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Auricular Acupuncture & ADDICTION

Mechanisms, methodology and practice

KIM WAGER
WITH SUE COX

CHURCHILL LIVINGSTONE
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Forewords by
Professor Alison Liebling and Mike O'Farrell

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Finally we must not forget the reason why we do this work at all: our patients. Ultimately this book is for them.

Foreword by Alison Liebling

I first encountered the idea of the treatment of addiction with the support of auricular acupuncture when Michael Wheatley was studying for his Masters' Degree in Applied Criminology at Cambridge University. He was inspirational in his determination to investigate the subject empirically, based on clinical trials. His acupuncture teachers, Kim Wager and Sue Cox, with contributions from Michael Wheatley, Caroline Doyle, Chris Nortley, Lee Ball and Karl Sheldon, have brought together the practical, theoretical and empirical foundations for this link, based on a thorough review of the available evidence, and constant evaluations of their own practice over a number of years. The book provides a highly readable and clearly understandable account of the addictive process, and shows how acupuncture can reduce withdrawal symptoms and cravings. The outcomes from trials are promising.

The book is written with passion and insight. It is informative and engaging, about the effects of alcohol, cocaine, heroin, cannabis, ecstasy, amphetamines, LSD and nicotine use on our physiological and emotional states, and about the mechanism of reducing dependence. The authors clearly regard their clients with respect as well as realism, and they understand the emotional power of addictive cravings, as well as the underlying psychological and other mechanisms supporting them. One of the many benefits of acupuncture is that, unlike traditional therapies, it 'does not require difficult verbal interactions'. It can co-exist with other therapies. At its most effective, it can bring about the kind of 'stillness' and 'return to natural rhythm' that the recovering addict needs to calm drives and redirect energy, interrupting chaos and encouraging individuals to 'turn that corner' towards health.

The chapters in the final part of the book provide powerful examples of applications of the method in penal settings. One study shows that treatment effects are generated following twice-weekly interventions of 40 minutes' duration over a four-week period. Benefits included improved sleep, relaxation, reduced cravings for drugs, improved psychological well-being and general health improvements. Another found that additional benefits included closer and more therapeutic relationships with staff and a feeling of respect and trust between prisoners and officers in a maximum security unit. These are significant and humanising outcomes. Well-received and carefully evaluated courses provided by SMART UK (Substance Misuse Academy Registered Training UK) in these and other settings have found that 'an ancient practice has been successfully integrated into mainstream addiction services'. This book provides a framework for understanding how and why acupuncture makes an important contribution to the treatment of addictive behaviours. It will make an important contribution to the research agenda and to practice in this valuable field. It will also appeal to those suffering from addictions who want to understand their experience and find a way out.

Alison Liebling, Cambridge 2008

Foreword by Mike O'Farrell

A telephone call one morning at our offices in London from a newly graduated practitioner was my first introduction to Sue Cox and Kim Wager, the authors of this book. I had been aware of the work done in the field of substance abuse by many practitioners and knew that the use of acupuncture as an holistic treatment was very beneficial.

I had just begun to appreciate how different applications of this therapy could benefit patients whose needs were quite specific and was considering how best to broaden the awareness of this particular approach and indeed how best to inform other professionals. The juxtaposition of these two events seemed too much of a coincidence to be ignored.

The caller who effected the meeting with Sue and Kim was so excited by the educational programme that was being offered that I felt I needed to know more and as a lay person in the field I was already on a steep learning curve. So the meeting appeared to be a logical step forward. I did not bargain for the enthusiasm and commitment from the authors for their course and neither did I realise that its participants would share the same enthusiasm.

I was soon to learn that the professionals they taught came from a wide range of backgrounds and disciplines and were all united by the common cause of helping people to work with their addictions. The course as represented by this text appears to be highly detailed and well researched but is so much more.

This publication, in my opinion, is an insight into what can be done using a protocol involving acupuncture as part of the treatment programme. The protocol in question uses only auricular acupuncture and is described in detail. There is also a great deal of background information to hold and enhance the reader's interest.

I believe it says a great deal for this educational programme and the authors that the key organisations whose employees have participated are also discussing outcomes within this textbook.

We live in an environment where the cost of substance abuse is a significant and growing concern to the community and where the impact goes far beyond the individual and even the immediate family. It is for this reason that I feel so enthusiastic about both the process used and the explanations given. Acupuncture is between two and three thousand years old and to be a fully trained practitioner takes an average of three to four years fulltime equivalent study. This publication allows other skilled professionals who need to have other tools in their armoury to appreciate what they can do to help needy patients.

You will learn from the contributors in this book the part that the SMART structure has played within their environment and also some indications of patient response and reaction. As an organisation representing professional acupuncture, the British Acupuncture Council believes that good treatment only comes from well-trained and educated practitioners and my view is that

this textbook written by Kim and Sue ensures that those professionals who use auricular acupuncture will have a real understanding of what can be achieved with the healing art that is acupuncture. This publication brings to the wider public an appreciation of just what acupuncture can do and as such I believe will make a significant contribution to an important sector within public health.

Mike O'Farrell, London 2008

Preface

Acupuncture has been around for a long time. Within the field of addiction it has been used for well over 30 years. Acupuncture is not considered to be a 'cure' for addiction, nor is it intended to replace existing treatment protocols. Inclusion of acupuncture in treatment programmes has been shown to reduce withdrawal symptoms and cravings. The theories presented in this text explain many aspects of both addictive behaviour and the mechanisms of auricular acupuncture. Outcome studies completed to date are very encouraging and it is hoped that these, as well as the theories included in this text, will lead to new avenues of research in the future that will show how acupuncture is well proven to be of benefit. Regardless of whether such research gets funded, it is undeniable that tens of thousands of addicted patients have reported benefits from acupuncture treatment and it cannot therefore be casually dismissed.

SMART UK (Substance Misuse Academy Registered Training UK) provides comprehensive teaching courses regarding the use of auricular acupuncture as an adjunct to the treatment of addictive behaviours. These courses have received widespread praise and SMART UK is now considered to be the provider of choice. The protocol we teach is used widely in HM prison service, the NHS, the armed forces, smoking cessation services and in many community drug and alcohol services. To date, we have trained around 5000 practitioners in the use of acupuncture.

The degree with which we have come to understand the treatment and the underlying neural processes of addictive behaviour has meant that the treatment has not only proven its worth in this limited sphere, but also in several other aspects of mental healthcare, such as the treatment of post traumatic stress disorder, attention deficit hyperactivity disorder, obsessive compulsive disorder and depression.

The success of the course reflects the fact that science can be interesting, exciting, understandable and fun. For some the course has proven to be the beginning of a career in acupuncture and for others just insight into the field. The course challenges preconceived ideas as to what acupuncture has to offer and has allowed thousands of patients to receive treatment that was previously out of their reach.

The course teaches not only the practicalities of acupuncture treatment but also includes very comprehensive modules regarding the integration of the treatment into the existing scientific models of acupuncture and addiction. In this way, an ancient practice has been successfully integrated into mainstream addiction services.

We consider that although acupuncture dates back thousands of years it must keep pace with the modern world. While the terminology of the past is endearing, it is the reluctance of many practitioners to challenge old models that may hinder the acceptance of acupuncture into the mainstream. This is not to say that the practices themselves must necessarily be outdated but that the previously described mode of action is incorrect. To illustrate, many acupuncture

practitioners use a particular formula treatment, often for the treatment of psychiatric disorders. The treatment, anecdotally, does seem to benefit some patients. The mechanism of the treatment is said to lie in the fact that psychiatric illness is rooted in the invasion of demons. The treatment releases dragons that kill the demons and so the patient improves. Hopefully, no-one today accepts that ghosts and demons are the transmitter of disease, but continued use of the terminology is not of benefit to the profession and could easily lead to considerable misunderstanding.

It is our desire that this text, although designed as our course textbook, will make a contribution not only primarily to the field of addiction science, but also to the wider acupuncture profession. We also hope that it will provide a valuable resource for other health practitioners who have the desire to help and understand more about their addicted patients; for example counsellors, psychotherapists, psychologists, psychiatrists, doctors, dentists and physiotherapists.

Science requires an enquiring mind. If this book raises more questions than it answers then all is well. If, in the years to come, the knowledge contained within this text should become outdated or discovered to be wrong, this will confirm the validity of the scientific method and should be celebrated as part of the evolutionary process of learning.

Kim Wager
Sue Cox

About the authors

Kim Wager has over 12 years of experience in the field, working both in private practice and in the NHS. He is a qualified acupuncturist and Chinese medical herbalist. He has also trained in the UK, USA and Germany. His primary interest is in the human brain and he is currently working towards his MSc in neuroscience at the Institute of Psychiatry at Kings College London. Previously, he has studied biochemistry, quantum mechanics and cosmology.

Sue Cox has over 30 years of experience in the field of addiction, working as a qualified counsellor and acupuncturist both in the NHS and private practice. She has trained in the UK, the USA and Germany. She has also studied diet and nutrition. She is currently working towards a degree in natural sciences. Sue's absolute passion remains the recovery from addiction.

Contributors

Chapter 15

Mike Wheatley
Senior Manager, Reducing Re-offending Unit, Directorate of High Security, HM Prison Service, Wakefield, UK

Chapter 16

Caroline Doyle
Head Nurse, Dangerous and Severe Personality Disorder Unit, Frankland Prison, County Durham, UK

Chris Nortley
Acupuncturist and Clinical Nurse Specialist for the Acupuncture Programme, Park House Mental Health Unit, North Manchester Hospital, Manchester, UK

Lee Ball
Team Leader, Salvation Army Day Centre, Cardiff, UK

Karl Sheldon
Team Leader, Stimulant Service, Addaction, Middlesborough, UK

Introduction

The mind is in its own place, and in itself
Can make a heaven of hell, a hell of heaven.

(John Milton)

Addiction can be defined as the uncontrolled, compulsive use of a substance, person, thought or behaviour for the purpose of changing a person's emotional state, regardless of any potential consequences, which they fail to admit to consciousness. The condition is rooted in the interaction of environment with genetically predisposed imbalances in brain chemistry; addiction is a symptom of this interaction. Addiction is not caused by one's environment nor is it caused by genetic predisposition; it results from a combination of the two.

Recovery from addiction is not inevitable. True recovery relies on abstinence. Unfortunately, abstinence itself is initially a powerful stressor both physically and emotionally. The patient has lost something perceived as dear: their source of pleasure, their painkiller and their emotional crutch. Relapse is very, very common. It is all too easy for a person to think that they cannot be addicted because they have managed to stop. They will convince themselves that the chemical is not a problem, and project the problem onto other things; for example, they only used because their marriage broke down or they lost their job. The get-out clauses are infinite. The downward spiral is then resumed, control is lost and the use of any addictor will then reinforce the conditioned learning of that behaviour.

It is our opinion, borne of years of experience and patient feedback, that recovery requires several steps:

1. The removal of denial
2. Abstinence
3. In-depth learning of the truth of one's condition
4. Sustained hard work in order to build the ability to respond to challenge
5. The improvement of status and self-respect
6. The reduction of feelings of isolation, and enhancement of connection to others
7. The provision of emotional safety and support without collusion (tough love)
8. The reduction of stressors
9. The empowerment of the individual

How can this be achieved?

1. Talking to the patient will not be effective until the craving mechanisms of the unconscious brain are supported.

2. Acupuncture makes an important contribution. Its focus is on modification of thought and feeling related to neurochemical imbalance in the brain.
3. Denial is a creation of the addictive process. The brain shields the truth as a protective mechanism in order that we continue to supply it with that with which it has fallen in love. The brain uses an unconscious process to manipulate our neurochemistry. Realisation that one is powerless to the dominance of the brain removes denial.
4. Education regarding the reality of the craving brain empowers the individual. No longer do patients assume themselves to have a moral deficit; instead they come to the realisation that their brain is hard-wired to be truly special and of significant value when harnessed correctly.
5. Recovery starts when the patient becomes aware that their condition lies in the 'wiring' of the brain. This means that they learn that they are powerless to control their use of chemicals and that, in fact, the chemicals control them. In this way, they learn that they must remain abstinent at all costs.
6. The support of others is of great benefit. Survival of the individual is improved with the help of the family, the pack, the group or the team. Natural selection has made it so.
7. External (systemic) stressors should be reduced as far as possible; poor education and poverty are examples of these. Schemes that offer education, jobs and housing are of incredible value. People need to be valued because they *are* of value.
8. Internal (process) stressors should also be tackled; a feeling of incapability to provide for the home or family, loneliness and depression are examples of these. Services that offer counselling and cognitive behavioural therapy are to be sought.
9. Non-drug related behaviours must be repeatedly reinforced to condition neural pathways.
10. Family and friends should also be supported. They will also feel the stress and shame of the user. They too must not deny the problem and enable the situation to continue. The enabler must reach the point whereby they realise that they are prolonging the situation. Organisations that provide for codependents are important.

Interventions that aid recovery are many. We have seen acupuncture benefit thousands of patients in the UK and tens of thousands have benefited worldwide. It should be noted that acupuncture once a week will be of minimal benefit; where resources allow, the ideal situation is to provide acupuncture once a day, even twice if possible.

Addiction is more than having problems associated with drug use. The key factors are that the person has lost control and is in denial of their situation. If a person could control their behaviour then they are, by definition, not addicted. They may appear to use a drug, like alcohol, in a way that appears to be alcoholic

but if they can stop and not revert back to their previous ways, they were not truly addicted.

It is true that some people who appear to be addicted can just stop using. To reiterate, they were not addicted. Unfortunately, the existence of such people gives those who are truly addicted a great excuse to try and continue controlling their drug use. Think about people you know. Could a heavy smoker limit their intake to just one or two cigarettes a week? Most usually they cannot, but they continue to try because they have heard of someone who can just smoke occasionally, and it suits them to convince themselves that they can do this too.

It would be incredibly naive to imagine that acupuncture can solve the problem of addiction. It can certainly form an important part of a patient's treatment plan, but used on its own, it will be ineffective. A multimodal approach is vital. Acupuncture will help address some of the underlying biological processes behind addiction but conditioned learning and any underlying stressors must also be addressed. Stopping acupuncture treatment before all of the other pieces of the jigsaw have been dealt with will result in relapse.

It is very much our feeling that although acupuncture does have demonstrable effects at the neurochemical level which are profound in themselves, it also offers more:

1. Acupuncture can harness the powerful effects of placebo. A placebo is a physiologically inert intervention which provides therapeutic benefit because it is psychologically determined to do so. All medical interventions, whether Western or Chinese, exert part of their influence through placebo effects. With regard to acupuncture, the effects are likely to be a consequence of the therapeutic alliance between the patient and therapist and the treatment setting. Practised correctly, acupuncture is perceived as a credible clinical intervention and so it is considered of benefit. It is also likely to be the case that the novelty of a new procedure has some beneficial effect. It is our feeling that even if all the positive effects of acupuncture were down to placebo alone, acupuncture still presents good value. It is a cheap intervention to administer, costing in the region of £0.40, and it is a treatment that patients evidently value as they request it themselves. Few interventions of value are so cheap, and thus acupuncture positively affects treatment programmes.
2. Patients feel better following acupuncture treatment. This means that they have learnt that they can change how they feel without the use of drugs. This carries with it a positively motivating emotional charge. Normally, in order to effect change they must take a drink, inject something, smoke something or snort something. Positive reward reinforces learning. It is vital that routes that strengthen natural rewards become favoured.
3. Acupuncture administered as often as possible results in cumulative effects. This is as a consequence of conditioned learning. The more often a person repeats the experience the more established the memory engram becomes. As will be learnt later in the text memory is more than the simple recall of events but also extends into the physiological realm. The

neurophysiological response to acupuncture becomes stronger with repetition.

4. Acupuncture strengthens the therapeutic alliance. Trust is required in the relationship before patients can allow the practitioner to touch them and insert potentially painful needles into their bodies. Acupuncture breaks down barriers. This is particularly the case when carried out by discipline staff within the prison service.
5. Acupuncture does not require difficult verbal interactions on behalf of the patient. This is particularly valuable for those who feel unable or who are not yet ready to communicate.
6. Acupuncture has proven itself to be a valuable holding treatment whereby patients are retained in treatment for longer. As such, this benefits the treatment service, and consequently offers the patient a better chance of recovery. Recovery takes time and persistence and so patient retention is vital.
7. Acupuncture requires that the patient sit or lie still for around 40 minutes in silence. This reduces sensory input and allows the patient to sit and be with their thoughts and feelings. This is seen as important because it is from these very things that they wish to escape. Sometimes it will be difficult but that is because recovery is difficult. To be difficult does not imply detrimental; quite the opposite is true. If a person is to gain lasting improvement then they must feel it. If recovery is made too easy then it will not be truly valued and so given away with ease. Recovery is to be cherished above all else.

The brain – target organ of addictive substances

If you look at the anatomy, the structure, the function, there's nothing in the universe that's more beautiful, that's more complex, than the human brain.

(Keith Black, quoted in *Discover* magazine, 21 April 2004)

Whose fault is it that the addict sitting in front of you has fallen prey to addiction and criminality? This troubled soul is the victim of his or her neurobiology. The person before you has been sculpted by evolution, constrained by genes, modulated by hormones and shaped by life experience, even in the womb. This by no means excuses criminal acts and, whatever their root cause, society must be protected. But this can be done with humanity; no-one 'decides' to become an addict.

Brain basics: introduction

We should not underestimate the power that our brain has over us. Nowhere in our body do we have a mechanism to control the brain. The brain is certainly influenced by the world around us but the world does not control the way our brain processes information coming in from the environment and directs our response to this information. We cannot think of a way to make our brains listen to our thoughts because our thoughts are the result of our brain talking to us. Our thoughts are purely a creation of our brain. Each time we experience a thought, a memory or an emotion, our brain reaches out and makes every single organ in our body work differently, such is its strength. The you in you is your brain.

This chapter seeks to explain the basics of how your brain is shaped to shape you. This is the biology of human behaviour.

The nervous system

The nervous system is highly specialised. It has evolved to allow us to experience and interact with our environment, and ultimately to keep us alive in the face of the challenges that life might throw at us. In humans it has also developed such that we have a profound intelligence and awareness of self. Why is it that only humans have developed a welfare state or have been able to invent the silicon chip? The answers are woven into the structures that comprise the nervous system.

There are two divisions to the mammalian nervous system: the central nervous system (CNS) and the peripheral nervous system (PNS).

The central nervous system

The central nervous system consists of the brain and spinal cord; all others parts of the nervous system belong to the peripheral nervous system. Although both are essential, the central nervous system could be considered more important because it is in charge of all information processing, including that gathered by the peripheral nervous system.

The spinal cord conveys information to and from the central control point that is the brain. The brain itself has many and varied functions. It integrates information that allows us to walk, talk, see, hear, smell, remember, have faith in God, laugh, cry, love and hate. It is here, in the brain that the chemicals of abuse target their action.

Importantly, the PNS interacts with the CNS via the spinal nerves to provide an exchange of information and so, in this way, the environment can influence higher brain function and vice versa.

The peripheral nervous system

The peripheral nervous system consists of two divisions:

1. *The somatic peripheral nervous system*. This division is the key to the ability of the individual to experience and interact with their environment. Somatic sensory neurons collect information from the skin, muscles or joints while somatic motor neurons command voluntary movement via the muscles.
2. *The autonomic nervous system (ANS; otherwise referred to as the visceral peripheral nervous system)*. This division governs those aspects of our being that are outside of our conscious control. The nerves of the ANS innervate internal organs (the viscera). Visceral sensory neurons collect information about, for example, blood pressure or glucose levels in the blood. Visceral motor neurons bring about change in function, for example the speeding up of the heart rate, relaxing a blood vessel or

initiating the secretion of insulin. It is the ANS that allows us the physical experience of emotion. When we experience goose bumps or blushing it is the ANS that is responsible.

The autonomic nervous system

Overall control of the ANS lies in the brain, in a structure called the hypothalamus. There are two parts to the ANS:

1. *The sympathetic branch*. The sympathetic branch is involved in the fight-or-flight response, it can be thought of as the body's accelerator pedal. Bodily systems are mobilised for emergency in favour of tasks of lesser current importance, for example digesting a meal.
2. *The parasympathetic branch*. Again using the analogy of a car, the parasympathetic branch of the ANS can be likened to the brake pedal and hence brings about a calmer bodily state. It looks after processes that work for the long-term good, for example the immune system response.

The goals of the two divisions are incompatible; the systems work in antagonistic harmony. Thus, instead of pressing both pedals to the floor at the same time, gentle release of one while slowly increasing the pressure on the other results in a much smoother drive. To illustrate, both divisions of the ANS innervate the heart – the sympathetic branch speeds it up, the parasympathetic slows it down – these processes cannot occur at the same time.

Regulation of the ANS is controlled by the brain using three integrated systems; the hypothalamus governs the various processes:

- Hypothalamic control
- Limbic control
- Cortical control

Hypothalamic control

The hypothalamus directly regulates the internal environment in response to a changing external environment. As such, it plays a chief role in homeostasis. For example, if our body temperature is raised significantly because we go for a lie down in a sauna then the hypothalamus will receive input from temperature sensors and activate physiological mechanisms such as sweating to cool down.

Limbic control

The limbic system is the seat of emotion. It is here that emotional responses may be evoked by a stimulus, such as the sight of an oncoming bus on the pavement. Emotions initiated by structures within the brain's limbic system are communicated to the hypothalamus in order to activate a very fast, hopefully life-preserving response. Has someone ever kicked you in the shins and made you angry? The pain in your shin was conveyed to parts of the brain controlling emotion and that then on to the ANS in order to ready you for conflict. Have you ever read a passage in a book that for, whatever reason, made your heart

beat just that little bit quicker or made you blush? Emotional arousal was conveyed to the ANS to initiate these physical changes. These examples illustrate that sensory experience can influence brain function and that just a thought or idea can make your body work very differently.

Cortical control

Humans (and other primates) are also able to communicate with the limbic system via neural connections from the frontal cortex (cognitive or thinking functions) into the limbic system. If we think about our next holiday and imagine lying on the golden sand under clear blue skies, we probably feel happier, calmer and our pulse might have slowed down. So to a degree, thought can influence the activity of the ANS. This means a threat does not even have to be real but could be perceived or even completely imaginary. Depression, for example, can sometimes be rooted in imbalance in this cortical or thinking part of the brain.

Imagine you go outside and the bus tearing down the street knocks you down. Your brain will turn on various life-saving mechanisms, for example, to stop you bleeding to death. Your brain will also take control of you so that immediate survival is of paramount importance. You are not going to feel very happy at all that you have been hit by a bus. You will not feel unduly inclined to eat or particularly open to sexual arousal. Most often in normal day-to-day life, these physiological changes do not arise because we have actually experienced disaster. In some individuals, the stresses and strains of everyday life may trigger the same physiological events as witnessed in the bus crash. In these people there need in fact be no actual stressor at all; the frontal cortex has spontaneously unhappy thoughts or imaginings and feels the need to tell the limbic system and consequently the hypothalamus all about them.[1] The body will then turn on its fight-or-flight responses, making the person feel depressed, anxious and low in libido and appetite, to name just a few effects.

The brain's control over the body

So, a thought or a memory can profoundly affect the internal workings of our body via the ANS, which can command every single organ and tissue in our body.

The neural tract connecting the frontal cortex with the limbic system is called the cingulum bundle. Severing this bundle of nerve fibres has been used as a treatment for intractable depression and addiction in an attempt to stop distortions of thought affecting the physical body. Interestingly, it was this very operation, a cingulotomy – for which the patient was being prepared using acupuncture – that led to the discovery that acupuncture could relieve some of the symptoms of withdrawal. This will be explored more fully later in the text.

It is perhaps no great surprise to note that a part of our brain can influence the workings of other parts of the nervous system. It is perhaps more amazing that the hypothalamus not only coordinates the ANS but that it also interacts

with the pituitary gland, and so can influence the secretion of all sorts of hormones that affect the body in profound and often long-lasting ways. To put this in perspective, the hormonal effects of chronic stress can, for example, create a situation of subfertility or even an absence of menstrual periods. Hormonal effects do not solely affect physical function either – they can also affect brain cells, and so therefore can profoundly affect one's mood, memory or cognitions. For example, consider the mood swings of an anabolic steroid user.

How is the brain organised?

The brain is made up of two halves known as hemispheres. All brain structures or modules are duplicated in either hemisphere except for one, the pineal gland, which secretes melatonin. The two hemispheres communicate with each other in order to function as one unit but as the two halves mature, each develops its own strengths and weaknesses, processing information in its own unique way. The left side tends to be better at 'thinking' and the right at 'feeling', and so broadly speaking, the left hemisphere is considered analytical and the right much more emotional. Normally both halves communicate seamlessly but what if the nerves connecting the two were severed? Both hemispheres view the world in their own unique way and so, in a sense, there exists in the brain two separate states of consciousness, two people in one brain. If you have ever decided that you do not really 'gel' with someone or a situation 'doesn't feel right' but do not know why, the problem lies in poor hemispheric communication. The right side of the brain may have processed some information but not communicated it to the left. Similarly you may have been told that your loved one has died in a car crash but 'it hasn't sunk in yet'. In this case the left side has not yet passed the factual information to the right side to allow for emotional processing.[2]

The anatomy of the human brain is inextricably linked to the evolutionary process. Three major evolutionary landmarks have been identified and so the structure of the brain is often referred to as triune. Around 500 million years ago the development of the brain started with a bulge at the top of the spine that served as a central control point. This part consists of the brainstem and cerebellum. The brainstem is responsible for maintenance of vital life functions such as breathing and the beating of the heart; the cerebellum is responsible for movement, posture and balance. This part of the brain is very old and sometimes referred to as the reptilian brain (Fig. 1.1). The easiest way to remember what this part of the brain does is to think – **heartbeat**.

Later on in evolutionary terms, a still rather old part of the brain, located above the brainstem (reptilian brain), expanded into what became known as the limbic system or mammalian brain. Basic limbic structures control temperature, hunger and thirst. It is in more advanced limbic areas that memory, complex processing of stimuli and emotions are generated. This part of the brain is still unconscious, so although emotion is generated here, it is not experienced in a conscious way.

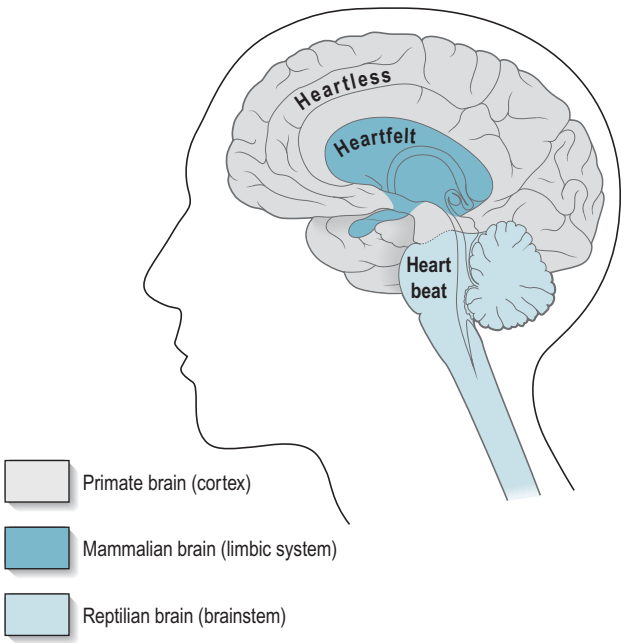

Fig. 1.1 Triune brain structure.

The easiest way to remember that this part of the brain deals with emotional regulation is to think – **heartfelt**.

Further down the evolutionary track, the cortex developed and increased in complexity; it is ultimately from this part of the brain that consciousness arose. The more advanced the cerebral cortex, then the more evolved the species. The cortex is responsible for complex sensory perception, recognition of stimuli and communication. What particularly distinguishes humans from other non-human primates is the massive expansion of the frontal cortex. This part is most concerned with thinking, planning, decision making and gratification postponement. It is this cortical expansion that caused human skulls to evolve their characteristic forehead and domed head.

This part of the brain is cold and clinical; it is a little like a computer. When trying to remember what this brain module is responsible for think – **heartless**.

Essentially, the more fundamental functions of the brain are related to structures close to the spinal cord, the further away you go the more the structure of the brain is related to 'higher' brain function.

You might have come across the term 'top down approach' in discussions about the brain. This refers to neural communication running from the top of the brain, the neocortex, down through the limbic system to the brainstem and ultimately spinal cord. The evolutionary age of the different areas of the brain is vital when considering the nature of addictive behaviours. As will be discussed fully later in this text, the areas of the brain that are affected by psychoactive substances affect behaviour at a powerful and fundamental level.

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CHAPTER 2

How nerves work

The brain has no knowledge until connections are made between neurons. All that we know, all that we are, comes from the way our neurons are connected.

(Tim Berners-Lee in *Weaving the Web: the Original Design and Ultimate Destiny of the World Wide Web by its Inventor*[1])

The structure of the nervous system

The organs and tissues that make up the human body are composed of cells. The specialised functions of these cellular building blocks depend on the roles they play. The cells of the brain work as individuals but are then 'glued' together in a way such that, when working together as a collective, incredible complexity of function is generated. It is from this intricate web that the amazing depth of human feeling, thought, spirituality, self awareness and perception arise. The 'glue' is life experience and so differs for every individual. There are absolutely no two people whose brains work the same way and therefore no two who perceive the world in the same way as another.

Consider the following situation, for example. Several people glance at a bowl of apples. One thinks 'Wow, look at the amazing colours', one thinks I'm hungry', one thinks 'I miss my Dad, he always used to buy me a toffee apple at the fun fair when I was a kid' and another thinks 'There's a fly on them, better not eat one, might make me ill'. Every single experience is uniquely moulded by memory and creates new neuronal wiring to influence future experience.

This text focuses on the function of one of the types of cell in the nervous system – the nerve cell or neuron. Neurons are the targets of psychoactive substances and it is their function, and how they communicate with each other, that underlies all behaviours, including addictive behaviour.

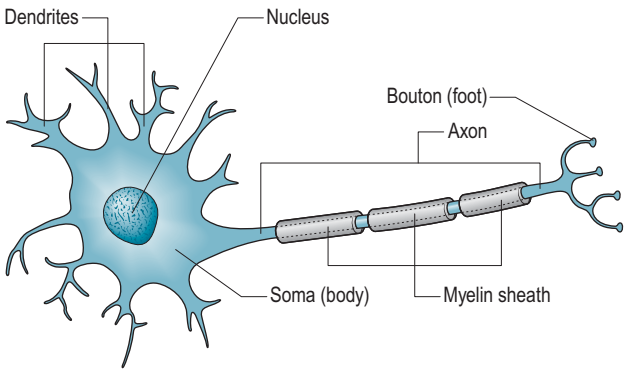

Fig. 2.1 A typical neuron.

The neuron

The neuron consists of three key parts: the cell body or soma, the axon and the dendrites (Fig. 2.1). The cell body stores genetic information, supplies energy and manufactures substances that are shipped out to the rest of the cell to enable it to function. The axon can be likened to a cable that allows information to be sent over large distances. The dendrites branch off from the cell body and receive incoming information. Metaphorically, the dendrites are the ears of the cell and the axon the mouthpiece.[2] Astonishingly, a single human neuron can vary in length between a thousandth of an inch and 3 feet. The human brain contains approximately 100 billion neurons and each of these cells can have up to 10000 inputs and 10000 outputs. Clearly, this means that a substantial amount of communication is taking place. It means that the total number of connections in the brain, if written out, would be followed by over 6 miles of zeros.

How do neurons communicate?

To understand how a neuron can become excited and start sending information, it is necessary to understand a little about electrical activity, which is essentially all about contrasts in electrical charge. The water contained in the fluid inside cells (the intracellular fluid) and outside the cells that bathes the neuron (the extracellular fluid) contains dissolved electrical charges in the form of ions. It is these ions that make the fluid salty and that allow electrical impulses to occur in neurons. It is the distribution of these charges across nerve cell membranes that allows neurons to be very quiet when they have nothing at all to say and to scream their heads off when they are excited. There are no between states – this is an all or nothing phenomenon.

Once a neuron is excited it needs to tell others about what it has to say. This is where the existence of the synapse is all important and is the root of the brain's

astounding power. The synapse is the site of action for many psychoactive drugs, is the root of mental illness and is the means by which life experience shapes us as individuals. It is at our synapses that we think, feel and remember.

The synapse

There are two broad types of synapse: electrical and chemical. An electrical synapse, also known as a gap junction, is a mechanical link between two neurons that allows for the conduction of electricity. Electrical synapses contain channels that allow charges (ions) to flow from one cell to another (Fig. 2.2).

In humans, most synaptic transmission is of the chemical type and it is this type that is affected by ingested chemicals. For these reasons, this text focuses on the chemical synapse (Fig. 2.3).

In chemical synapses the flow of information tends to be unidirectional. The first neuron in a communicating pair is referred to as presynaptic and the second postsynaptic. It should be noted that the communicating neurons are not in physical contact. Due to this lack of physical communication there exists the need for a means to bridge the synaptic gap. Communication across the synapse is brought about by neurotransmitters. The function of a neurotransmitter is to convert the electrical signal of the presynaptic neuron into a chemical signal that can cross the synaptic gap and reach the postsynaptic neuron, where the chemical signal is converted back to an electrical one. In this way,

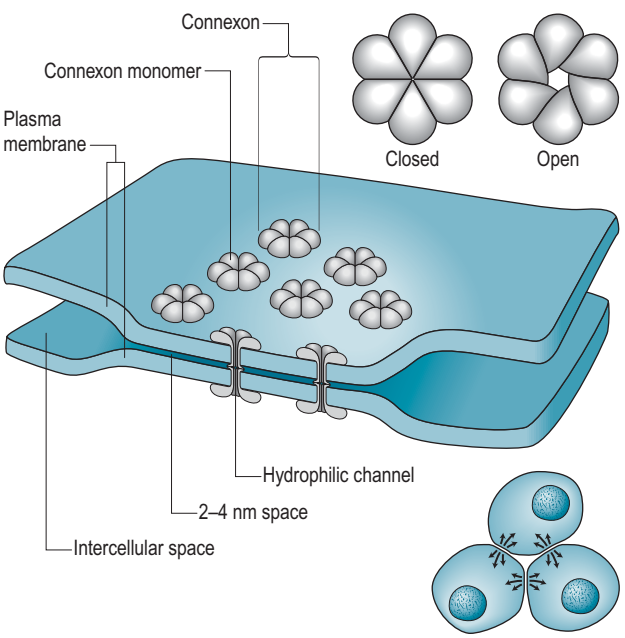

Fig. 2.2 A gap junction.

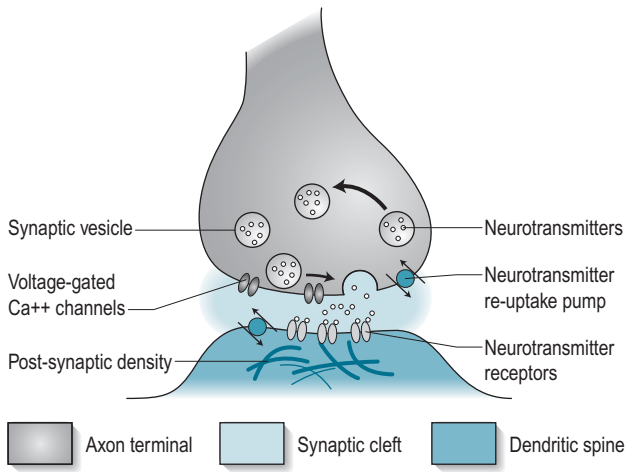

Fig. 2.3 A chemical synapse.

neurons can exchange information, in a sense have a conversation with each other and – via complex chain reactions of interconnected neurons – converse with millions of others. From out of this neuronal chit-chat springs human behaviour.

Neurotransmitters

These chemical messengers are stored in and released from the presynaptic neuron. Depending on their chemical structure they are released either from secretory granules or vesicles. The concept of a neuron only having one neurotransmitter is often referred to as Dale's principle. New research suggests that a given neuron has the ability to release several different types of neurotransmitter under different conditions. Nevertheless, according to Dale's principle most neurons produce and release only one type of neurotransmitter. For this reason, neurons tend to be named according to the type of neurotransmitter they release. For example, neurons that release serotonin are termed serotonergic neurons. It is the control of neurotransmitter release that adds 'colour' and complexity to the brain rather than simple linear electrical connections. Each neurotransmitter is associated with either specific brain areas or specific brain functions and so, in a sense, one's individuality is rooted in their mechanisms of neurotransmitter activity. Neurotransmitters can have either an excitatory effect or an inhibitory effect on the nervous system. For normal functioning, neural circuits depend on there being a delicate balance between synaptic excitation and inhibition. Most importantly, how psychoactive chemicals cause changes in physical and mental behaviour is a function of their actions at the synaptic level.

Neurotransmitters are released by the arrival of an electrical signal in a neuron. This electrical impulse causes an alteration in the structure of the cell membrane, which causes the vesicles or granules that store neurotransmitters in the neuron to release them into the synaptic gap.

Neurotransmitter receptors

Neurotransmitters have specific shapes due to their molecular structure. In order for a neurotransmitter to have an effect on a postsynaptic neuron it must bind to an equally specific receptor site. A useful analogy is to consider the neurotransmitter as a key and a receptor site as a lock. Only the key that fits the lock perfectly will allow it to be turned and the bolt unlocked. Often, many of these keys will have to be turned in order for a signal to be generated in the postsynaptic neuron (Fig. 2.4). So in a sense, neurons are like a door with a combination of several locks, only when the correct number of locks is opened will the door open. This open door is analagous to the generation of an action potential, a nerve impulse.

There are several types of receptor site, and these act quite differently. Activation of the sites can produce rapid excitation or inhibition of neurons or even longer-lasting widespread metabolic effects.

The effect that a given neurotransmitter may have upon the nervous system is not so much related to the neurotransmitter itself but rather to the particular neurons that they affect. Hence the same neurotransmitter can have very different effects depending on where in the body or brain it acts. For this reason it is important to know not just what neurotransmitters are affected by certain drugs but perhaps more importantly where in the nervous system they target their action; location, location, location as the saying goes.

The beauty of the brain is that a specific brain area exerts fine control over the release of particular neurotransmitters. However, drugs flood the whole brain and so, rather than targeting a small region, overwhelm many areas, which can produce a broad range of effects or, as in the case of many prescribed medicines, undesirable side-effects. To illustrate, many of the symptoms of schizophrenia are thought to be caused by an excess of a neurotransmitter called dopamine in a brain pathway called the mesolimbic system. Antipsychotic, dopamine antagonist (blocker) drugs can be prescribed to help the situation. However, a common side-effect is the development of parkinsonian-like tremor because normal

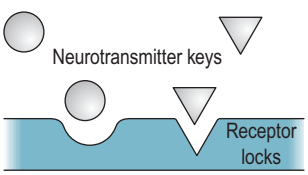

Fig. 2.4 Lock and key analogy.

dopamine levels are depleted in another part of the brain, the basal ganglia, responsible for smooth motor control.

Neurotransmitter recycling

When a neurotransmitter has done its job in the synapse it is important that it is removed. Neurotransmitters may be enzymatically destroyed or reloaded into synaptic vesicles to be used again. If this process does not occur normally, as is the case with drugs such as opiates, which mimic a naturally occurring neurotransmitter but remain in the receptor site for a long time, they may have continued effects for several hours. These sustained high concentrations in the synapse may also lead to a process of desensitisation of the receptor sites. When this occurs, despite the continued presence of a neurotransmitter the nerve stops firing. It is this process (among others) which is responsible for drug tolerance.

To illustrate the importance of the recycling process, consider the agents used for chemical warfare. Many of these prevent the degradation of a neurotransmitter involved in muscle contraction; the neurons in question become desensitised to the continually high levels so that the muscles they control no longer function, causing respiratory collapse.

The collective processes by which synaptic transmission occurs are chemical in nature. It is for this reason that drugs, which are of course chemicals, can have profound effects on its mechanisms. The effect of drugs on the nervous system is known as neuropharmacology.

Pharmacologically intervening with the various re-uptake mechanisms has led to the development of medicines such as Prozac, so illustrating the importance of the recycling mechanisms with regard to mood and behaviour. Prozac slows down the degradation of a particular neurotransmitter. In so doing, the neural signaling is increased and mood is elevated.

How drugs can affect the nervous system will be fully explored later in the text.

Neural regulation

It is important that neurons can integrate all of the many incoming signals in order to transmit an appropriate signal; remember that a single neuron may have 10 000 inputs so this is quite an impressive task. Neurons therefore, in effect, process reams of incoming information, decide what it all means and then reply accordingly by choosing to send a signal or not, as the case may be. Some inputs may be trying to excite a neuron and others to inhibit it; the skill of the neuron is in the correct analysis of the information.

As with all body systems, neurons can self-regulate in an attempt to make sure that incoming information is not misleading. This process of self-regulation

ensures that the multitude of neural systems work in harmony and so one module does not get inappropriately over or under active.

Neuronal down-regulation

One such inbuilt safety mechanism is the ability to down-regulate function in several ways. As mentioned above, neurotransmitter receptor sites may become less responsive or desensitised. It is also the case that not only do postsynaptic neurons possess neurotransmitter receptor sites but the presynaptic neuron that actually releases the neurotransmitter also has these active sites. These receptors are known as autoreceptors. When activated, these autoreceptors either inhibit further neurotransmitter release or even its synthesis. It is also quite possible for neurons to decrease the number of its receptor sites. These processes thereby combine to function as a 'volume knob', which will reduce the response (turn down the volume) to a given neurotransmitter should its levels become inappropriately high. It is this process that allows for the down-regulation of neuronal activity and hence is one – but not the only – contributory factor leading to the development of tolerance to a given drug. This mechanism is also partly responsible for the phenomenon of withdrawal anhedonia. To illustrate, neurons may become deafened to a drug due to this down-regulation and so more of the drug is needed to have the same effect: this is tolerance. Additionally, when the levels of the drug are reduced due to it being metabolised (removed), the body will continue to release less of a given neurotransmitter and have fewer receptors for a time and hence there will exist subnormal neural function; this contributes to some sensations of withdrawal and also manifests in the observation that naturally rewarding behaviours, such as a good meal thereafter, also carry less positive impact. How specific neurotransmitters and neural networks might be affected will be discussed later in the text.

It is also true that should too little of a neurotransmitter be present then the nervous system will try to compensate by up-regulating the system by manufacturing and releasing more of the neurotransmitter, increasing receptor sensitivity or the number of receptors. It should be borne in mind, however, that there are biological constraints to these mechanisms of regulation and that these vary from individual to individual according to genetic traits.

Dependence can also result from neuronal down-regulation. If the use of a drug is stopped after repeated consumption, withdrawal symptoms manifest due to the fact that the body now has fewer active neurotransmitter systems and has got used to having artificially raised neurotransmitter levels; it takes a while for the body to re-up-regulate the mechanisms to more normal levels. It is important to note, however, that the existence of tolerance and dependence leading to withdrawal symptoms does not define addicition; it is quite possible to be physically dependent on a drug and experience withdrawal when it is discontinued, without being addicted. The neural basis of addiction will be covered thoroughly later in the text.

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CHAPTER 3

Types of neurotransmitter

I don't do drugs. I am drugs.

(Salvador Dali, Spanish painter 1904–1989)

Our brains are awash with chemicals: neurotransmitters. Neurotransmitter systems are responsible for the governing of behaviour. Some behaviours are innate, genetically predetermined mechanisms that allow for the optimisation of our physiology; these are known as instinctive behaviours. An example of a broad-reaching instinctive behaviour is the seeking of pleasure and the avoidance of pain, springing from the drive for survival. Instinctive behaviours tend to be beneficial to survival and so are rewarded with pleasurable sensations that encourage their repetition; this is known as positive reinforcement. The pleasurable sensations that drug users experience result in positive reinforcement and hence the desire to repeat the drug taking. Undesirable behaviours are not beneficial to the individual and so are announced by what we perceive as unpleasant sensations to discourage repetition: this is known as negative reinforcement.

In addicted persons, negative reinforcement manifests with the individual making adjustments to their behaviour to avoid withdrawal symptoms. Often, this avoidance behaviour manifests with the repetition of their drug use. It should be made clear, however, that the avoidance of unpleasant withdrawal symptoms is not the sole driving force behind addictive behaviour. Addicts are driven by the need to experience pleasure. In our clinics we see this all the time. Patients may be on medication to relieve their withdrawal, but they still crave the pleasure of drugs. This has been shown experimentally with rats, using food as the source of motivation.[1] Destruction of dopamine axons failed to reduce the hedonic impact of food, even though the rats stopped eating. If food was given to the rat with these lesions, the rat would still behave as if the food evoked pleasurable sensations and would eat the food. The destruction of dopamine axons therefore causes a lack of motivation, or craving to actively seek out food, but the animal does enjoy it if it is available. The rat *likes* food but does not *want* food. This provides evidence that dopamine neurons control behavioural motivation and are the drivers of the craving process.

Much of this information is fairly obvious: we instinctively seek out food to provide energy, we seek out a partner to perpetuate our deoxyribonucleic acid

(DNA), and our brains tell us to repeat the processes appropriately because the associated sensations of reward are reinforced through memory. Should we put our hand into a fire, it hurts and we withdraw our hand quickly, and the associated pain informs us not to do it again. What is less immediately obvious is that it is the altered physiology of the brain resulting from those behaviours that acknowledges that the event has occurred: how pleasurable or otherwise it felt and the learning process can alter our reaction to stimuli in the future. So learning through our environment can influence all behaviour, including that of instinctive behaviour. All these changes are firmly rooted in the activity of neurotransmitters.

Although the brain has evolved these functions of reinforcement and avoidance, neither function is particularly advanced. Very primitive brains from far less evolved organisms are capable of these functions; even single-celled organisms with no nervous system manifest these same characteristics. Humans are, however, able to implement higher brain function (intelligence if you like), such that we, unlike less evolved organisms like insects, are not entirely bound by instinctive drives. It is this higher brain function that enables us to resist the temptation to have sexual intercourse whenever the mood takes us.

Should, for some reason, a neurotransmitter system related to reward be underactive, normal behaviours that should be perceived as pleasurable will have a subnormal impact. Because the experience of pleasure is linked to survival, and its pursuit is an innate desire, the individual is motivated to carry out one or more of the following: the associated behaviour (particularly if it has felt good in the past), a substitute for it (like a chemical) or more rewarding behaviours in an attempt to find out if these will stimulate a greater release of the related neurotransmitter and consequently provide the desired effect. This means that our emotions serve to optimise our physiology. Should we experience a 'bad' emotion, it serves as a signal for us to change our behaviour in such a way as to alter our physiology in a favourable way. If a given neurotransmitter is related to pleasurable sensations or to the overall good of the individual, a deficiency in its activity makes the individual feel suboptimal. These unpleasant sensations make us actively seek out behaviours that increase the activity of the given neurotransmitter in order to maintain previous levels or even exceed them.

Human brains are 'hardwired' to motivate us to seek out certain kinds of behaviour. This hardwiring lies deep inside our genetic makeup and so is biologically determined. The psychological 'bonus' is that these instinctive behaviours feel good, or at least should do for the majority of people. The downside is that if we do not get to carry out the instinctive behaviour, or if it does not have a particularly strong impact on the individual, then the lack of neurotransmitter release in the pleasure circuitry produces a lack of satisfaction. This means that we are driven to actively seek out the behaviour that induces the best expression of a neurotransmitter system that elevates the mood and makes us feel 'normal' or hopefully great. Addicts are therefore pleasure seekers not in a hedonistic sense but in that, on a day-to-day basis, they just do not feel that much pleasure because their reward systems are underactive and they explore ways of changing this situation.

The different substances of abuse have diverse effects on several neurotransmitter systems and hence have equally diverse actions. However, all such substances are addictive because they all impact on the innate reward systems of the brain that subconsciously govern certain instinctive behavioural traits. In truth, the factor that implicates a psychoactive substance as being addictive is the fact that it must affect the reward circuitry of the brain. If the drug does not affect this part of the brain, it will not become psychologically addictive. It is for this reason that our clinics are not full of patients addicted to the contraceptive pill or antibiotics. Patients might well develop tolerance to many different classifications of pharmaceutical medication via neuronal downregulation and other mechanisms, and could even present with withdrawal symptoms on drug discontinuation, but should they not be able to obtain the drug for a time they will not be motivated toward drug-seeking behaviour in the same way as an addict is. This is because these other drugs do not affect the brain's reward circuitry.

There continues to be much debate in this field. The mechanisms of addiction are exceedingly complex and neuroscience is in its relative infancy, but it seems to be that at the level of current understanding the key neurotransmitters involved in addictive behaviour are dopamine and serotonin (however, these are not the only ones).

There is much evidence to suggest that animals are motivated to perform and repeat behaviours that stimulate the release of dopamine in the reward circuitry of the brain.[1] Should a behaviour release dopamine it is strongly reinforced, meaning that your brain tells you that repetition of the behaviour is beneficial. The common ground that all addictive drugs share is that they increase the levels of dopamine in the reward circuitry. Serotonin is also important because this neurotransmitter signals the 'like' in the pleasure circuitry. The actions with which they cause this increase are different, depending on the pharmacological properties of the drug but the net result is the same, 'that felt good, do it again'.

Dopamine

The function of dopamine (Fig. 3.1) is often misunderstood. It does not signal pleasure sensations as such. In fact, with reference to addictive behaviours it has two key roles:

1. It converts stimulus into action or motivation.
2. It is a facilitator of conditioned learning.

Dopamine makes neurons more receptive to incoming stimuli; it creates mental focus to promote survival and it allows associational connections to be made. If we are hungry, for example, then the sight and smell of food is heightened by raised dopamine levels. The release of dopamine therefore more accurately informs the process by which the individual becomes aware

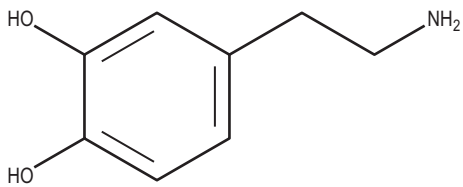

Fig. 3.1 Dopamine molecule.

of the possible presence of reward. Its release grabs the attention and so prompts the individual to continue to carry out reward-seeking behaviours, which in themselves have some degree of hedonic impact. These behaviours carry with them sensations of excitement and anticipation. So dopamine does have actions within the so-called pleasure circuits of the brain, although its release in itself is not responsible for the emotion of pleasure, it is only part of the picture.

It seems to us that the use of the word 'pleasure' is too broad; we prefer to use the terms 'anticipation' and 'satisfaction', both of which could be described as pleasurable. Dopamine drives anticipation and also helps the individual sub-consciously record exactly how rewarding a behaviour was; dopamine thus drives needing, wanting and craving. Normally, dopamine levels are high when seeking food, company or sex, for example. In fact, it is thought that sleep is important to replenish the brain's supply of dopamine in readiness for the stimulation associated with wakefulness.[2] For example, if food cannot be found, then more and more dopamine is released to encourage you to work harder to get it. Dopamine is powerful and hard to resist; it wants you to survive. Without it, life is lost.

Dopamine's other key function is the attribution of high-incentive saliency values. This means that something that proves itself to be very rewarding is memorised as such and takes precedence over other rewards perceived to be of lesser value. So, normal behaviours in an addicted person (or one predisposed to addictive behaviour) do not provide much stimulus. Little dopamine is released in response to say, hunger, because the reward system is much more interested in powerful stimuli. Powerful stimuli, like alcohol, actually manage to register in the brain because they release much greater amounts of dopamine than 'normal' behaviours and do so incredibly quickly. The excess dopamine drives the person to take more and more. This is why, for example, alcoholics are not satisfied with the drink they are having but are obsessed with getting more. The first time the brain experiences the dopamine rush it is saying, in effect, 'This alcohol is really interesting to me, I've never felt like this before, this is important stuff, I must remember to do this again'. Dopamine increases our ability to learn associations. The brain has now created a memory associating alcohol with feeling better. These memories get whispered to the rest of the brain whenever the brain senses dissatisfaction and dopamine is released in anticipation of finding another drink, driving the desire for a big hit. Dopamine tells you 'Go on, its going to feel amazing!'. Dopamine is impulsive.

Serotonin

At some point, once a behaviour has been carried out our feelings should change. We need to feel relaxed and satisfied. We now are no longer driven to carry out the behaviour we initially so desired. The sensations of pleasure related to satiation itself are regulated by the neurotransmitter serotonin (Fig. 3.2). This is a crucial function; without it action would never cease.

Serotonin modulates dopamine. Dopamine makes stimuli seem more important and serotonin less so. This means that if serotonin levels are high we are satisfied. This concept is fairly well known and has led to the development of drugs that affect the amount of serotonin available at the synapse, such as Prozac. Research has shown that abnormally reduced levels of serotonin manifest in depressed individuals. Low levels have also been shown in addicts, bulimics, the suicidal and the homicidal, amongst many others. Serotonin levels are reduced in the premenstrual phase of the reproductive cycle. It is this that leads to low mood, irritability, and food cravings.[3] It has also been shown that depleting serotonin levels using *p*-chlorophenylalanine, produces compulsive sexual activity in male rats, cats and rabbits (as long as testosterone is present). The low serotonin levels cause dopamine to be released in order to seek out behaviours that supply satisfaction, whatever the cost. If something lowers serotonin levels, like addiction, then dopamine searches for a solution.[4]

Serotonin gives individuals the ability to reflect on their internal state and to decide when they feel satisfied. Serotonin moderates dopamine; it applies the brakes so to speak. Individuals need to experience a balance between dopamine-driven impulsive behaviour and serotonin-mediated self-control. The implications of this are, therefore, that wildly fluctuating dopamine levels in the brain or levels higher relative to serotonin lead to impulsive behaviour, whereas low serotonin levels, or at least relatively lower than dopamine, lead to low impulse control (or both at the same time!). This makes individuals irritable as their threshold to tolerate discomfort is diminished. This deficiency in serotonin relative to dopamine means that the brain drives people harder and harder to find something that satisfies them. The drive becomes obsessive, to the detriment of all else, and this often ends in drug taking. It has been shown experimentally that even punishment delivered by electric shock does not deter compulsive sexual activity in rats with serotonin removed from their

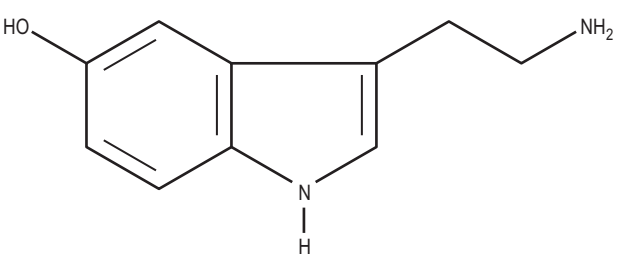

Fig. 3.2 Serotonin molecule.

brains.[2] Serotonin tells you "job done, don't do it again." Serotonin is patient.

Homeostasis of dopamine and serotonin

Addiction occurs not only when dopamine levels are raised in a part of the brain called the nucleus accumbens, which plays a key role in the reward circuit, but importantly, when serotonin levels are reduced. How behaviours affect serotonin might reflect on the pattern of their misuse. If a drug or behaviour raises serotonin levels then seeking stops; if a drug or behaviour does not strongly raise serotonin then a binge will occur. Alcohol, for example, has little impact on serotonin and so users tend to drink until they either pass out or empty their pockets. If dopamine levels are too high people will search everywhere for that which they desire, frequently switching purpose. Serotonin needs to modulate this behaviour to increase focus. When a task initiated by dopamine release has been completed and an individual's needs have been met then serotonin rises to signal closure on that event.

Dopamine circuits are linked to those of serotonin and also to memory. If a deficit is registered in the serotonin satisfaction circuit, then dissatisfaction turns to craving. Dopamine is released and seeking or wanting behaviour is initiated to gain satisfaction. The degree to which dopamine is released depends on how rewarding a potential behaviour is perceived to be. If a previous behaviour proved to be enormously pleasurable then the next time it is considered the concurrent dopamine release is proportionately larger and so wanted more vehemently. This is why addictors, as opposed to normal behaviours, create such profound wanting. The normal behaviours never felt very important because they did not register in the dopamine circuit.

As mentioned above, if excessive neurotransmitters are released – much greater than the brain would naturally release – then the nervous system adjusts through down-regulation. This means that an identical behaviour will have a less profoundly rewarding effect and so more drug is needed, a 'harder' drug is sought out or a more potent drug administration method is chosen. This time the brain is saying 'So, that felt OK but not like it did last time, maybe I'd better try a bit more'. Since it can be readily observed that 'liking' reduces in addicted persons, this suggests that serotonin neurons get down-regulated; dopamine neurons, however, as a mediator of learning appear to be sensitized to drug cues and so compulsivity increased. The brain will regulate the reward systems to optimise physiology and these adjustments support this. Research has shown that even a novel environment triggers more dopamine release and even results in increased risk of overdose. The adjustment of reward saliency according to relative dopamine levels also means that normally rewarding behaviours, like eating, have little impact and so lose some of their motivational significance.

Initially, dopamine release (and hence seeking) is triggered by a key stimulus, such as the smell of a pheromone, for example, or a memory associated with past pleasurable experiences, like a familiar pub or the sound of a gurgling wine bottle.

Dopamine drives the 'wanting' of an individual, not the 'liking' associated with serotonin. So, if these interacting neurotransmitter systems are weak, naturally rewarding behaviours (those that most individuals would like to repeat because they provide satisfaction, such as sex) do not provide much effect. Due to this fact the brain does not reinforce normal reward behaviours particularly strongly.

Those individuals with weak wanting/liking systems need something stronger and, when they find it, its use is particularly strongly reinforced; the brain very carefully takes note of what activities 'hit the spot' so to speak. Low satisfaction levels drive the individual to seek out new and more powerful rewards.

When a goal is reached, neurotransmitter levels should normalise at the point at which the individual is satiated and loses interest in seeking more. Drug users do not get this fall in interest because, unlike natural rewards, drugs cause a prolonged, unnaturally high release of dopamine that is often not removed from the synaptic cleft for a long period of time due to interference with re-uptake mechanisms, further triggering shifting reward saliency.

Dopamine release, driving the 'want', is triggered by the environment associated with reward and this is borne out by rat research. Dopamine levels are indeed raised in individuals even before they carry out the actual gratifying behaviour. The research has shown that rats placed in a cage in which they had previously been administered cocaine released dopamine even without the presence of the drug. The amount of dopamine released is proportional to the perceived potential for the individual to experience pleasure. If a given behaviour does prove to be gratifying then the anticipatory release of dopamine will be correspondingly higher next time the behaviour is considered; this creates higher 'wanting'. If tolerance causes the drug to be less pleasurable at the same dose then dopamine continues to rise to make us take more. It therefore seems that dopamine is actually a facilitator of learning. Dopamine release helps the individual to remember the various sources of gratification. The incentive for pleasure seeking is survival and is driven by dopamine but wanting and liking are not synonymous. This phenomenon is leading to the possible development of addiction-inhibiting drugs that deplete dopamine.

As dopamine reinforces desirable behaviours, it seems a little odd that one would ever stop using a reinforcer. Why do we not continue to eat or procreate all the time if it is essential to survival? This is where the modulating effects of serotonin are brought into play, regulating satisfaction. In order that an individual is able to carry out a wide variety of beneficial behaviours one must be made aware of when a given behaviour has fulfilled its purpose for the time being.

Current research implies that individuals with a genetic predisposition to addiction have under-responsive dopamine and serotonin receptors. This seems to create a situation in which normal behaviours do not provide normal reward salience values and so life feels different for individuals in this situation;[5] they feel like a square peg in a round hole, 'other people find reward in life, why not me?' They go through the world seldom experiencing pleasure and so are not particularly motivated towards supposedly pleasurable behaviours, instead they are subconsciously in perpetual search for something that for them is potent.

Low levels of dopamine receptors decrease the sensitivity to salient stimuli. Again, rat research substantiates this. If alcoholic rats are genetically manipulated to encourage overexpression of the number of dopamine receptors they possess, they then consequently reduce their alcohol intake.[6] These rats did not need excess amounts of alcohol to stimulate them because their pleasure circuit was now more receptive to dopamine. Normal behaviours would also now register more normally for them. It has also been shown that addicted rats that subsequently have their dopamine neurons destroyed do not crave; they simply cannot crave because the neurons of memory no longer have dopamine neurons to talk to and there is no dopamine to provide motivation. We just end up with a bunch of miserable rats with no idea that a change in behaviour could change the way they feel. This begs the question 'Why not "cure" addicts by destroying their dopamine neurons?' Well, we could in theory but they would also lose a vital part of their nature along with their neurons, which seems inhumane. They would forever be unable to realise that life can feel good. What is more realistic is the manipulation of dopamine receptor sites. Some pharmaceuticals, like pramipexole and ropinirole, are being explored to try to block the action of dopamine; this might well reduce the drug reinforcement but because dopamine has diverse effects throughout the brain these drugs also cause undesirable side-effects. These drugs may also further numb the addict to seek natural rewards, in a sense making the situation of anhedonia worse.

Once an addict has found a behaviour that causes an associated increase in dopamine, the brain records the details for use later on. Addicts therefore are now in possession of a dopamine system that, although suboptimal, is driven by the reinforcement of what caused dopamine levels to be higher, the dopamine system has become sensitized to drug-related behaviours. This is compounded by their inherently weak serotonin system. They are therefore impulse driven in relation to their drug use and never know when 'enough is enough'. Of course, this is exacerbated by the fact that an already underactive serotonin neurotransmitter system will, relative to the greatly raised dopamine, be further suppressed following a torrent of drug-induced neurotransmitter release. This will again trigger the desire to experience their effects, driven by both behavioural reinforcement through strong memories and unpleasant withdrawals.

To summarise, although it seems sensible to assume that liking and wanting are part of the same process, neuroscience research has shown that these behaviours are mediated by different but interconnected neural circuits. Liking is linked to feelings of pleasure and is mediated by serotonin. Wanting attributes a motivational value to a stimulus and is seen as essential behaviour governed by dopamine. This can be observed in addicts because repeated drug use does not increase the pleasure associated with their use, although wanting is certainly intensified by their use. Drugs sensitise the dopamine systems that mediate incentive salience and so lead to pathological wanting of high reward.

> *'So, all experience is chemically conditioned. If we imagine some of them are purely spiritual, intellectual, aesthetic it is merely because we have never troubled to investigate the internal chemical environment at the moment of their occurrence.'*[7]

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CHAPTER 4

Learning

Memory is a way of holding on to the things you love, the things you are, the things you never want to lose.

(Kevin Arnold)

Adaptive mechanisms

As we have seen, like other body systems, neurotransmitter levels and even synaptic connections are self-governed by homeostatic mechanisms. The sum goal of these mechanisms is to increase the likelihood of survival. However, different parts of the brain respond differently to stimulation – depending on the role of that particular part of the brain – sometimes becoming more excitable and sometimes less. It appears that in addicted patients two kinds of neural adaptation are occurring simultaneously; the pleasurable effects of the substance and ordinarily rewarding behaviours tend to be weakened while cravings for the drugs are increased.

When an individual is experiencing sensations such as anhedonia, pain or withdrawal, the nucleus accumbens (which plays a key role in the reward circuit) becomes more sensitive. This means that it releases dopamine more strongly in order to initiate behaviours that will solve the problem. To illustrate, if we are thirsty the nucleus accumbens releases dopamine, which motivates us to walk to the kitchen, turn on the tap and take a drink. Learned or conditioned responses actually cause the brain to release dopamine more swiftly and in larger amounts. This increases our ability to connect incoming stimuli, a phenomenon known as pattern recognition. Drug users become conditioned to release more dopamine in response to drug-related stimuli.

Memory circuits related to drug-related behaviours become more responsive to stimulation whereas other circuits that govern day-to-day behaviours often tend to become less responsive because they do not have such a profound effect. The methods with which these regulatory processes occur are very much affected by the drugs of misuse and are responsible for withdrawal, craving and addictive behaviour. So, in an addict, some parts of the reward circuit are suppressed and others sensitised. Neural pathways using serotonin, relating to the experience of

pleasure itself are down-regulated, whereas pathways related to drug cravings, which connect with dopamine pathways, are sensitised. In withdrawal, dopamine levels are likely to be very low due to down-regulation. However, when drug use is considered, for whatever reason (a feeling of loneliness, the sight of a teaspoon or abdominal cramps), then dopamine levels rise strongly, indicating the possible presence of reward and thus driving the desire for drugs. The addict is reminded of how much better things could be, and due to the resetting of the neurotransmitter thermostat now needs even more serotonin release to better the previous experience. If the neurotransmitter level does not rise significantly then the brain craves more of the drug, maybe more powerful drugs or a stronger administration method. If these newer, better behaviours work then yet again neurotransmitter levels will rise higher than ever before, and this new level is recorded, thus resetting the thermostat still lower. The addict is caught in a vicious circle.

The sensitised pathways are those of memory modules (amygdala) that talk to the dopamine modules that make up the reward circuit itself (mesocorticolimbic). The dopamine pathways are sensitised to drug-related stimuli as opposed to those of normal stimuli because of their input from neural memory networks, and so day-to-day behaviours do not have the same profound response as drug-related behaviours. The salience of drug rewards carries more weight than any other.

It is also true that factors such as genetic variation allow for individual differences in the homeostatic processes and that this helps shape one's psychology, hence also one's predispositions toward mental health problems and of course, most importantly substance misuse issues.

Learning

Addicts often say something along the following lines: 'The first time I had a drink I found what I had been waiting my whole life for; everything fell into place and it just felt right. Before I always felt like something was missing, it always felt like a piece of the jigsaw didn't fit. When I found drink, it fitted like a glove'.

Once an addict has experienced these new sensations they are never forgotten. Drugs chemically activate the neuronal circuits associated with learning. This is illustrated by the observation of intensified behavioural responses: the addict wants more or better. All addictive drugs cause an increase in dopamine in the mesocorticolimbic system. Of particular note are the ventral tegmental area, which sends projections to both cortical and limbic areas, and the nucleus accumbens, which projects to the prefrontal cortex. The knock-on effect of this is a rise in glutamate, the memory neurotransmitter.

The process of learning is vital. It allows beneficial behaviour modification. Learning as a phenomenon is present not only from the moment we are born but actually begins in response to our prenatal environment. The brain receives sensory input, processes it and modifies neural function thereafter. These modifications may lead to the acquisition of new skills, facts or emotional responses.

Unfortunately, however, in modern society the changes resulting from learning mechanisms can be less helpful than in more ancient times. For example, most of us do not any longer need to be scared of snakes or spiders but, should our predisposition to fear them be triggered by experience, we learn to fear them anyway. Indeed, addiction in itself is not of any benefit whatsoever but it becomes intertwined with powerful mechanisms that evolved to increase the likelihood of survival of the individual, i.e. life-promoting behaviours with which pleasure sensations were associated. Drugs influence the neuronal plasticity of these memory pathways and the brain is tricked into thinking drugs are necessary for survival. The phenomenon of craving itself is a learned or conditioned behaviour.

What mechanisms are behind learning?

Somehow, learning seems hard to put your finger on. Is there a specific place in our brain that holds a memory and if such a place exists what form does a memory take? Is there some sort of cellular organelle that is like a bag of memories? What is a memory anyway, how can it seem so real if it is constructed of no physical form?

We might easily marvel at how amazing modern information storage devices are. It is now possible to store thousands of books, photos, videos and songs in a tiny device that slips into your pocket. Brains are not, however, organic magnetic storage devices; they are made of billions of cells, have the consistency of wobbly jelly and a seemingly limitless storage capacity. Memory to a human being must therefore be somehow special, more special than any technological device we have yet created or probably ever will.

Until relatively recently no-one had any real idea how memories could be formed. Some scientists thought that new brain cells must be manufactured whenever we learnt something new. When synapses were discovered, towards the end of the 19th century, it was felt that new synapses must be made and it was these new connections that allowed for memory. Eventually these theories were ridiculed and it became clear that what actually happens is that synapses grow a little stronger when they successfully participate in the firing of a post-synaptic neuron. Just to complicate the issue, it has recently been discovered that some parts of the brain do actually manufacture new neurons and that brains can form new synapses.[1] However, the majority of the physiology of learning is still very much considered to be rooted in the ability of synaptic function to change over time.

Current research suggests that memories are not held in a single brain module but that different types of memories are stored in different places. Conscious memories appear to reside in the hippocampus and unconscious ones in the amygdala and striatum; the locus coeruleus also seems to be important for memory. The frontal cortex deals with the working memory that enables the planning of behaviour, for example gratification postponement.

A stimulus might excite a network of neurons. These neurons then make the brain respond in a multitude of ways, depending on the stimulus. When a stimulus has stopped it leaves metaphorical footprints. These do not represent what the stimulus was in itself but a pathway in the brain. Where that pathway leads is most important, as it is here that the stimulus held meaning; this meaning will be slightly different for different individuals, depending on their previous learning. How easily the footsteps are retraceable denotes the ease with which the meaning – and hence the memory – can again be experienced.

It is interesting to note that the brain of a newborn has a relatively smooth surface. As the brain ages and learns from experience it starts to develop characteristic wrinkles as brain structure adapts, so, much like the wrinkles on our faces reflect our life experience so do those of the brain.[2] The changes in shape result from a change in the physical structure of neurons (and hence the brain) as a result of a process of synaptic change known as synaptic plasticity. To demonstrate how this might manifest, consider Einstein's brain, which was found to be 15% wider in the parietal lobes than 'normal' (control) brains. The parietal lobes are involved in mathematical and spatial reasoning. This illustrates how the more we use a given part of the brain the more it grows, thinking is like weight-lifting for the brain.

Synaptic plasticity: learning at a cellular level

Synaptic communication is a variable process and can change as a result of experience; this is the basis of learning. It appears that a number of possible mechanisms contribute to the learning phenomenon:

1. Neural pathways work more efficiently the more they get used. It might be useful to consider the following analogy. The Highways Agency notices that a B road is struggling to cope with the volume of traffic. It is decided that it be expanded, strengthened and reclassified as an A road. This process is what is referred to as long-term potentiation (LTP).
2. New synaptic connections can be synthesised. This process is known as synaptogenesis. This allows for further strengthening of neural communication and also associational memory.
3. Although still a hotly debated topic, it also appears that a new neuron could be formed in response to stimuli. So in this case the Highways Agency decides that it would be inappropriate to upgrade the B road because it runs too near a school, so they build a bypass. This process is known as neurogenesis. Until recently it was thought that brains only generated new cells in early development. This now appears not to be the case. Adult neurogenesis can occur but it is limited. This is why brain damage can be irreparably destructive, even though neurogenesis has been shown to occur in various areas of the brain. As neurogenesis is limited, this text focuses on LTP as the dominant paradigm for learning.

Long-term potentiation

In short, LTP means that a synapse between two neurons can not only alter in order to work more efficiently, but that these changes last a long time. In a healthy individual, these changes can last a lifetime; do we ever forget how to ride a bicycle, can we always remember snippets of our childhood?

Should a synapse be stimulated repeatedly, in quick succession, the next time it is stimulated something different happens. The wave of excitation is larger than last time. This synapse is now more responsive than it was before.

LTP occurs in particular neurons that use a neurotransmitter called glutamate and several factors lead to LTP in addicted persons:

1. It occurs when a neuron receives a dense cluster of rapid action potentials (inputs). When enough glutamate has been released, calcium is able to enter the cell. In response to the influx of calcium several important changes occur. The result is that the neuron becomes hyper-responsive. This means that the neural pathway is stronger and increases the likelihood that a single neuron can fire an action potential.
2. Should a behaviour or a chemical be ingested that either mimics or causes the release of a neurotransmitter torrent causing very potent pleasure sensations, the neurons responsible for memory, which use glutamate, will also be wildly stimulated. Memory circuits do this because pleasure is attached to behaviours that are favourable to survival and hence repetition is reinforced. So pleasure-inducing drugs or behaviours trigger the learning mechanism to associate the sensations with the ingestion of the drug and the associated behaviours. The memory neurons (glutamatergic) link with dopamine neurons, which thereby learn to predict the occurrence of reward and are sensitised to do so.
3. This hyperstimulation causes spare receptor sites to be brought online as a result of the calcium ions pouring into the neuron. The postsynaptic neuron becomes more attentive.
4. A molecule of phosphorus is also added to the receptor site, which causes it to stay open for longer and so neurotransmitters can sit around for longer in the receptor exciting the neuron.
5. The shape of the cell membrane on the dendritic spine changes shape allowing more efficient conduction of the wave of excitation.
6. It has recently been discovered that postsynaptic neurons can actually send a neurotransmitter backwards to the presynaptic neuron to tell it to release even more glutamate and thus send a stronger signal.

The consequence of these changes is that the presynaptic neuron releases more glutamate and the postsynaptic neuron now has more receptors, and these receptors are more sensitive. Metaphorically the presynaptic neuron is talking more loudly and the postsynaptic neuron's hearing has also become more acute.

LTP is also facilitated by unpleasant sensations such as withdrawal symptoms. The experience of unpleasant withdrawal symptoms is often also potentiated

because dopamine neurons in the withdrawal phase have hypersensitive AMPA receptors (a subtype of glutamate receptor). These changes can create an inappropriate fear of withdrawals in much the same way as a traumatic event might lead to post-traumatic stress disorder (PTSD). In fact, the brain has evolved to remember even more information about distressing events than pleasant events, just in case a piece of subtle information might save your life some time. To illustrate, imagine an individual sitting in a coffee shop, with a song playing on the radio, when a bomb goes off outside. Although the individual would not be aware of it, the brain might have memorised the song just in case it was important. Months later, hearing the song on the radio again would unconsciously set up feelings of panic and terror.

LTP is most studied with respect to parts of the brain that are mostly associated with memory, various limbic structures, the hippocampus and amygdala, but it seems to occur all over the brain. In this way, pretty much any experience can lead to memory formation. Learning is also not the exclusive domain of the part of the conscious brain that remembers the dates of the battles but, as will be shown later in the text, much animal behaviour is also a learnt phenomenon.

The means by which LTP occurs are fascinating. The physical structure of the synapse alters in response to a stimulus. Think about that for a second: it means that just a word on a page, which is nothing more than a bunch of photons hitting your eye, can affect profound changes in how your body works thereafter.

Learned behaviour

There are two distinct types of learning: declarative and non-declarative.

Declarative learning

Declarative memories are those that most people think about when they use the term 'memory'. These memories can be accessed for conscious recollection, such as being able to quote pi to the umpteenth decimal place or reel off the date of the gunpowder plot. Declarative memories are generally easily formed but are also unfortunately all too easily forgotten. Declarative learning requires cognitive processes to create the memory. To illustrate, if an addict is being taught harm-minimisation techniques, such as safer injecting procedures, the interaction involves cognitive processing and memorisation of the information, and so falls into the category of declarative memory. The multitude of counselling techniques start to do their work at this level of learning; by enhancing the underlying mechanisms it is hoped that cognitive changes can be used to alter subsequent behaviour. Unfortunately, however, declarative memories are often easily forgotten. Consider the earlier analogy of memory footprints. These memories are like footprints in the sand and can be washed away (Fig. 4.1). For example, can you remember all the facts you learned at school, or have they been washed away?

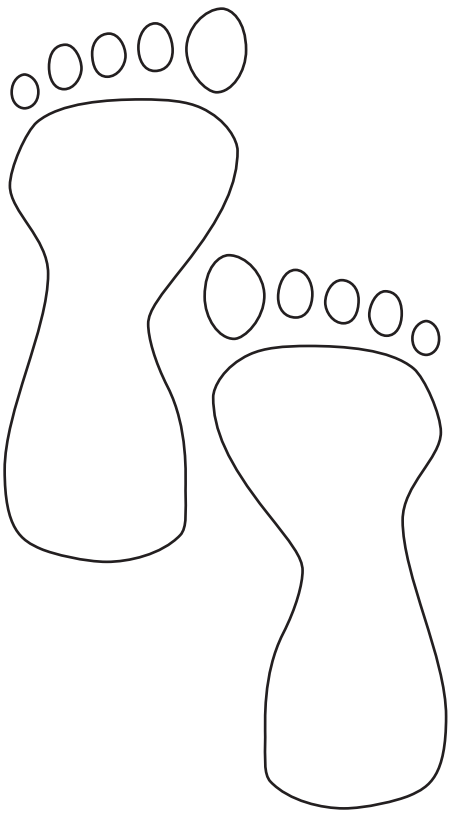

Fig. 4.1 Weak memory traces.

There are multiple types of memory. Some memories are stored in short-term memory and are selectively transferred to long-term memory, usually by the process of repetition. Repetition causes glutamate to keep being released until enough has been released to result in the aforementioned calcium influx thus triggering LTP.

Non-declarative learning

Non-declarative memories cannot really be thought about. It is difficult, for example, to describe how you learnt to ride a bicycle but, once you have learnt the skills you never seem to forget them. These types of memory become part of our very being, resulting in new skills, habits and unconscious emotional behaviours and responses. The important point about these memories is that they are much, much harder to forget, if at all – as the saying goes, 'you never forget how to ride a bicycle'. These procedural memories become interwoven into the fabric of the brain as a result of experience. The footprints created by these memories are like those in concrete; once set they are not so easily washed away

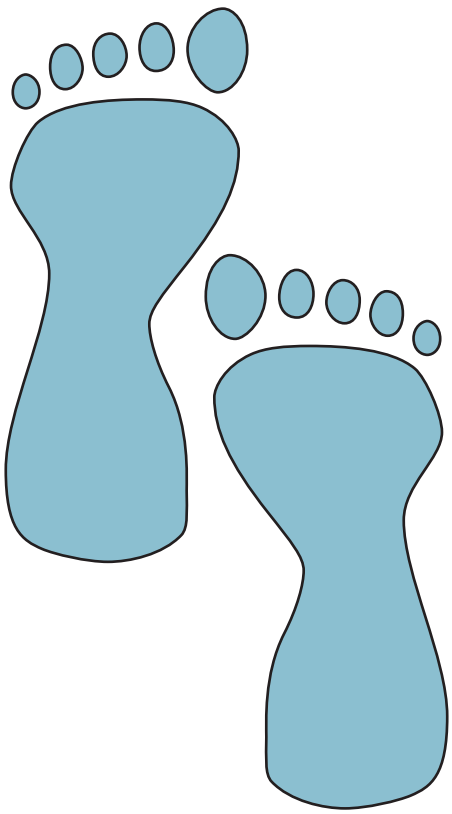

Fig. 4.2 Strong memory traces.

(Fig. 4.2). It is unfortunate but true that psychoactive chemicals do their damage at this level and hence to the detriment of the individual, their memory can last a lifetime.

The tricky part of treating addiction is teaching new skills to the declarative, conscious brain in such a way as to have the knock-on effect of re-educating the notoriously strong non-declarative, unconscious pathways. The easiest (and perhaps most obvious) way to get the unconscious brain to be receptive to new information is to avoid psychoactive chemicals. In this way the newly built memory A roads of the reward circuitry can be avoided. Fortunately, it seems likely that, although the A roads will always be there, there is nothing to stop you building a new by-pass (modified behaviour).

Two key factors contribute to the ability of the brain to remember. Either one factor, or a combination of the two, results in learning:

1. Repetition consolidates memory. So the more times an experience is repeated, the more ingrained in the brain it becomes. In effect, repetition creates deeper footprints. Repeated neural stimulation will eventually release enough glutamate to trigger the process of memory. This is the 'Ah ha' moment and important in forming treatment strategy.

2. The brain easily remembers 'big' things, often described as a 'flashbulb memory'. If something is heavy it creates deeper footprints. This means that if something carries with it a powerful emotional charge or if it challenges one's preconceptions it is likely to be remembered and does not require repetition. This is the strongest factor in learning; think about the strongest memories you have. They tend to be about emotional times such as weddings, birthdays, funerals or the first time you met your lover. This is because emotions are a fundamental part of human processes and, as such, great importance is attached to them. In terms of addiction this phenomenon implies that if an emotional charge can be applied to something it has more profound effects. This therefore relates to the fact that because drugs affect the part of the brain that governs emotions they affect us at a very powerful and fundamental level. Drugs are emotional charge.

It is also true that when patients get to 'the right place' and are ready to attempt recovery it is often because they hit 'rock bottom'. Every patient's rock bottom will be a very personal place but the important factor is that it is a place within each individual that is so horrible and uncomfortable that the person seems to experience a realisation that he or she has become powerless in the face of the chemicals. We have heard stories of many rock bottoms. They can seem relatively minor to some. One woman realised she had a problem because she woke up next to someone she had never met before, another because she wet the bed, another because she noticed how wrinkled her face was becoming and how big the bags under her eyes were getting. Some rock bottoms are much more profound; one patient had an awakening because he woke in the morning to find a toddler impaled in the radiator grille of his car. Think about how you responded to that story. Absolute horror, anger or abject sadness? Will you ever forget that story? That is the power of emotional charge.

Associational memory

Early in the 20th century, neuroscience research led scientists to realise that memory engrams (memory traces) cannot be localised within the brain but that memories are distributed between vast numbers of neurons that become simultaneously active in response to stimulus. This group of simultaneously active neurons is known as a cell assembly. Neurons are not linked in simple chains with one neuron connecting to another; one neuron can receive inputs from as many as 10 000 other neurons.

Activity of a pre-existing cell assembly does not just lead to strengthening of the existing synapses but also initiates the formation of new synaptic connections.[3] This discovery led to the phrase 'neurons that fire together, wire together'. The new connections are not entirely new relationships but are added to pre-existing connections. It is these new wiring configurations that, in addition to changes in synaptic function, contribute to memory. This fire-wire phenomenon is known as

Hebbian plasticity after Donald Hebb – the man who proposed the theory – and essentially describes the aforementioned processes of synaptogenesis.

Should activation of the cell assembly persist for long enough then adaptive processes occur such that these interconnected neurons work more efficiently together. Subsequently, only a proportion of these interconnected cells need be activated by a later stimulus to activate the whole cell assembly and trigger the associated memory. This interconnectedness allows subtle environmental stimuli, such as the sight of a needle or the smell of smoke, to trigger powerful memories; this is explored below.

This fire-wire hypothesis also means that LTP in dopamine circuits is related to drugs specifically, as opposed to any behaviour that might use the same circuitry. The specific network of neurons activated is related to the drug use and the environment that is unique to that person. So dopamine neurons will be more strongly activated by drug-related memories due to LTP than normally salient stimuli.

Associative learning: relapse triggers

One of the ways in which we learn is known as associative learning. This simply means that associations are formed between two events and often referred to as conditioning. It falls into two types, both of which are implicated in certain characteristics of addictive behaviour:

1. *Classical conditioning.* This is the form of conditioning well known as a result of the classic Pavlov's dog experiments. Some key stimuli create a response in an individual without conditioning, for example the sight or smell of food. What Pavlov wanted to discover was if a secondary stimulus could be linked to the first by learning mechanisms. The way he carried out his experiment was as follows. First he observed the response that dogs made to the primary stimulus, the sight of a slab of meat. The dogs consequently started salivating in anticipation of a meal. The secondary stimulus he used was the sound of a bell, which clearly did not evoke salivation. Next, he paired the presentation of the meat with the sound of the bell and repeated the process several times. He then sounded the bell but withheld the meat. Because the sound of the bell had become associated with the presence of the meat, the dogs had learned that the bell predicted that a meal would soon arrive and salivated in readiness. This is a prime example of the conditioned response. This phenomenon is quite easily observed in addicted patients. For example, a smoker will associate having a meal with also having a cigarette. An individual who is trying to quit will often comment how difficult it is to have a meal without also fantasising about smoking a cigarette. The phenomenon of needle fixation also fits into this category, as does the sight of a crack pipe or the chink of glasses which trigger pleasurable memories. Memory therefore tends not to be rooted in single stimuli but in patterns of stimuli that occur together. Déjà vu, for

example, occurs when several patterns overlap and are reminiscent of another situation.[4] The brain seeks out familiarity because we want significant things to be quickly recognised and acted upon. When craving a cigarette for example the sight, sounds and smell of another person lighting up more easily cross our threshold of awareness. This is achieved by the actions of dopamine, bringing environmental stimuli to the forefront of our sensory systems.

2. *Instrumental conditioning.* In this type of conditioning the individual learns that a given behaviour is associated with a particular consequence. The typical experiment used to illustrate this phenomenon used a rat placed in a box with a lever that when depressed deposited some food reward. The rat would accidentally bump into the lever and food would magically appear. After a few accidents the rat learned that pressing the lever released food and would continue to press it until it was no longer hungry. This type of association can be illustrated by the fact that very quickly a user will realise that a hit of heroin or smoking a cigarette creates altered states of consciousness.

Interestingly, associative learning is unconscious and does not need an advanced nervous system. It requires no cortical activity and has even been demonstrated in sea slugs. While conditioned learning takes place unconsciously during drug taking it is also true that the unconscious brain communicates with the cortex and vice versa. It is through this communicative process that various counselling techniques work. Behaviours are consciously explored in the cortex that will then, in effect, try and explain what it has learned to the unconscious limbic areas. If the new neural connections are used regularly they remain strong; if not then they are weakened. Considering the example above, this means that the more times a meal can be eaten without also smoking a cigarette, the less potent the associational memory. These associative, non-declarative learning mechanisms therefore respond well to therapies that focus on altering behaviours that may trigger craving by association. The only difficulty with these therapies is that the regular presence of drugs in the brain makes it very difficult to 'reach' a person such that behavioural adjustments get a chance to do their work. The continued drug use continues to reinforce learning. Another major difficulty lies in the fact that the limbic system can quite easily make itself heard over the frontal cortex. This means drug use inhibits cortical activity. This is explored fully later in the text.

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CHAPTER 5

Emotion: addiction is an emotion

An intellectual is a person who has discovered something more interesting than sex.

(Aldous Huxley)

The key point we would like to introduce here is that addiction is based on emotion, not intellect. Drugs and alcohol are no respecters of persons; an addict can belong to any position in society regardless of perceived intelligence, whether the person is a doctor, lawyer, member of the police force, shop assistant or cleaner. Addiction is not a character defect, a moral weakness or a deficit in will power.

To fully understand addiction it is necessary to realise how important emotion is from a human perspective. Try to imagine what life would be like if we did not have emotion. It is almost impossible to do this because emotions are so fundamental to our being. We glance at our loved one and a smile creeps across our face. We walk home on a dark cold night and think we spy an attacker in the bushes out of the corner of our eye. Although just a trick of the light, our heart starts racing and our palms sweat. These are just simple examples of the unconscious hold that our emotions have over us all of the time. Essentially, an emotional experience is a response to sensory input, or as in the above examples, perceived input, perhaps influenced by a film that we might have watched.

It might seem strange that something intangible like a feeling has a biological basis but neuroscience is beginning to unravel these mysteries. It is, for example, possible to produce a given emotion by electrically stimulating a specific brain area via the insertion of an electrode. One such experiment on a 16-year-old girl produced great amusement and giggling; in another, electrostimulation caused the individual to experience a spiritual awakening and the participant believed he had actually seen Christ.[1] It is also now commonplace to 'see inside' the mind using functional neuroimaging to observe how the brain changes its physiology while an individual is experiencing an emotion. It is no longer possible to believe that the self stands above scientific reason.

The spectrum of human emotion evolved to direct us towards behaviours that have a positive impact on survival, and away from experiences that may have detrimental effects. Emotions are one way through which the human body can try to maintain internal homeostasis in response to changes in the external

environment. So emotion is the process of attaching importance to a stimulus.[2]

No single area of the brain creates emotion; each has a specific neural basis. However, the collective structures that create emotion are located in an area known as the limbic system. It is the limbic system that generates drive and emotion such that we actively seek food, reproduction or even shopping (hunting). It is also in the limbic system that emotions such as fear and anger are generated. So emotion is a feeling distinguishable from a thought because it is used to influence a biological function. Some thoughts can bring about emotional change and therefore physical change, but emotion, not thought, is in the driving seat.

Although emotion is generated in the limbic system it is actually registered in a region known as the frontal cortex. What is registered is not however the emotion itself, it is the physical effects of the emotion that are interpreted as the emotion. For example, a loud bang unconsciously creates fear, the limbic system tells your body to respond by making you duck and your heart beat faster. Your conscious brain detects these physical responses and registers the fear. The above-mentioned brain structures will be discussed in more detail shortly.

It is important to note that being able to experience emotion is not the same as being conscious. An emotion is a survival mechanism whereas consciousness makes emotions into feelings. Insects, for example, all have to eat and flee from danger but they are unlikely to be conscious in the way that humans are. Emotions are generated unconsciously and cannot be controlled directly. This is why we cannot fake an emotion; we can act out an emotion but doing this does not mean we are consciously feeling that emotion.

The only way we can really influence emotion is by attempting to manipulate our environment so that it triggers emotional change, for example by smoking crack cocaine or having sexual intercourse. This environment could also be rooted simply in a memory or a thought; it need not even be physically 'real' or present; the anticipation of injecting the next heroin hit perhaps would be more than sufficient. If this is the case, it is the brain that creates that changing environment. However, it is almost impossible to control emotion consciously: you cannot think an emotion. Feeling easily overpowers thinking. If you have ever been depressed, you will soon realise that no matter how hard you try, you will not be able to think yourself happy; if only it were that simple! Also, try to imagine the following situation: you are jealous that your lover is flirting outrageously in a nightclub. Your conscious brain tries to rationalise the situation, and you say to yourself 'it doesn't matter, it's me he wants' or 'she only does that because everyone likes attention' but this is easier said than done. Emotion is so much more powerful than thought. It is also important to note that unconscious mechanisms do not consider the consequences to, or the feelings of, a distressed partner or young child; in this respect they are utterly selfish.

Emotion is also more than just a simple feeling. Emotional responses include physical effects. For example, the emotion of fear creates physiological responses that allow fight or flight: the rate of breathing quickens, the heart beats more rapidly and even the pupils dilate to gather more visual stimuli. So, remember, emotion can reach out and take charge of the internal organs and in fact, every one of the billions of cells that we each possess.

The relative strengths of emotion and thought result from the fact that the emotional centres evolved much earlier than thought in the evolutionary process and so are, in a sense, more fundamental to survival. The human species has survived because our ancestors evolved mechanisms to increase the chance of survival. Natural selection is driven by these mechanisms. It is also true that the neural connections that link the emotional systems to the thinking part of the brain are much stronger than those that run in the opposite direction. In health there does exist a degree of two-way conversation between the two brain centres but there is nevertheless always a bias in the direction of emotion.

To illustrate this further, consider the psychiatric condition Cotard's delusion.[1] In this condition, patients, despite overwhelming evidence to the contrary, and with absolute conviction, believe that they are dead. Although the thinking brain processes information normally, the emotional centre refuses to go along with it. Imagine living in a world in which we feel we no longer exist but are being shown round hell, and we dress ourselves in a shroud and demand to be buried; our brain creates our reality.

These factors are of vital importance with regard to addictive behaviour. This means that you cannot simply think your way out of addiction because the parts of the brain affected by the substances lie in the limbic system and so are largely out of conscious control. The drugs create such a profound response in the limbic system that any degree of input from the frontal cortex is ignored. For addiction to be overcome the key factor must be that the drugs must not be allowed to influence the limbic system. Once the limbic system is filled with drugs it becomes impossible for the thinking part of the brain to have any say at all with regard to behaviour because it is being overpowered. Going back to the example of the jealous lover, after six pints of beer, rationalising is no longer an option and an argument often ensues. Logically, this means that abstention must be the only way to prevent the brain being manipulated. Once the chemicals have been eliminated the brain can start to return to a more stable balance between emotion and cognitive function. These concepts will be discussed much more fully later in the text.

Pain

The emotional impact of pain or discomfort is critical to survival. It is hard-wired into our biology and so present from birth. A new-born baby must survive and therefore is appropriately equipped. Mother nature in her wisdom chose pain as a motivator. When the child needs food the discomfort is registered and the child cries. The sound of the child's cries impacts on the mother and milk engorges her breasts, causing discomfort. When the child suckles, he or she is relieved of pain and instead feels contentment, enhancing the bond with the mother. The child has no appreciation of the fact that it is 3 o'clock in the morning or there is currently a wedding going on; he or she feels uncomfortable and is motivated to act on this feeling. This is powerful, over-riding and subconscious behaviour. The more uncomfortable a situation becomes then the more strongly we are

informed to adjust our situation. Hopefully this next example has not happened to us but I think we could imagine that it might: you are at the front of a rock concert and need to urinate. You are enjoying the band and so you put the sensations to the back of your mind. Suddenly it gets really painful and you really have to go. Now you are more motivated to move back through the crowd to find the toilet. Unfortunately, it is so busy that you cannot get through and you become so motivated to feel relief that you wet yourself. This is highly embarrassing but strangely tinged with pleasure, or at least relief.

So what can cause us pain? Pain is more than just the ache we feel when we bang our elbow or the fullness of our bladder. It can be anxiety, insecurity, a lack of money, loneliness or a poor relationship. In the case of a drug user it is often abstinence distress. Pain is anything that can detrimentally impact on survival. Its result is to focus our attention on adjusting our behaviour until it is removed. Craving is the biological response to pain in order to initiate change. All of this occurs in the brain.

Pleasure

The emotion of pleasure evolved as a reward to reinforce the behaviour that causes its sensations. These behaviours tend to be fundamental to survival: eating, and sexual intercourse, for example. You might be wondering why something essential like breathing does not have pleasurable feelings attached to it. The answer is that it does but we tend not to experience it on a day-to-day basis, this is because air is very abundant and so we do not need to actively seek it out; pleasure is attached to things we have to seek out. If you really want to test this, try holding your breath for as long as you can. The first breath you take when you can hold it no longer will feel really quite good. This means that the value of a stimulus varies according to need. This is important because it means that a brain adapted to the presence of drugs will assume it needs them when they are metabolised out of the system and adds extra importance to them.

What the brain will also try to do is to seek out those behaviours that carry with them the greatest reward and choose those over lesser ones. The dopamine and serotonin-driven anticipation-satiation circuit is designed to, in effect attach a numerical value to a reward, which is then memorised and used to remind the individual which are the most rewarding behaviours. So, should serotonin levels start to fall when pleasure is not being experienced, then the memory and/or panic circuitry tells the body there is a problem, raising dopamine, thus motivating the individual towards those behaviours that subsequently raise serotonin levels again. Remember, the brain has emotionalised drugs and feels like it must have them to survive. If it does not get them it thinks the situation could be detrimental to survival.

This phenomenon of pleasure seeking has been well researched using rats that have had an electrode implanted in the part of the brain that is involved in the reward mechanism. If the rat pressed a lever it received a pleasure-giving electri-

cal stimulation to its brain. It soon spent all of its time pressing the lever in preference even to food and drink, until the point of collapse.[3]

The majority of texts refer only to the pleasure circuit and the role of dopamine. This can be a little misleading. In light of current research, we have chosen to view the circuitry in a more holistic fashion and so use the term 'anticipation/satiation circuit'. The parts of the brain involved in this circuit use the neurotransmitters dopamine and serotonin. The anticipation of pleasure is driven by dopamine but not the sensation of pleasure itself; pleasure sensations are controlled by serotonin. This relationship has been borne out of interesting rat research regarding short-term feeding behaviour. If dopamine neurons are destroyed it does not reduce the hedonic impact of food on the rat. When the rat is given some tasty food it continues to exhibit the reactions of sensory pleasure. The rat's behaviour does however change: it now lacks the motivation actively to seek food, although it still does eat if food is available.[3] This is due to the fact that the power to induce seeking through raising dopamine levels is lost and subsequent memory salience could not be attributed to the food. The rats are now incapable of craving and so are unaware that food can impart beneficial sensations. Consequently they do not seek food out over and above normal long-term feeding levels governed by separate mechanisms under the control of several hormones. It is also true that memory circuits may send impulses to the dopamine neurons all they like about how food used to feel, but nothing will happen because the nerves were destroyed. So in effect they do not remember that food feels nice either. On the other hand, if dopamine neurons are stimulated the rat shows increased craving for food and actively seeks it out, because a greater salience is attached to it when it does feed, but no greater expression of actual hedonic impact is observed.

In humans 'normal' rewards are not attributed a large degree of salience if the dopamine and serotonin receptors are under-responsive. A degree of enjoyment might be experienced, but it will be a sub-normal amount. For these reasons such individuals will not be unduly motivated towards the repetition of those behaviours. These individuals, in the search for stronger sensations may repeat the behaviour over and over in attempt to experience satisfaction. If repetition is unsuccessful they might explore other behaviours on a mission for satiety. If a stimulus is very powerful it actually registers in the anticipation/satiation circuit and is recorded as being of benefit. This is why more or better seems like the logical choice to an addicted person whose memory serves to remind them of how good some things, like heroin, can feel.

The difference in the rat experiment is that the dopamine neurons were destroyed, so no value at all could be attributed to the food. The rats were unable to remember the consequences regardless of whether or not the food tasted good. It is also the case that as these dopamine neurons drive seeking behaviour, if they are totally destroyed, motivating this type of action becomes impossible.

The interesting thing about all the substances of misuse is that, albeit through different mechanisms, they stimulate dopamine and serotonin release and hence their use is strongly reinforced. It is, however, a common phenomenon that the effects of a drug no longer get a user particularly 'high', but its memory (hence anticipation) is enough to encourage compulsive use. Hypersensitivity of the

dopamine system to memory inputs creates excessive wanting but down-regulated serotonin systems create insufficient satiety. It seems that the inter-relationship between serotonin and dopamine is very important and that balance of the two systems is vital:

1. If serotonin levels are relatively lower than dopamine the individual is unsatisfied and so experiences craving.
2. If serotonin levels are relatively higher than dopamine the individual is satisfied and so does not crave.

Ideally, these neurotransmitter levels exist in homeostasis – dynamic equilibrium – both triggering behaviours and being modulated by them. Behaviours are nothing more than manipulation of one's external environment to manipulate the internal chemical environment.

The mechanisms with which rewarding behaviour are modulated are of particular interest with regard to substance misuse. A stimulus creates an urge in the brain that needs to be satisfied. In health this stimulus will be something such as a drop in blood sugar levels or a decrease in blood volume, any stressor in fact. This stimulus might also, however, be rooted in a predisposition to an imbalanced brain chemistry manifesting as, say, a feeling of emotional emptiness, pointlessness, inadequacy, self-disgust or social inhibition. Various factors might contribute to this predisposition, such as genetic factors, lifestyle or experience; these all shape the biology of the nervous system. Withdrawal symptoms due to drug use also fall into this category either by artificially imbalancing normal brain chemistry or by compounding an often already imbalanced neurochemical environment.

The action created by the stimulus, in this case drug taking, is rewarded by pleasurable sensations. In fact, even the anticipation of the forthcoming reward and the context in which it is received contribute to the process. For example, a glucose drip will stop hunger and the individual actively seeking food, but it will not provide pleasure and true satisfaction; we have not evolved to expect an intravenous drip to satisfy hunger. The ritual of meal preparation and the very action of chewing is part of the process because they form part of the associated memory of the process. It is for these reasons that a patient might develop needle fixation or experience strong cravings in a particular social situation; satisfaction results from the compound behaviours.

So, as a reminder, dopamine is not related to pleasure itself but more to the anticipation of pleasure, which in itself is quite stimulating and the subsequent memorisation of how pleasurable a stimulus feels. It is for these reasons that many people would rather not know what they might be getting for their birthday: anticipation and gratification postponement feel good, but only if the ultimate goal is in sight.

The degree to which the environment and ritual are intertwined with addictive processes is more important than many imagine. More dopamine is released in a novel environment and so the situation has a more profound effect on the individual. Research has highlighted this importance; addicts are more likely to overdose if they take drugs in a novel environment.[4] To illustrate this, consider the different effects alcohol might take in a different environment. Four pints of

beer drunk at home while listening to Mozart will have quite different effects to four pints drunk at a raucous hen-night party.

The final part of the process is satiation or fulfillment, and this is mediated by serotonin. Sexual intercourse or a good meal satisfies healthy individuals. This part should be the full stop at the end of the sentence; it is the sensation of 'enough is enough'. Of course, addicts often feel that they are never satiated and always crave more of the substance that once gave them a degree of relief. A social drinker can have one drink, feel satiated and go home. Have you ever heard an addict say 'I've had enough'? An alcoholic has little interest in the drink he or she is consuming but is driven by the anticipation of the next due to a lack of satiation. Dopamine levels are relatively much higher than serotonin and so craving is high. An addict feels improved sensations during use because of the relative avalanche of dopamine and initial increase in serotonin that the drug provides. The anticipation and motivation of the next drink is driven by dopamine and is experienced as pleasurable, but the climax rooted in serotonin release is seldom reached – the user will tend to fall unconscious first.

So, one mechanism by which addicts differ from healthy individuals is that their serotonin 'thermostats' can be too easily reset downwards or are set rather low in the first place. This means that satiation is a rather elusive sensation. To illustrate: an addict might smoke some crack cocaine, which on a pleasure scale of 1 to 10 reaches a 10, and feels so great that he or she does not take any more. If the 'thermostat' is susequently reset such that when the initial hit has worn off another hit only reaches 8 out of 10, then the brain craves just that little bit more. This is the mechanism of tolerance and craving; serotonin levels struggle to rise and so it is so much harder to get satisfaction. It is also true that addicts have been shown to have dopamine circuits that are insensitive to natural reward behaviours and so the individual in question is classed as a pleasure seeker; they only want what they do not have. It seems odd that nature would select for low activity of the reward circuitry but it would appear that this harks back to a time in history when rewards such as food were harder to come by and so the behaviours carrying the highest rewards were favoured. It is for this reason that fatty food carries more hedonic impact than most others; in times of hardship food with a greater calorific value would be more important and so our brains have evolved to bear this factor in mind. When dieting, we crave calorific foods – those of high fat or sugar content – because the brain thinks there is famine. We also tend to crave salty food. Salty food gives us more pleasure because in times of drought, when clean water is scarce, fluid retention is life saving. Salt retains body fluids. So craving a curry when on a strict diet is truly evolution in action.

Interestingly, dysregulation of a 'thermostat' is not the only way in which the nervous system adapts in response to stimuli. Sometimes, a given pathway will become sensitised. This process intensifies the response to a given stimulus and is the mechanism of memory. Once an addict has experienced the profound sensations associated with drug taking, the brain forms a strong memory that feeds back into the dopamine circuitry. Anticipation evolved to drive an organism to seek reward and so we are actually evolved to want more of them. Sensitisation therefore seems to occur in this part of the brain by consolidating memory in order to further encourage rewarding behaviours. It does not seem to make evolutionary sense to down-regulate a mechanism that promotes seeking of

actions that allow survival. This means that drugs and drug-related behaviours create a situation of hyper-responsivity in the dopamine circuitry to them above all other stimuli.

It should be noted that in healthy individuals these neural circuits are finely tuned and in homeostasis. Natural stimuli, such as food, tend not to create huge deviations from the norm. However, the drugs of misuse are so powerful that they provide stimuli never attainable through normal day-to-day life. If imbalance arises for whatever reason though, even food or other more normal stimuli can be abused. In some ways, these have a weaker hold because they do not change the brain chemistry as dramatically as drugs, but in a sense they can be harder to deal with because, for example, we cannot abstain from eating.

To conclude, all addicts want is more and to the detriment of all else. Their persistent and denied quest for satiation is such that normal behaviour, such as the urge to keep clean or eat, often pales into insignificance. It is also often the case that due to the down-regulation of satiation systems, no act creates satisfaction, hence the development of conditions such as obsessive-compulsive disorder (OCD). Individuals with OCD might obsessively wash their hands because something gnaws away inside to persuade them they are not yet clean. But however much they scrub, they do not get very far up the pleasure/satiation scale. Similarly, in sufferers of post-traumatic stress disorder (PTSD), a syndrome of hypervigilance is observed due to a relative deficiency of serotonin to dopamine.

Addiction is a prime example of this reward/deficiency syndrome. Blum and Comings – who discovered the D2R2 allele that is present in 50 to 80% of alcoholics, drug addicts, compulsive eaters and gamblers – suggest its presence to be one factor involved in reward/deficiency syndrome. This allele prevents dopamine binding to the postsynaptic neuron and hence the stimulatory feelings of anticipation and the ability to memorise pleasurable behaviours are not readily achieved by normal activities.[5] Similarly, another genetic trait that results in individuals possessing fewer of a particular dopamine receptor subtype, D2, means that individuals go through life with most behaviours carrying little salience, they find that life is pretty anticlimactic and find little joy in existence; often, that is, until they find something so powerful it does hit the spot, and this is usually found in drugs.

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The limbic (emotional) system

The advantage of the emotions is that they lead us astray.

(Oscar Wilde)

We have already established that the brain does not consist of an unorganised homogenous mass of neurons. It is instead made up of a number of functionally specific and interconnected modules. The module collectively responsible for the regulation of emotion and the emotional associations with memory is known as the limbic system (Fig. 6.1). The limbic system therefore governs behaviours driven by emotion. The term 'limbic' is derived from the Latin word for 'border' because the limbic system forms a sort of border around the brainstem.[1] In short, the limbic system governs survival behaviours, such as the search for food, the avoidance of danger and reproduction. It is the limbic system that drives you to order a take-away, to jump when you see a spider and to make sure you look your best in those tight jeans.

The role of the limbic system is to gather sensory information essential to survival. The limbic system processes information about our emotional state and uses it to assess need. It can then influence the rest of the body through its actions on the hormonal system and the autonomic nervous system. As addictive drugs and behaviours are strongly linked to emotion this part of the brain is highly implicated in the pathology of addiction.

The limbic system itself comprises many submodules, which communicate with each other and with the hypothalamus – another key brain module. The hypothalamus is the master gland that controls hormonal release.[2] In fact, the over-riding desire of every limbic structure is to pass on its information to the hypothalamus. Limbic structures are in a sense selfish and when they have something important to say they want exclusivity. You could think of the limbic structures as being like a group of journalists who think they have a great angle on a story, and the hypothalamus is the newspaper editor. The editor is going to run the story that shouts to him the loudest. No disrespect to journalists, but not only do the limbic structures present their story vehemently, they also have tactics that they can use to keep the others quiet and so prevent them from influencing the hypothalamus.

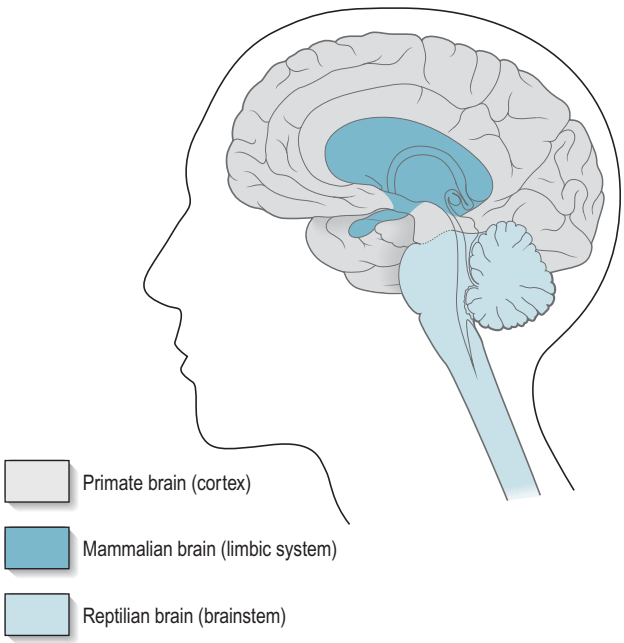

Fig. 6.1 Limbic system.

Hypothalamic function is discussed later in the text. At this point it is sufficient to say that the hypothalamus is the route through which the brain can reach out and take control of automatic bodily responses, thereby governing the behavioural expression of emotion.

To summarise therefore, the neurons of a given limbic structure send excitatory projections into the hypothalamus, and lateral inhibitory projections out to the other limbic modules, trying to keep them quiet.

With regards to substance misuse, the key limbic structures are the ventral tegmental area, nucleus accumbens, locus coeruleus, hippocampus, amygdala and the frontal cortex. As discussed earlier, the cortex evolved much later than the limbic system but despite this, the wiring of the prefrontal cortex (as discovered by Walle Nauta, a famous neuroanatomist) ensures it can now be considered part of the limbic system.[2] There are many neural projections traveling up to the prefrontal cortex from the limbic system and also some, although fewer, running back down from the frontal cortex to the limbic system. Let us now explore these areas in more depth.

The prefrontal cortex

The collective functions of the structures comprising the prefrontal cortex (Fig. 6.2) are often referred to as executive function. The most important parts of the prefrontal cortex with respect to addiction are the orbitofrontal cortex and the dorsolateral prefrontal cortex. These form the part of the reward circuit

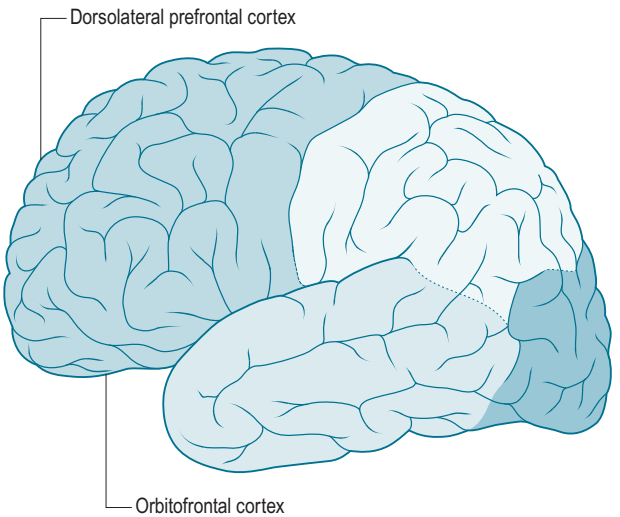

Fig. 6.2 The prefrontal cortex.

associated with expectation and the planning of behaviours. The orbitofrontal cortex differentiates conflicting thoughts, helps us to determine if an action is likely to have positive or negative connotations and whether the outcomes of a given behaviour are favourable or not. It therefore has a role in being able to determine the future consequences of current activities. The implications of these functions are that this part of the brain allows an individual to exhibit (or not) social control based upon the prediction of outcome. It processes the input received from key 'emotional' structures of the limbic system and has the ability to decide if it would be prudent to act upon emotional urges that might be socially unacceptable or illegal. The neural connections allowing for these functions are shown in Figure 6.3.

In fact, it has been suggested that the connection of emotional centres to the orbitofrontal cortex explains why pleasure can be derived from problem solving. Dysregulation of this area can lead to a plethora of problems, most importantly (as can be deduced from its function), an inability to control compulsion, thus leading to addictive behaviour, rash decisions and poor social interactive ability.

The dorsolateral prefrontal cortex is also involved in the conscious control of behaviour. It does not reach full maturity until the early 30s. It receives input from the ventral tegmental area and the substantia nigra. It sends out projections to the locus coeruleus and raphe nuclei. If this area is inhibited the individual exhibits social withdrawal, impairment of goal directed behaviours, poor motivation and poor ability to problem solve.

The ventral tegmental area

The primary role of the ventral tegmental area (VTA) is the assessment of need. The VTA processes information to ensure satisfaction; it then forwards this

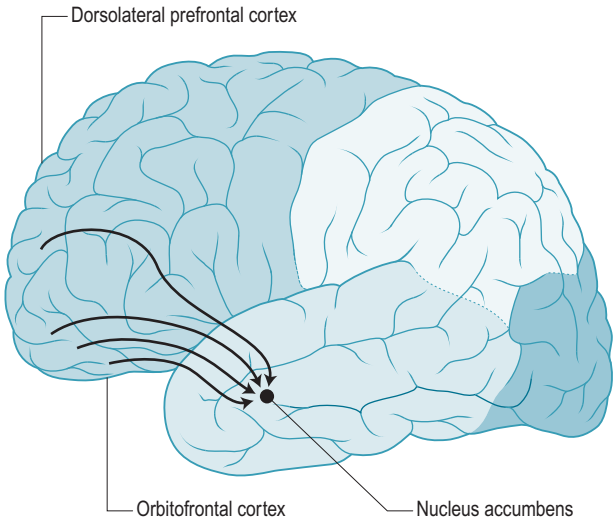

Fig. 6.3 Inhibitory projections from the prefrontal cortex to the limbic system.

information to the nucleus accumbens (NA) using the neurotransmitter dopamine. If there is an increase in dopamine in the VTA there is a concurrent increase in the NA. The VTA and NA are connected by a group of nerves called the medial forebrain bundle (MFB), often referred to as the reward bundle. The VTA also sends dopamine projections into the prefrontal cortex and other regions of the limbic system such as the amygdala. The VTA forms part of what are known as the mesolimbic and mesocortical systems, which are discussed below. The VTA is part of the reward circuit in the brain; psychoactive drugs directly influence the release of dopamine in this area, so leading to addiction and its associated behaviours.

The nucleus accumbens

The NA receives information about need from the VTA and then motivates activity to address the need. It is therefore key to survival behaviours and also plays a vital role in the reward circuit. The relative activity of dopamine and serotonin in the NA plays a crucial part in the development of addiction. Dopamine promotes wanting and serotonin satiation. All drugs of addiction have been shown to raise dopamine levels and lower serotonin levels in the NA.

The NA does not work out what might actually be needed in itself but rather how intense the response to that need should be. In response to need, dopamine is released. When one 'needs' drugs or anything else key to survival, the NA is sensitised to incoming stimuli. These stimuli might be thoughts, memories, smells, pretty much anything. Should these stimuli be associated with a means of stopping the need, then dopamine is released. The amount of dopamine release is proportional to the degree of need. If more dopamine is released then the need

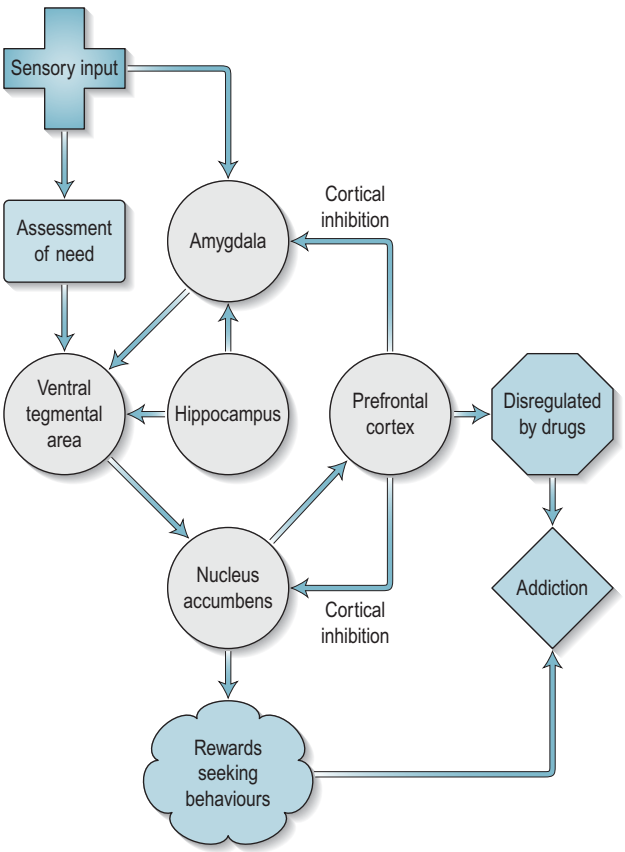

Fig. 6.4 The addiction circuit.

is greater. It is this dopamine release that motivates behavioural modification: to phone a friend, eat a meal, snort some coke.

Note that, normally, potential benefit and risk are weighed up against need by the frontal cortex. However, if the need is great enough, such that survival is considered to be at risk, then inhibition of the frontal cortex removes future consequences from the equation. This inhibition is mediated by the neurotransmitter gamma-aminobutyric acid (GABA), also used in the NA. Excitation of the neurons in the NA by dopamine causes its GABA neurons to fire, thus inhibiting the prefrontal cortex. The result of this is that the NA motivates the individual to carry out the task necessary to address the appropriate need. If dopamine levels are high enough this inhibition will occur regardless of undesirable consequences (Fig. 6.4).

The hippocampus

The hippocampus lies in the temporal lobe of the brain and is so called because it is supposed to resemble a seahorse (hippo = horse, kampos = sea

monster). Its function is largely to lay down declarative memories of our conscious experience and it is a key structure of the limbic system. It is within the hippocampus that several inputs converge in order to remember people, places and things. Sensory input from the visual, olfactory and auditory systems are connected by the hippocampus to form a biographical memory. It is the hippocampus that remembers the experience of the nightclub, the flashing lights, the song that was playing, the smell of dry ice and the faces of the friends we were with that night. The hippocampus itself both receives input and sends output to many areas including those of the VTA (need) and the amygdala (emotion). This means that the memories of the hippocampus can provide sensory input to drive need, and that memories can also trigger strong emotions.

The amygdala

The amygdala is shaped like an almond (in fact, its name comes from the Greek word for almond). It is located very near to the hippocampus, in the temporal lobe, and its role is largely one of emotional perception, in particular of perceived potential threats. The amygdala receives input from many regions, such as the hippocampus, but also, significantly, from the prefrontal cortex.

Recent research suggests that the amygdala, like the hippocampus, is associated with memory, the difference being that its memories are unconscious, which means that the amygdala is responsible for conditioned responses and, most importantly, emotional learning – of course all mediated by long-term potentiation (LTP). The amygdala is a very sensitive brain area that needs little stimulation for its neurons to fire. When it is activated, its information is sent very quickly to the hypothalamus and, much more slowly, to the conscious brain: the cortex. It is this phenomenon that allows us to act on impulse without thinking hard about it first.[3] If we see something slithering on the ground in the corner of our eye we jump without thinking. After the initial jump, we process the information in the cortex to discover it was only a garden hose and make the decision not to run away.

It is the amygdala that decides whether or not an experience was pleasurable and hence if it is worth repeating. It is in this area of the brain that we experience emotional memory or conditioned incentives. The role of the prefrontal cortex is in choosing the appropriate course of action that can best deal with the situation. After the initial conditioned, automatic response, the prefrontal cortex can – when functioning normally – allow for the voluntary, conscious change of reaction. Role-playing in the context of addiction treatment is used to strengthen the prefrontal cortex such that, over time, a conditioned response from the amygdala can be overcome.

Both the VTA and NA (in the pleasure circuit) receive input from the amygdala. These structures use the information to direct the individual towards a given behaviour. The information is then sent further on, to the prefrontal cortex, for processing in order to encourage or inhibit the emotionally driven behaviour. The

long-term memories of the amygdala are those that underlie drug relapse after long abstinence; addiction is, at least in part, a phenomenon of learnt behaviour.

The locus coeruleus

The locus coeruleus (from the Latin for 'blue spot') communicates closely with the amygdala. It is the brain's main source of the neurotransmitter noradrenaline (norepinephrine). This chemical is excitatory and is released in response to pain or stress, stimulating what is referred to as the 'fight-or-flight' mechanism. This means that it activates the sympathetic nervous system. In the brain, noradrenaline (norepinephrine) is a neurotransmitter, but in the body it acts as a hormone and is released by the adrenal glands.

When an addict is in withdrawal it is the resultant activation of the locus coeruleus that creates the unpleasant symptoms and sensations, such as insomnia, anxiety and panic. This occurs because activation of the VTA and NA applies the brakes to the locus coeruleus. When this activation stops, due to down-regulation, the brakes can no longer be applied. Remember, limbic structures want exclusivity and so, when talking, make other areas be quiet. The stress response as a result of activation here is very much linked to depression, panic and anxiety disorders and PTSD.

The reward pathways: mesocorticolimbic system

The mesolimbic pathway

This pathway is a conglomerate of two primary limbic brain structures. All the nerve axons in the mesolimbic pathway communicate using dopamine and are therefore known as 'dopaminergic neurons'. These axons originate in the VTA and project towards the forebrain, penetrating the NA (Fig. 6.5). It is part of the medial forebrain bundle that allows for this communication.

Dopaminergic axons do innervate many other areas of the brain but these are not concerned with addictive behaviour and so will not be discussed here. The structures of the mesolimbic pathway work together to inform the individual of how rewarding a behaviour might be. They therefore control behavioural arousal according to incentive salience.

Even very simple organisms have a reward circuit; the human circuit is, however, very complex and integrated with other brain modules. It integrates with two other important limbic structures, the hippocampus and amygdala. This allows for the reinforcing effects of drugs to be linked to memory; these two structures directly innervate the NA and VTA. To serve as a reminder, all substances of abuse cause a profound increase of dopamine into the limbic system and so their use is heavily reinforced. Drugs are thereafter attributed primary

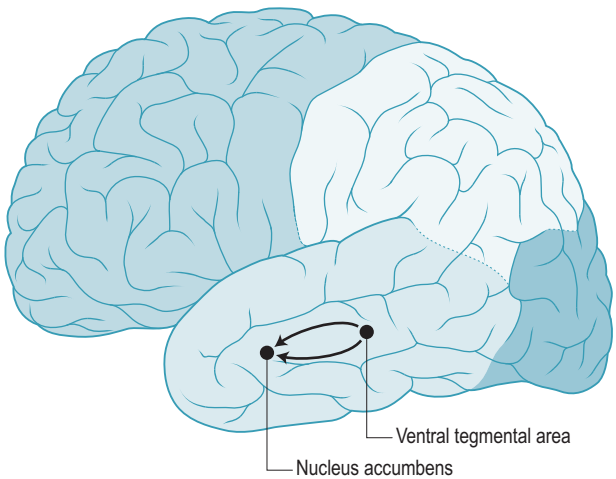

Fig. 6.5 Mesolimbic pathway.

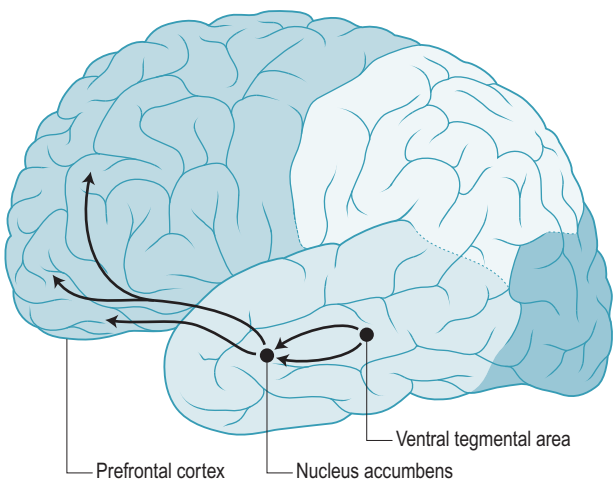

Fig. 6.6 Mesocortical circuit.

incentive salience values over and above that of normally rewarding behaviours. This makes them seem all the more attractive.

The mesocortical pathway

This system starts in the VTA and projects via the NA to terminate in the structures that comprise the prefrontal cortex, orbitofrontal cortex and anterior cingulate. Collectively, we will refer to it as the 'frontal cortex' for simplicity (Fig. 6.6).

Broadly speaking, these structures allow for conscious experience and, when disregulated, for the compulsive administration of addictors. Essentially, the frontal cortex acts as a filter for impulses from the limbic system, allowing some degree of conscious control over emotional drives. This part of the brain must decide whether strong emotional drives generated lower down in the brain are appropriate and, when necessary, suppress them. The presence of excess dopamine in the mesocortical circuit fools the frontal cortex into thinking that the associated behaviours are essential to survival because profound pleasure is attached to them and so encourages us to continue doing them.

If we think about it, there must be more to addiction than the ability of drugs to strongly raise dopamine levels in the reward circuit. As these increases are just as apparent in non-addicted as addicted patients, this implies there is more to the story. The role of the frontal cortical area in addictive behaviours must not be overlooked.

Cortical control

Human beings stand out from other animals because of their superior processing power. A key feature of our humanity is that we, unlike animals, have much greater control over impulse and we can feel guilt and remorse if we make a mistake. The part of the brain largely responsible for this ability to reason and make a decision is the frontal cortex. In fact, the frontal cortex is the only part of the cortex that sends descending serotonergic (serotonin-containing) neural projections to the limbic system where they connect directly to the VTA and amygdala. So the two-way traffic between the limbic system and frontal cortex plays a key role in balancing drive with common sense. Excessive activation of the frontal cortex by dopamine-enhancing drugs suppresses the serotonin-mediated inhibition of the mesocorticolimbic system leading to disinhibition of sensory-driven affective responses. This means that frontal lobe, top-down processes are reduced and so behaviours that are normally constrained are released. Inhibitory control is suspended and stimulus-driven behaviour is accentuated. These stimuli may be a thought, memory, craving or use of the drug itself, forming a vicious circle of addictive responses. The neural connections are shown in Figure 6.3.

To function in a social environment, we must not only evaluate a situation on its emotional merits, but also integrate feeling with knowing. We have the benefit of being able to use past learning to predict the best future action. The frontal cortex is also the site of working memory, necessary for decision making. It contains glutamatergic neurons (memory) that innervate the NA and VTA.

Interestingly, this part of the brain does not fully develop until our mid to late twenties, and so our decision-making ability in the face of emotional and instinctive drives is somewhat poor in our youth.[2] Consider your teenage years – perhaps your first love. How easy was it to make careful, well-thought-out decisions while your heart strings were being tugged; did you make any errors of judgement?

The frontal cortex allows you to choose to make difficult choices in the face of emotional drive. If you have small children you might have noticed how hard they find it to make these choices. An older sibling knows that he should not lose his temper with his little sister when she wants to play with one of his toys and you can almost see the battle raging in his cranium, but his ability to assess 'good' or 'bad' behaviour is quickly defeated by emotion and he lashes out anyway.

The function of the frontal cortex was first discovered following an accident to an unfortunate railroad worker called Phineas Gage in 1848. While working on the railroad, an explosion caused a 6-kg iron rod to be blown through his skull, destroying part of his brain when it made a 9-cm-diameter exit hole in his forehead. He survived and even managed to walk to the doctor's office but he was a changed man. Before the explosion, Gage was an archetypal good worker, husband and father; afterwards he was unable to control his more animal characteristics, becoming profane and sexually disinhibited. He also found it impossible to make future plans. As soon as he constructed some, they were abandoned in favour of others that seemed more feasible. In fact, his friends commented he was so altered that he was 'no longer Gage'.[1] In health, individuals can moderate their instinctive drives by activating the frontal cortex. They can decide, for example, that it might be unwise to eat another chocolate because they have had three already. This is not so if the frontal cortex is underactive.

Many lessons can be learnt from this:

1. Be really careful when working on the railways.
2. The frontal cortex allows us to make decisions.
3. The frontal cortex can inhibit certain sensory-driven behaviours.
4. Perhaps more importantly, that which defines you is constructed in your brain and hangs by a thread that can be so easily broken that you lose yourself forever.

One sure way to break that thread is by taking drugs, which so stimulate the mesolimbic system that the controlling power of the frontal cortex is lost and can no longer compete. Thus, individuals lose themselves to drive, instinct and emotion. Brain imaging research confirms these frontal-lobe deficits, revealing substantial volume deficits in addicted patients.[4] It is also hypothesised that long-term depression (LTD) occurs in the neural pathways connecting the frontal cortex to the limbic system in response to a lack of use; 'if you don't use it, you lose it' as the saying goes. Damage to the frontal cortex thus inhibits its behaviour-controlling abilities in the long term.

Fortunately, a drug user can rebuild the thread of connection. The key is that the mesolimbic system must not be overactivated by drugs such that it shouts 'go on, it feels amazing' over the frontal cortex whispering 'don't do it, don't do it, bad idea'. The behaviours and altered emotional states at the heart of addiction are the loss of this conscious, self-directed behaviour to that of automatic, emotionally driven ones. This is the root of compulsive behaviour.

From the perspective of neurotransmitters, it is serotonin projections that give the frontal cortex the power to show restraint. Only when there is enough

serotonin stimulation in the frontal cortex will it be able to tell the limbic system to quieten down. It is the serotonin 2A receptor on the VTA dopaminergic neurons that communicate with the frontal cortex. If the serotonin receptor is stimulated it inhibits the release of dopamine to the frontal cortex. If serotonin is low then this blocks the inhibition normally produced by serotonin and this leads to the VTA releasing more dopamine to the frontal cortex.

Serotonin fibres also project to the amygdala to control anxiety levels. As serotonin levels rise, serotonin excites GABA neurons, which inhibit the excitatory projections of the amygdala, which feed the locus coeruleus that produces noradrenaline (norepinephrine) and hence anxiety. In fact, this is exactly how Prozac seems to produce a reduction in anxiety levels.

Remember also that the wiring of the brain is weighted towards emotion, with relatively fewer projections from cognitive systems running in the opposite direction. It is perfectly possible to function on drive alone, without the brain asking the frontal cortex for advice: the so called 'quick and dirty route' that Joseph LeDoux refers to.[3] Humans inherently favour the limbic system because it is – in evolutionary terms – fundamentally more important as it drives survival behaviours. From the evolutionary perspective, it is a much more ancient structure that can therefore quite easily overpower the frontal cortex, making the easier thing, emotion, seem irresistible. Effective treatment must lie in attempting, not only to quiet the limbic system, but to try and strengthen the frontal cortex by potentiating new pathways involved in gratification postponement and behavioural inhibition. It is in this way that therapies such as cognitive behavioural therapy can be of benefit.

It has in fact been shown that, on post-mortem (adjusted for post-mortem delay and age), addicted individuals have substantially lower serotonin transporter densities, in fact up to 35% lower in the frontal cortex.[5] This would seem to add additional weight to the theory that addicts have a number of very real physiological reasons for their seemingly irrational ability to make decisions against their best interests and an inability to learn from their mistakes. So, the old phrase of 'do what you've always done and you'll get what you always got' does truly have a biochemical basis.

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CHAPTER 7

The physiology of relapse, bingeing and the permanency of addiction

The fog is like a cage without a key.

(Elizabeth Wurtzul in *Prozac Nation*)

The drugs of misuse provide a severe spike of dopamine in the reward circuit, which triggers off a process of neuroadaptation. The strong rise in neurotransmitter levels causes a temporary suppression of the reward circuit. Research shows that cAMP response element binding (CREB) protein is a key factor in this suppression of activity. CREB is a type of protein known as a transcription factor; this kind of protein essentially controls the ability of a gene to manufacture another protein during a process known as transcription. They therefore control gene expression and hence, ultimately, depending on what protein the gene codes for, neuronal function.

When a drug is ingested it causes a strong rise in dopamine levels in the nucleus accumbens (NA). As a consequence, dopamine-responsive neurons increase their production of cyclic adenosine monophosphate (cAMP).[1] cAMP is known as a second messenger, the key role of which is to modulate synaptic transmission rather than to cause an action potential. cAMP activates CREB, which enhances the gene expression of genes that manufacture the protein, dynorphin. The activation of CREB makes the reward circuit less responsive to stimulus. Recently, it has also been shown that raised levels of dynorphin are a molecular trigger for depression. This lack of pleasure – also known as anhedonia or dysthymia and commonly associated with drug use – is also rooted in part in this phenomenon; the brain has also become less responsive to natural reinforcers and so finds it much harder to derive pleasure from non-drug stimuli. This results in relapse and bingeing of drug-related behaviours in an attempt to compensate for insufficiencies in the natural reward-satiation pathway.

Neurons in the NA now manufacture dynorphin and loop back to the ventral tegmental area (VTA), where dopamine is manufactured, to limit production. This process is likely to contribute to the phenomenon whereby subsequent exposure to rewards becomes less reinforcing. If this process alone occurred then it is less likely that people would become addicted. The down-regulation of the reward mechanism should reduce the reinforcing ability of drugs. If this were the

case, drugs would be wanted less. Obviously, this does not occur; natural rewards are wanted less but drugs more so. This means that some other processes must also be taking place, which raises the following questions:

1. Why is it that drug users release more dopamine in relation to drug-related behaviours and less dopamine in relation to natural rewards?
2. It is also the case that CREB production is switched off relatively soon after drug exposure. So this down-regulation will wear off reasonably quickly, but drugs clearly have a very long lasting hold over a person. Why is this?

This is where long-term potentiation (LTP) fits in. Remember the synaptic changes that allow for learning? As the result of memories formed by experience, addicts crave in response to the expectation of either a drug high or of the reduction in some negative physical or emotional state. Structural neuronal changes causing sensitisation (and, as a result, learning) are there to stay, in contrast to the short-lasting effects of neuronal down-regulation or desensitisation mentioned above. Both phenomena are modulated by gene expression and the transcription factor CREB. However, depending on which proteins are affected, the changes result in either short- or long-term neural modifications.

As both sensitisation and desensitisation involve CREB, something else must be going on. Another transcription factor called deltaFosB would appear to be the major influence on the long-lasting neuronal changes contributing to craving. Chronic substance abuse causes a subsequent gradual rise in the levels of deltaFosB, primarily in the NA (in the reward pathway) but also in other brain modules. DeltaFosB is a very stable protein and therefore has a long-lasting effect. This is in contrast to the rise in CREB, which is very quick but short lived.[2]

The abnormally high levels of deltaFosB are responsible for the rise in sensitivity of memory pathways that feed into the reward circuitry. This change also would appear to be present in many compulsive behaviours, so the neurobiological basis for all compulsive behaviours seems to be rooted in the same imbalances in the reward circuit and is not the exclusive domain of the chemical addictors. Most importantly, chronic exposure to deltaFosB induces neurons in the NA to sprout new side branches off dendritic spines. These make new synaptic connections, thereby amplifying input signals from drug-related memories and cues. So drug taking even has an effect at the level of the genes, and can make nerves grow new connections. It is little wonder that it has such profound effects.

The reward circuitry is not isolated from the rest of the brain but communicates with structures that are key to certain types of memory. The amygdala, hippocampus and prefrontal cortex all shunt information to and fro between the VTA and the NA of the reward circuit. These three memory areas communicate using the excitatory neurotransmitter glutamate that is so key to learning. When there is an increase in dopamine there is a consequent rise in sensitivity to glutamate. Remember that dopamine is used to decide how important a behaviour is and then to file the information away for later. This rise in glutamate is the key to learning, and so strengthens the pathways linking the memories of drug effects with high reward. In fact, glutamate levels must necessarily be high for LTP to

occur because glutamate uses a two-receptor system.[2] When the first glutamate receptor is filled, the neuron sends its normal action potential to the next neuron. It is not until there is enough of a glutamate hit – the point at which all first receptors are filled – that the second receptor is then filled. When the secondary receptor is full there is a sudden explosion of excitation and ionic changes, which cause potentiation of the pathway; the lightbulb goes on and something is learned. The importance of glutamate has been illustrated by research on mice. Mice engineered to have no mGluR5 (a glutamate receptor) do not become dependent on drugs.[3]

To summarise, short-term variations in CREB and cAMP lead to tolerance and dependence, but not addiction as such. These phenomena do not define addiction. The long-lasting changes of deltaFosB and glutamate do, however, linger for a

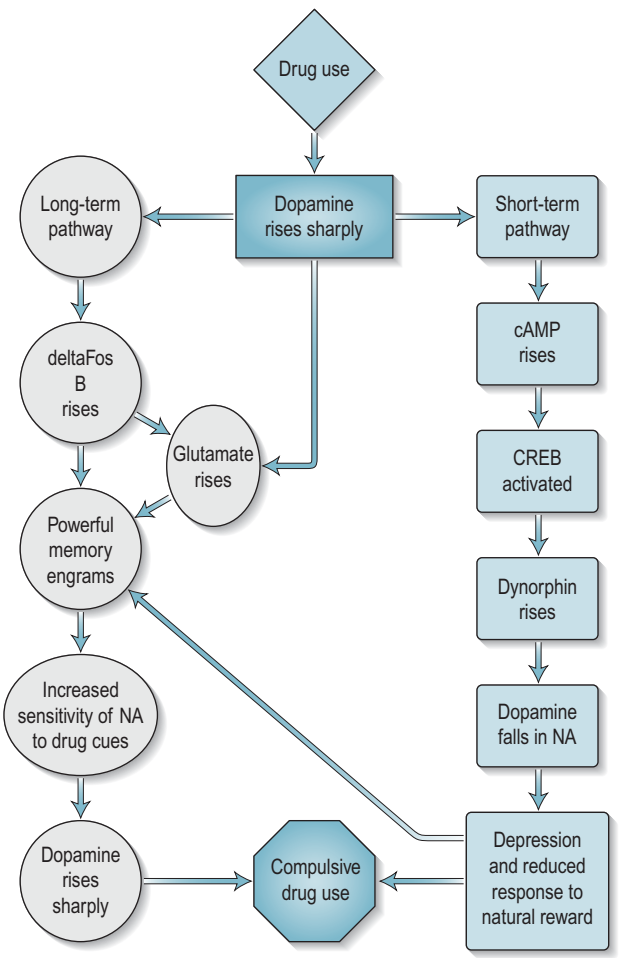

Fig. 7.1 Short-term desensitisation and long-term sensitisation pathways of drug-related behaviours. cAMP = cyclic adenosine monophosphate; CREB = cAMP response element binding; NA = nucleus accumbens

lifetime. Should an addict ever lapse after a period of abstinence, the learned pathway will have remained potentiated and so increased sensitivity to the reinforcing drug effects and associated behaviours sends the addict back to square one and craving wildly again. This phenomenon is known as rapid reinstatement syndrome and is associated with a concurrent rise in the risk of overdose because metabolic tolerance will have also reduced.

Simply put, it does not seem to make any sense whatsoever to take 'controlled' amounts of any drug. The lack of satiation experienced as a result of tolerance is a result of these adaptive mechanisms and research shows that low doses of a drug serve as nothing but a cue, indicative that a larger dose is on its way and thus increases the anticipation of it.[4] Rat research has shown that an animal that has been clean for months will revert to its compulsive behaviours when given a taste of cocaine, or even if it is put back into a cage with which it associates previous highs. Several phenomena trigger craving, including low drug exposure, drug-related cues and stress. If addiction was merely about the reduction of withdrawal symptoms, this would not be the case.

The two pathways, one illustrating short-term desensitisation and one illustrating long-term sensitisation of the drug-related behaviours and how they interact, are outlined in Figure 7.1.

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CHAPTER 8

How does the brain exert influence on the rest of the body?

All day long I think of things
But nothing seems to satisfy
Think I'll lose my mind
If I don't find something to pacify

(Black Sabbath in *Paranoid*)

The hypothalamus

The brain controls the function of organs throughout the body via the autonomic nervous system, influenced by the limbic system (see Ch. 6). However, this is not the only way in which the brain can exert control.

The brain is the most complex structure in the known universe. If this was not enough, the brain, while being a complex of nervous tissue, contains areas that are known as endocrine glands. This means that they secrete hormones, which travel in the bloodstream to reach cells all over the body and influence how they work. Many textbooks refer to the pituitary gland, which is located at the base of the brain, as the 'master gland'. However, this is incorrect. The true master gland is in the brain itself: the hypothalamus. The hypothalamus produces various hormones that exert their influence on the pituitary. Some hormones in the body are under direct control of the brain, such as the release of oxytocin, some under partial control, such as the release of insulin, and some entirely independent of the brain, such as interleukin secreted by white blood cells.

But what have hormones got to do with addiction? Well, let us think about what hormones do. They affect cells and, as cells are the structural and functional units of the body, including the brain, this means that hormones affect the way the brain works. This is not news to most of us; we are aware that fluctuating hormone levels can affect mood, for example, think about a woman suffering from premenstrual syndrome or the anabolic steroid user suffering 'roid rage'. If we consider the fact that brains work because of neurotransmitters released by

nerve cells, then this means that hormones affect neurotransmitters. In fact, research has shown that the hormonal fluctuations that occur at different stages of a woman's menstrual cycle influence brain activity, particularly with respect to reward; consider the development of chocolate cravings. During the follicular phase, when oestrogen levels are raised, the orbitofrontal cortex and amygdala show higher activity both when women are anticipating reward and when they receive it. It could therefore be hypothesised that behaviours involving reward systems, such as drug addiction, might be enhanced during the follicular phase. It is speculated that this mechanism may have been of evolutionary benefit. Increased receptivity and desire during the ovulatory period would facilitate procreation.[1] The primary sex hormones, oestrogen and testosterone, both lower serotonin levels. This is why we lust, to remove the pain of desire. Young people who are not engaging in sexual activity are under a kind of stress and crave satisfaction, which is why they are irritable. It is for these reasons, in addition to the underdevelopment of the frontal cortex, that adolescents are particularly vulnerable to addiction, anorexia and other compulsive disorders. This is why there are laws discouraging young people from drinking alcohol: they are at higher risk of falling prey to its power.

The hormone class we are particularly concerned with in reference to addiction are the glucocorticoids. These hormones can affect dopamine release and also neural plasticity in the amygdala. Short-term stress raises glucocorticoid levels, which in turn results in dopamine release, which can feel quite stimulating and exciting. This is the reason why some people love rollercoasters.[2] In health, one or two rides will satisfy our need for stimulation; serotonin levels have risen. The individual no longer experiences the desire to continue to repeat the ride over and over again. This is why rides at the fun fair do not go on for hours. In the long term, however, the usual adaptive processes occur. Dopamine release is down-regulated and serotonin depleted, resulting in normally-rewarding behaviours becoming less salient and less pleasurable. In an attempt to address this we might ride more and more, or try a more scary ride. Intoxication also activates this stress response, creating similar complications to a perpetual rollercoaster ride.

Chronically raised levels of glucocorticoids also enhance long-term potentiation (LTP) in the amygdala. This is why unpleasant withdrawal symptoms seem to be etched into the brains of addicts with disproportionate ease. The amygdala is going to record as much information about the unpleasant experience as possible, so that the next time it happens it is ready for it and sets off the fight-or-flight mechanism. This is revealed by feelings of anxiety, a racing heart beat and sweaty palms. Chronic or extreme stress, however, disrupts LTP in the hippocampus. This means there is little actual conscious memory of events but the amygdala can go ahead and influence the hypothalamus anyway. If we think about severely traumatic events that strongly raise glucocorticoid levels, something like a car crash, we tend to forget the details of what happened. The hippocampus went offline, while the amygdala went overboard filing away as much information as possible about the crash. We never know when some of the stored information might save our lives.[3] These memories are however unconscious. So when weeks later we pass the same colour of car that caused us to hit the tree,

for no reason apparent to us, the fight-or-flight response is triggered. So we now have an irrationally large fear of red cars. To an addict, withdrawals and cravings are like big, red cars. When in drug withdrawal, the brain is convinced that it is now experiencing a life-threatening event because it no longer feels the pleasure or satisfaction that is attached to behaviours essential to life, and so it initiates the fight-or-flight response. Once the amydala is hyper-reactive to stress the slightest stressful provocation can trigger relapse because conditioning means that addicts have learnt that they can blunt these sensations through the use of chemicals.

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CHAPTER 9

Addiction and genetics

A chicken is only an egg's way of making another egg.

(Samuel Butler in *Life and Habit*[1])

There must be something peculiar about addicts. Clearly we do not mean this in a derogatory sense. Drugs do exactly the same thing to everybody; they increase the levels of dopamine in the reward circuit (as does any rewarding behaviour), but not everybody who uses these chemicals becomes addicted, this happens only to a minority. Consider how many people drink alcohol or even abuse it through binge drinking at the weekend. They will certainly be doing themselves damage but are they all addicted? Not so. This strongly implies that addiction does not lie within the substance as such but more so with the person that the substance interacts with. This also means that the treatment of addiction involves addressing the *individual* who is addicted (i.e. their common neurobiology) and not their chosen addictor. It is for this reason that acupuncture can be used to treat all manner of addictions: drugs, alcohol, cigarettes, overeating, gambling, the list goes on.

For example, the physiological effects of cannabis compared to other substances are relatively poorly understood, perhaps because it was – and to a degree still is – felt to be a 'safe' drug. However, in the late 1980s it was noticed that more of the patients admitted to the Maudsley Hospital due to the development of psychosis were users of cannabis. Initially, it was thought that perhaps this drug use was a form of self-medication in an attempt to deal with their symptoms, but later it was suggested that perhaps the link was causal.

Psychosis is associated with an excess of dopamine in the brain, hence its development in drug users. Dopamine is released when something is novel and interesting and it signals the brain to pay attention. If dopamine levels are high then all stimuli seem hyperimportant and so the brain tries to understand why these events might be important using its associative circuitry. This is why psychotic patients think that the television is sending hidden messages. The patients are under the illusion that everything that happens to them is incredibly important and that they must also be terribly important; if this is the case then it does not seem unreasonable to them that MI5 must also think that to be the case and so are spying on them.

Clearly, not all cannabis users become psychotic. This means that some individuals must be more susceptible; this is substantiated by genetic research. The gene *COMT* produces a protein that breaks down dopamine. There are two types of this gene, MET and VAL. The research shows that patients of the MET/VAL type are at twice the risk of developing psychosis as patients of the MET/MET type. Individuals of the VAL/VAL type are at a tenfold risk of developing psychosis if they smoked cannabis in their adolescence. Adolescence is a particularly risky time to be abusing psychoactive chemicals because the brain is still maturing and is more easily damaged. With regard to risk, one quarter of the population is of the VAL/VAL type, one quarter MET/MET and the rest are MET/VAL.[2]

It is often stated that addicts use as a means of dealing with life trauma, poor relationships, rape, stress and so on. Undoubtedly these are terrible experiences, which can cause untold psychological damage, but sadly, they happen to a lot of people, not all of whom become addicted to a chemical substance. Addicts, therefore, not only differ from each other but also from 'normal' individuals; they differ in that – at some level – there is an imbalance in the physiology of their brains. For a multitude of reasons, a brain that is predisposed to addiction responds to drugs by producing abnormally high amounts of dopamine, and so drugs become highly significant to the owner of that brain.

We are not suggesting that an individual's genetic inheritance inevitably predisposes that person to becoming an addict. Predisposition is not the same as predetermination; genes provide tendencies not inevitabilities. However, the environment and an individual's genetic make-up can interact and result in addiction. A different environment might result in an entirely different outcome. By 'environment' we mean that which influences us. This can include the prenatal environment and encompasses anything supplied by the bloodstream such as hormones, nutrients or even those less direct influences like sounds. For example, if a pregnant woman is beaten by her partner, the stress hormones released can affect gene expression in the fetus, starting the process of neuronal down-regulation, which can be life-long. A pregnant woman who suffers trauma or takes drugs will shape the genetic expression of her unborn child; equally, neglect of a young infant will affect that individual's genetic expression. Thus, trauma triggers addiction in a susceptible individual; it does not *cause* it. This has been shown in mice: baby mice separated from their mother demonstrate modified gene expression and show increased vulnerability, anxiety and aggression.[3]

The converse is also true – environmental enrichment has been shown to alter gene expression and even neurogenesis.[3] A good environment can therefore be very beneficial to a patient, but should this person use drugs again, the good work is all too easily undone. Let us now look at all this in more depth.

What do genes do?

Contained in a cell's nucleus are structures called chromosomes, comprised of a material called DNA (deoxyribonucleic acid). The information contained within DNA is the blueprint used to manufacture a person or any other living thing. It is segments of DNA that form genes, and we have around 30 000 of these.

Our DNA has been passed on to us from our ancestors for millions of years. Examining our DNA is like stepping back with a time machine. It is incredible to think that a pair of organisms that found each other attractive enough to mate with all those billions of years ago resulted in us.[4] Us being alive today is dependent on millions of ancestors. In fact, the simplest forms of life that lived about 3.85 billion years ago eventually led to us. Considering that most species that have ever lived are extinct, this is a privileged evolutionary line. It appears that all life is derived from the same set of blueprints or DNA. In fact 60% of our genes are found in fruitflies and at least 90% in mice. So, do not ever think that we are not special; one tiny hiccup billions of years ago and we would not be here at all.

What genes actually do is pretty simple. They contain a code that provides the information to instruct the body how to manufacture a specific protein. Proteins are strung together from an 'alphabet' of twenty amino acids. Genes specify the sequence of the chain of amino acids, which can be enormous. The complexity and diversity of protein structure provides the human organism with a huge array of specialist tissues. It is estimated that there exist as many as a million proteins in the human body. With regard to substance abuse it is important to note that many neurotransmitters, particularly the ones that we are concerned with, neurotransmitter receptor sites, and enzymes, are all made from proteins.

All cells with a nucleus (and that is nearly all of them; only red blood cells do not possess a nucleus) contain every gene. How these cells differ in structure and function depends on which genes are turned on or off (known as epigenetic modification). The turning on or off of genes itself is known as gene expression, and is mediated by the cellular environment and hence also external environmental influences, like drugs. Let us look at it like this:

- The cell's nucleus is like a library.
- The chromosomes within the nucleus are like books.
- The genes found in the chromosomes are like words on a page.
- DNA is like the alphabet.
- Gene expression is like reading.

To summarise, a string of DNA letters is called a gene that codes for a protein. Genes are located on chromosomes, which are found in a cell's nucleus.

How do genes affect behaviour?

First, a word about genetic mutation. Gene mutations are a permanent change in the DNA sequence that makes up the gene. There are two types: inherited mutations, which are passed on via the sex cells to the offspring, and acquired mutations, which can occur at any time in the process of DNA copying. These gene mutations are not passed on to any offspring. Environmental influences certainly have a very important part to play in the expression of genes in a fairly predictable way, as is the case in substance misusers. Of course, some

environmental influences can trigger permanent mutations in an individual. Cigarette smoke, for example, can cause cancerous mutations, but this aspect of mutation is not a heritable trait.

The thing to note about proteins is that they are made from building blocks called amino acids, and that there are twenty different amino acids. They can be linked together in any sequence and the chains can be of any length. How these chains are constructed defines the shape of the resultant protein and this distinctive shape determines its function.

Recall that in the section on how neurons work (see Ch. 2), the key and lock analogy was used. Neurotransmitters have a specific shape, like a key, and the receptor site has a correspondingly specific shape, like a lock. Only congruent shapes will cause the desired change in the neuron. These shapes are determined by the structure of the protein. Also remember that enzymes are used both to manufacture and to deconstruct neurotransmitters. These enzymes are also proteins. In fact, many hormones are also proteins. Thus, proteins are central to the functioning of the nervous system, and hence individual differences in proteins can account for individual behavioural traits.

The problem here is that should just one amino acid in the protein chains be changed due to a genetic mutation, then the shape of the molecule is correspondingly different and so the protein will differ in function. For example, if a receptor site is a tiny bit different to 'normal', a neurotransmitter might not bind to it at all or, if it does bind, it does so loosely and might leave the site before it has fully conveyed its message. The converse could also be true, the neurotransmitter might stay longer and convey a stronger message and so, depending on the specific change, an advantageous or detrimental change might have occurred. This also means therefore that a given gene might code for two different neurotransmitters or two different receptor sites.

An enzyme known as a 'splicing enzyme' is involved in the process by which the genetic code is copied to manufacture the required protein. As enzymes themselves are proteins, they need to be coded for by genes too. Should there be an error in the functioning of a splicing enzyme due to a mutation, the result is that a gene sequence can actually end up coding for different proteins than intended. Therefore because of an accident in the 'photocopying' process, the enzymes, in effect, have invented a new protein.[3] So it is not only our genes that determine our destiny, our enzymes do too.

The new protein might or might not be a favourable change to the species, but if such a change occurs in a sex cell or at fertilisation (early enough to become a heritable trait), natural selection will take care of the long-term consequences to the species. This is the basis of evolution: variation, consequence and heritability. If the mutation occurs later on, it may well have profound effects on that individual but will not affect the family line because it is not passed on.

The variability in the manufacture of the protein chains is rooted in our DNA. If for some reason the genetic code is mistyped, different proteins are produced. There are various ways in which these 'typos' can occur but they all boil down to mutations in the sequence of the genetic code. If the mutation causes the new version of the protein to work better than the previous one, then more copies of your genes are likely to be passed on. This is how natural selection

occurs, survival and reproduction of the fittest leading to a change in the species over time.

Of course, if the new protein does not work better than the original one then it might not be an error so severe that the organism exhibits traits so detrimental that they are unable to survive or breed, but oftentimes, much more subtle differences are apparent. In fact, most mutations have neutral effect or are identified and repaired by the cell. With regards to the brain, these subtle changes may be observed as behavioural differences, and may relate to how the individual suffers anxiety or depression. In fact, the shape of an individual's personality is in part a result of the shape of that person's proteins! As for what causes acquired mutations, it is most commonly an error in the several steps of the copying process of DNA, or some environmental factor like a dietary toxin, cigarette smoke or sunlight. Mutations that occur later in life (acquired mutations) cannot be passed on to the next generation.

To reiterate, mutations do not only occur when reproductive cells divide to change the function of an organism's offspring, they can occur whenever a gene is being copied to make a protein. This means it can happen at any time. Your present body function is therefore not necessarily a predictor of the future, it is on a kind of knife edge. It is quite possible, to pick an extreme example, that you could suffer a gene mutation that so affects your brain function that you become polygamous instead of monogamous, develop a passion for pornography, become a fundamentalist religious zealot or even become institutionalised. Generally, these instances are rare because our body is very good at correcting mistakes, but it does happen. If nothing else, this serves to remind us that our biology makes us who we are, we should take nothing for granted, and that we should never be judgemental in healthcare.

How might drugs affect genes?

The genetic information that codes for protein manufacture sits in the nucleus of our cells, the nucleus being a huge library of information. The total number of all the books in the library is necessarily pretty vast. After all, the sum of these is the instruction manual for a human being. It is estimated that we have 10 thousand trillion cells, each one of which knows exactly what it should be doing, whether it be a piece of muscle or an eyebrow and whether it should produce insulin or adrenaline (epinephrine).

Our DNA never leaves the cell nucleus and yet our cells collectively manufacture an array of up to a million proteins (noone is quite sure yet how many). So how is the information passed from the nucleus to the protein manufacturing parts of the cell? Another molecule called ribonucleic acid (RNA) is the messenger of genetic information; it basically makes a photocopy of the DNA sequence and transports the information out of the cell nucleus and off to the parts of the cell whose business it is to make protein. Rather than waste paper and photocopy every page of every book in the library, a cell will only make a copy of a gene if it is activated, in effect when it is told to do so.

Not all of our DNA code actually codes for protein. In fact, a staggering 95% codes for nothing. So what is it all for? Some of these non-coding genes tell the cell where a piece of genetic code starts and stops, so the protein code is 'sandwiched' between start and stop DNA. The 'start' section of DNA is called a promotor sequence and the 'stop' a terminator sequence. A gene is turned on when the cell decides that a photocopy of a gene should be made. This decision to start turning a gene on is controlled by an enzyme called RNA polymerase and regulated by several other transcription factors. So, some of this 'excess' DNA is responsible for the process of turning genes on or off. Remember, if all cells have all the genetic code, they need to work out which bits to use and when, as appropriate.

The rest of the 'excess' DNA is often termed 'junk' DNA. Sections of 'junk' DNA are interspersed between coding sequences and are removed by an enzyme when the RNA photocopy is made. These sections are called introns. Introns seem to be used to detect errors in the photocopying process or are old portions of code that are now redundant. The parts of a gene actually converted to the final sequence of RNA that is used to make the protein – called mRNA – are called exons (Fig. 9.1).

Clearly this process is not random or we would become a mass of non-differentiated cellular confusion. The regulation of which genes are turned on or off is controlled by proteins called transcription factors, which bind to that part of the gene that says 'start'. These transcription factors are very important and govern gene expression. They are present inside the cells but are themselves activated by messengers from outside the cells. This means that the extracellular environment decides whether genes are turned on or off. So what is happening in another cell or another organ regulates genes. It is at this level that psychoactive chemicals can have profound effects on gene control. Research has shown that, once altered, the transcription factors can remain so for years, if not permenantly.[5]

The extracellular messengers that activate the transcription factors are often neurotransmitters. Thus, the external environment – the real world outside – through its influence on our nervous system, can regulate gene expression. Most people find this idea striking. Genes are thought of as 'hardwired' entities that cannot ever be changed. However, we have now discovered that mutations, and even the external environment, can change the functioning of our genes.

To illustrate this, consider what happens when we smell something. A smell is just a chemical, a molecule that can signal our olfactory (smelling) neurons to fire. Your olfactory system then relays this information to our limbic system. The limbic system then informs our hypothalamus, which then passes the information on to the pituitary gland. The pituitary secretions then tell our adrenal glands to release stress hormones. These hormones may then act as messengers and activate photocopy factors that go about turning a gene on or off.[3] It turns out the smell was a perfume that an ex-partner used and it brought back some very bad memories linked to stress, fear and anger. The environment changed the regulation of our genes, genes are not therefore our everything. Evolution is thus not just about making new genes by random mutations in sex cells or at fertilisation, but more so about regulating how genes respond to environment.

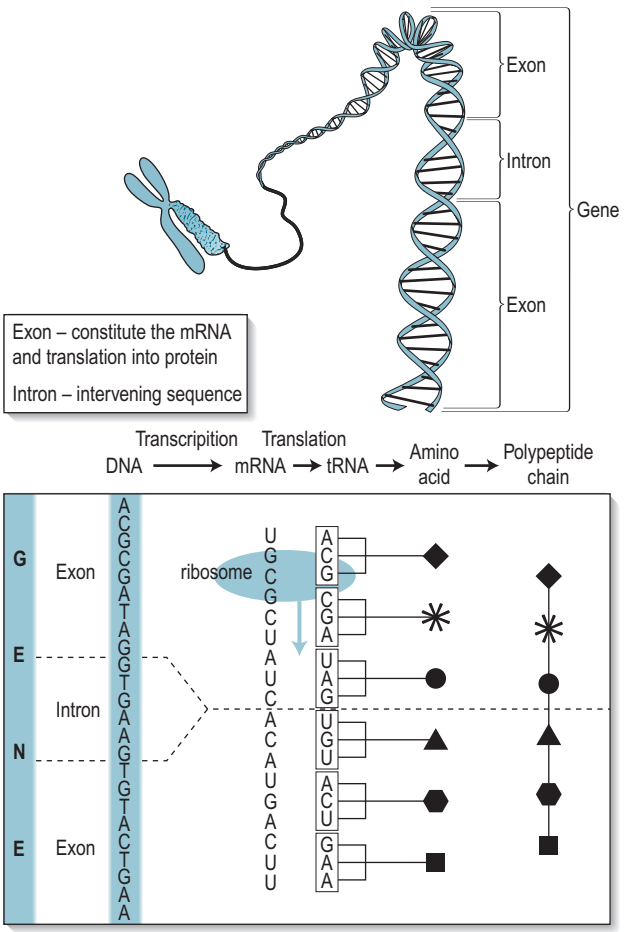

Fig. 9.1 A gene (sourced from National Human Genome Research Institute website www.genome.gov).

The upshot of this is that our environment moulds us on a fundamental level. If we suffer trauma in childhood, for example, or if we are brought up in a non-stimulating environment, or if we abuse chemicals, we are changed at the genetic level, not by what genes we possess but by the control of our existing genes. A type of serotonin transporter gene, for example, has been shown to increase our risk of depression but only if we are raised in a stressful environment.[3]

Heritable genetic traits appear to account for between 40 and 60% of an individual's risk of becoming an addict. To date, no single gene that predisposes towards addiction has been found, although many seem to contribute. There are no easy answers to the problem at any level. The ongoing argument as to whether addiction is rooted in genetics or environment seems a little redundant, as both factors are significant and neither can be taken in isolation. The debate should not really be focusing on which factor is the sole problem, but rather on an investigation of how the two factors might interact to result in addiction.

The genetic problem is, however, very real. Kryger and Wilce (reported by Volkow et al) found that 772 genes were expressed differently in alcoholic patients.[6] A survey of 20 000 people also linked the serotonin transporter 5HTT-LPR to a predisposition to addictive behaviour. Dopamine has also been implicated. D2 receptors have been shown to be insufficient leading to reward insufficiency but D4 receptors can also be overexpressed, manifesting as outgoing personality types with a leaning towards novelty seeking and hence drug misuse.[15]

Studies by the addiction researcher, Volkow, show that the insertion of dopamine D2 receptors, via a viral vector, to increase gene expression results in a decrease in alcohol intake. A greater number of D2 receptors therefore seems to reduce the risk of substance abuse. Neuroimaging techniques have demonstrated underactivity of D2 receptors in the brains of cocaine addicts. Individuals with a low D2 receptor activity who take drugs feel stimulated. Conversely, individuals with a high D2 receptor activity who take drugs find the result unpleasant.

To reiterate, the problem of addiction is very, very complex and there is, as yet, no way to unravel all the interactions. The influence of genes on behaviour cannot be separated from environment, except for innate behaviours present in the absence of environmental experience. For example, animals that have been raised in social isolation still demonstrate submissive behaviour if shown pictures of dominant males. These animals have had no opportunity to learn this behaviour, but it exists regardless because it has been passed down through many generations. In humans, smiling is a good example of an innate behaviour. We do not learn to smile. In infancy we perform natural smiles automatically. We do, however, learn fake smiles, so-called Duchenne smiles, according to our experience of social situations (in fact, a Duchenne smile uses slightly different muscles and so, if you know what to look for, it is possible to spot a fake).[7] Aspects of our behaviour could be thought of as similar to this example of smiling. We have an innate tendency to seek pleasure but addiction itself is learned in response to our experience.

Non-genetic heritability

Having pointed out that acquired genetic mutations or alterations to the activation of 'photocopy' (transcription) factors by messengers cannot be passed on, we must add a further complexity. The genetic code is not the only mechanism by which heritable traits are passed on; changes in gene activation can be passed on regardless of the genetic code. Therefore it is incorrect to assume that, if an individual has had no postnatal experience of a given stimulus, behavioural responses to a later exposure to that environment must be a genetic trait. Our environment starts prenatally and so any given trait could have been inherited from the mother's environmental influence.

The prenatal environment is both rich and diverse. The fetus shares its circulatory system with the mother and so is influenced heavily by the mother's environment for the 9 months of pregnancy. In fact, even identical twins can have

non-identical prenatal environments because they might share a placenta (monochorionic monozygotic twins), which might result in a disproportionate distribution of blood between the two. Very quickly after birth of course, environments become different for identical twins regardless of prenatal blood supply, and so all twins, although having identical DNA, will have different genes turned on or off due to epigentic modification and so become the unique individuals that we observe.

Hormonal influences are a key environmental factor and can have profound effects on a developing fetus because many hormones can cross the placenta. Stress hormones are a prime example of this, and maternal stress can lead to non-genetic inheritance of certain traits. Research has shown that stress hormones easily cross the placenta and cause the fetal brain to develop more slowly, resulting in a smaller brain.[3] The parts of the brain most sensitive to stress hormones are those of the limbic system, in particular the part of the limbic system that serves to shut off the stress response. If this occurs, the child has a brain that finds it much harder to turn off the stress response. This individual may therefore be predisposed to anxiety. This is not a genetic trait but it is heritable nevertheless. Taken a little further, maybe years down the line, this anxious individual has a child. Since their stress hormones are always high, this trait is again passed on to the offspring, and so on through the generations, albeit getting a little weaker each time. Bearing in mind that stress can contribute to the likelihood of abusing chemicals, we can see how a vicious circle could start.

Mothers who use drugs profoundly influence the fetal environment in a multitude of ways. There is, of course, the direct influence of the abused chemicals that cross the placenta but also the additional influence of stress hormones.[8] During drug withdrawal, it has been shown that levels of stress hormones in the blood and of stress-related neurotransmitters in the brain rise. This response becomes potentiated over time, resulting in a user having an exaggerated response to stressful stimuli or an inappropriately large response to minor stressors. It is easy to see how a vicious circle can be set up revolving around stress and the use of chemicals. Individuals might seek out pleasure-inducing chemicals to reduce their perception of stress, but the drugs then induce a physiological state in which it becomes more difficult to cope with stress, thus causing them to turn again to drugs.

Mothers who abuse chemicals raise the levels of cortisol (a stress hormone) in their unborn babies and so predispose them to an inability to cope with stress. Even a traumatic birth or a forceps delivery can have similar consequences, illustrating the importance of environment on development. Robert Sapolsky has shown that more socially dominant individuals have lower levels of cortisol, thus one's social ranking (at school, in the workplace or in society at large) can help us understand how hierarchy might influence predisposition to addiction.[9] High stress levels, and hence higher levels of cortisol, cause a down-regulation of D2 dopamine receptors. This increases the risk of addictive behaviour due to natural reward insufficiency. It is easy to see therefore how important it is to increase our perception of family and societal value during treatment. Increased self-respect transforms us at the level of the neuroreceptor.

Postnatally, a stressed family environment can clearly adversely affect the newborn child. It has been shown that children of alcoholic parents have high levels of cortisol; primate studies concur with this. Monkey mothers who do not know where their next meal is coming from are less focused on their offspring. This stress causes raised levels of cortisol and noradrenaline (norepinephrine) in the offspring, who exhibit the symptoms of depression. If one considers modern society, it is not at all hard to see how it is that addiction is rife, particularly (although far from exclusively) in those from a socially and economically deprived demographic.[10] To demonstrate how all strata can be affected, regardless of status, consider the words of Rachel Cusk, who has written widely about parenthood:

> *'To be a mother I must leave the telephone unanswered, work undone, arrangements unmet. To be myself I must let the baby cry, must forestall her hunger or leave her for evenings out, must forget her in order to think about other things. To succeed in being one means to fail at being the other.'*[11]

Thinking back to the prefrontal cortex, the decision-making, self-controlling part of the brain that allows us to become social animals is not mature at birth and not fully mature even until our late twenties. This means that it is vital that a baby is nurtured in the right way, and at the right time, to aid the maturation of this part of the brain. Primate research confirms this and more strikingly, so does some research on Romanian orphans. Orphans who were left in their cots all day with little adult contact, and so no chance to develop social bonds, have been shown to have a virtually non-existent orbitofrontal cortex, a key structure of the prefrontal cortex.[12] Thus lack of emotional expression or social referencing has profound effects on the crucial part of the brain that a child needs later in life to avoid falling prey to addiction. The experience of reward, a cuddle or a kind word is more important than we could imagine in early development. Our old favourite neurotransmitter, dopamine, triggered by these actions, enhances the uptake of glucose in the prefrontal cortex, hence helping in the growth of new tissue in the area.[13] So although parental availability is not the only factor, the quality of their presence is vital.

It should be noted that 'stress' is a word now used so casually that it has, in a sense, lost its true meaning and the importance that should be attached to it. Stress is not just a word that happens to us but a complex biochemical response to a given stimulus. Stress can be caused by many things, really anything that could be seen as a threat to survival. Loneliness is for example a stressor; in terms of survival of the fittest there is safety in numbers. It is no coincidence that we speak of colonies, herds, flocks or packs in other species. Humans have instead, family, community and football teams. Why is it that native indigenous peoples have a tendency to abuse drugs and alcohol when they lose their land and culture?[14] And why is it that so many deculturalised individuals turn to gang culture? The herd is important. Significantly, addiction and the consequent lack of control over one's life are additional chronic stressors.

The stress response is triggered by the hypothalamus, ultimately resulting in the release of cortisol from the adrenal glands. Sustained periods of excess cortisol cause a reduction in the ability of the prefrontal cortex to cope with limbic input. A child left to cry will have raised cortisol levels, which will

disrupt the maturation of the neural pathways yet to be firmly established. Stress hormones also increase the propensity with which the nucleus accumbens releases dopamine. This increases our ability to seek out ways of reducing the stress. To further complicate the issue, it is also possible that low cortisol levels predispose to addictive behaviour. Low cortisol can be triggered in an infant by emotional or physical abuse. The initially high levels of cortisol caused by the stressor may be down-regulated as a result of the homeostatic mechanisms, causing a switch to low cortisol levels. In a sense, the low cortisol levels allow the body to cope by subconsciously allowing the individual to detach from the situation and so avoid painful feelings. It enables the individual to be comfortably numb, but unfortunately also emotionally unavailable. This suppression of emotion, however, also means that pleasure is seldom experienced, triggering the craving of it, and that drugs are a profound source of these feelings, from which the individual cannot disassociate. It is also the case that at some point, suppressed emotions might build to the point that they must be vented leading to socially inappropriate or aggressive behaviours.[10]

Very importantly, these social environments, and the infant's biochemical responses to them, facilitate the aforementioned gene expression. Positive experience triggers the synaptic plasticity a brain needs to mature and this process is governed by the genetic messengers discussed above.

How to build an addict

The interaction of genes and environment converges on the brain and thus shapes behaviour (Fig. 9.2). The resulting imbalance affects four key brain circuits:[6]

- Reward circuit – nucleus accumbens and ventral tegmental area
- Control circuit – prefrontal cortex and anterior cingulate gyrus
- Memory – hippocampus and amygdala
- Drive and motivation – orbitofrontal cortex

Why would evolution allow for 'bad' genes?

Before investigating the phenomenon of evolution it is important to note that evolution is not just a theory. This suggestion is often made by proponents of creationism and intelligent design. However, there is a wide range of evidence for evolutionary processes. In brief, this evidence is found in paleontological records (fossils), comparative anatomy (the similarity of the basic structures of living things), vestigial organs (such as the appendix), geographical distribution of species and the commonality of DNA in all living things. Evidence that is perhaps more 'real' to most of us is the development and spread of antibiotic-resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA).

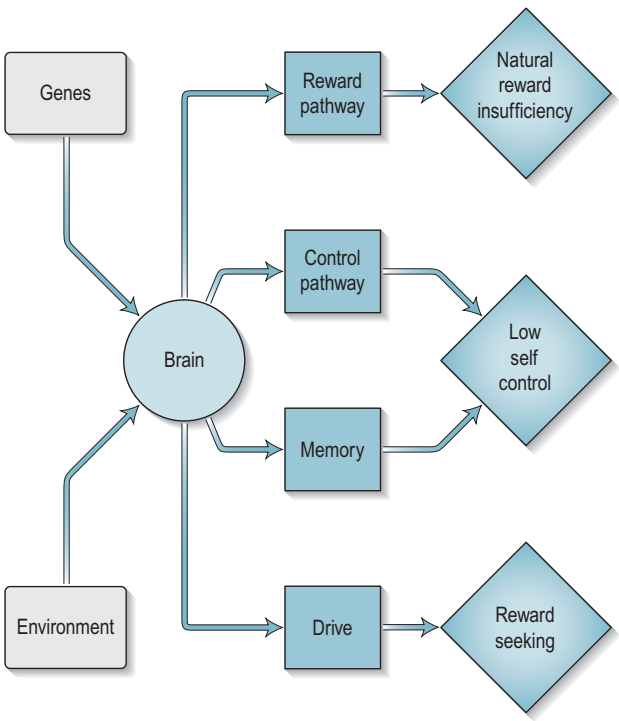

Fig. 9.2 Genes and environment converge to produce addictive behaviour.

The basic premise of natural selection is that favourable heritable traits become more common in successive generations and unfavourable traits less so. It therefore seems odd that natural selection would allow a genetic predisposition towards addictive behaviours to be perpetuated in the species. Clearly, destructive behaviours are not beneficial to the survival of either the individual or of the species, so why is this?

It is worth noting that the existence of genetic codes that produce underactive reward systems are not in themselves disadvantageous. On the contrary, it seems that natural selection allows for these types of low-reward activity to stimulate the activity of instinctive survival behaviours that produce the highest reward. In times gone by, we can see why it would be of great benefit to have members of our pack who were more driven and motivated to actively seek out reward, such as food and clean water. In modern society, however, natural rewards have tended to be replaced by powerful chemicals. Those of low-reward activity are subconsciously motivated to seek out the highest rewards in society. It is therefore modern society that is at fault, not the person.

This concept of no fault is important. As mentioned earlier, our perception of self impacts on the physiology of our reward and satiation pathways. When society, counsellors or recovery groups perpetuate the myth that addicts are at fault this severely hampers the ability of individuals to recover. Recovering addicts are far from inadequate; they possess strengths that can benefit society.

Addicts should be encouraged to understand this, and all aspects of their condition, in such as way as to empower them. To give up our power to another person, power or chemical, maintains only subordinacy. When addicts learn to remove their attention from drugs toward natural rewards they are driven and unrelenting in their focus. Often to our advantage, the natural reward that carries for them a strong enough emotional charge to transpose their drive is the desire to help others through the mire that is addiction.

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CHAPTER 10

The drugs of misuse

Canst thou not minister to a mind diseased,
Pluck from the memory a rooted sorrow,
Raze out the written troubles of the brain,
And with some sweet oblivious antidote,
Cleanse the stuff'd bosom of that perilous stuff
Which weighs upon the heart?

(Shakespeare in *Macbeth*, Act 5, Scene 3)

Alcohol

We have chosen to start this chapter with a discussion of alcohol for one simple reason: alcohol destroys the lives of more people than all the other drugs combined, partly, we suspect, because its use is not just socially tolerated but actively encouraged. It is legal in most parts of the world and so exposure to it is more commonplace. It is also very easy to manufacture, simply made by the fermentation of sugar.

Although chemically the simplest substance of abuse, in terms of its chemical effects on the body, alcohol is arguably more complex in action and more damaging than other substances of abuse. Chemically speaking, there are many different types of alcohol; ethanol is the alcohol referred to in the case of alcoholic beverages.

Interestingly, alcohol is the only substance of misuse that has any calorific value. Alcohol contains eight calories per gram. Alcoholic beverages also tend to contain sugar, which of course increases the calorific content. A pint of beer contains around 250 calories. It is for this reason that weight gain often accompanies alcohol use.

Alcohol consumption tends to be measured in units. One unit of alcohol corresponds to 8 g. The damage caused by alcohol is not related in any way to the type of beverage chosen but solely to the amount of alcohol consumed. This means that a beer of 4% alcohol is just as damaging as vodka at 40%. The difference is that one would have to drink a larger volume of

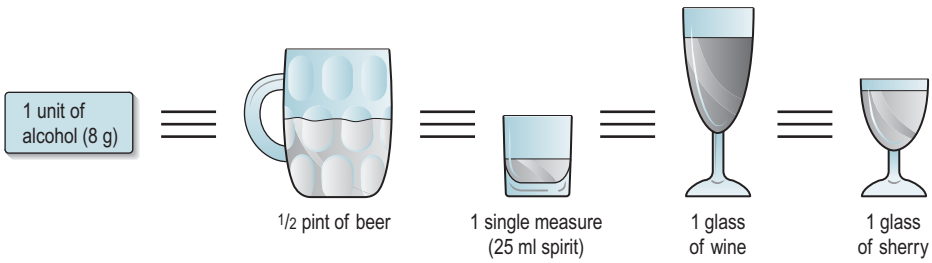

Fig. 10.1 Alcohol units. © Elsevier. (Reproduced from Kumar & Clark: Clinical Medicine 6e – www.studentconsult.com)

beer to consume the same amount of alcohol as a small volume of vodka (Fig. 10.1).

Counting the units of alcohol a patient consumes has very little benefit. Alcohol affects people differently due to genetic variations in their ability to metabolise alcohol and in its psychoactive effects thereafter. With reference to addictive behaviour, the amount of alcohol patients consume does not matter. It is what happens to them because of their drinking that is paramount. Some treatment centres advocate controlled drinking, whereby patients are asked to moderate their alcohol consumption to within recommended 'safe' limits. Although perhaps limiting some of the physical damage alcohol causes, this approach is not beneficial with regard to addiction. If addicts were able to control their drinking, they would, and so by definition they would not be addicts. Addicts who try to count their drinks, or spread them over a given time, think of nothing else but alcohol. They become obsessed by the anticipation of the next drink, fuelling their addiction still further.

With regard to the physical damage of drinking, three units a day for men and two per day for women is thought to be a maximum. The effects of alcohol are worse for women, hence the lower values. It is also important that women do not drink at all during pregnancy. Alcohol can damage the fetus, resulting in fetal alcohol syndrome. This condition manifests with mental retardation, abnormal features and growth impairment.

At the start of the chapter, we stated that alcohol was the most damaging of all the addictive chemicals. The following list, outlining the body systems affected and the conditions caused or contributed to by alcohol, clarifies this statement:[1]

- Central nervous system (CNS)
  - epilepsy
  - Wernicke-Korsakoff syndrome
  - polyneuropathy
- Muscles
  - acute or chronic myopathy
- Cardiovascular system
  - cardiomyopathy

  - beri beri
  - heart disease
  - cardiac arrhythmias
  - hypertension
- Metabolism
  - hyperuricaemia (gout)
  - hyperlipidaemia
  - hypoglycaemia
  - obesity
- Endocrine system
  - pseudo-Cushing's syndrome
- Respiratory system:
  - chest infections
- Gastrointestinal system
  - acute gastritis
  - carcinoma of the oesophagus or large bowel
  - pancreatic disease
  - liver disease
- Haemopoiesis
  - macrocytosis (due to direct toxic effect on bone marrow or folate deficiency)
  - thrombocytopenia
  - leucopenia
- Bone
  - osteoporosis
  - osteomalacia

Alcohol is a depressant drug. This means that in moderate doses it leads to sensations of relaxation and to a reduction in social inhibitions. From these observations it can be deduced, as verified by research, that alcohol must affect the prefrontal cortex. This part of the brain provides executive function, including the ability to control the appropriateness of behaviour. If one considers the behaviour of those who have consumed alcohol, it is apparent that their experience of self and social interactivity is much changed. How often do those under the influence of alcohol behave in a way they would previously have found embarrassing, for example, suddenly realising they had missed their vocation as a pole dancer, stand-up comedian or action movie hero?

In higher doses, alcohol causes vomiting because it irritates the lining of the stomach. In fact, vomiting may save a drinker's life by eliminating alcohol from the stomach. It is important to note that smoking cannabis and drinking heavily could prove fatal, as cannabis suppresses vomiting. In the long term, the effects

of alcohol on the gastrointestinal system can be devastating. This includes damage to the mouth, oesophagus, stomach, liver and pancreas. Alcohol is an irritant and can inflame any of these structures, increasing the risk of cancer in these areas. This inflammation impairs the ability of the body to extract nourishment from food, which can result in malnutrition problems.

Alcohol also contributes to abnormal perceptions of temperature. Initially, drinkers feel a warm glow and flushed cheeks because alcohol causes vasodilation in the skin. However, this results in heat loss (as drinkers are somewhat anaesthetised and so numbed to the cold), which can result in hypothermia, a cause of death common in street drinkers. In larger doses still, the drinker might fall unconscious. This risks death from inhalation of vomit or subsequent pneumonia as the stomach acid digests the fragile tissue of the lung.[2]

Alcohol is very quickly absorbed. It passes directly from the digestive tract into the bloodstream within minutes and is distributed throughout the body, most importantly to the brain.

Alcohol and the brain

Alcohol affects the neurons in the brain in a multitude of ways. It enhances the gamma-aminobutyric acid (GABA) neurotransmitter system. The role of GABA-receptor-containing neurons is to reduce neural activity, notably of the locus coeruleus and the CNS. This is achieved by controlling the flow of chloride ions to the postsynaptic neuron. When chloride ions enter the postsynaptic neuron, the neuron becomes less excitable. Alcohol-induced changes to the cell membrane of the postsynaptic neuron cause the ion channels to open, allowing extra chloride ions to enter the neuron in those parts of the brain containing GABA receptors. Alcohol can also bind directly to GABA receptors, which enables the ion channels to stay open longer and more 'calming' chloride ions to enter.

These phenomena explain the sedative, anti-anxiety effects of alcohol. These sedative effects are enhanced by the fact that alcohol blocks the excitatory effects of the neurotransmitter glutamate. This is why we lose our memory when drunk; glutamate is used to help form memories.

As ever, adaptive processes occur in the brain to combat these effects. GABA neurons become less sensitive to the sedative neurotransmitter GABA and hence become overexcitable. This results in the common excitatory symptoms of withdrawal, such as anxiety and insomnia. The brain adjusts to the blocking effects that alcohol has on the excitatory neurotransmitter glutamate by becoming hypersensitive to glutamate, resulting in excitatory symptoms. In fact, withdrawal symptoms from alcohol can be so severe as to be life threatening in a syndrome known as delerium tremens (the DTs), with mortality rates as high as 35%. Again, this ability to cause life-threatening withdrawals sets alcohol apart from all the other drugs of abuse, except for the benzodiazepines and barbiturates. The DTs can cause epileptic-like seizures due to the hypersensitivity of the glutamatergic neurons. They also manifest with primarily visual or tactile hallucinations, anxiety, paranoia, rapid pulse, high blood pressure and fever due to the lack of opposition to sympathetic activation by GABA.

The addictive nature of alcohol relates to its ability to curtail the action of the enzyme that breaks down dopamine, thus leaving more dopamine available at the synapse to have its affect. Alcohol is also thought to promote the release of dopamine by stimulating the delta opioid receptors (which explains why the opiate blocker naltrexone is useful for some patients). Remember, dopamine signals that a behaviour is important and so worth repeating.

Alcohol and the liver

The liver has many functions, one of which is the metabolism of chemicals such as alcohol. This process involves breaking down alcohol, through a series of metabolic steps, into its constituent parts, ultimately carbon dioxide and water (Fig. 10.2). Some of the intermediate chemicals produced, chiefly acetaldehyde, are toxic in their own right.

Alcoholic liver damage essentially comes in three types:

1. Fatty liver
2. Alcoholic hepatitis
3. Cirrhosis.

Alcohol metabolism invariably produces fatty deposits in the liver due to both an increase in fatty acid synthesis and decreased fatty acid oxidation. There are often no clinical features of this disease. If severe, inflammation accompanies the accumulation of fat, which can lead to the development of cirrhosis. Fatty liver disease is diagnosed when blood tests detect alterations in normal liver

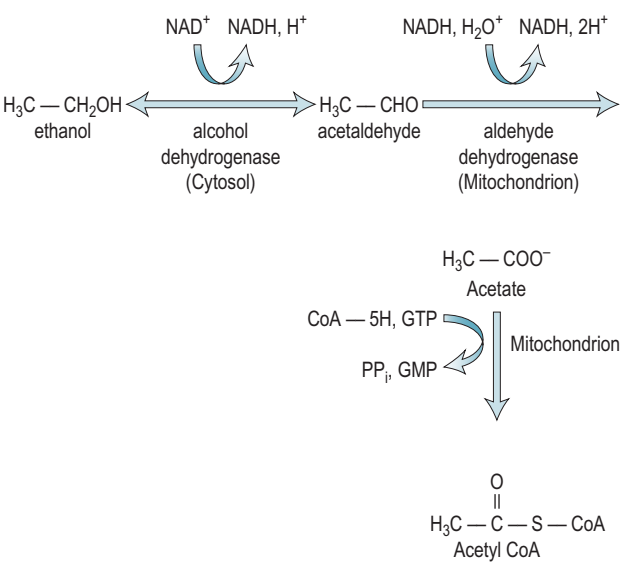

Fig. 10.2 Alcohol metabolism.

biochemistry. It is then usually further investigated using ultrasound or computed tomography (CT) scanning. The good news is that, on discontinuation of alcohol, the fat will gradually disappear and the liver biochemistry usually returns to normal.

Alcoholic hepatitis is an acute inflammation of the liver, usually accompanied by severe liver malfunction. This may result in the striking condition of jaundice in which the skin and whites of the eyes turn yellow. Pale stools and dark urine are often also present. Quite often, however, patients appear well, with inflammation being apparent only on biopsy. If alcohol consumption continues, alcoholic hepatitis may progress to cirrhosis. If alcohol is discontinued the liver usually recovers.

Alcoholic cirrhosis is the final stage of liver damage from alcohol abuse, the next stage being death. Surprisingly though, patients can appear to be healthy and present few symptoms. It is more normal, however, for patients to present with physical symptoms of chronic liver disease, jaundice being common. Other possible signs are neurological problems such as disorientation, personality changes, red palms, nail clubbing, spider naevi distributed above the nipple line, skin ulcers, xanthomas and oedema to name but a few. Due to the interference with blood-clotting mechanisms and blood flow there is a risk that the patient may suffer internal bleeding and die as a result. Should abstinence for life be implemented, the 5-year survival rate is 90%, if not, it falls to 35%, usually with death occurring in the first year.[1] Essentially, if the liver does not function properly, blood poisoning occurs, which can be fatal.

Pancreatitis is also caused by excessive drinking. In this condition the pancreas becomes inflamed. In fact 60–80% of chronic pancreatitis cases are due to alcohol. An attack may follow an alcohol binge. Pancreatitis can be acute, which is a temporary condition whereby normal function resumes after an episode, or chronic, meaning that there is continuing inflammation and irreversible damage. Pancreatitis is one of the most painful of all diseases and can be fatal. The pain is usually located in the middle of the abdomen between the rib cage and abdomen and is knife like in character. Often the pain can also be experienced penetrating through to the back. The abdomen will be very tender and the patient exhibits guarding. If severe there may be bruising around the belly button (Cullen's sign) or on the flanks (Grey Turner's sign).[1] Patients must be referred to hospital immediately and without fail as multi-organ failure and death are a very real possibility. The easiest way to understand what is happening in a case of acute pancreatitis is to consider the enzymes present in the pancreas digesting the tissue of the pancreas itself, thus destroying it. In chronic pancreatitis, damage to the pancreas results in its inability to produce digestive enzymes and/or insulin which can result in digestive problems or diabetes.

Alcohol abuse often also leads to anaemia, in which there is a reduction in the number of red blood cells and various other cardiovascular problems. There is increased blood pressure, increased risk of stroke and cardiomyopathy, a condition in which the heart muscle can no longer pump efficiently.

The abuse of alcohol easily leads to the deficiency of vitamin B1, thiamine. Thiamine is used as part of the process by which energy is provided to nerve cells. It is found in many foods including nuts, seeds, meat and cereals. A

deficiency in thiamine results in a condition known as Wernicke's encephalopathy (a type of brain damage). This condition manifests primarily with a loss of short-term memory, partial paralysis of the eyes and difficulty coordinating movement. If treated very promptly this condition is reversible, if not, Korsakoff's syndrome develops. Korsakoff's syndrome manifests with terrible memory loss and confabulation, whereby memories are invented or imagined and taken as truth. The severity of brain cell damage in Korsakoff's sydrome is usually so severe that treatment is unsuccessful or incomplete with less than 20% even approaching recovery. Certainly thiamine replacement is no longer successful. In fact, 15–20% of patients with this disorder die from it.

Western medical treatment of alcohol dependency

One of the most used drugs for this clinical situation is Antabuse (disulfiram). This drug interferes with the mechanism by which alcohol is metabolised, so that when alcohol is ingested the chemical acetaldehyde builds up in the body causing very unpleasant sensations such as skin flushing, headaches, nausea, vomiting, high blood pressure, rapid heart beat and shortness of breath. Sometimes it can even cause death. The theory is that drinkers will be so afraid of these unpleasant sensations, or of dying, that they become less inclined to drink.

However, there are some problems to consider regarding Antabuse. Drinkers can easily stop taking the drug and resume drinking. In fact, chronic alcoholics rarely find that the aversion to unpleasant symptoms is outweighed by the desire to experience the positive effects of alcohol. Addiction is defined by the user's pursuit of pleasure, not the avoidance of unpleasant sensations. The desire for the effects of alcohol is so strong that even if Antabuse is implanted under the skin it has been known for addicts to cut the implant out themselves.

It is also very easy for addicts to change their drug of choice in their search for pleasure. Antabuse is specific for alcohol and does not stop an individual experiencing the positive effects of other drugs. However, this can cause other problems. If Antabuse is combined with stimulants or some antidepressants it can result in insomnia, anxiety or even psychosis. This occurs because Antabuse also interferes with the removal of dopamine from the synapse, resulting in excitatory symptoms.

So Antabuse is no magic bullet. It is not a cure for alcoholism, it merely reinforces to a patient the fact that stopping alcohol consumption is highly desirable. What it can sometimes offer is a window of opportunity. For a time, while alcohol is not inhibiting the frontal cortex, it is possible for patients to begin to make some effective decisions. Antabuse alone, however, cannot drive recovery. What must initiate the process is the realisation that at a profound emotional level, alcohol has become so all-consuming that it must be avoided at all costs.

Another drug, acamprosate, has shown some promise but is not effective on its own and must be combined with other support methods. It seems to reduce the cravings for alcohol by increasing the levels of the inhibitory neurotransmitter GABA. There is also some evidence to suggest that acamprosate is neuroprotective, and so may reduce the brain damage caused by the surge in glutamate

associated with alcohol withdrawal. Experience shows that the drug appears to be useful only in preventing relapse and so the patient should be abstinent before trying it. It also has some undesirable side-effects, such as allergic reactions, heart arrhythmias, blood pressure problems, headaches, digestive disturbance, insomnia and impotence.

Cocaine

Welcome to the world of extremes. In one fell swoop cocaine is responsible for both ultimate pleasure and abject desperation. This is the case not only for those who become addicted to it, but also for those involved in the cocaine industry – misery for the poorest farmers and riches beyond compare for the principal dealers.

Cocaine is now the second most used illicit drug after cannabis. A survey conducted by the Home Office in 2003/2004 showed that three-quarters of a million individuals aged between 16 and 59 years in the UK have used cocaine over the past year.[3] In the US it is estimated that 6.6 million people, or 3% of the entire population, use cocaine.[4]

Cocaine has been used for many thousands of years. Its use is thought to have started when the leaves of a coca plant were tentatively chewed to discover how they tasted.[4] Coca leaves themselves do not have the same profound effects that the isolated drug has, but it does increase mental alertness and reduce hunger and fatigue. Such was the power of the leaf that the Inca religion regarded the leaf as divine and magical. It was chewed during rituals and burnt so that its aroma pleased the gods; its ashes were scattered to keep the fertility goddess happy and placed with the dead to discourage their spirits from haunting the mortal world. Even today, one Colombian tribe practises a ritual whereby one 'marries' the coca leaf.[4] So, clearly, something about how this drug makes you feel is regarded as pretty special, and herein lies the problem. Cocaine makes you feel like nothing else in the world you have ever experienced. In 1860 a doctor called Paolo Mantegazza published the results of some experiments on cocaine that he had tried out on himself following the successful isolation of the coca alkaloids by Friedrich Wohler a year earlier. Dr Mantegazza stated:

> *'I sneered at all the poor mortals condemned to live in the valley of tears while I, carried on the wings of two leaves of coca, went flying through the spaces of 77 438 worlds, each more splendid than the one before. An hour later I was sufficiently calm to write these words with a steady hand: God is unjust because he made man incapable of sustaining the effects of coca all life long. I would rather live a life of ten years with coca than one of 100–000 (and here I inserted a line of zeros) without it.'*

It was statements like these that led to the commercially minded becoming interested in cocaine. Initially, cocaine was sold mixed with wine to form a perfectly legal elixir much used by such famous names as Arthur Conan-Doyle, Sigmund Freud, Louis Bleriot, Jules Verne, Thomas Edison, HG Wells and former

US presidents William McKinley and Ulysses S. Grant. During most of cocaine's history, no taboo has existed surrounding its use. In fact, when alcohol was banned in Atlanta, Georgia, in 1885, coca was added to soda water and Coca Cola was born.[4] Cocaine also became of great interest to the pharmaceutical industry as a very powerful local anaesthetic and is in continued use for eye, throat and nasal surgery.

In its isolated form, cocaine is most commonly a salt called cocaine hypochloride. This form can be snorted and is absorbed through the nasal mucosa. Its absorption is relatively poor, at around 20–30%, because the drug tends to cause vasoconstriction. In this form the cocaine looks like a white powder. This appearance means that, on the street, cocaine tends to be 'cut', or diluted with similar looking powders such as baking soda or dextrose. Clever dealers cut the cocaine with local anaesthetics, such as benzocaine, which mimic the numbing effect of cocaine on the nasal mucosa. In addition to snorting, this form of cocaine can be mixed into drinks or dissolved in water for injection because it is water soluble. Snorting cocaine produces its maximum psychoactive effects within around 10 minutes, and these are sustained for about 40–60 minutes. A typical single dose is in the region of 100 mg.

Freebase is produced by dissolving the cocaine hypochloride salt in water and then treating it with ammonia to free the base from the salt. To recover the freebase, a solvent such as ether is added to the solution. The freebase dissolves in the ether when shaken vigorously. As ether is insoluble in water it can be siphoned off and evaporated, leaving behind the freebase cocaine. Ether is extremely flammable and can spontaneously combust, bringing with it added dangers. Freebase is smoked, allowing it to enter the bloodstream very quickly. The euphoria associated with smoking freebase cocaine is experienced almost immediately, reaching the brain in about 5 seconds, at least as fast as through injection but without the associated risks. The speed with which euphoria is reached is associated with the speed with which dopamine levels are raised and so the addictive potential for freebase cocaine is immense.

Due to the fact that the use of ether to extract freebase can be risky, baking soda is often preferred to ammonia in production of the freebase, and ether is not used at all, leaving the cocaine bicarbonate salt in the mixture. This method produces what is known as crack cocaine. Its texture ranges from crumbly to a hard crystal with a yellowish colour. Not only is this safer but it increases the profitability to the dealer. The resulting crack cocaine is not soluble and so cannot be snorted or injected. It is usually smoked in a pipe or burnt on a piece of tin foil. When it is heated, any water present boils and makes a crackling sound as it evaporates, hence the name 'crack'. Crack pipes are readily available but it is just as easy to smoke crack using any narrow metal tube, such as a radio aerial. To avoid burning the mouth and fingers, paper may be wrapped around the tube and metal wool used as a filter. The rock is placed at one end of the pipe and the other end in the user's mouth. The rock is then heated with the flame from a cigarette lighter. As the rock heats it melts and the vapour is inhaled.

Freebase and crack cocaine are particularly rapidly metabolised and so the euphoria is short lived, typically subsiding within 5–10 minutes. This leaves the user needing more. It is not unheard of for users to smoke crack at 15-minute

intervals for 72 hours solid without stopping to eat or sleep. Crack affects the reward system so powerfully that all else becomes insignificant in the shadow of cocaine. 'Crack houses' have developed in response to this quick demand for more. These crack houses provide a place where people can go to smoke crack and also provide a ready supply of crack rocks. A rock of cocaine will on average provide 30–60 minutes of effect if smoked intermittently. Crack cocaine is often surprisingly cheap to purchase, costing around £20 for a rock but these can sometimes be cut into smaller sizes to encourage people to buy. Cocaine costs between £40 and £80 per gram. Recently, however, prices have been as low as £10 per gram, which is perhaps why cocaine is the fastest growing recreational drug among 20 to 24-year-olds.

To illustrate how profitable crack dealing can be at the level of the street, the wholesale price is typically half the street price and bought in bags of 50–100 rocks. So one bag of 100 rocks will have a street value of around £2000. For dealers higher up in the chain the profits are even greater. Some dealers have been known to make £70 000 profit in a day. The head of the largest drugs cartel, Amado Carillo Fuentes had an annual income of £7 billion.

To further illustrate the magnitude of the cocaine problem, in 1999 a BBC survey conducted by forensic chemists discovered that out of 500 banknotes circulating in London, 99% carried traces of cocaine. About 1 in 20 of these notes were highly contaminated, suggesting they had been used to snort cocaine. The rest had probably been contaminated by users and dealers. This means that the cocaine industry handles so much money that nearly every banknote in circulation has been touched by it. A frightening thought.[4]

Cocaine and the brain

As was mentioned earlier (see p. 50), the brain has evolved in such a way that pleasurable sensations have become attached to behaviours that are of benefit to the individual. The big issue with drugs is that they affect the brain in an unnaturally powerful way. The sensations that can be created by drugs far outweigh those that can be experienced from natural behaviours. Mother Nature considers the single most important act for the survival of the human race to be sexual intercourse, and so for most people, intercourse provides the strongest sensations of pleasure that are naturally achievable. Pleasure reminds us that a behaviour is beneficial and should be repeated. Cocaine feels better than sex; it feels about 1000 times better. The reward 'thermostat' in the brain is reset to anticipate reward at these kinds of level. As natural rewards cannot provide anywhere near this level of stimulation, they are disregarded in favour of cocaine.

Cocaine produces its effects largely by working on the neurotransmitter dopamine (among others). Normally, once a behaviour has resulted in a given level of a neurotransmitter, levels return to normal because of neuronal reuptake mechanisms. Neurons behave in this way so that behaviours are partaken of in moderation. Cocaine disables the dopamine reuptake transporters. This means that dopamine continues to float around in the synapses, signalling to the brain how great and important cocaine is, providing sensations of concurrent euphoria.

When cocaine is metabolised, the brain removes all the dopamine it can. As a result of down-regulation, there are therefore subnormal levels of dopamine. There are now fewer dopamine receptors and so the nerves are deprived of stimulation. This is experienced as the cocaine come-down or crash. Although not yet fully understood, it appears that in some cases dopamine receptors become permanently damaged, resulting in the brain remembering cocaine as the only thing that creates pleasure. It is hoped that the various approaches used in treatment can help a user to resist the craving until more dopamine receptors come back online and normal life becomes pleasurable again. It is hypothesised, through behavioural observation, that auricular acupuncture influences this process.

Stimulating that part of the brain involved with reinforcement (the part of the brain encouraging the 'Go on, it's going to feel great' mechanism) also reduces the effect of the satiation mechanism (that part of the brain saying 'Don't do it, enough is enough'). Cocaine affects this mechanism perhaps more than any other drug, resulting in the all-consuming bingeing effects observed in cocaine users. To demonstrate cocaine's ability to take control, consider the following research. A chimpanzee was trained to press a lever to receive a dose of cocaine. When the animal had learned that pressing the lever provided cocaine, the researchers adjusted the equipment so that the chimpanzee would have to press the lever more than once to receive his dose. The researchers were expecting to find that at some point the chimpanzee would get fed up with pressing the lever and stop trying. The experiment was stopped after the animal pressed the lever 12 800 times for a single dose of cocaine. As well as being inhumane, this experiment provides astounding evidence as to the power of cocaine.

Crack cocaine is even more addictive than the standard form of cocaine because it is so quickly absorbed into the bloodstream. It is the resulting rapid increase in dopamine that makes the effects of crack cocaine so intense, although short lived.

Part of a drug's addictive potential lies in its administration method. This is why users will start to smoke cocaine after first experimenting with snorting and why heroin users may start smoking it but then end up injecting. In a sense, most of us are aware of this; people do not get addicted to nicotine patches but they certainly do to cigarettes. This is because the patches provide a much more steady release of nicotine and so the brain does not experience any pleasure or reinforcing effects. This is why nicotine patches miss the point. Many who use nicotine patches continue to smoke because they need the pleasure that cigarettes provide. They need more than the reduction in nicotine withdrawal symptoms that the patches provide. For some, removal of the discomfort provides enough relief to give them an opportunity to quit; for others there is still much more work to be done.

The effects of cocaine

As with every drug, the effects vary according to time scale, i.e. the immediate effects of the drug and its later withdrawal effects.

Short-term effects

- Increased energy
- Talkativeness
- Dilated pupils, increased temperature, sweating, blood pressure and heart rate
- Decreased need for food and sleep
- Feelings of invulnerability
- Increased libido
- Restlessness and irritability

Long-term effects

- Runny nose and nosebleeds
- Destruction of the nasal septum
- Burst blood vessels
- Heart attack
- Severe phlegm (crack use)
- Skin crawling ('coke bugs')
- Intense paranoia
- Anxiety
- Insomnia despite lethargy
- Depression
- Increased risk of human immunodeficiency virus (HIV)/hepatitis infection

Pharmacological interventions

Unfortunately, at the present time, no medications can provide much in the way of help for cocaine addiction. Antidepressants tend to be the most prescribed, but appear to be of little benefit. It is hoped that drugs will be developed that will prevent the binding of cocaine to neurotransmitter reuptake transporters, thus reducing the associated euphoria. While perhaps offering some benefit, it is our opinion that this will simply leave users craving the pleasure they are no longer experiencing; they will continue to equate pleasure with cocaine.

We are not suggesting that auricular acupuncture will provide a 'cure' but there is evidence to suggest it helps. Researchers at Yale University studied 82 cocaine-addicted patients, who received auricular acupuncture for 45 minutes five times a week, and who were tested for cocaine use after 2 months. More than half the patients in the acupuncture group returned negative urine samples compared to 23% and 9.1% in two control groups.[5]

HIV/hepatitis risk

Users of cocaine often assume that because they tend not to inject the drug they are not at risk from blood-borne viruses. This is a dangerous assumption to make. Snorting cocaine works because it is absorbed through the blood vessels lining the nasal mucosa. Snorting damages these blood vessels, which is why nose bleeds often occur. Users sharing a snorting tube, even if it is just a rolled up £10 note, are therefore at high risk of blood contact. In addition to this, cocaine users often feel invincible and so often do not care about risk anyway. Research has also shown that cocaine helps destroy the body's defence against HIV, so in cocaine users it can replicate much more quickly, allowing the disease to progress more rapidly.

Heroin

The very existence of heroin is an irony. Heroin was first synthesised from the opium poppy in an attempt to deal with the problem of addiction to morphine – clearly it was unsuccessful. It is now believed that around 10 million people use heroin worldwide. The income of the drug barons from heroin is estimated to be around £345 billion per annum. The profit to a drug cartel of 1 kg of heroin can be as much as £250 000, depending on the size of the organisation. Small-time street dealers can convert £1000 into £3–4000. In the UK, around 30 tonnes of heroin are used annually, with a street value of £2.3 billion. Although the price of heroin fluctuates according to market conditions, it tends to cost around £40–£50 per gram. According to the 2001 Home Office report 'Sizing The UK Market For Illicit Drugs', a regular heroin user will therefore spend approximately £28.80 a day on heroin and will use on around 24.6 days out of 30, about £8 516 per annum. The report also shows that nearly 20% of users who class heroin as their drug of choice also take crack cocaine, and that 83% of crack users also use some heroin, which increases their annual bill to £16 500. In 2007, as this book is being written, prices have not significantly gone down nor the problem lessened. Heroin is arguably responsible for more health and social problems than any other illicit drug, and so more drug treatment resources are devoted to its users.

Heroin starts life as the sap of the opium poppy. Once extracted the sap is dried, washed and boiled to form opium. In this form it is ready to be smoked. Chemically, opium is a complex mixture, the active ingredients of which are the alkaloids morphine, codeine, noscapine, papaverine and thebaine. The use of opium is by no means a recent phenomenon. There is some archaeological evidence to suggest that Neanderthal man may have used it over 30 000 years ago.[6]

Refining raw opium into heroin takes a while. First, the opium is refined to isolate the alkaloid, morphine, a very powerful painkiller used by the pharmaceutical industry. First isolated in 1805 by the German scientist, Sertürner, morphine was named after the Greek god of sleep and dreams, Morpheus. The

morphine is then heated with acetic anhydride to form 3,6 diacetylmorphine, now known as heroin. Diacetylmorphine was first manufactured in 1874 by an English scientist called Wright. Later, in 1895, the drug manufacturer Bayer named diacetylmorphine 'heroin' from the German word for hero, '*heroisch*', as it was so revered.[6]

Impurities are removed via various purification processes but the reality on the street is that the purity of heroin varies enormously. Pure heroin is a white, odourless powder with a bitter taste. To further complicate the issue of purity, heroin is cut to maximise profit. Adulterants include flour, talcum powder, milk powder, brick powder or even strychnine (rat poison). The colour on the street therefore varies enormously, although it is often brown. This variability in purity and the variety of contaminants contribute significantly to the deaths associated with the use of heroin. In fact, pure heroin actually does no physiological harm (aside from overdose risk) to the internal organs; it is the contaminants that are the real menace. Many of these additives do not dissolve well and so, on injection, can reduce the blood flow to vital organs causing tissue damage.

Several synthetic versions of heroin that do not rely on the opium poppy are produced in laboratories. Contrary to popular belief, these are not safer, pharmacologically speaking. Provided the labs in question are not illegal, these drugs are at least not adulterated with various potentially damaging fillers, but many of these opiate analogue drugs, such as fentanyl, are actually much more potent than heroin, so can kill in an instant. Two of the most famous of these analogues are buprenorphine and methadone, which are prescribed to help patients deal with their addiction. These are discussed below.

If heroin is mixed with other drugs its effects can become even more dangerous. It is often mixed with alcohol, tranquillisers and barbiturates. These combinations can cause severe depression of the CNS, which can result in death. Perhaps the most famous combination is the use of heroin with cocaine, known as a speedball. The use of this method is an attempt to experience the best of both worlds, that of a stimulant and a depressant.

Heroin can be administered in many ways. In fact, the real medical concerns surrounding heroin use are more related to its means of administration than its physiological effects on the user. It can be smoked, inhaled, swallowed, snorted, or injected under the skin into muscles or into a vein. The sniffing of heroin is the same process as that of cocaine, through a rolled-up banknote or tube. This method is not particularly common, however, because heroin tastes very bitter. Heroin is rarely swallowed because it does not provide the desired quick effect and is much less potent because the liver manages to process the drug before it has much effect.

When smoked, the heroin is placed on a piece of aluminium foil and heated. The heat makes the heroin writhe about and the resultant swirling smoke is said to look like a dragon's tail, thus the method is often referred to as 'chasing the dragon'. The peak effects experienced from snorting or smoking take around 10 minutes. Smoking heroin is a rather inefficient process and so this method is often seen as rather wasteful. It does, however, remain attractive to those worried about injection risks. Pulmonary complications are common in those who smoke heroin.

Chronic breathlessness and phlegm are most common, but in tandem with general poor health, pneumonia is a real risk.

When heroin is injected under the skin the technique is known as 'skin popping', whereas injection into a vein is referred to as 'mainlining'. Subcutaneous and intramuscular injection produces a lesser high and so intravenous injection is more popular, creating euphoria within around 8 seconds. The process of injection is typically carried out four times per day.

To convert the heroin into an injectable form, a small amount of drug is placed on a spoon, sometimes a drop of citric or ascorbic acid is used to help it dissolve. Vinegar and lemon juice are sometimes used because they are easily available, but these more readily cause infection. This mix is then heated with a lighter flame to encourage the heroin to dissolve. When cooled, the liquid is drawn up into the syringe through a filter, often from a cigarette. This will remove some of the undissolved impurities but is by no means a clean or sterile technique. One of the major disadvantages of injecting heroin is that there is no way of assessing the quality of the batch. If it is of unusually high quality the user may well overdose and not survive to tell the tale.

The most accessible veins tend to be chosen, lying near the inner aspect of the elbow joint. In order to make these veins stand out further a tourniquet may be applied. Over time, these injection sites scab over and so the needle site is moved a little further along the vein. As this process continues the lines of scabs are referred to as needle tracks, which can leave permanent scars.

Repeated damage to a vein may cause it to collapse and so a vein in another location must be found. As the user declines the injection sites become more extreme. Long-term users may well inject into the jugular vein on the neck, a vein in the groin or a vein on the penis might be chosen in desperation. This can be very dangerous. Worryingly, the trend for heroin users to start injecting in the arm and then to move onto other locations is diminishing, particularly among young women. Because the veins in the groin are hidden from common view, they are becoming preferred sites. It is easier to deny heroin use if there are no track marks on the arms.

Even 'chasing the dragon' carries with it dangers that are not at first apparent. Aluminium foil is backed with a thin film of plastic to make it easier to roll. The combination of aluminium and plastic fumes causes damage to the lungs, leaving the smoker with bronchitis. The added problem is that heroin suppresses the cough reflex and so phlegm cannot be expectorated thus increasing the risk of pneumonia.[6]

Heroin physiology

Heroin itself is not biologically active. It does not bind to opioid receptors. It is, however, metabolised to active metabolites, 6-acetyl morphine and morphine. Heroin is preferred to morphine by users because it is lipid soluble and crosses the blood–brain barrier more quickly, and so the euphoria is more intense.

Heroin works because it mimics chemicals naturally produced by the body. These chemicals are referred to as endorphins (or endomorphines) because they

are naturally produced (endogenous) and pharmacologically speaking have an action similar to morphine. Endorphins are manufactured from amino acids and so are called opiate peptides. The manufacturing process occurs in the pituitary gland located at the base of the brain and in the hypothalamus. The pituitary gland releases endorphins into the bloodstream, while the hypothalamus releases them to the brain and spinal cord. It is of course the endorphins released into the nervous system that are responsible for behavioural modification.

Endorphins are produced in response to pain. Their role is to inhibit the neural signalling of information relating to pain. Opiates do not, strictly speaking, inhibit pain but rather modulate the sensation of pain by reducing its emotional implications.[2] They also mediate emotions such as anger and arousal and have a role in the regulation of hunger, thirst and immune response.

There are at least three types of opiate receptor: mu (μ), delta (δ) and kappa (κ). Opiate drugs have such a profound action because they bind to the same receptors as our endogenous opioids. These are found in various locations in the body and are stimulated to various degrees by three types of endorphin: alpha (α), beta (β) and gamma (γ)-endorphin. It appears that β-endorphin is the most involved in pain modulation.

Stimulation of the μ-opioid receptor is most implicated in addiction to heroin and morphine. Activation of this type of receptor inhibits the release of the inhibitory neurotransmitter GABA by neurons in the ventral tegmental area. These neurons usually inhibit the amount of dopamine released in the nucleus accumbens. Inhibition of the release of GABA results in the dopamine pathways becoming disinhibited and so more dopamine is released. This excess of dopamine is responsible for the inappropriate synaptic plasticity that leads to addiction (as described in the section on learning, p. 44).

In an attempt to balance out the increased opiate activity in the brain, the body drastically down-regulates its production of endogenous opiates. This results in the many uncomfortable sensations that accompany opiate withdrawal.

Chronic opiate consumption, through quite complex mechanisms, results in an overproduction of the cellular messenger cAMP, resulting in increased neural activity and craving for the drug.

How does heroin affect a person?

The effects of heroin are to shield the person from physical and emotional distress with concurrent sensations of tranquillity. The person feels sedated, relaxed and time appears to slow down. The 'rush' is said to start as a warmth that spreads through the body, dissolving pain, fear, hunger and anger as it penetrates. It is often described as inducing a sensation of being wrapped in a cocoon of cotton wool, safe and sound. The emotional contentment can also manifest as losing one's appetites, whether it is for food or sexual intercourse.

Unlike depressant drugs such as alcohol, heroin has no effect on coordination and mental acuity. It can, however, cause drowsiness in very high doses. Heroin can be extremely dangerous because opiate receptors are located in several locations other than the limbic system. The respiratory centre in the brain is one such

location. When heroin binds to the receptors in the respiratory centre it inhibits these neurons, reducing the depth and frequency of breathing. In the event of an overdose, breathing may cease altogether resulting in coma and possibly death.

It is quite common for novice heroin users to vomit. This is due to the stimulation of receptors normally activated by contaminated food or drink. Regular heroin use can also cause hormonal irregularities through its direct effects on the hypothalamus. In women this may manifest as irregular or non-existent menstrual periods. Constipation is also common in regular heroin users because receptors in the intestines are stimulated, thus inhibiting its rhythmic contractions. Possibly the most famous and easily observed effect of heroin is its ability to constrict the pupils of the eye, resulting in pinpoint pupils, regardless of light conditions.

Tolerance to opiates is differential, meaning that different parts of the body exhibit different levels of tolerance with continued exposure to the drug. This results in users needing more of the drug to experience changes to their psyche, whereas tolerance to the slowing of intestinal function and constriction of the pupils is minimal.

The physical dependence that develops in heroin users manifests as a predictable withdrawal syndrome, often referred to as going 'cold turkey' (due to the appearance of goose bumps on the skin). Withdrawals typically commence within about 6 hours of drug discontinuation and can last for up to a week. To avoid this, heroin users tend to use three or four times a day. The withdrawals typically manifest with:

- Pain in muscles and joints
- Restlessness (movement seems to reduce unpleasant sensations)
- Insomnia
- Profuse sweating
- Fever
- Piloerection (goose bumps)
- Diarrhoea
- Vomiting
- Abdominal cramps
- Rhinorrhoea (runny nose)
- Excessive lacrimation (production of tears)
- Anorexia (loss of appetite)
- Pupillary dilation
- Muscle twitches

One of the most uncomfortable and irritating symptoms is that of incredibly itchy skin resulting in compulsive scratching that leads to bruising, bleeding and scab formation. This is sometimes termed 'itchy blood'. In a sense this is not far from the truth. The itching arises due to the widening of veins induced by the

release of histamine. It is this release of histamine that also accounts for the observed flushing of the skin and the sweaty appearance.

Overdose from heroin use is common. It may be almost immediate or may take hours. Overdose can occur for several reasons. Should a batch of heroin be more pure than a user is accustomed to, in preparing their usual amount, they are actually taking much more than intended. Equally, if a user has been abstinent for a while, perhaps due to a spell in prison for example, then their tolerance to the effects of heroin will have reduced. If the user prepares a dose that they used to be comfortable with, it may well have a much more potent effect than predicted. To minimise this risk a small amount of a new batch should be used first in order to serve as a test for potency. It has also relatively recently been shown that there exists a phenomenon known as place conditioning whereby a user may exhibit tolerance to the effects of taking a drug within the confines of a known ritual or context of a known setting. If a user takes the drugs in a novel way or in a novel setting the addict may overdose. It is thought that the familiarity with the environment triggers a release in the enzymes used to metabolise the drug. In novel experiences this increase in enzymes does not occur.

A heroin overdose is actually very easy to treat, the key of course being that, a patient must be found and diagnosed quickly. The application of an opiate antagonist such as naltrexone has such a high affinity for opiate receptors that not only does it block any empty receptors (without stimulating them) but it displaces any heroin that may be occupying a receptor site. This results in an immediate return of consciousness and the onset of withdrawals.

The key signs of opiate overdose are:

- Slow, laboured breathing
- Cold, clammy skin
- Slow, weak pulse
- Cyanosis (bluish colouration of the skin)
- Pupillary constriction (pinpoint pupils)
- Drowsiness
- Delirium
- Unconsciousness

Should a user be found in an overdose situation an ambulance must be immediately called and then the A, B, C of first aid adhered too. If possible try to keep the patient awake by walking them around and talking to them.

As mentioned earlier in the text, the most damaging physical effects associated with heroin use tend to be more associated with its methods of administration. The only major threat to health from the drug itself, although not to be underestimated, is overdose via respiratory depression. The major impact of regular heroin use is on the psychological state of the user due to the addiction to pleasure. Heroin becomes the major goal of a person's existence, and so they neglect normally desirable and essential behaviours such as sleeping and eating, leading to a subnormal physical condition. This can often be observed in a user's pallid

complexion and undernourished physique. Additionally of course addicts all too often have to resort to criminal behaviour in order to fund their habit and end up existing in a grim and dark world surrounded by crime, poverty and poor living conditions.

It is well worth mentioning that heroin abuse can cause more complications in women than in men. Menstrual irregularities and anovulation (absence of ovulation) are common. Heroin affects the hypothalamus so that it does not release the pituitary-regulating chemicals that it would if there was normal health. This has the knock-on effect of irregularities in the production of both luteinising and follicle stimulating hormones. Should a user be pregnant, the fetus is at significant risk. Miscarriage and stillbirth are common. If the baby is born safely they are at heightened risk of Sudden Infant Death Syndrome, are often below average size and are susceptible to congenital and developmental defects. It is also true that the child will be born addicted to heroin and will suffer withdrawal symptoms after birth. Because the child is addicted in the womb, expectant mothers' must not withdraw suddenly from heroin but must be medically managed to protect the fetus.

Pharmacological interventions

The approaches used to attempt to help addicts stop using heroin tend to be aimed at easing the withdrawal symptoms whether they are physical or psychological. In order to relieve the physical symptoms of withdrawal the most common approach is to use opiate drugs that have a longer-lasting action than heroin. The most common of these are methadone, naltrexone and buprenorphine.

Methadone is a synthetic opioid drug first discovered by scientists in search of a non-addictive analgesic. The therapeutic goal is to avoid the symptoms of withdrawal. It is known as an opiate agonist which means that it binds to an opiate receptor site, just like heroin does. Agonist drugs are like keys that have the right shape to operate the lock. Their shape is like that of the relevant neurotransmitter, and so the door opens and the neuron is stimulated. Methadone, however, works slightly differently to heroin because it is metabolised much more slowly. This allows it to be administered just once daily. It can be delivered by injection but in order to eliminate this possibility it is manufactured in a form suitable only for oral administration. Those on a methadone maintenance programme develop tolerance to it, so its dose is gradually increased until the patient is comfortable. Due to the development of tolerance, patients exhibit withdrawal symptoms on discontinuation. These symptoms are generally less severe than heroin but last significantly longer, and can continue for weeks. For this reason the dosage is very slowly tapered off. Methadone is seen as quite an attractive option by society because it is cheap and is the only drug to which one can remain addicted but which allows users to function reasonably normally and without intoxication. Its use is intended to stabilise the patient, therefore reducing the need for heroin and consequently reducing criminal behaviours. It is of course, on balance, much safer than using heroin, because it is not injected, it is of pharmaceutical grade and its dosage is precise. Unfortunately, patients may be placed

on a methadone replacement programme for years, even for life. They thus remain a user, feeling stigmatised and worthless, thereby perpetuating their reward insufficiency. Keeping a patient addicted is not a treatment for addiction.

Addicts who take methadone orally do not experience a sensation of euphoria because the drug produces only a steady level of opiate in the bloodstream. In a sense, this lack of a high is the big problem regarding methadone use. Addiction is not defined as the search for the reduction in withdrawal symptoms, but by the fact that users crave pleasure, and so there is a higher risk of users 'topping up' their methadone prescription with heroin. Addicts choose heroin because of its very fast-acting effect on the raising of dopamine levels in the pleasure centre of the brain. The steady approach of methadone is not therefore desirable to them. Another major drawback relating to the use of methadone is that overdoses are relatively common, particularly in young children who chance upon the drug and drink it without knowing what it really is. Naltrexone can be used to treat methadone overdose, just as it can for heroin overdose. However, because methadone is much longer acting than heroin, repeated doses of naltrexone are necessary to avoid relapse into a coma and subsequent death.

Naltrexone is referred to as an antagonist drug. This means that it blocks the receptor site for opiates. An antagonist can be thought of as a key that fits in a keyhole thus preventing any other keys from fitting in the same keyhole; however, the key cannot turn the lock and the door is jammed shut. This means that the neurotransmitter receptor sites are blocked and the nerve cannot therefore be stimulated by the neurotransmitter. If a user takes heroin it has no effect because the opiate receptor sites are blocked by the naltrexone. In fact, even if some heroin is already sitting in the opiate keyhole, the naltrexone can knock the heroin key out of the lock and replace it. Naltrexone is used by some rehabs to provide a rapid opiate detoxification. Some centres will even administer it while the patient is unconscious under general anaesthesia; others prefer a more gentle sedation. In our opinion, detoxification methods that cushion the patient from their discomfort, while seemingly more humane, are not to be recommended. It is considered that detoxification should be difficult and uncomfortable. If it is seen as easy it acts as little discouragement from relapse. There is no easy route to recovery. Successful recovery can only come about as a result of hard work and commitment.

Naltrexone is most commonly administered orally, but more recently is being prescribed as an implant inserted under the skin in the abdomen. This implant is seen as advantageous because it does not require patient compliance. It is, however, not unheard of for patients to cut them out themselves because it prevents them getting high – this is clearly a risky procedure. The main downside though is that drug users crave pleasure, and while naltrexone prevents pleasure mediated by opiates it does not inhibit the desire for pleasure per se. Its effectiveness is therefore limited. One path to pleasure has been blocked by medication, but there are plenty of other drugs out there offering alternative paths to pleasure.

Interestingly naltrexone is now used mainly for the treatment of alcohol dependence. The mechanisms of its action are not fully understood, but it seems

that blocking the opiate receptor has the knock-on effect of modulating the production of dopamine associated with the consumption of alcohol.

Buprenorphine, commonly known by its brand name Subutex, is another opiate drug with partial agonist and antagonist actions. This means that it fits in the keyhole and turns the lock but the door cannot open fully because someone left the chain on. The drug therefore prevents other opiates getting into the neurotransmitter receptor site, but it also provides a very small amount of neural stimulation in itself. Clinically it can be used as an analgesic for conditions, such as arthritis, in addition to its use for opiate dependence. Similarly to other opiates, buprenorphine can cause undesirable symptoms such as respiratory depression. Should it be taken in combination with depressant drugs such as alcohol, or benzodiazepines, it can lead to death. Buprenorphine is most commonly taken sublingually, although it is also available as a transdermal patch brand named Transtec. Most importantly, it should be noted that buprenorphine has a very high binding affinity to the μ-opioid receptor which makes it difficult for an antagonist such as naloxone or naltrexone to remove it. This means that overdose cannot easily be reversed. Overdose is, however, unlikely in an individual who exhibits opiate tolerance. Due to the fact that buprenorphine is also a partial opiate antagonist it is often recommended that heroin users are abstinent for a time before starting buprenorphine. If not, an opiate withdrawal syndrome is triggered that cannot be easily reversed. Ordinarily, the withdrawals from buprenorphine are much less than from methadone. If buprenorphine is to be chosen following a methadone treatment programme the patient can expect a difficult time if they are still taking methadone. They should not start taking buprenorphine until withdrawals have already started. The withdrawal symptoms associated with this switch from methadone to buprenorphine tend to be much worse than from street heroin because of the more long-lasting action of methadone.

Common side-effects associated with the use of buprenorphine, as with opiates generally, include nausea, vomiting, headaches, dizziness, decreased libido and constipation. More rarely, liver problems can occur and so liver function is often monitored during treatment.

Since buprenorphine is not a full opiate agonist it has little euphoric effect, less even than methadone. This means that it is much less likely to be used and sold on the black market. However, some euphoria can be obtained if the tablets are crushed and inhaled or prepared for injection. This provides further evidence that addicts will continue to crave pleasure and will attempt to shape their environment in any way possible to achieve it. To avoid this abuse risk it is possible to receive a drug combination of buprenorphine and naloxone brand, named Suboxone. The addition of naloxone blocks any possible euphoric effects from the buprenorphine. Buprenorphine has a longer half-life even than methadone, which means that it can be dosed every 2 or 3 days, while methadone must be administered daily. One of the largest factors in favour of buprenorphine over methadone is that there is little awareness of it in the public domain. In contrast, most people have heard of methadone. There is therefore less of a stigma attached to buprenorphine, aided by the fact that it can be used less frequently and it is easier to take more discreetly. Since one's self respect and perceived position in

social hierarchy can influence brain function, this reduction in social stigma should not be dismissed.

Several countries, notably Switzerland, Spain and The Netherlands, prescribe heroin to addicts. There exists some support for this approach in the UK. The set up of 'shooting galleries' (safe places to inject heroin) certainly has some advantages. Patients can get a health check and are supplied clean equipment. The heroin supplied will be of pharmaceutical quality and so damage from adulterants is not an issue. However, there are also problems associated with this approach. Heroin is expensive; 1 year of treatment per patient costs £10–15 000, while methadone is nearer £2000 per annum. The risk of the prescribed heroin leaking onto the black market is also high. Most importantly, this approach does nothing to address the possibility of a user pursuing a healthy, drug-free life. While abstinence is not an easy route, it is surely the only way to real and true freedom. Something worth having is never easily obtained.

Cannabis

The first recorded use of cannabis for medical purposes was over 4 800 years ago, and for spiritual and recreational use significantly earlier than that. In short, it has been around for a long time. Even after all this time however, the debate as to its safety and legality still rages on. There are two factors that in particular seem to continually rise in debate: its safety and its potential use as a medicine. To take the first of these, many people including some notably famous individuals, have called for the legalisation of cannabis on the basis that it is less harmful than tobacco. Richard Branson, for example, signed a petition calling for the legalisation of cannabis and stated that he would not rule out selling it in his stores if it was decriminalized.[7] Certainly, this school of thought has a point in terms of the dangers of tobacco. This does not, however, make cannabis safe, it just makes the sale of tobacco immoral. The same could be said of alcohol. These drugs are so intertwined with society and culture that we are probably stuck with them; but because we have two big killers already, adding a third damaging chemical does not seem a sensible option. We also consider that the 'medical use' argument is not valid. Cannabis has, for example, some pain-relieving properties, so it is used by some for arthritis pain. This is not a convincing excuse. Countless over-the-counter medications are much more potent painkillers. Heroin is also an excellent painkiller but it does not mean that people should blindly self medicate with it.

Cannabis is also historically connected to various religious and spiritual practices; historians associate its use with ancient Pagans, Jews, Christians, Muslims, Hindus, Sikhs and Rastafaris. Most religions have discontinued its use and many actively oppose it, considering that those who interpret ancient texts in this way are making excuses for their desire to take drugs. Some sects still do, however, promote its use. Users of cannabis for religious purposes believe it to be the key to understanding the self, the universe and God.

Famously the Dutch have decriminalised the use and sale of cannabis in order to try and control its use. It is partly for this reason that so many tourists visit Amsterdam. In Amsterdam many coffee shops sell cannabis to be smoked and/or as an ingredient in their cooking, the aptly named 'space cakes'. The advantage to the Dutch government must be considerable: tourism brings with it a good deal of revenue, and as a legal product, cannabis can be legitimately taxed. This is a complex issue. Decriminalisation can be argued to reduce the profit available to criminals through the sale of cannabis, and perhaps drug-related crime. It could also, however, be argued that decriminalisation is a form of state condonement. Many suggest that if Holland can do it and not have a drug problem then the UK should follow suit. However, in Holland there has been a substantial rise in the use of recreational drugs amongst secondary school children and surely no-one would argue that that is a positive trend. Holland is also the market leader for drug consumption and distribution throughout Europe.[8]

Cannabis is derived from the female of the plant Cannabis sativa. The major psychoactive ingredient is Δ9-tetrahydrocannabinol (THC). The concentration of THC is variable. Several breeds available on the black market are now extra potent and so have a powerful action. It is likely that other cannabinols also contribute to the effects. Herbal cannabis is the dried leaves and flowers of the plant, often referred to as marijuana, 'weed' or 'wacky backy'. Cannabis resin is made by compressing the leaf and stem sap into blocks, often known as 'hash' or 'pot'. Cannabis oil is made by dissolving the resin in ethanol, which is then allowed to evaporate. This is often referred to as 'oil' or 'diesel' and is the most potent form.

Cannabis is most commonly smoked, either in a type of cigarette known as a 'joint', in a pipe or a bong. A bong is essentially a type of water pipe that concentrates the smoke allowing more cannabis to be consumed. Smoked cannabis starts taking effect almost immediately.

Cannabis can also be eaten. THC and other cannabinoids are absorbed more efficiently into the bloodstream if combined with fats such as butter. This lipid solubility is the reason why cannabis can be traced in the body for up to 30 days after taking it. The cannabis is often ground and blended with the butter, known as 'cannabutter'. This cannabutter is then used to make cakes, brownies or biscuits. There is also much less waste than is produced if smoked. Cannabis taken in this way takes longer to have an effect, usually around an hour, but its action is more intense and prolonged. In fact the experience can be too intense for some individuals. If the cannabis is ingested on an empty stomach it can cause nausea.

Cannabis effects

The active ingredient of cannabis, namely THC, mimics naturally-occurring brain chemicals and thus mimics their action. Those who promote the use of cannabis suggest that, since it is tapping into naturally-occurring brain pathways, it cannot be harmful. However, all drugs tap into naturally-occurring brain pathways. If they did not, then they would not work at all. This clearly has no relation to

potential harm. Heroin for example, works in exactly the same way but can kill you in an instant. Similarly to heroin, cannabis has been used medicinally for thousands of years and so is thought by definition to be safe. Again the same could be said of heroin but it is certainly not considered safe.

The endogenous cannabinoids are neurotransmitters called anandamides. The name anandamide is taken from the Sanskrit word 'ananda' which means bliss or delight. Anandamides are involved in regulating pain, memory, cognitions, emotions, appetite and sleep patterns. THC can therefore interfere with all of these functions. Anandamide is also important for implantation of the embryo and so cannabis could quite conceivably interfere with early stage pregnancy.

Cannabis has quite a varied physiological impact, as it affects several parts of the brain, namely the hippocampus, cerebellum and rostral ventromedial medulla. Cannabinoid receptors are, however, present almost everywhere in the brain. The hippocampus is largely involved in memory, the cerebellum in movement and balance and the rostral ventromedial medulla mediates pain sensations.

THC begins altering physiological processes by binding to the CB1 anadamide receptors. These receptors then modify the activity of several intercellular enzymes including cAMP. A reduction in cAMP activity results in a subsequent reduction in an enzyme called protein kinase A. This decreases the activity of the calcium channels, so reducing neurotransmitter release and hence lowering brain activity. In the reward circuit this results in a paradoxical release of more dopamine (as do all addictive drugs). The dopaminergic neurons themselves do not possess CB1 receptors, but are inhibited by GABAergic neurons which do have them. Cannabis inhibits the release of the inhibitory neurotransmitter GABA on the dopamine neurons and so more dopamine release is activated, resulting in behavioural reinforcement.

In chronic cannabis users the down-regulation of CB1 receptor expression in the arteries feeding the brain reduces the flow of blood to the brain, in effect starving the brain cells. This results in amotivational syndrome, attention deficits, memory loss and impaired learning ability. The symptoms of chronic cannabis use will be discussed further shortly.

Common sensations described by cannabis users include slight euphoria, relaxation and amplified auditory and visual perceptions. These perceptual changes are said to enhance one's enjoyment of music. It is for these reasons that cannabis is so often abused by musicians. The sensations are, however, strongly influenced by one's pre-existing mental state and environment. Sensations of agitation and paranoia are also especially common.

Cannabis users often report a substantial increase in appetite following cannabis use, commonly described as the 'munchies'.

According to the International Classification of Disease the general criteria for a diagnosis of acute cannabinoid intoxication must include at least one of the following:

- Euphoria and disinhibition
- Anxiety or agitation
- Suspiciousness or paranoid ideation

- Temporal slowing (in which time appears to pass very slowly)
- Impaired judgement
- Impaired attention
- Impaired reaction time
- Auditory, visual or tactile illusions
- Hallucinations with preserved orientation
- Depersonalisation
- Derealisation
- Increased appetite
- Dry mouth
- Conjunctival injection (bloodshot eyes)
- Tachycardia (rapid heartbeat)
- Interference with personal functioning

An argument often put forward by those in favour of the decriminalisation of cannabis is that it is safer than, for example, alcohol. This may be true, but being safer than a very dangerous chemical does not make it safe and harmless. Cannabis overdose is, however, pretty difficult. In order to overdose on cannabis one would need to ingest around 95 g of THC. That means a typical man eating around 1.8 kg of average strength (5%THC) cannabis or smoking thousands of 'joints' in one go. For this reason no overdose attributable to cannabis alone has ever been reported. It should be borne in mind, however, that cannabis smoke contains many of the same carcinogens as tobacco smoke.

The biggest problem is not the physical effects of cannabis but its effect on the psychology of a person. Nobody knows how cannabis is going to affect them. Some will be able to smoke cannabis occasionally without too much detriment to their lives, and others will develop cannabis-induced psychosis due to a reasonably common genetic susceptibility. This is discussed more fully in the section on addiction genetics on p. 80. Unfortunately, most people start getting involved with cannabis in their teens, when the adolescent brain is immature and particularly at risk. A paper published in the *British Journal of Psychiatry* highlighted these risks, stating that adolescent cannabis use can lead to developmental problems, permanent cognitive impairment and psychosis.[9] The diagnosis of cannabis-induced psychosis is not always easy, as often, patients do not mention their use of cannabis. They tend not to consider it important because it is not perceived to be particularly harmful or dangerous. Often, family and friends have no idea that a patient is using it, and so the patient's using history is vague. Cannabis-induced psychosis manifests with one or several of the following, as outlined by the International Classification of Disease:

- Apathy and sedation
- Disinhibition
- Psychomotor retardation
- Impaired attention

- Impaired judgement
- Interference with personal functioning
- Drowsiness
- Slurred speech
- Pupillary constriction
- Decreased level of consciousness

Chronic users of cannabis can be left with permanent and well-recognised symptoms. The pattern of symptoms is known as Chronic Amotivational Syndrome manifesting with memory loss, apathy, loss of motivation and paranoid ideation.[10] This chronic state does not necessarily mean that a patient has had or will have a psychotic episode. There also exists much evidence that even moderate cannabis use causes deficits in frontal lobe function.[11] It appears that cannabis can cause or exacerbate the symptoms of schizophrenia or bipolar disorder, especially in young people who are poorly equipped to cope with stress, or in whom antipsychotic therapy has proved unsuccessful.[12] In a follow-up study of schizophrenic patients, those with a previous history of cannabis abuse had a significantly higher number of hospitalisations, tended to have worse psychosocial functioning and scored significantly higher on the psychopathological syndromes 'thought disturbance' and 'hostility'.[12] A large prospective study has been carried out which has shown that there exists a linear relationship between the frequency with which cannabis has been used by the age of 18 years and the risks over the subsequent 15 years of a diagnosis of schizophrenia.[13]

Ecstasy

The street drug ecstasy is known in chemical terms as methylenedioxy-N-methamphetamine or MDMA.

Ecstasy is a powerful psychoactive drug that has a distinctive impact on the emotional being of a person. It is sometimes referred to as an entactogen,[14] a term that conveys some of the drug's effects. It induces the desire to produce tactile sensations as a response to increased desire to feel emotional empathy with others, for example by hugging. It is for this reason it is sometimes referred to as the 'love drug'. It is not, however, strictly speaking an aphrodisiac because it does not cause hyperarousal, although it can reduce social inhibition and increase sexual pleasure.

The effects of ecstasy are rooted in its ability to stimulate the secretion of the neurotransmitters serotonin, dopamine and noradrenaline (norepinephrine) in the brain. In addition, it also slows the re-uptake of these chemicals from the synaptic cleft. This causes the user to experience the aforementioned sensation accompanied by euphoria.

In contrast to the majority of illicit drugs, ecstasy has not been in use for very long at all. The patent for MDMA was originally filed in 1912 by the pharmaceutical company Merck. The initial intention for the use of MDMA was as an

intermediate chemical involved in the manufacture of a haemostatic drug to control bleeding that was previously discovered naturally occurring in the buttercup. In the late 1930s, pharmacists started getting interested in the effects of MDMA itself as a possible appetite suppressant. Due to the existence of undesirable side-effects it was shelved as an appetite suppressant in 1941.

The exploration of MDMA as a psychoactive agent was pioneered by the chemist Alexander Shuglin, famed for his skill in producing and testing the effects of psychoactive and hallucinogenic drugs. He believed they held great potential for learning and exploration of the unconscious mind. Shuglin felt that rather than using drugs to escape some aspect of oneself they should be used to increase one's understanding of self. As a result, much of his research was in fact carried out on himself or his friends; animal research was not favoured because he could not see into the mind of the animals and so they were of no use. This ultimately led to the development of a drug ranking system called the Shuglin Rating Scale that provided detailed information on the subjective effects of the chemicals. As a result of Shuglin's experiments using MDMA he introduced it to the psychotherapist Leo Zeff, and it soon developed a reputation for being able to enhance one's communication skills, through its ability to reduce inhibition and increase one's capacity for introspection. In fact it is still used in Switzerland as the 'marriage guidance drug', because it reduces hostility and improves interactions and feelings of intimacy between couples.

Since the 1980s, ecstasy has become a popular recreational drug, which is felt to enhance one's musical and social experience. It is usually sold in pill form, although the use of powder is on the increase. In the early years, ecstasy was costly – as much as £20 per tablet. Now, however, £3 is nearer the average.[15] Once taken, effects take an hour or two to manifest and last for about 8 hours. These pills come in many different designs, usually named in accordance with their colour or embossed logo. As an appropriate illustration 'yin yangs' have the yin yang symbol printed on them. One of the biggest dangers is of course that it is impossible, without chemical testing, to ascertain the ingredients of the pills. Some dance clubs will in fact provide a testing service on site in an attempt to increase safety. Quick tests like this are, however, fairly inaccurate and no real substitute for a proper laboratory analysis.

The manufacture of ecstasy involves relatively straightforward isomerisation techniques that any chemist could carry out. However, obtaining the raw ingredient is less easy. The process is started using a yellow, oily liquid called safrole. Safrole is often extracted from the root bark or fruit of the sassafras plant. Safrole is actually found in many plants and has a familiar smell akin to that of a sweet shop. Safrole was once added to the soft drink, root beer, but has now been banned following the discovery that it is a carcinogen (causes cancer).

MDMA pharmacology

Essentially, MDMA acts simultaneously as a stimulant and hallucinogen because in terms of its molecular structure it is similar to both amphetamine and lysergic acid diethylamide (LSD). Serotonin reuptake transporters (SERTs), in particular,

have been focused upon by researchers. Like other stimulants such as cocaine and amphetamine, MDMA blocks the neurotransmitter re-uptake transporters for various neurotransmitters and so their effect is prolonged. This, therefore, prevents serotonin recycling. Not only does the MDMA block the transporter but it also causes it to run in reverse, serotonin being transported back out from the axon into the synapse, further perpetuating the high serotonin level.[16]

In fact, ecstasy fires the release of serotonin faster than any other process and its levels rise exponentially. MDMA actually enters the neuron via the reuptake transporter because it has a higher affinity for the transporter than serotonin. MDMA starts to do its work once it has entered the neuron.

The hallucinogenic effects of ecstasy are due to the fact that MDMA stimulates a type of serotonin receptor called 5-HT2A (2ARs). Normally when serotonin binds to the receptor it is rapidly recycled. Hallucinogens, however, bind more tightly to the receptor, causing greater than normal activation. This overstimulation is not the whole story though, as excess serotonin in itself does not cause hallucinations. The process is actually more complex. Serotonin binding causes what is known as a phosphoinositide hydrolysis response, a rise in intracellular calcium levels and hydrolysis of the receptor itself. Hallucinogens do not produce the concurrent rise in calcium and limited phosphorylation of the receptor. It is this difference in the signaling cascade which seems to cause the distortions in sensory perceptions. For example, altered neural signaling in the visual cortex of the brain mimics the effect of light falling on the retina, causing altered images or even interpretations of vision when the eyes are closed.

Of course, as with all addictive chemicals, dopamine is also released in the reward circuit. This effect is both direct and indirect. The release of dopamine is thought to involve both transporter and impulse-mediated processes. Activation of the serotonin 2A receptor in fact stimulates the synthesis and release of dopamine. The impulse-mediated processes are a result of the knock-on effect of serotonin increase. The transporter-effected processes relate to the fact that the MDMA molecule also fits into dopamine re-uptake transporters, thus preventing the removal of dopamine from the synapse. It was not until 1988 that it was realised that dopamine was also involved. It was discovered that pretreating rats with methyl- p-tyrosine, which inhibits dopamine, prevented MDMA toxicity.[17] It has also been shown that destroying all of a rat's dopamine neurons prior to giving them ecstasy, prevents serotonin axonal loss.[18] Further, if L-DOPA, a dopamine precursor, is administered to rats they sustain more neurotoxic damage.[18]

Initially, therefore, MDMA increases the amount of serotonin and dopamine available. This is, however, later reversed. The serotonin deficit is due to the fact that the activity of the enzyme tryptophan hydroxylase is reduced and so less serotonin can be manufactured. Perhaps even more disturbingly there is a lot of evidence to show that both serotonin and dopamine neurons are actually damaged and even destroyed by MDMA. A single high dose of MDMA in rats has been shown to completely destroy 90% of the serotonergic neurons.[19] Similar effects have been shown in primate research at dosages approximating that of recreational users. This leaves us with a potentially big problem, as dead neurons tend not to grow back very well. If they grow back, they tend to do so abnormally.

Monkeys dosed with MDMA, and given 7 years in which to recover, still exhibit abnormal patterns of serotonergic innervation due to incomplete regrowth. These effects of ecstasy are referred to as its neurotoxicity.

Research conducted in 1999 by Hatzdimitrou et al clearly shows microscopic evidence of the damage to serotonergic neurons. The results can be seen in Figure 10.3.

The extent and permanency of the damage to users is likely to be the result of a combination of dose dependency and genetics. Basically however, the more ecstasy used the greater the damage caused. Since a user has no idea what dose they are taking or how their metabolism is likely to deal with ecstasy, it is not a good gamble to take.

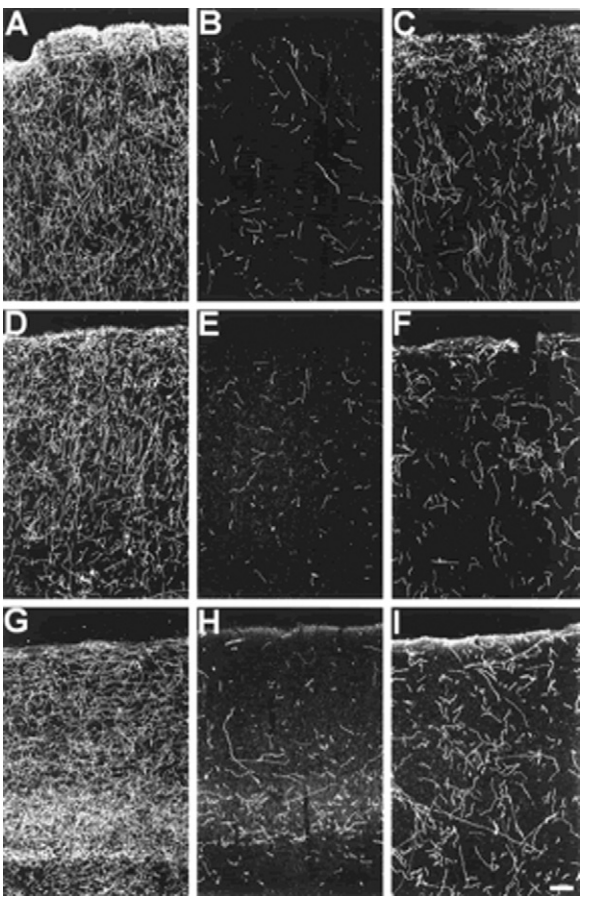

Fig. 10.3 Serotonergic neuron damage. The white lines are the serotonergic neurons running through the cortex. A, D, and G are of healthy monkey brain and show a dense network of neurons. B, E, and H illustrate the brain of a monkey 2 weeks after twice-daily doses of ecstasy; the serotonergic neurons have nearly disappeared altogether. C, F and I illustrate the monkey brain that has had 7 years to recover (mentioned previously); it is still very far removed from that of the healthy monkey brain.[20] PET scans on living human brains shows that this translates to humans in the same way.

The damage to dopaminergic neurons has been shown in the brain areas relating to the pathological changes present in Parkinson's disease and other movement disorders. This appears to be particularly prevalent if ecstasy is taken in combination with amphetamine, which is not at all uncommon.

Research is also showing that cognitive and memory impairments resulting from ecstasy use continue for a year after use, even when biochemical markers return to normal.

Perhaps the most famous problem associated with repeated use of ecstasy is the development of depression that is thought to be a result of serotonin depletion.

This decrease in serotonin is longer lasting than the initial surge and results in the ecstasy 'come down'. When a user starts 'coming down' it is because the number of activated serotonin receptors is reduced, as there is far less serotonin available in the storage vesicles of the serotonin neuronal axon terminals. Users may take more ecstasy to try to relive the positive sensations, but this does not work very well because the serotonin supply is pretty much exhausted; ecstasy does not produce more serotonin, it simply releases it, and so depletes the pre-existing store. It is thought that replenishment of the serotonin store takes around 2 weeks. As the 'come down' proceeds the serotonin depletion manifests with depression, tiredness and irritability. Further compounding this process is the usual neuro-down-regulation of serotonin receptors, in order to try to maintain homeostasis and neural damage.

Serotonin is manufactured from an amino acid called 5-hydroxytryptophan (5-HTP). 5-HTP enters the neuron directly through the cell membrane rather than through a reuptake transporter, then the enzyme tryptophan hydoxyalse turns it into serotonin to be stored in the vesicles. Serotonin takes a while to be manufactured because a few metabolic changes to the protein in the diet have to occur before realising the molecule 5-HTP. Under normal circumstances there is no need for the brain to make vast amounts of serotonin quickly. In contrast, however, the brain can replenish dopamine levels very quickly and so dopamine levels do not reduce at the same rate as serotonin. Ecstasy users often self administer 5-HTP in an attempt to reduce the depression and discomfort experienced after ecstasy usage.

The neurotoxic effects of ecstasy are in fact rooted in dopamine. Following ecstasy use the serotonin reuptake transporters are left vacant. When this happens, dopamine can capitalise on these empty transporters and enter the serotonergic neuron, a place it is not meant to be. Dopamine is actually toxic to serotonergic neurons when it gets inside them. Furthermore, dopamine gets broken down by the enzyme mono-amine oxidase B (MAO-B) as part of natural metabolism, a process which produces hydrogen peroxide (bleach). Hydrogen peroxide is great at oxidising chemicals, known as a reactive oxygen species (similar to a free radical) and it does this inside the serotonergic neuron, a location that is not normally oxidised. This oxidative stress is ultimately what destroys the neuron. It has also been shown that these neurotoxic effects are increased by a hyperthermic (too hot) environment, typical of ecstasy use.[21] Drugs that inhibit the activity of MAO-B, so inhibiting the breakdown of dopamine to hydrogen peroxide, reduce neurotoxic damage.[17] The use of MAO drugs with ecstasy is

however, contraindicated, as there is a risk of life-threatening serotonin syndrome which may manifest with hypertension, tachycardia, sweating, nausea, agitation, tremor, shock and seizures.

Drugs such as Prozac, which are selective serotonin reuptake inhibitors (SSRIs), seem to prevent this neurotoxicity. SSRIs prevent dopamine entering the serotonergic neurons because they block up the reuptake transporters. Prozac appears to be the most effective SSRI for this purpose as it has a very high binding affinity for the reuptake transporter, more so even than serotonin.

People on Prozac tend not to experience very much when they take ecstasy, as the MDMA cannot get into the neuron through the reuptake transporter because the Prozac is blocking it. Some effects are experienced because of its direct impact on dopamine and noradrenaline (norepinephrine), but nothing like what a non-medicated user would experience.

Studies have shown that free radical scavengers such as alpha lipoic acid, vitamin C and L-cysteine can reduce the oxidative stress caused by ecstasy.[22] Whether this is of significant benefit is as yet unknown but it is possible that it might reduce some of the drug-related harm. Further research has shown that transgenic mice, treated to over-express CuZn superoxide dismustase (an antioxidant enzyme) demonstrate neuroprotective mechanisms from ecstasy-induced serotonin depletion.[23] It could be hypothesized, therefore, that increasing one's intake of antioxidants may be neuroprotective.

How does ecstasy feel?

Users take ecstasy primarily because it substantially increases their sensations of connection and affection towards other individuals. It is particularly popular in dance music culture because it also greatly increases one's energy levels so that one can continue dancing without the need for rest or sleep.

Ecstasy seems to tap into a fundamental part of being human, our desire to belong to a collective, a tribe. From an evolutionary perspective, behaviours exist to promote survival of the individual such that they procreate. In more primitive times the chances of survival were greater in a group, hence the positive feelings we experience when connected to others. There is also something tribal and primitive about the music that often goes hand-in-hand with ecstasy use. Often based around repetitive beats and loops the music seems to encourage the development of a trance-like state. In fact, neuroscientists have discovered that loud music actually intensifies the effects of ecstasy at the level of the neuron.

Many individuals also feel that they become more insightful and have a more profound awareness of self and purpose.

Physiological effects

- Pupillary dilation
- Trisma (jaw clenching)

- Bruxia (teeth grinding)
- Increased heart rate and blood pressure
- Insomnia
- Dehydration
- Anorexia (loss of appetite)

Adverse effects

- Death by unknown causes
- Liver damage
- Hyperpyrexia (heatstroke)
- Hyponatremia (low sodium levels)
- Depression
- Mouth ulcers

Ecstasy can lead to hyperpyrexia for a number of reasons. It decreases heat loss by causing constriction of blood vessels in the skin. It masks normal responses to thirst and exhaustion. Users will tend to dance for hours on end and so the increased metabolic activity of their muscles generates a lot of heat. Eventually the body cannot cope with the excessive heat exposure and the internal temperature of the body rises significantly. Should the body temperature rise from the average of 37.2°C to around 40°C the situation becomes life threatening. At 41°C brain death begins. The signs of heat exhaustion are mental confusion, headache, rapid heart beat, muscle cramps and absence of sweating. This may be accompanied by nausea and vomiting. The individual will not be sweating at this stage because dehydration prevents the production of sweat in order to conserve body fluids. When sweating stops the body temperature rises quickly and significantly. Unbeknown to the patient their blood will thicken, increasing the likelihood of clots, particularly in the lungs (pulmonary embolism). If heatstroke is suspected, hospitalisation is necessary. The patient must be cooled immediately. The patient must be moved to a cool area, clothing removed as appropriate and cold compresses (water soaked clothes) applied. The patient must be given water. Alcohol and caffeine are prohibited.

It is worth noting that the dehydrating effects of dancing for hours on ecstasy are well documented, so most users consciously make an effort to drink water. There have, however, been a number of deaths attributable not to dehydration but to water intoxication, in which so much water is drunk that electrolyte concentrations become over-diluted. It was this that killed Leah Betts, in one of the most publicised ecstasy-related deaths. Water intoxiation causes water to move by osmosis from the extracellular fluid into the cells causing them to swell. When this occurs in brain cells they may rupture and be destroyed. This is further complicated by the fact that excessive sweating from prolonged dancing leads to

the excessive loss of electrolytes. Furthermore, ecstasy can affect the pituitary gland such that it produces extra antidiuretic hormone, leading to further water retention. Water retention is more common in women because of their hormone balance.

Teeth grinding and jaw clenching are very common and easily observed. In order to reduce the associated jaw ache, many ecstasy users chew gum or a baby's dummy (a common part of a raver's apparel). Sometimes users may take a supplement of magnesium to try and relax the jaw muscles. Biting of the lining of the mouth frequently leads to mouth ulcers.

Worthy of inclusion are some of the effects related to the behaviours associated with ecstasy use, as opposed to the chemical itself. Vigorous and intense dancing for many hours can take its toll on the body:

- Joint and back problems
- Fungal infections (fungi love warm, moist skin)
- Friction burns on the buttocks ('raver's rash')
- Damaged feet ('techno toe')

Ecstasy and death

Ecstasy is metabolised via several methods of processing in the liver. These processing methods do not work faster with increasing dosages of the drug and so, over a given threshold, higher and sustained drug concentrations will exist. These higher drug concentrations, through taking too many ecstasy pills, may be responsible for ecstasy-related deaths.

It has also been hypothesised that death caused by ecstasy use may be related to one of the enzymes involved in its metabolism called CYP2D6. If this enzyme does not break down the drug, it is thought that it may kill. Some individuals do not possess the gene that makes enzyme CYP2D6 and so die the first time they use ecstasy.

The majority of deaths, thought to be around 100 per year, are believed to be caused not by MDMA itself, but by contaminants. Without chemical analysis it is impossible to know what is actually in the pill. Pills showing the same symbol guarantee nothing, as any drug manufacturer can emboss what they like on the pills; there are no trademarking laws attached to criminals who make drugs. Capsules are particularly dangerous because they are very easy to tamper with. The most common contaminants are methamphetamine, ketamine and PMA (para-chloroamphetamine). Administration of any of these drugs may contribute to the increased likelihood of death.

Ecstasy and addiction

Like other drugs of misuse, ecstasy stimulates the reward circuit and so its use can become addictive in nature. Clinically, what seems more often to be the case

is that ecstasy initiates the addictive processes in the brain and other rewarding drugs are chosen in preference to ecstasy.

Amphetamines

Amphetamine or phenylisopropylamine is a stimulant drug available on prescription that has become illicitly available and much abused on the club scene. Like most of the drugs of abuse, amphetamine has been with us for quite a long time and can be traced back to its herbal roots. Amphetamine is chemically related and so similar in structure and function to a plant-derived alkaloid called ephedrine, isolated from the traditional Chinese medicine ma huang (Ephedra sinica) that has been in use for more than 5000 years.

It was first manufactured back in 1887 at the University of Berlin. Research focused upon the observation that amphetamine had properties as a bronchodilator. Amphetamine became more frequently used after 1928, when it was marketed as the bronchodilator Benzedrine.

Following the later discovery that amphetamine could temporarily relieve fatigue and improve performance through its actions on the central nervous system, it was taken up for use by various military forces. Methamphetamine was much used in World War II by the German and Japanese armed forces. In terms of its abuse it became more popular following the declaration of cocaine as an illegal drug. Amphetamine was still legal, and therefore became the obvious alternative. Medically, amphetamines have been used as decongestants, appetite suppressants and as a remedy for fatigue and narcolepsy.

Amphetamines tend to be subdivided into three groups whose chemical properties and actions are pretty much identical. What differs is their potency, as shown below in order of their varying potencies:

1. Methamphetamine
2. Dexamphetamine
3. D-Amphetamine

Methamphetamine, an amphetamine-related psychostimulant is also synthesized from ephedrine. Both amphetamine and methamphetamine have also been isolated from the foliage of two acacia species without the need for ephedrine as a chemical precursor. The active ingredient of ecstasy, MDMA, is also a derivative of amphetamine. As a point of interest to all the chocoholics out there, amphetamine is a homologue of phenethylamine. This means that it is in the possession of the same chemical functional group and so has similar chemical properties. Notably dopamine also possesses the same functional group. Phenethylamine is found in chocolate and a range of fermented food products. It is therefore chemically quite feasible for one to become addicted to not only chocolate but also cheese. Realistically, however, to experience true psychoactive effects from these foods one would be required to consume a very large quantity, in order that sufficient concentrations reach the brain.

Amphetamine abuse has been widespread. It is the drug of choice for anyone needing to stay alert for prolonged periods, such as long distance drivers, students, doctors and clubbers. It must of course be mentioned that amphetamines are also anorectic. This means that it not only increases energy but also suppresses the appetite. For these reasons amphetamines have been used to treat obesity and so have been abused by many wanting to lose weight for cosmetic reasons, such as catwalk models.

Amphetamine usually takes the form of a white, odourless, crystalline powder. More recently however, as a marketing ploy to make the drug more appealing, colourants might be added. It is usually ingested orally and has a bitter taste. Sometimes, however, amphetamine is snorted as opposed to orally ingested because it is absorbed faster and so takes effect more quickly. It dissolves readily in water and alcohol so can be mixed into drinks for ingestion. Its ability to be dissolved in water also makes it suitable for intravenous injection, which creates a greater rush and sense of elation.

Relatively recently, amphetamine has begun to be smoked. The smokable form is actually methamphetamine hydrochloride commonly known as 'ice' or 'crystal meth'. Previously, in powder form a very high temperature was needed to cause vapourisation. 'Ice' crystals melt much more easily and produce a potent vapour. Ice tends also to be less adulterated due to the difficulty of cutting the larger crystals with bulking agents.

In the past, non-chemists have tried to extract methamphetamine from Vick's inhalers by soaking them in hydrochloric acid and then separating the mix with alcohol. However, this method is ineffectual. The methamphetamine used in the inhalers is the L- isomer which is not particularly potent, but sufficient as a decongestant. It is the D- isomer that has potent physiological effects. To fully eliminate any potential for abuse, the Vick inhaler's formulation was changed in 2001.

Currently, several methods of making amphetamines are possible, but the easiest simply requires ephedrine, lots of boxes of matches, some iodine, water and ethanol.

Amphetamine effects

- Increased energy and stamina
- Decreased appetite
- Increased alertness
- Increased confidence
- Increased sexual drive

Adverse effects of chronic use

- Sweating
- Restlessness

- Nausea
- Rapid heart beat
- Irregular heart beat
- High blood pressure
- Headaches
- Insomnia
- Anxiety
- Irritability
- Panic
- Depression
- Aggressiveness
- Paranoia
- Psychosis
- Schizophrenia

Fatal toxicity

Deaths directly attributable to amphetamine use include hypertensive cerebrovascular haemorrhage, ventricular fibrillation or hyperpyrexia.

Amphetamine pharmacology

Amphetamine binds to the monoamine transporters and so increases extracellular levels of monoamines including dopamine, noradrenaline (norepinephrine) and serotonin. The behavioural reinforcement associated with addiction to amphetamines is related to its actions on the dopaminergic activity in the mesolimbic system and so this text will focus on this aspect.

This dopamine rise occurs because amphetamines are similar in molecular structure to dopamine, and so can enter the presynaptic neuron via its dopamine transporters. Additionally, amphetamines can diffuse directly through the neural membrane. Once inside the presynaptic neuron, amphetamines force the dopamine molecules out of their storage vesicles and expel them into the synaptic gap by making the dopamine transporters work in reverse. To compound the problem, amphetamines also appear to work as monoamine oxidase inhibitors and so reduce the re-uptake of dopamine.

Sustained high doses of amphetamines produces a persistent depletion of dopamine in the reward circuit. The brain interprets this as being of potential detriment because it is not any longer receiving reward. This results in activation of the excitatory fight-or-flight mechanisms and drug craving.

Lysergic acid diethyl amide (LSD)

LSD is categorised as an hallucinogenic or psychedelic drug. These kinds of drugs have been in use for thousands of years in quite diverse ways. In more recent times, following the discovery of the semi-synthetic LSD, much of the use of psychedelics has focused on their influence upon the creative process. Users often describe the feeling that all creative boundaries are removed allowing unhindered contact to expression of one's inner self, in a sense to touch the mind. LSD often provides the user with an extraordinary experience that may, for example, inform and inspire their creativity.

LSD is synthesised from a granular fungus called ergot that is parasitic on certain grains and grasses, typically rye. Ergot itself contains several alkaloids that can affect neurotransmission and the circulatory system. Historically, since the 12th century, ergotamine poisoning has been documented, and entire villages have been known to suffer from its ill effects after the village bakery used infected grain. Commonly, the symptoms of ergotism include diarrhoea, nausea, vomiting, headaches, hallucinations and psychosis. Gangrene may also occur as a result of vasoconstriction in poorly vascularised areas like the extremities.

Historically, many cultures and religions have used hallucinogens to enhance the spiritual experience. Typically, psychoactive mushrooms, iboga bark or peyoti cactus were taken to trigger states of introspection and insight into the metaphysical realm.

Albert Hofmann is the Swiss scientist who is creditied with the discovery of LSD in 1938 while studying the fungus for use as a pharmaceutical stimulant of uterine contractions. It was only 5 years later, however, when Dr Hofmann discovered the psychedelic effects of LSD after accidentally absorbing some on his fingertips. In his book *LSD: My Problem Child* Hofmann was quoted as saying 'In a dreamlike state, with eyes closed (I found the daylight to be unpleasantly glaring), I perceived an uninterrupted stream of fantastic pictures, extraordinary shapes with intense, kaleidoscopic play of colours'. Three days later, intrigued by his experience, Hofmann intentionally ingested a large dose of LSD. The dose was large enough to cause him to experience such abnormal cognitions that he believed he had been possessed by a demon, that his next-door neighbour was a witch and that his furniture was threatening him. Gradually, the experience became less intense. 'Now little by little I could begin to enjoy the unprecedented colours and plays of shapes that persisted behind my closed eyes. Kaleidoscopic, fantastic images surged in on me, alternating, variegated, opening and then closing themselves in circles and spirals, exploding in coloured fountains, rearranging and hybridizing themselves in constant flux'. The following day Hofmann felt refreshed, 'Breakfast tasted delicious and gave me extraordinary pleasure. When I later walked out into the garden, in which the sun shone now after a spring rain, everything glistened and sparkled in a fresh light. The world was as if newly created'. Famously, others such as Aldous Huxley later recorded their own experiences of LSD, his in the infamous text *The Doors Of Perception* which was the source for the name of the equally infamous band The Doors.

When introduced as the drug Delysid by Sandoz Laboratories in 1948, LSD was marketed as a psychiatric panacea, a remedy for schizophrenia, criminality, homosexuality (!) and alcoholism. Amazingly, in the late 1950s, Dr Humphrey Osmond gave LSD to alcoholics in Alcoholics Anonymous who had failed to quit drinking. After 1 year, around 50% of the study group had not had a drink. No other study has ever been so successful. Clearly however, substituting one drug for another is not recovery. As scientific data started to build it became clear that the drug had no lasting affect in the treatment of psychiatric disorders, and carried with it a high potential for abuse and so was made illegal. In fact, psychotic crises and acute panic disorders were frequently triggered by its use in high doses.

LSD was of such great interest for a time that the CIA conducted a secret project called MK-ULTRA with the intention of researching the use of LSD as a pharmaceutical route into mind control. MI6 was also involved in similar research in order to find a 'truth drug'. Many research subjects committed suicide or ended up in psychiatric hospitals and so the project moved onto the investigation of other substances instead.

Surprisingly, when initially chosen as a drug for recreational use, most users were academics and medical professionals. A little later during the 1960s, much interest was generated around the use of LSD due to the success of bands such as The Grateful Dead, Jefferson Airplane, The Beatles and The Rolling Stones. LSD became symbolic of a generation of hippies, an almost religious movement that supported sexual liberation, the opposition to war and the rejection of the establishment.

The popularity of LSD dwindled in the 1980s but made something of a comeback with the advent of the acid house scene in the 1990s. Acid house music focussed upon the use of simple tone generators, drum machines and samplers, leaving LSD to fill in the creativity gaps! The usage trends of LSD are currently pretty stable. The majority of users are young, between the ages of 16 and 23 years. In the UK it is estimated that around 83 000 individuals are regular users.

In its pure form LSD is typically a colourless and odourless, slightly bitter tasting liquid. LSD is usually dropped on to small squares of blotting paper called tabs. Often, these tabs have cartoon like pictures on them as a form of branding. A typical tab of LSD may contain anything between 100 and 500 micrograms although effects can be experienced using as little as 20 micrograms. Small tablets called microdots are also available. Due to the fact that an active dose of LSD is so small it is easy to manufacture and supply, 5 kg of LSD could provide 100 million doses. One dose costs in the region of £2–3. It is of course impossible to know what dosage one is taking. This can be problematic because undesirable effects are more likely in response to higher doses.

LSD pharmacology

LSD affects a large number of postsynaptic neurotransmitter receptors including those of many dopamine, serotonin and adrenoreceptor subtypes as indicated in Figure 10.4.

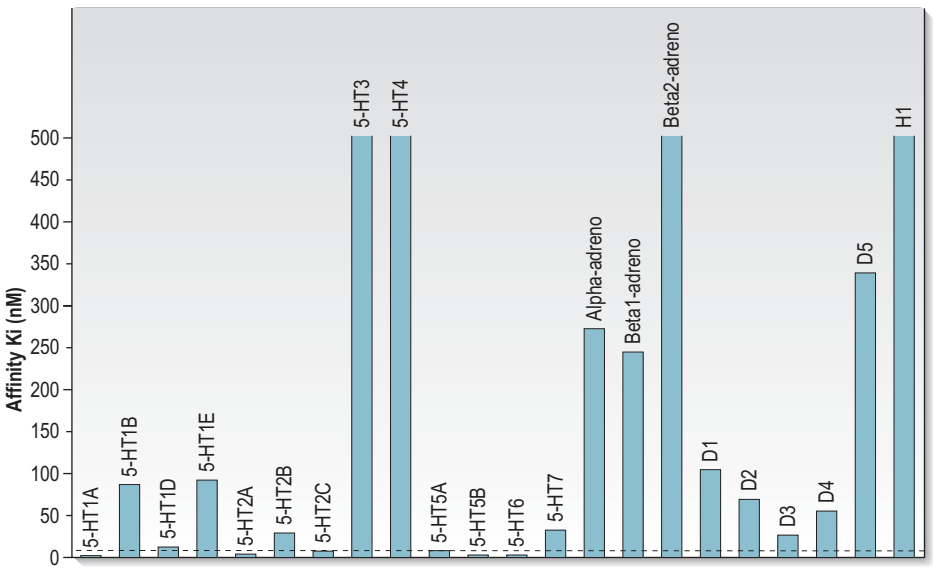

Fig. 10.4 The neurotransmitter sites affected by LSD.

With reference to the hallucinogenic effects of LSD it appears that its binding affinity for the 5-HT2A receptor is responsible. 5-HT2A antagonists effectively block any hallucinogenic action. So what LSD seems to do is artificially activate serotonin receptors when there is actually no serotonin being released. Typically the neuromodulatory effects of the serotoninergic system moderates awareness of one's environmental surroundings and filters the information prior to processing. In this way only enough information is processed as deemed necessary for survival. The result of this is that the filter is opened by LSD so that neural pathways get stimulated, even though the brain had no intention of it happening as there was no causal stimulus. For example, LSD might fool the visual cortex into thinking that it is receiving input from light falling on the retina when this actually is not the case. It has been suggested that LSD shifts action potentials toward the right hemisphere, the side of the brain predisposed to creativity.[24]

Although most research into LSD focuses on serotonin transmission, it is becoming clear that dopamine is also profoundly affected and so influences the addictive potential of LSD. It is generally accepted that LSD itself is not addictive because it does not produce compulsive drug-seeking behaviour. Its dopamine agonist actions can, however, stimulate reward pathways which leads users to try other rewarding drugs with greater addictive potential. Research conducted on pig brains using PET scans indicates that LSD has a similar magnitude of effects on dopamine receptors as amphetamine, but of longer duration.[25] LSD trips occur in two temporal phases, the first phase mediated by serotonin and the second by dopamine.

The effects of LSD

Due to the broad spectrum of pharmacological activity of LSD its effects are wide reaching and highly variable. The effects depend on the dosage taken, the user's personality, mood and expectations. The effects take 30–60 minutes to start and last for up to 12 hours.

The hallucinogenic experience appears to affect consciousness in several ways. At the level of sensory perception, sensations of vision, touch and hearing can all become distorted. It is also quite common for sensory information to be coupled to another, a condition known as synesthesia. For example it is possible for sounds to be seen and colours heard. In terms of cognitive functioning one's experience of self or consciousness appears to be expanded. Apparently day-to-day experiences may take on a symbolic or cosmic meaning. This is seen as an attempt by the brain to integrate the intensified sensory input with equally intense meaning. The hallucinations themselves take on an infinitely variable form because they are subconsciously informed by one's previous experience. It is common for static surfaces to appear to move and moving objects to leave trails. Music appears intensified and sound often manifests with echo-like distortions.

The effects of LSD may include the following:

- Hyperthermia
- Pupillary dilation
- Tachycardia
- Hypertension
- Insomnia
- Dry mouth
- Hallucinations
- Temporal distortions
- Fear
- Depression
- Psychosis
- Schizophrenia

So called 'bad trips' can occur. This is usually the case if the user takes the drug in an unsettling or unusual environment. LSD can also trigger a state in which the user may lose the ability to make adequate judgments and may not be aware of their actions.

Due to the fact that LSD can trigger uterine contractions it is not considered safe for use by pregnant women. Some research also implies that LSD may cause developmental abnormalities in the fetus. This data is however limited and complicated by the fact that illicit users may have used contaminated samples, or used other psychoactive drugs concurrently.

Many users talk of a phenomenon commonly known as 'flashbacks' whereby a user perceives themselves to be experiencing LSD effects days, months or even

years after actually consuming the drug. While often the sufferer is aware that the experiences are not real, some individuals experience severe anxiety or derealisation whereby they feel divorced from reality. Typically these flashbacks are of short duration but in some may persist. Psychiatry now recognises a disorder known as Hallucinogen Persisting Perception Disorder (HPPD). This condition is more highly reported in those individuals who also suffer other psychiatric conditions, so it could be hypothesised that they are more vulnerable to LSD effects. The mechanism of HPPD is not yet known but tends to focus upon changes to the occipital lobe causing visual distortions. It has been shown using electroencephalograms (EEGs) that HPPD patients have significantly shortened occipital visual evoked potential latency than experimental control subjects.[26] Certainly the suggestion that LSD remains in the body has been experimentally disproved.[27]

Nicotine

Nicotine is the chemical constituent of tobacco that causes dependence. It is the most widely used addictive drug in the world. Although banned by many European and Asian nations in the 17th century it is now legal in most countries. Smoking is the principal, avoidable cause of premature deaths in the UK. It kills more people than alcohol and all the other drugs combined. It is the only known powerful carcinogen legally produced and sold. In the UK, it kills 114 000 people every year, accounting for one-fifth of all deaths.[28] It is also estimated that 364 000 patients are admitted to NHS hospitals each year due to diseases caused by smoking. This translates to 7 000 hospital admissions per week or 1000 per day.[29]

The tobacco plant, *Nicotiana tabacum*, is named after Jean Nicot, a French ambassador, who sent tobacco from Portugal to Paris in 1550. Its first use appears to have been by the Native American Indians over 2000 years ago. Nicotine is a naturally occurring chemical found in several of the 'nightshade' family of plants, which includes tomatoes, potatoes and aubergines. Nicotine is quickly absorbed, reaching the brain in around 7 seconds when inhaled, as is the case with most smoked drugs. Nicotine is a stimulant drug with neurotoxic effects. The neurotoxic effects are particularly strong in insects and nicotine has been used as an insecticide historically.

Most commonly, tobacco is smoked whereby much of the nicotine content is burned away. Nevertheless, enough is absorbed to provide significant effects. Chewing tobacco and snuff deliver a much stronger dose of nicotine.

Nicotine is a highly addictive drug with widespread effects on the nervous system. It stimulates the release of dopamine, vasopressin, arginine, noradrenaline (norepinephrine) and beta endorphin in the brain. Tobacco also contains other ingredients that have an effect on raising dopamine levels due to their inhibition of the monoamine oxidase (MAO) enzyme that normally breaks it down. Nicotine also binds directly to the brain's acetylcholine receptors causing an increase in blood glucose levels, heart rate, blood pressure and respiration rate.

Tolerance builds to the effects of nicotine and so users will increase the number of cigarettes smoked until they get to a level that seems to suit them. If users switch to a brand with lower nicotine content they then seem to increase the number of cigarettes smoked until the brain receives the dose it requires. Nicotine differs from the other substances of abuse not in its potential for causing addiction but in that it does not produce intoxication and cognitive impairment. It is currently socially acceptable (although at the time of writing this is changing) and is intertwined with powerful social forces, being somewhat glamourised by the young. It does not therefore tend to cause the breakdown of the family unit or the loss of jobs. It simply kills most of those who use it.

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CHAPTER 11

Qi, the story so far

Rainbows are beautiful. Who needs leprechauns?

(Kim Wager)

Introduction

Qi is the fundamental concept underpinning Chinese medical thought and indeed permeates many aspects of Chinese culture. Unfortunately to the Western mind it tends to be the first stumbling block in our understanding of the system. Chinese medicine is based around the concept of *Qi*. It is therefore essential to elucidate what *Qi* is; this is perhaps the biggest hurdle to traditional Chinese medicine (TCM) being accepted into the mainstream.[1] *Qi* is often translated into English using esoteric language such as 'life force' or 'vital energy'. Of course, in a sense, these terms are absolutely correct but they do not help us to actually conceive of what *Qi* is or help us to understand anything about its nature. The vast majority of acupuncturists subscribe to such definitions, suggesting that *Qi* is an indefinable, unmeasurable power behind everything. Clearly this does not serve to increase understanding. Western medical professionals or those lay people with a vague knowledge of science are often quite dismissive and do not believe in *Qi* because it cannot be measured, unlike electricity for example. It is our fear that a potentially powerful system of medicine will be lost to ridicule if it is not allowed to leave behind some of its outdated concepts. It is hoped that through works such as this book, models of Chinese and Western medicine might ultimately be brought closer together, or at least that discourse is opened between the two schools of thought. It is too often the case that neither school understands the other, nor attempts to do so. This thereby perpetuates a mutual lack of respect which cannot be constructive.

We would suggest that *Qi* is unlikely to be something new or different, it is just a foreign word for us to translate. Whether one is geographically rooted in the East or West the laws of physics, and hence biology, must work the same. In fact, the concept that no place in the universe is 'special' and that the laws of physics are the same for everyone is the fundamental meaning of Einstein's theory of special relativity.[2]

The notion that the body possesses some energy vital to life is certainly not unique to Chinese medicine. Hindus refer to *prana*, the Tibetans to *rlun*, the Japanese to *Ki*, the Hebrews to *ruach*, the Greeks to *pneuma*, the Romans to *spiritus* and countless others. These all refer to a non-material, often supernatural medium that imparts life to otherwise inert matter.

The metaphysical doctrine of Vitalism suggests that life is caused by some non-physical entity. It suggests that the laws of physics alone cannot explain life. Upholding this mysticism is often quite attractive to practitioners of Chinese medicine because it sets it apart from Western medicine, but it also hinders its acceptance into the mainstream. To be part of an integrated healthcare system we need at least a degree of mutual understanding. So, to that end we need to start some sort of translation process.

Mechanistic Materialism theorising that life emerges as a result of scientific law sits much more easily in the modern world, is no less exciting, but can be conceptually understood. It is within this paradigm that we firmly stand. Acupuncture must work according to the laws of science because nothing can stand outside of these laws.

The laws of physics governing the very creation and workings of the universe are scientific fact. It makes no sense to ask what lies outside the universe because space is a property of the universe itself. We cannot create new phenomenon. Even Chinese medicine must lie within the confines of scientific reality. Biological systems are of course subject to the laws of science, as is the rest of the universe. As soon as we look for something outside of the laws of physics we are going to start having conceptual problems. The 'New Vitalism', the search for *Qi* or some other kind of energy unique to life is, in our view, bound to end in disaster and renewed scepticism. The nature of *Qi* must already be a known quantity; if any 'new' energy existed it would undoubtedly have been discovered by X-ray telescopes or in particle accelerators. We are therefore stating that *Qi* as an entity does not exist. It is only a word that we must seek to comprehend. Its understanding is often hindered by describing it through the use of language that is generally not part of a typical Westerners' vocabulary. It is also true that in searching for something magical or mystical one is distracted from the magnificence of the truth that already envelops us. *Qi* is not a 'new' kind of energy and should be explainable by current scientific knowledge.

It is our opinion that acupuncture is, or at least should be approached like any other science and, if it is to be accepted in the West, then it needs to be treated as such. From the standpoint of science, if there exists no proof for the validity of any theory it remains just that, theory. Until a theory is substantiated it cannot be accepted as fact. From the perspective of the authors there is, as yet, no scientific proof for the existence of any mystical 'life energy'. Beyond doubt, life energy exists, but it must surely be explicable? If we work with the human body we must, by definition, be working with biology and therefore by reduction, chemistry and by further reduction, physics. By no means is it considered that this approach invalidates Chinese medical practices but that the explanations of their ingenuity are no longer valid in the face of current scientific knowledge.

This chapter seeks to critically review many of the current postulates as to the nature of *Qi*. This will form a springboard for the following chapters which will

explain our standpoint on the subject of *Qi* and the mechanisms of acupuncture.

Current state of knowledge

Biology is simply the study of life and has fascinated us since the dawn of time. At the time of the yellow emperor Huang Di, who reigned from 2697 to 2598 BCE, ghosts, spirits and demons were believed to be the transmitters of disease. Physicians of the day were shamans who used medicine in conjunction with incantation and ritual.[3]

By the later Han dynasty there was a great shift in the medical paradigm. Health and disease were seen as subject to the principles of natural order and could be observed and understood. Like all scientists, the Chinese have sought to discover that which animates us. It is this energy of animation that is described as *Qi*. Unlike many ancient cultures the Chinese did not bestow this power of animation on the gods, instead, life was considered a result of certain universal guiding principles, governing all things: the *Tao*. Taoists believe that *Qi* pervades the entire universe and that all phenomena are 'immersed' in *Qi* whether alive or dead.[4]

Some authors describe *Qi* as life energy; *Qi* is seen as being that which animates living things. A living being is full of *Qi* and a dead one has no more *Qi*.[5]

Defining life is in itself a difficult problem. Its definitions are many and varied. The distinguished evolutionary biologist, John Maynard Smith, describes life as any population of entities that has the properties of multiplication, heredity and variation. Information theorist, Stuart Kauffman, states that life is an expected, collectively self-organised property of catalytic polymers. Equally reknowned experts propose that life is the flow of energy, matter and information or that life is a self-sustained chemical system capable of undergoing Darwinian evolution. Currently, biologists rely on the presence of deoxyribonucleic acid (DNA) or diagnostic proteins to identify life.

Importantly, *Qi* is also considered to impart consciousness, mental acuity and spirituality. With regard to human life, the medical and legal profession consider that the activity of the brain is the indicator of life.[6] Others consider the converse to be true – that the brain translates a signal generated by some uplifted consciousness.[5] In Western thought these 'higher' states are considered to be a result of physiological processes; notably neural activity in the brain. The neurons are the channels through which we think, act, imagine, feel and remember. It is through the synapses themselves that our fundamental traits and beliefs are encoded. The self is shaped by a blend of genetics, environment and experience.[7] To understand what it is to be a human, a spiritual being, the storage of information at the synaptic level and the complex interaction of information systems in the brain must be understood. Indeed it is now possible, using neuroimaging techniques, to locate and observe the mechanics of rage, violence, humour, mother-love and even self-awareness,[8] and so it is felt that the brain will

ultimately comprehend itself scientifically. Several researchers have shown that acupuncture produces specific changes in the metabolic activity of several areas of the brain and so is proven to have real physiological effects.

Some authors, however, suggest that *Qi* actually pervades all things whether they are alive or inanimate. Kaptchuck states 'Chinese thought does not distinguish between matter and energy, but we can perhaps think of *Qi* as matter on the verge of becoming energy, or energy at the point of materialising'.[9] While still being referred to as 'that which animates life' it is seen as 'Immaterial yet essential, the material world is formed by it.'[9]

Traditional Chinese medicine has never considered energy and matter to be separate, but as extremes of a continuum. In this way matter is understood to be made up of energy of a certain density. As shown in Figure 11.1 below, the Chinese character for *Qi* supports this concept of the duality between energy and matter. It indicates a subtle substance (steam) deriving from a coarse one (rice) during the cooking process.

Some suggest that *Qi* can be directly seen using various methods. Kirlian photographic phenomena are, for example, sometimes referred to as being capable of imaging the radiant *Qi* of the body, sometimes referred to as its aura. Semyon Kirlian himself claimed the images were physical proof of the life force.[10] This concept will be explored more fully later in the text but it is sufficient to say at this point that this seems rather unlikely.

To complicate the issue, there exist within the field of Chinese medicine several different types or aspects of *Qi*, depending on context. In a sense there are two aspects to *Qi*, one as life force, and one as a communication medium through acupuncture meridians.

Western scientific thought also describes fundamental concepts of energy in general terms and then seeks to describe all phenomena with respect to these concepts:

1. Energy is a physical property possessed by an object that measures its capacity to make changes to other objects. These changes may include speed of motion, temperature or position.[11]
2. The four fundamental interactions concerned with existence itself are gravitational interactions, the weak and strong nuclear interactions and electromagnetic interactions.
3. The concept of duality in matter and energy is not uniquely Chinese and is not at all unlike Einstein's theory of relativity which also

Fig. 11.1 Chinese character representing *Qi*.

considers matter and energy equivalent and interchangeable according to the famous equation $E = mc^2$. It describes a situation whereby anything with energy has mass and the mass is related to the amount of energy.

So, the human body and life is seen as a direct result of the above-mentioned fundamental interactions.

We will now seek to explore several possibilities with regard to Western scientific correlates for *Qi*.

Qi as 'life force'

Several authors, notably Cohen,[5] and Beinfield and Korngold,[12] suggest that *Qi* is that which creates life and is in fact only present in living things.

It is our opinion that some fundamental energy which could be described as *Qi* permeates all things organic, inorganic, alive or dead. Clearly not all matter is alive, but its apparent inanimacy implies that there is no movement or energy within its structure. However, this is an incorrect assumption; atoms, the building blocks of all matter and of course the human body too, are never at rest. Even a seemingly inert lump of rock is teeming with activity at the atomic level. At absolute zero, atoms still move and therefore exhibit an inherent energy. To be motionless would contravene Heisenburg's Uncertainty Principle. This principle is seen by some to be the central feature of quantum theory. It basically describes the fact that it is impossible to know both a precise momentum and a precise position for small particles such as atoms or electrons, for example.[13] In relation to the above-mentioned atoms, this means that atoms cannot stop moving because if they did, we would know where they were and that they had zero motion, and that is against the Uncertainty Principle.[14] So, the energy of movement or animation, kinetic energy, is present in all things, dead or alive, always.

Kirlian photographic phenomena are sometimes referred to as being capable of imaging the radiant *Qi* of the body, sometimes referred to as its aura, and even of proving the presence of acupuncture points and channels.[15–20] Our opinion is that this is a fallacy. Kirlian photography is a form of high-voltage contact print photography. When an object on the photographic plate is subjected to an electric field, an image is created on the plate. Many studies have now proved that the images are related to corona discharge effects due to the fact that moisture in the objects is ionised by the high voltages used. It is the corona discharge that colours the photographic dye. This has been proved by the fact that when an organism dies its image should disappear. This is not however the case, the image remains the same as long as the water content of the corpse remains constant.[10] It is not a phenomena exclusive to living things, for example electric power cables exhibit it. The use of corona discharge is also the way with which photocopiers and air ionisers work and is clearly not related to any life force as such.

Meridian *Qi*

The concept of *Qi* and the concept of the channel as a means for its transmission and the acupuncture mechanism are so closely related that most research to date focuses on attempting to comprehend meridians in order to define *Qi* and so this is well worthy of review. Our opinion is actually that there is no such thing as an acupuncture meridian. The meridian concept just served as a hypothetical descriptive model that ancient Chinese doctors used in order to attempt to explain phenomena that they could not yet understand. This is exactly the kind of thing that human beings have done through the ages; if they do not understand something they invent an explanation satisfactory at the time. For example, until relatively recently it was accepted that the movements of the stars and planets was due to the flapping of the wings of invisible angels.

It is now a well-verified fact that there are numerous locations on the surface of the body that have lower electrical resistance compared to the surrounding tissues, and that the distribution of these points delineate several fixed routes.[1] These points correspond to those accepted by TCM theory. It is postulated therefore by some that *Qi* is a mixture of electromagnetic and subtler energies.[21] To our minds, 'subtler energies' is rather a vague phrase. It implies some kind of energy that remains unknown to the laws of science; this is an unlikely prospect. We consider that it might be the case that some feel the need to uphold some mysticism around the concept of *Qi*; is electromagnetism itself not worthy of investigation?

Electrical properties of 'meridians'

Interestingly, research has shown that the low electrical resistance property of acupoints remains after death.[1] This implies that low resistance properties are not attributable to physiological processes but to a physical property and again to the fact that *Qi* is perhaps not present in only living organisms. If this is the case, then, in some way, the anatomical structure of human tissues must have inherent electromagnetic properties. Factors which could contribute to this phenomenon could, for example, be tissue density or relative ion permeability. We would also like to mention that some caution should be taken in blind acceptance of some of the information regarding electrical properties of the meridians. For example, many studies compare the impedance of acupoints relative to the whole body by getting the subject to hold one of the electrodes. This is likely to be rather inaccurate since, without doubt, enormous electrical variability exists throughout the body. It is also true that the pressure with which electrodes are applied to the skin, proximity to blood vessels, moisture differences and even emotional state (via autonomic effects) can all affect the readings.

Yung postulates that a meridian channel could be a lossless electromagnetic transmission line and that *Qi* is a wave riding on the line with acupoints as its nodes.[1] We have some issues with this hypothesis. In order for the acupoints to be at the nodes of an electromagnetic wave the acupoints would need to be

evenly spaced exactly one wavelength apart; clearly, assuming the standard locations are correct, this is not the case. Yung goes on to explain that in health, although the distance between the acupoints varies, due to variations in electromagnetic properties such as the dielectric constant in the tissues, the corresponding distance in the transmission line does not vary. Yung also postulates that when the standing wave is propagated under healthy conditions energy does not get lost. Yung suggests that if the corresponding organ to a channel is diseased its transmission properties change, the line is no longer lossless and energy is lost at the acupoints.[1] This postulate means therefore that there should exist an internal conducting line that communicates with the surface of the skin at the meridians. We believe this to be inaccurate because this would imply that in order to be lossless, in health the entire transmission line (not the line at the skin's surface) would exhibit identical transmission properties. This is unlikely to be the case as the structure of human tissue is so variable. It also implies that in health energy is not lost at the acupoints; they should therefore not be electromagnetically definable unless there is ill health and this is not the case.

It should also be considered that, by definition, a transmission line stores energy and moves it from one place to another. In order for this to be a lossless line it must absorb energy from a generator and return it back to source without dissipation. It is the opinion of the author that whether the body is in health or disease it is an unrealistic postulate in that ohmic loss due to the resistance in the line (tissues) is inevitable. Bearing in mind the existence of research into the thermal characteristics of the acupoints, whereby they are warmer than adjacent tissues, this energy loss (as heat) is implicit.[22]

Yung uses this idea that energy loss exists during a diseased state to suggest that acupoints are like capacitors that can be charged or discharged according to the needle technique chosen; how this might occur is not explored. In terms of electronics, capacitors store electromagnetic energy, like a battery. In order for a capacitor to hold energy, its stored charges must be separated in space (perhaps across cell membranes). Should the capacitor be short circuited it will be discharged. Should this theory be valid, we therefore postulate that needling could 'short circuit' the acupoints and thereby drain energy. With regard to charging the capacitor (acupoint), the mechanism must be more complex in that energy needs to be supplied. It is possible that the mechanical energy introduced to the system via the needle technique be converted to electromagnetic energy through some property of the tissues. Certainly according to the first Law of Thermodynamics this mechanical energy must be converted; some will be converted to heat but it is feasible that some energy then is transferred to the capacitor (acupoint). Piezoelectrical properties (mechanical deformation creating electrical energy) are a possible mechanism for this phenomenon. It is also possible that acupoints could be considered as variable capacitors and the needle as an inductor. An inductor is a passive electrical device usually made of wire, often a coil. The manipulation of the needle could cause the circuit to store or release energy due to the disruption of the electromagnetic field. This could result in altered oscillation characteristics of the electromagnetic wave due to Lorentz forces (forces exerted on charged particles like electrons in an electromagnetic field) acting on the electrons in the needle during its manipulation.

Through this method it is suggested that the wavelength of the electromagnetic wave might be changed such that total capacitance, resistance and impedance then behave so as to once more form a steady state electronic circuit. We would suggest therefore that rather than implying a system of lossless transmission lines, Yung is really modelling his system in a way similar to electronic circuit diagrams and that loss maybe is considered small enough to ignore in practical terms.

This steady state circuit model is very interesting given the fact that the very nature of a human body is to provide homeostasis and that acupuncture seeks to support the process. It is, however, at this time just conjecture. This model in effect describes an electronic circuit that, when in a steady state implies health; the wave is in a natural oscillation state and in disease a disordered oscillation state is occurring. As for what makes up the conduction medium this needs more investigation.

Electrical transmission

Electromagnetic current conduction can occur in three ways: metallic, ionic and semi-conductor. Metallic conduction is best visualised as a cloud of electrons moving along the surface of a metal. Since the human body contains no wires this means of conduction is excluded as a possibility. Ionic conduction occurs in solutions by the movement of ions. Ions are electrically-charged atoms or molecules. Ions are much larger than electrons and so move somewhat laboriously through their conducting medium. Due to this fact, ionic currents only travel short distances, for example across nerve cell membranes. Semi-conductors can only carry small currents because they lie somewhere between a conductor and insulator but do conduct over large distances.

Semi-conduction only occurs in materials that have an orderly molecular structure such as in a geometrical crystal lattice (Fig. 11.2).

The interesting fact here is that Gyorgyi pointed out that the molecular structure of many parts of the cell was regular enough to produce semi-conduction.

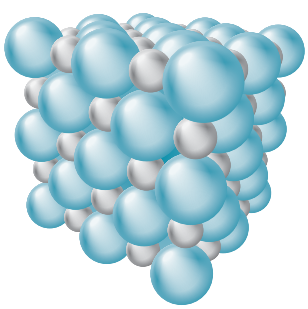

Fig. 11.2 A crystal lattice.

He suggested that protein molecules could be linked in a way such that electrons could flow along the chains over long distances.[23]

Gyorgyi likened this process to electron flow in photosynthesis (in plants) whereby electrons cascade step by step down a staircase of molecules, losing energy with each bounce. However, he suggests that in protein, semi-conduction energy could be conserved. We would like to suggest that electron transport chains that occur in mitochondria (in humans) in order to convert energy to adenosine triphosphate (ATP), the energy currency of life, are a phenomenon worth further investigation later in this text. Experimentally, semi-conduction in tissues has been proved by observation of the Hall effect in mammalian limbs whereby the application of a magnetic field diverts charge carriers perpendicular to the direction of current flow and creates a separate, measurable voltage. True conductors do not exhibit this phenomenon due to the nature of the metal.[10] However, semi-conductors do, and so mammals do exhibit semi-conduction properties.

It is therefore implicit that there is a structure to the line. There must be some structure that forms the 'path' for energy flow. In order to be a conductor with little or no resistance, that medium would have to be a periodic ion lattice (a type of crystal) which would produce coherent constructive interference of the wave. It is also possible that the medium could be a heavily doped semiconductor or some other form of superconductor. The only issue regarding superconductors is that they operate at temperatures around absolute zero and hence superconductivity is not a likely transmission route in living organisms. It is important to note that crystals are not necessarily hard substances like diamond but in living tissues the structures are flexible crystalline arrays called liquid crystals.

It is well known to biochemists that cell membranes, steroids, glycolipids, DNA and many other structures are liquid crystals. It is also known that some viruses organise themselves as liquid crystal arrays.

This field of research into biologically occurring liquid crystalline nanostructures is known as bio-mimetic chemistry. It could be hypothesised that considering proteins are chiral (handed) molecules they could behave as ferroelectric liquid crystals. This could be confirmed by the fact that ferroelectric crystals respond very well to applied fields and so perhaps give some clue as to how acupoints appear to respond to the application of magnetic fields.

It is also interesting to note that acupoints are temperature sensitive. Some liquid crystal molecules change orientation according to temperature change, a property known as thermotropism and so their conductive properties would also change. This could provide clues as to how moxibustion, a method used to apply heat energy to an acupuncture point, might provide its apparent therapeutic effects.

It is possible that the transmission lines Yung refers to are nerve fibres, but these are not a lossless medium; synaptic potentials are decrementing.[24] However, that said, the nervous system compensates for this by virtue of the neuronal axon hillock serving as an analogue to digital converter such that action potentials are not generated until a certain threshold of membrane depolarization is reached and therefore, in a sense, this might support Yung's concept of a lossless line. This process, the massive inflow and outflow of ions does, however, use some energy.

We would suggest therefore that the energy that drives physiological processes should also be explored as a correlate for *Qi*.

Interestingly, the aforementioned semi-conductivity is a concept postulated by Becker with regard to the possible means of energy transmission.[10] The work of Becker was much informed by that of Gyorgyi. It was Gyorgyi who pointed out that at some point when mechanistically minded biochemists broke living things down into their constituent parts, somewhere along the line, life slipped through their fingers and they found themselves working with dead matter. Gyorgyi also suspected that this '*elan vital*' could be electromagnetism. He investigated this concept in his book *An Introduction to a Submolecular Biology* in 1960.[23]

So, while this theory is a fascinating idea as to the mechanism of acupuncture it does not suggest where the energy comes from in the first place; it only postulates how it might be influenced by needles. With regard to the nature of *Qi*, however, Yung and Gyorgyi clearly believe it to be electromagnetic in nature. To reiterate our position so far: we do not consider that acupuncture can be explained by mystical energetic concepts and do not imagine that meridians exist. We consider that acupuncture is merely a means of stimulating the nervous system to bring about physiological change. The nervous system is an electrical means of communication and, as such, should remain the focus for acupuncture research.

Qi and electromagnetism

Dr Shui Yin Lo also proposes a theory whereby electromagnetic radiation and ions flow along the meridians.[22] He also says that infra-red light flows along them. Infra-red is electromagnetic energy, however, so we are unsure as to why this was mentioned as a separate concept. Dr Lo then goes on to propose that the meridians themselves have a structure comprised of polarised water molecules and it is along these that energy flows. We do not find this an adequate description in that water is a permanent electric dipole and the only array of organisation that we are aware of pure water forming is ice; clarity is therefore needed. Whatever crystalline array he is considering, we would suggest that it would be detectable using either electron microscopy or radioisotope tracing.

Dr Lo maintains that acupuncture must work at a more fundamental level than biochemistry, at the level of electrons and nuclei, whereas Western medicine concentrates on the molecular level. We again think that Dr Lo should be clearer because chemistry (and therefore life) works the same, however you look at it. Chemistry is governed by the communication of charged particles (in this case, the electron) via the process of photon interaction, and so is ultimately explained by quantum electrodynamics.

Dr Lo does, however, point out some very interesting information although he does not say where he found it. He states that acupoints analysed using magnetic resonance imaging reveal that they consist of a complex system of connective tissue interwoven with capillaries, nerves and lymph vessels. Assuming this to be true, the fact that acupoints are rich in nerves particularly interests us. The

insertion of needles can stimulate the nervous system and thereby the brain. If the brain function is altered any body system can thus be affected. That needles stimulate the nervous system cannot be debated – as for the full implications of this, there is much to learn.

The fact that brain function is altered by acupuncture is becoming well researched using functional magnetic resonance imaging and so far provides, from our perspective, the biggest clues as to the mechanisms of acupuncture.

Through vast amounts of research into how electromagnetic phenomena are at the root of many physiological processes, Becker also concluded that the foundation of life itself, healing and consciousness are governed by electromagnetism.[10] Although his research focused upon the use of electromagnetics with regard to tissue regeneration; his work led him to also ponder upon how electromagnetic signals might be communicated through the body and so to how perhaps acupuncture might work. Ultimately, Becker wanted to understand what made living things alive. The flows of current through the body were, in his opinion the vital spark.

Penninger and Zhao have also demonstrated that natural electric fields and currents in tissue play a vital role in wound healing and have even identified the genes responsible for controlling the cell migration factors. They have shown that cells and tissues essentially behave as chemical batteries with positive potassium ions and negative chloride ions separated by membranes. This creates electric field patterns all over the body (Fig. 11.3). For a current to flow a channel must open to link the two sides, either through damage or deliberately. If a current flows, an electric field follows. Injury disrupts the fields and cells are attracted to the area to repair it.[25]

The role of electric fields in biological processes is not limited to wound healing or nerve impulses but is also involved in, for example embryonic development, cell division and gene expression. How cells sense and respond to electric fields seems to be controlled by calcium ions. Voltage changes open calcium channels, thus initiating a signalling cascade. This has been experimentally verified by removing or blocking calcium in cell cultures; the cells then stop responding to electric fields.[26] We would hypothesise, therefore, that acupuncture could alter calcium ion permeability by influencing calcium channels through initiating voltage change in the tissues.

Qi and bio-electronics

It seems that two major schools of thought are developing: the phenomenon of biological electricity and the concept of biological electronics. Biological electricity is well recognised and due to ionic flow across cell membranes, for example. Biological electronics involves the flow of smaller charged particles such as electrons, protons and electron holes.

Solid state bio-electronic semi-conduction is also a concept explored by Oschman.[27] He suggests that physiologists are reconsidering their model of the cell as a 'bag of solution'. We now know that this is not the case but that the cell

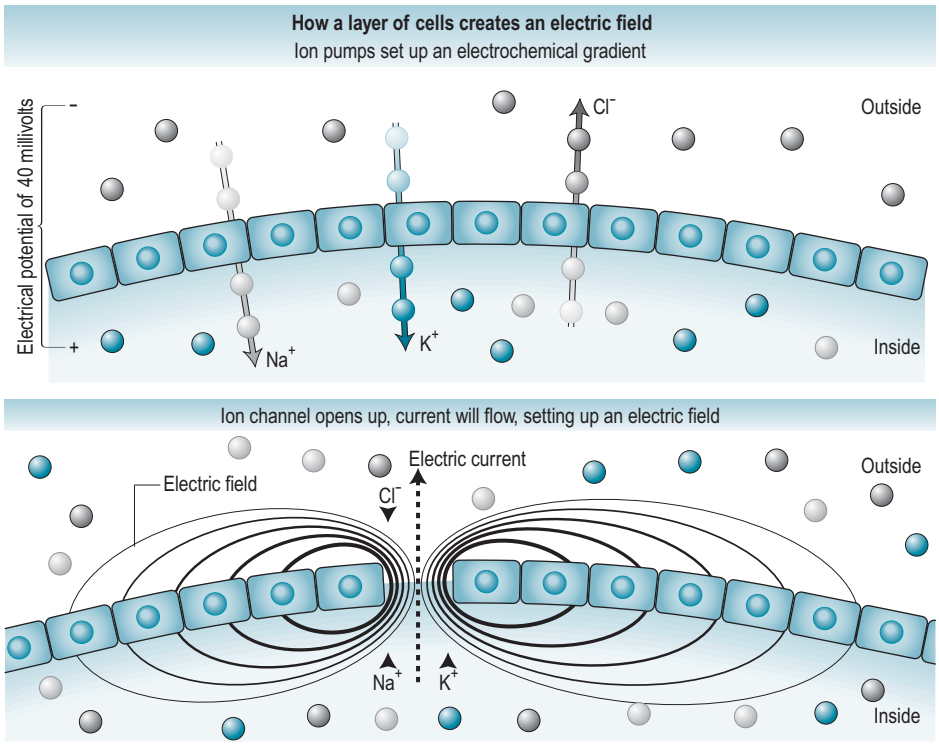

Fig. 11.3 How a layer of cells creates an electric field. (Adapted with permission from Penninger J, Zhao M. To heal a wound, turn up the voltage. New Sci 2006; 191(2562):15.)

is embedded in connective tissue made of a protein called collagen.[27] We think that this is a simplified view. The matrix is actually composed of several different materials. Collagen is present in many structures but mainly that of bone, cartilage, tendons and ligaments. It is also true that some matrix materials have no specific shape. These include hyaluronic acid that maintains the shape of the eyeballs for example.[28] That said, a specific family of proteins called integrins may be of particular interest. These proteins could be important if Gyorgyi is correct in his assumption that protein could semi-conduct.

Oschman also points out that the interior of the cell is filled with microfilaments and microtubules.[27] Together, these are referred to as the cytoskeleton. Microfilaments consist of a protein called actin. They provide support and shape and assist in the movement of cells and movements within cells. Microtubules consist of a protein called tubulin. These also provide support for the cell and also form conducting channels through which substances can move through the cytoplasm, the substance inside the cell (Fig. 11.4).

Oschman states that linear biochemical pathways occurring in solution lose sight of the fact that molecules are not simply floating around but are bound to the cytoskeleton.[27] It is, however, also known that the chemical activities of the cell do not occur within the cytoplasm but within structures known as organelles. This system of compartmentalisation allows many reactions to occur

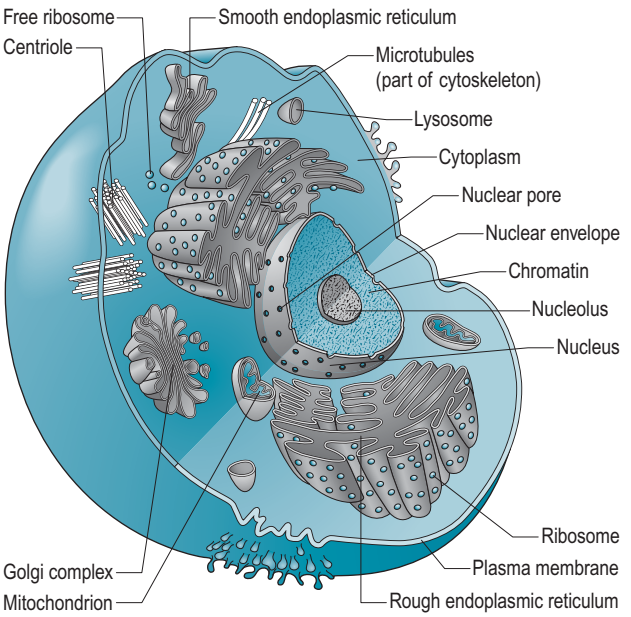

Fig. 11.4 An animal cell.

simultaneously without interfering with each other. Therefore, the cytoskeletal structures have no direct involvement with the cell chemistry.[28] We therefore consider that more clarity is needed here. The cytoskeleton does move molecules around the cell but it has no part to play in biochemical reactions.

Oschman is of the mind that it is an oversimplification to show a metabolic pathway as a sequence without its structural context.[27] In light of the above-mentioned system of compartmentalisation this seems a little ambiguous.

Oschman also states that the cellular matrix is physically linked to the extracellular matrix via transmembrane linking molecules.[27] He states therefore that any cell is inextricably linked to all others via these linking molecules and even goes so far as to say that the intention of a practitioner sets up specific electromagnetic changes in their nervous systems that could be transferred to others via the matrix when any part of their skin is touched. Although it appears rather unlikely to us, many acupuncturists consider that one's intention during needling is at least as important as the choice of acupoints, if not more so and many more are now performing 'acupuncture' without the needle even penetrating the skin. If it is the case that these observations and practices are valid (which seems very unlikely), then this model may explain the underlying mechanisms of action. We would consider that it is far more likely that any change in the patient in these cases occurs as a result of the placebo effect initiated by the therapeutic alliance, post hoc reasoning, touch and the complex rituals involved in such 'acupuncture' practices. Intention is therefore important with regard to treatment outcome but is not part of the physiology of acupuncture itself.

Transmembrane proteins span the internal to external surface of the phospholipid bilayer that makes up the plasma membrane. Although X-ray diffraction

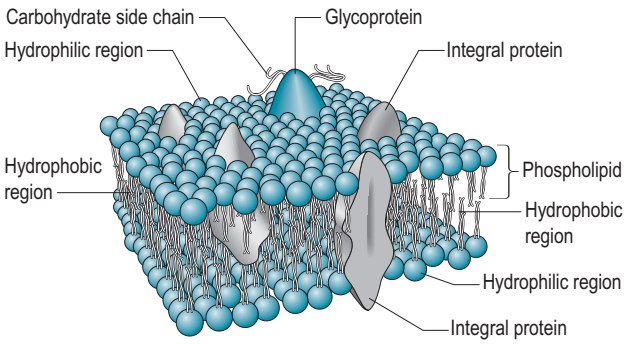

Fig. 11.5 The cell membrane.

and nuclear magnetic resonance spectroscopy have demonstrated that most do not provide any structural link, some specific transmembrane proteins – called integrins – do provide the structural link that Oschman suggests (Fig. 11.5). Integrins seem of particular interest with regard to the possible process of acupuncture as a means of cellular communication and hence possibly an important aspect of the mechanism of acupuncture.

From a biochemical perspective it is known that integrins play a role in signal transduction from the cell to the extracellular matrix. This is the process by which the cell converts one kind of signal or stimulus into another. The process involves a series of biochemical steps referred to as a signalling cascade. The actions of hormones or neurotransmitters are examples of this process. An important aspect of signal transduction is signal amplification. A small change at the cell membrane can activate much larger downstream processes. From the perspective of *Qi* correlates, cellular ion channels can be opened by a change in cell potential; that is the difference in electrical charge across the cell membrane. In fact, Ionescu-Tirgoviste and Popa demonstrated that 'tonification and dispersal techniques can be distinguished by ionic changes in the vicinity of the needle'.[29] In neurons it is ionic processes that underlie their action potentials. We consider therefore that the nervous system has a vital part to play, partly due to the *De Qi* (sensation felt during needling) phenomenon. Many (although not all) acupuncturists consider the sensation of *De Qi* to be vital with regard to whether the acupoint has been located and stimulated or not. The *Ling Shu* states 'When the *Qi* arrives, the treatment is effective. This is the essential of needling'. Although this is referred to as a *Qi* sensation, clearly it must be communicated via the nervous system because that route is the only way that the brain can experience physical sensation initiated by environmental change. So, to say that acupuncture has nothing to do with the nervous system but more mystical mechanisms seems a little farfetched. Research has shown that the sensation relates to changes in electromyogram (EMG) readings used to measure myoelectric potentials and that if injury to the nerves is present, neither the *Qi* sensation nor the EMG reading

could be aroused.[30] The needle 'grab' sensation often described by the practitioner as their experience of *De Qi* seems to be caused by a contraction of muscle around the needle. Some research has also shown that in using neurotransmitter antagonist drugs, the effect of acupuncture and the *De Qi* sensation is blocked.[30] This confirms that the *De Qi* sensation must be mediated by neurotransmitter release. It also seems that even humoral responses to acupuncture can be traced back to changes in cerebrospinal fluid and so also relate to the neural paradigm.

So integrins are not simply hooks that attach cells to the extracellular matrix but provide the cell with critical information about its surroundings. These proteins form an important part of the mechanism with which cells make a decision on which biological action to take; they thus lie at the heart of cellular biological processes. Integrins are also important in the role of transferring the information from mechanical stimuli to the extracellular matrix through the cytoskeleton. In this way it is possible that vibratory interactions through signal transduction have potential regulatory importance at the cellular level. It is also the case that needling in the close proximity of a nerve can consequently stimulate it due to the communication of the needle stimulus via integrins. Physiologists are also aware that electricity can be created by the movement of body tissues, perhaps for example, during needling. Two phenomena could be at play here: piezoelectricity and streaming potentials. Both are worthy of investigation from an acupuncture perspective.

Piezoelectricity is the phenomena whereby mechanical deformations of a crystal lattice cause a current to flow. It is in this way that the diamond needle on a record player creates electrical signals that reflect the nature of the groove. In 1954, Yasuda (cited in[10]) showed that bone was piezoelectric. This was later confirmed by Becker, who showed that semi-conducting proteins in connective tissue exhibited this property. It is clear therefore that oscillations set up in the crystalline structures of proteins in connective tissue by an acupuncture needle's movement or compression could generate small bio-electronic signals that could be carried by the semi-conducting network of the extracellular matrix.

Streaming potentials are developed by the flow of fluid containing ions over electrically charged surfaces. Electrostatic interactions are set up between the fixed tissue charge and the fluid charge. Potentials of this type are generated by blood flow and propulsion of extracellular fluids through the extracellular matrix as a result of tissue deformation.[31]

To reiterate, messages could be transferred through the matrix via the interstitial fluid or by electronic conduction along the protein backbone of connective tissue matrices.[27]

So it could be hypothesised that acupuncture meridians, the pathways of *Qi* flow, the *Jing Luo* are the semi-conductor electronic network which allows communication via the cytoskeletal transmembrane proteins. Whether this is true or not, stimulation of the nervous system is the end goal.

Interestingly, it has now been observed that coherent lattice vibrations in solid state semi-conductors emit electromagnetic radiation.[32] It has also been shown

that all organisms emit light (biophotons) at ultraweak intensities which are strongly correlated with the metabolic cycles of the cell.[33] It is possible that these phenomena occur due to the fact that metabolic pumping cycles excite cell membranes (which have an electric field across them) which then interact with adjacent cells via linking proteins until there exists coherent excitations of phonons and photons.[34]

Becker suggests that acupuncture meridians are DC electrical conductors of an injury message to the brain. He then goes on to suggest that the brain sends back a current to initiate a healing response in the area. This hypothesis arose from his research into the regenerative capacities of the salamander. So Becker considers that the meridian system is really one of signal transduction. Becker describes the acupoints as booster amplifiers for this electrical signal. He proposes this idea due to the fact that current grows weaker along a transmission cable due to its electrical resistance.

There seem to be questions that spring out of this hypothesis, however; what biological structure forms the transmission cable and should not the current and voltage increase at each acupoint if it is proposed as being a signal amplifier? Unfortunately, Becker lost his funding so he never found out if the points were booster stations. So to our knowledge this is still an unknown and worthy of further investigation. As for the structure of the transmission cable Becker considered that rather than being related to neurons it was the perineural cells that were of most interest. His experiments proved that bone healing was not mediated by nerves but the Schwann cell sheaths. So, it turned out that what biologists had considered merely insulation were, in actuality, wires themselves. It seems that the main difference between the current of nerves and Schwann cells is that the Schwann cells uses DC potentials as opposed to the back and forth (AC) ion currents of the nerves themselves. The existence of DC potentials has been confirmed by the use of SQUID (super conducting quantum interferometric device). These devices are super-sensitive magnetic field detectors and are sensitive enough to pick up the steady magnetic field produced by the direct current perineural system. This DC network corresponds to Becker's supposition of meridians being DC networks. Becker's research, however, has only investigated this DC perineural network as a mechanism of the control of the healing response to tissue damage. Therefore, bearing in mind the broad physiological effects of acupuncture, more investigation is needed. It is not clear in Becker's text as to how the mechanism behind needling an acupoint might effect electrical change. Assuming he is right that the meridian circuit is DC, we propose that the acupoints could be likened to a battery. Body tissues are immersed in electrolyte (ion-containing fluid) and so are an electrically conductive medium, much like inside a battery. If ion flow is influenced by the introduction of a needle into the medium then a current flows. It is perhaps possible that altering the ion flow in a given direction 'charges' the battery while reversing this process 'discharges' it. In our opinion, research is needed to see if ion flow changes occur wherever a needle might be inserted or if it is a phenomenon unique to the acupoints. In a sense, the needle could be providing a short circuit whereby two parts of a circuit with different potential differences (voltages) become connected.

Could *Qi* be chemical in nature?

A novel integrative approach for *Qi* into Western medical concepts again centres around intercellular communication. Ralt suggests that the use of nitric oxide (NO) is a prime candidate for the signalling molecule of the meridian system.[35] NO exhibits widespread usage in physiological functions, notably that of neurotransmission, synaptic plasticity and immune responses. Its use as a neurotransmitter is of particular interest to us due to the fact that, unlike most neurotransmitters which connect a presynaptic to a postsynaptic neuron, NO, being a gas has the unusual ability to stimulate several nearby neurons, even those not connected by a synapse. In this way its effects can be considered more diffuse. It is been shown that the NO content in the skin surrounding acupoints is consistently higher than those of non-acupoints and that this phenomenon is associated with their low electrical resistance. While fascinating information as to what may be the transmitter of needling information, this model does not help to explain *Qi* as an energy source for physiological process. Again, NO levels are regulated solely by synthesis reactions and so these biochemical reactions require a source of energy. We therefore feel that the *Qi* correlate is not NO itself but rather what drives its synthesis.

Quantum *Qi*

Dr Lo postulates that quantum oscillations are related to energy flows in the body and proposes the existence of a particle called a *Qion*. He suggests that meridians interact through *Qion* exchange. We think the fundamental problem here is that Dr Lo is like so many others looking for something 'new'. If a '*Qion*' existed at low energies (like in the body) then it is unrealistic to suppose that particle physicists, using particle accelerators capable of working at very high energies, have not stumbled upon it. It is possible Dr Lo is referring to a *Qion* not as a literal particle but rather as a quantised mode of vibrations according to wave-particle duality and quantum theory. Dr Lo states that the theory of acupuncture and meridians is supported by 2000 years of clinical practice and that therefore *Qi* must exist. We would disagree with this statement in that, just because something happens to a person when needles are inserted, it does not mean that *Qi* or meridians exist, it just means that acupuncture has some physiological basis.

Some acupuncturists propose that *Qi* is electromagnetic energy which is part of the quantum energy connecting everything in the universe including ourselves, known as the zero-point field.

The concept of the zero-point field is explored by McTaggart in her book *The Field*.[36] The zero-point field is defined as being the energy present in matter at the lowest possible energy. This energy is due to the residual jiggling of quantum particles due to quantised harmonic oscillations according to Heisenburg's Uncertainty Principle. McTaggart suggests that the zero-point field could correlate to the concept of *Qi* pervading the entire universe.[36] This is suggested due to the

quantum theoretical concept of the atom, not as a billiard ball-like entity, but as a concentrated centre of a force stretching out into infinity. It is this phenomenon that McTaggart describes as being responsible for the quantum property of non-locality whereby a quantum particle can influence another quantum particle instantaneously over any distance. This quantum coherence, she suggests, could be explained if all particles, and therefore all things in the universe were inextricably interconnected by the fabric of the zero-point field; this is all a very Taoist concept.

With regard to the human body, McTaggart refers to the work of theoretical biophysicist Fritz-Albert Popp. Popp suggested that the energy of living systems was driven by photonic interaction and that biophotonic emissions transferred cellular information; this is, however, speculation and has not yet been experimentally validated.[33] Photomultipliers can detect ultra-weak photonic emission from living tissue and so the existence of this radiation is not disputed. However, the hypotheses of Popp are dismissed by the wider scientific community; these emissions are generally regarded as by-products of electron transport reactions involved in cellular metabolism. Popp even went on to suggest that the coherence of these emissions with the zero-point field led to health or disease and that acupuncture meridians might work like wave guides transmitting this energy. It is true that injured cells exhibit more photonic emission than healthy cells but whether this is some form of distress signal or a consequence of greater oxidative stress is not yet understood.

Quantum theory predicts that space is filled with a sea of zero-point energy but there are difficulties around the concept. Currently zero-point energy is undetectable because although the amount of it is technically infinite it is in the lowest possible energy state, at the level of the Planck scale. In order to probe these small scales, very high energies are necessary; current particle accelerators probe with only a millionth of the required energy.

At the level of the Planck scale the universe would appear 'grainy', the grains being the minimum possible compromise between location and velocity according to the Uncertainty Principle; space is thought to break up at 10–33 cm. Synchroton radiation (radiation caused by electrons accelerating through a magnetic field) observation from the Crab nebula has shown this graininess is not apparent; as relativity theory predicts, space appears continuous. The energy of synchrotron radiation is proportional to the energy of the electrons; the radiation from the Crab nebula is so energetic that the electrons move close to the speed of light and so the 'graininess' should appear in radiation spectra but it does not. It is possible that atom synchronisation interferometry experiments may finally answer the 'graininess' question but to our knowledge these have not yet been conducted.

It is also true that since mass and energy are equivalent, zero-point energy should gravitate, thus curving space time. If zero-point energy is infinite and does extend to the Planck scale its energy density would be massive, around 1093 g/cm^3 contracting the universe to less than an atom in diameter. If, however, zero-point energy exerts a negative pressure such as dark energy, space time would expand. Observations of cosmic acceleration show that the order of magnitude is insufficient and that in order to be correct, 120 orders of magnitude per cm^3

greater would need to be observed. Were this to be the case the universe would have accelerated into oblivion within seconds of the Big Bang.[37]

This implies that the zero-point postulate is most unlikely to be involved in the mechanisms behind acupuncture. It is possible that when better understood, or if relativity theory and quantum theory are combined, the zero-point field could be the energy underlying the theory of everything; currently, however, much more research is needed but the postulate is nevertheless fascinating.

Some cutting edge theoretical physicists trying to merge general relativity with quantum theory are proposing the theory of loop quantum gravity. Similarly to zero-point field theory it sees the world as 'grainy' complex braids in space-time. This model therefore considers atoms and people as a consequence of space-time tangles and therefore also at one with the universe.[38]

Conclusion

While all the postulates mentioned in this chapter are very interesting, our standpoint is perhaps simpler. We conclude that since there is no hard evidence for any of these postulates it is better to stick to what is known. Acupuncture has an effect at the level of the nervous system and it is this that should be further investigated rather than incredibly complex hypotheses. The physiology of the nervous system is in itself probably the most fascinating subject in existence and requires no new 'energies' to understand.

The following chapter will further explore the fact that there is enough already known to answer the inevitable 'What is *Qi*?'

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CHAPTER 12

A new model for *Qi* energy

'Poets say science takes away from the beauty of the stars – mere globs of gas atoms. I, too, can see the stars on a desert night, and feel them. But do I see less or more?'

(Richard Feynman in The Feynman Lectures on Physics 1961)

Introduction

It is our opinion that acupuncture is, or at least should be approached like any other science and if it is to be accepted in the West then it needs to be treated as such. From the standpoint of science, if there is no proof for the validity of any theory it remains just that, theory. Until a theory is substantiated it cannot yet be accepted as fact. From our perspective there is, as yet, no scientific proof for the existence of any mystical 'life energy'. Beyond doubt, life energy exists, for without this functional energy we die, but it must surely be explicable? If we work with the human body we must, by definition, be working with biology, and therefore by reduction chemistry, and by further reduction physics. By no means do we consider that this approach invalidates Chinese medical practices; what is of more concern to us are the ingenious explanations given for Chinese practice, which we consider to be no longer valid in the face of current scientific knowledge. If we try to accept *Qi* as a fact, but one that we do not yet understand, we are likely to be disappointed. However, if we accept that *Qi* describes a fact that is already scientifically proven, then we stand much more chance of it exciting us.

The structural unit of the human body

Several texts, most notably *The Foundations of Chinese Medicine* by Maciocia, comment on the possible relationship of *Qi* to matter. Maciocia states that nowadays many sinologists in fact propose that *Qi* corresponds to matter.[1]

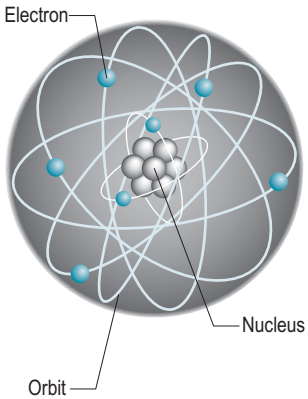

Fig. 12.1 An atom.

But what exactly is matter anyway? What are things made of? This is an important question to think about because human beings clearly are made of matter and so what we are made of must have some relationship to our physiological processes. Were we to dismantle the human body, we would, from a reductionist perspective, ultimately discover that it is made of atoms.

Atoms are the smallest unit of matter that exists independently. The word atom is derived from the Greek, '*a-tomos*', meaning indivisible. An atom consists of a nucleus that contains a number of positively charged particles called protons (contained in the nucleus) and an equal number of negatively charged particles called electrons that orbit around the nucleus in fixed quantum energy levels, sometimes called shells. The nucleus of an atom, in addition to protons is also made up of neutrons that have no charge (Fig. 12.1). (Some 200 or so other particles do exist but are out of the scope of this chapter.) An atom, therefore, has no overall charge but is nevertheless held together by the electrostatic force of attraction between the electrons and protons.

The Tao, often translated as The Way, describes the changeless properties of the universe, and therefore, by extension, could also describe the laws creating the universe and the resultant atom, the building block of all matter. To our mind, the guiding principle of *The Tao*, life, the universe and everything, is physics, and so the same notion that life is a result of the interaction of certain guiding principles is also true of Western science. The properties of the atom have endured for billions of years and the order resulting from these physical laws creates everything, living or non-living. As Lao Tsu described in the *Tao Te Ching*:

'Tao produced the One.
The One produced the two.
The two produced the three.
And the three produced the ten thousand things.'[2]

The atomic hypothesis is a very old concept; only until relatively recently did it become the atomic fact. The Greek philosopher Democritus, who lived from 460 to 370 BCE, suggested that the external complexity of the world could be

reduced to more simple entities allowing for a kind of internal unity. Democritus summarised his thoughts thus: 'By convention there is sweet; by convention there is bitterness. By convention hot and cold; by convention colour. But in reality there are only atoms and the void'.

As we can now see, if something exists, i.e. is made up of atoms, it possesses inherent energy of various types and so by this definition, *Qi* corresponds to matter, and *Qi* must be everywhere and in all things, living or not. So, humans are a pile of atoms, but this does not mean merely a pile of atoms; each human being is a pile of atoms so complex that never again is replicated, and that walks, talks, thinks and feels – this in itself is a miraculous concept.[3]

The building blocks of matter itself are chemical elements, which are of course atoms of various sizes. If we have an atom of the element carbon, for example, although it is almost infinitesimally small, it is nevertheless matter. What makes it a carbon atom is the fact it possesses six protons and six electrons (its atomic number) as shown in Figure 12.2.

A difference of just one proton makes an atom so radically different to another that it is in fact another element altogether. For example, an atom of nitrogen contains seven protons (and electrons).

Because protons and electrons are charged particles, we are not just talking about matter but energy too, so if an atom contains different numbers of protons and electrons to another its energy must also be different.

It is also worth reiterating at this point that modern physics does not consider energy and matter to be separate. In this way matter is understood to be made up of energy of a certain density. As aforementioned, Einstein's Theory of Special Relativity, represented by the equation $E = mc^2$ describes a situation whereby anything with energy has mass and the mass is related to the amount of energy. So, the intrinsic mass of an object is just one form of energy. For a compound object, the mass of the composite is not just the sum of the masses of the constituents but the sum of their energies. This means that the mass of the body changes as its speed (kinetic energy) changes; the faster a body moves, the more mass it has. This also means therefore, that if, for example, you charge your mobile phone it weighs more than when the battery was discharged. A more true statement is that energy manifests as mass. This can be proven during particle

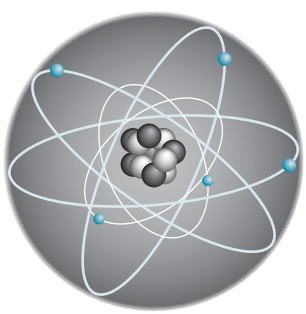

Fig. 12.2 A carbon atom.

acceleration experiments whereby two particles are forced to collide at high energies. During the collision they split into pieces. These pieces are, however, the same as the original pieces and not smaller. This is because the particles were created out of the kinetic energy of the collision.[4] So, it seems that relating *Qi* energy to matter is a useful model to help us understand that we are made of atoms and that atoms are inherently energetic. This model alone does not yet, however, help us to understand how the body goes about its day-to-day physiological processes or how acupuncture might work.

Qi and physiology

While channel *Qi* seems to be linked to structural/cellular communication and this area is quite well researched, we feel that the source of energy must be investigated; after all, the energy must come from somewhere before it can be used to drive physiological processes. We would therefore now like to explore further what might be the energy that animates us. In order to understand this aspect of energy a more fundamental understanding of energy is required.

Let us consider the fundamental workings of the universe. This is the area in which scientists have thought since the dawn of humanity. Until relatively recently, such questions that could not be answered were assumed to belong to the realm of the gods. Now science can answer an incredible number of searching questions, but it has taken a long time and the most incredible minds that ever existed to get to this point; it has not been an easy journey.

Just before the 'Big Bang' there was nothingness. At the time of the Big Bang all energy was created in just the right amount for the universe to exist. If the amount of energy had been any different there would be no universe. This is in itself both strange and miraculous.

The four fundamental interactions concerned with existence itself are gravitational interactions, the weak and strong nuclear interactions and electromagnetic interactions. So which of these energies is responsible for the inner workings of a human being? This is an important question to answer because surely it is to this energy that the Chinese are referring to when they use the word *Qi*? It is that which animates us. Remember that *Qi* is unlikely to be something new or different; it is just a foreign word for us to translate. Whether one is geographically rooted in the East or West the laws of physics must work the same.

Energy is a physical property possessed by an object that measures its capacity to make changes to other objects. These changes may include speed of motion, temperature or position.[5] We believe that *Qi* does, therefore, fit this broad definition in that it drives the physiological processes of life, our fundamental chemical reactions.

Gravitational interactions, according to Newtonian physics, represent the attractive force between any two masses as a result of their separation[5] (modern physics describes it as a result of mass curving the fabric of space-time, the Theory of General Relativity). It makes apples fall and holds the Earth in orbit around the Sun. Its influence is, however, irrelevant within the atom due to the

diminutive sizes of the masses involved. So although it influences certain physiological processes such as lymphatic drainage and led to the evolution of our musculoskeletal structure, it has nothing to do with body chemistry. We would therefore suggest that this energy has no relationship to *Qi*.

The weak nuclear interactions were responsible for most of the interactions in the early universe during which subatomic particles changed from one sort to another. Radioactive decay is an example of this type of interaction. Again, these are not the sorts of processes responsible for human physiology and so are not likely candidates for a *Qi* correlate.

The strong nuclear interactions enabled fundamental particles to bind together to form atomic nuclei of which the universe is composed. It is the force that binds quarks inside protons and neutrons. A small residual interaction binds the nuclei of atoms together but still is not responsible for the formation of molecules, the existence of chemistry, its life-giving processes and hence *Qi*.[5]

Electromagnetic interactions cause the behaviour of particles within atoms and molecules; they involve the interaction between charged particles. Charge creates a disturbance in space-time (a field) such that other charges in the field feel a force.

Quantum electrodynamics (QED) is currently the most complete explanation of electromagnetic interactions we possess. It is needed to understand the complexities of our subatomic world. It led to the realisation that light is nothing but a rapidly alternating electromagnetic field. In QED all electric and magnetic forces arise from the exchange of photons between charged particles.[5] These interactions are the origin of atomic and molecular activity, therefore ultimately of body chemistry and hence life.

So therefore, by definition, we propose that *Qi* in the context of Chinese medicine must correspond to electromagnetic force or energy, in that the other three fundamental energies are clearly not responsible for the body processes that make us alive. By our definition, *Qi* is electromagnetism and therefore experimentally proven. It is no longer an indefinable mystery.

To clarify, electromagnetism seems to be the energy that drives all body cells, the functional energy or *Qi*. This is of particular interest in light of most research to date. It largely focuses on the electromagnetic concept. In fact, as shall be seen, even the approach of Ralt, who proposed the nitrogen oxide model, could be described in terms of electromagnetic interactions.[6]

In Chinese medicine, *Qi* is a more generic term than merely functional energy, used to describe various, more far-reaching concepts. There are several different types of *Qi* depending on their location and function in the body. Broadly however, *Qi* is always functional energy and we propose that it is electromagnetic in nature.

It should also be noted that electromagnetic energy has properties of both waves and particles. This theory is known as wave particle duality and further substantiates the traditional Chinese medicine (TCM) view that energy and matter are the same. Waves possess some properties of particles, and vice versa, particles also exhibit properties of waves.

We also feel it is important to note that electromagnetic radiation is emitted or absorbed (as photons) in processes involving the electric and magnetic forces

and that when charged particles change speed or direction of motion, they emit electromagnetic radiation. It is these sorts of processes that occur during chemical reactions.

In order to de-mystify the concept of *Qi* further we also need to understand the Western theory of electromagnetic interactions with regard to the human body.

Energy and life

All living organisms need energy to survive. The beating of the heart, thought processes, growth and reproduction, require energy. The cell is the fundamental unit of life and every cell is capable, by means of catalytic change, of deriving and then utilising energy from its environment.

Even a dead cell has energy, according to $E = mc^2$, because it exists, but a living cell must also harness a different type of energy. This different energy is the *Qi* we consider in TCM when discussing a living organism. It is that energy that makes us alive.

To most people, these metabolic processes are thought of as purely chemical reactions. But let us consider things further.

Body chemistry

The number of protons an atom possesses determines the chemical properties of the element. The proton number gives an atom its identity, and its place on the periodic table. For example, if an atom has six protons it is an atom of the element carbon; if it has seven protons it is an atom of nitrogen. The proton number also determines the number of electrons that orbit the atomic nucleus. If positively charged protons are added to an element, then an equivalent number of negatively charged electrons must also be added to maintain an overall neutral charge.

To further understand how chemical reactions work we need to understand molecular organization.

The electrons orbiting an atomic nucleus occupy what are termed as shells. The electron configuration determines the atom's chemical bonding behaviour. It is therefore the electrons that give the atom its personality. There are a fixed maximum number of electrons in any one shell, each with its own energy level. An atom is most stable, i.e. least chemically reactive when its outermost (valence) electron shell is full. Often, though, this is not the case. The outer electron shell is not full and so the atom is unstable. An atom always attempts to fill its outermost electron shell; to do this the atom may give up an electron, gain an electron or share an electron. When an atom requires one electron to complete its outermost electron shell, e.g. hydrogen, it is said to have a combining power or valency of one. This property of valency allows atoms to combine in order to form more

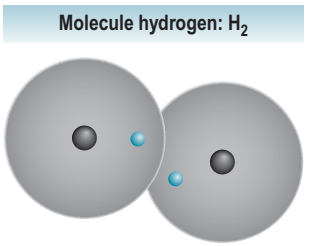

Fig. 12.3 Shared electrons – covalent bonding.

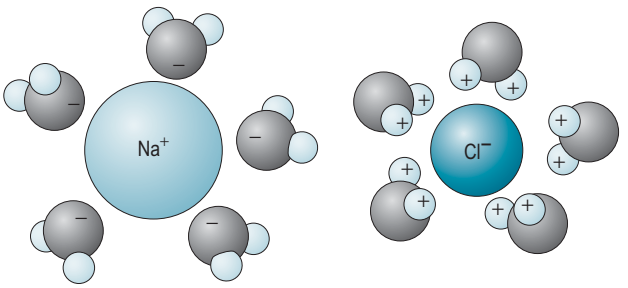

Fig. 12.4 Sodium chloride (table salt).

stable molecules in which its constituent atoms all have full outer electron shells; it is this that allows chemical reactions to occur.

For example, when two atoms of hydrogen combine they both share an electron. This results in both atoms having a full shell of electrons and a stable molecule; H_2 is formed. This sharing of electrons is called covalent bonding (Fig. 12.3).

In addition to atoms forming covalent bonds by sharing electrons, atoms may stabilize themselves by gaining or losing electrons to form charged ions. Oppositely charged ions attract one another to form ionic bonds.

For example, sodium tends to lose an electron to form a Na^+ ion. Chlorine tends to gain an electron to form a Cl^- ion. These two oppositely charged ions form ionic bonds to form sodium chloride or common salt which has the chemical formula NaCl (Fig. 12.4).

The atoms in a molecule are held together by these chemical bonds: when bonds are broken energy is released; when bonds are formed energy is required.

So we now understand how chemical reactions occur, it is all down to the interaction of electrons; so these reactions are therefore energetic (electromagnetic). When discussing Chinese medicine it is often referred to as energy medicine, and we think of Western medications working purely chemically, but when we get to the root of what actually happens we discover we converge at the same place.

Energy and the human body

When atoms combine with or break apart from other atoms, a chemical reaction occurs. Chemical reactions are the foundation of all life processes. The chemical reactions that occur within organisms are collectively known as metabolism. The fundamental chemical reaction by which means the human body obtains its metabolic energy for life is cellular respiration and this occurs in the mitochondria (Fig. 12.5). Organic compounds are taken up as nutrients from the environment and oxidised to release energy. Simply put, this process requires food and air.

Whatever form the food we take is in, it is converted to glucose that is then broken down in the presence of oxygen (oxidised) to release energy, and water and carbon dioxide as waste products.

If we look at an oxidation reaction more closely we will see that it involves the loss of electrons from the hydrogen atoms in the glucose molecule to yield free energy stored in adenosine triphosphate (ATP) molecules. ATP is considered the energy currency for living cells. Fundamentally the process must therefore be electromagnetic, and is known as the electron transport system (Fig. 12.6).

Current biochemical research suggests that cellular metabolism is regulated by proton currents (hydrogen ions); this is a concept referred to as proticity.[7] Enzymes located on the mitochondrial membranes are functionally related to the transfer of hydrogen ions (protons) and drive them across the membrane. An electrochemical proton gradient is therefore created. This gradient consists of two components, a difference in hydrogen ion concentration (pH) and a difference in electric potential; collectively this is known as the proton-motive force. So again, fundamentally, electromagnetic interactions form its basis.

The overriding feature of energy mobilisation in living systems is the use of the above-mentioned stored energy. In fact, the electron transport system as key to life has been considered for many years.

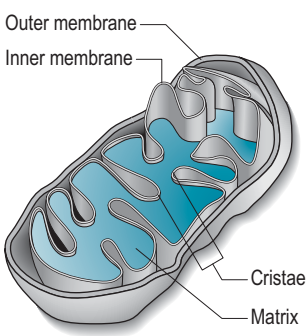

Fig. 12.5 A mitochondrion.

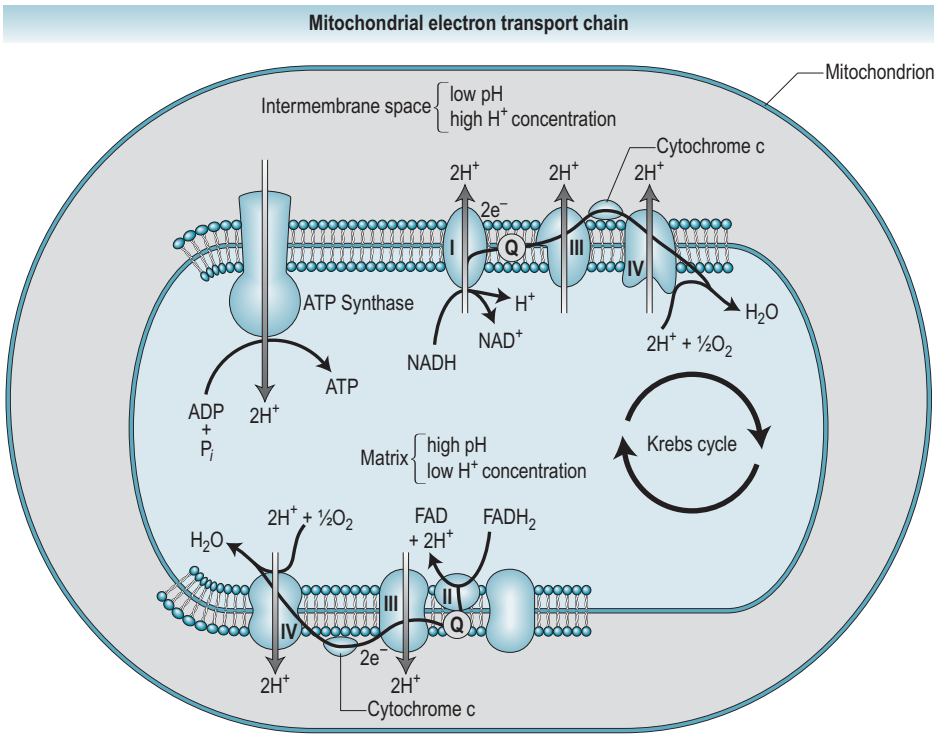

Fig. 12.6 The electron transport chain.

Formation of *Qi*

It has been established that *Qi*, or electromagnetism exists all over the body because it is in the very atoms that make us up; by formation of *Qi* we mean the type of *Qi* that corresponds to the energy used by body cells stored as ATP. In TCM this type of energy is referred to as *Zhen Qi* or True *Qi*.

In TCM, *Gu Qi* (Food *Qi*) is said to be derived from food and drink by the action of our digestive systems and combines in the chest with Air *Qi (Kong Qi)*, derived from air by the action of the lungs to form Essential *Qi* (*Zong Qi*). *Zong Qi* is then transformed into *Zhen Qi* (True *Qi*) with the assistance of *Yuan Qi* (Original *Qi*, the functional aspect of our Essence or *Jing*).

Food *Qi* + Essential *Qi* → True *Qi* (+ Impure *Qi*)

As already mentioned above, in Western medical terms energy is derived through respiration as follows:

Glucose + Oxygen → Energy + Carbon dioxide and Water

There is a direct correspondence between these two equations; they are really one and the same, illustrated using different terminology as further described below.

Types of *Qi*

As previously explained, when discussing *Qi* we consider there to be different types dependent on its location and function in the body. These types of *Qi* are, however, essentially the same energy but in order to explain their different manifestations they are assigned attributes particular to them. It should be considered that in Western medicine a general cell does not actually exist but is discussed in texts for ease of explanation. Actually, cells differentiate themselves in terms of function and structure according to their location and function required of them; the same is true of *Qi*.

Food *Qi*

In TCM this is called *Gu Qi* and is derived from food and drink by the digestive action of the body. *Gu Qi* is the basis for the formation of all *Qi* and Blood in the body. Ultimately, therefore, the entirety of our body's existence has its root in *Gu Qi*. So *Gu Qi* fundamentally correlates with our nutritional energy.

Essential *Qi*

Essential *Qi* is described in various ways in different texts. Essential *Qi* is often described as being the product of the interaction between Food *Qi* and air which is then used to make True *Qi*.[1] The energy released by the interaction of glucose and oxygen is used to add a phosphate group (PO_4^{3-}) to adenosine diphosphate (ADP) to synthesise ATP, this energy could be referred to as Essential *Qi*. ATP is not the energy itself that our body uses but is a potential energy store that is released as necessary. Essential *Qi* is the energy produced by respiration but also refers to the energy in oxygen, essential for aerobic respiration. It is obviously, therefore, directly related to the Lungs in that the oxygen from air must be supplied to metabolise the glucose; but also to the Heart which through its pumping action circulates oxygenated blood throughout our tissues where respiration can then take place.

True *Qi*

True *Qi* is known as *Zhen Qi* in Chinese. This is the final stage in the transformation of *Qi* so it is the energy actually used by the body's cells. It therefore corresponds to the energy liberated from ATP when it is broken down by the removal of a phosphate group to ADP. In TCM, True *Qi* assumes two forms which describe its different functions in the body. These are Nutritive *Qi* (*Ying Qi*) and Defensive *Qi* (*Wei Qi*).

Original *Qi*

Original *Qi* is thought of as the agent of change in the transformation of Essential *Qi* into True *Qi*.

As the source of energy, mitochondria are of particular interest here. These structures consist of two membranes, similar in structure to the plasma membrane where energy is generated. The inner folds of the mitochondrial membrane called cristae provide the surface for chemical reactions (Fig. 12.6). The enzymes involved in the above-mentioned energy-releasing reactions, are proteins and are located on the cristae.[8] It is these enzymes that we associate with Original *Qi* (*Yuan Qi*). An individual's genetic information codes for the manufacture of proteins, nothing more and nothing less. The enzymes involved here are proteins and so are related to the Original *Qi* which could be considered as our deoxyribonucleic acid (DNA).

Nutritive *Qi*

This aspect of *Qi* is considered as having the function of nourishing every cell of the body, allowing them to produce numerous chemicals in order to maintain life itself. For example, these chemicals may form new body components, hormones, antibodies or enzymes. These anabolic reactions require the energy of Nutritive *Qi*.

Defensive *Qi*

This aspect of energy protects the body from pathogenic influence. The concept of *Wei Qi* (Defensive *Qi*) therefore encompasses a variety of mechanisms to help us resist disease. Our immune response is a product of our lymphoid tissue. This consists largely of lymph nodes but also the spleen, gastrointestinal tract and bone marrow. In TCM, *Wei Qi* is thought of as circulating in the superficial aspect of the body, in the skin. Clearly this is not truly the case but this description was used to describe the observation that the skin has a role to play with regard to the defence from disease. From a Western medical perspective the skin, as in TCM, also has a role to play in resistance to disease. This is achieved through the action of keratinocytes, Langerhans cells and Granstein cells in the epidermis.

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CHAPTER 13

Yin-Yang theory

There are forces in nature called Love and Hate. The force of Love causes elements to be attracted to each other and to be built up into some particular form or person, and the force of Hate causes the decomposition of things.

(Empedocles 430 BCE[1])

Yin-Yang theory

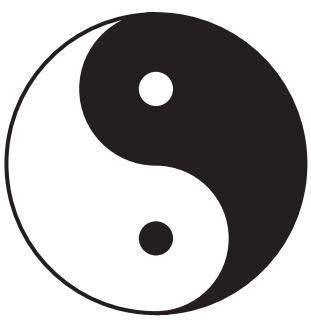
The theory or philosophy of *Yin-Yang* is one of the fundamental concepts of Chinese medicine. The earliest reference to it is in the *I Ching* ('The Book of Changes') written around 700 BCE. It was elaborated upon in the Warring States Period (476–221 BCE) primarily by Tsou Yen, a scholar of the Naturalist School who interpreted natural phenomena and observed how this might be related to the understanding of human health and disease.

Contrary to popular thought, the theory of *Yin* and *Yang* is not a belief system, quite simply, because there is nothing to believe. Essentially, it is a model that can be applied to help us to understand the world around us. *Yin* and *Yang* do not exist because they are not matter. They exist only as words, with meaning only attributed to them contextually, just as heat and cold do not exist in themselves but are terms we use to understand something about the energetic nature of the object being described. Neither *Yin-Yang* nor hot-cold is more real.

The development of the *Yin-Yang* theory sprang out of the ancients' observation of the cyclical flow between day and night, the day corresponding to *Yang* and the night to *Yin*. From this starting point it was noticed that the physiology of the body also seemed to follow this trend of alternation between two opposite poles. For example, humans tend to wake and be active in the daytime and then rest and sleep in the night-time. In modern times this observation has now found scientific verification leading to a new field of science known as chronobiology; in essence the study of circadian (*circa*, about; *diem*, a day) rhythms. To the chronobiologist, time is not the abstract, intellectual structure

that most of us consider it to be but a fundamental structure of the universe. Our bodies have evolved to beat to the rhythm of the planet we live on and this is no coincidence. Biological clocks are found in living systems from bacteria to humans, all inextricably linked to the rotation of the earth on its axis and its movement through the heavens. This is not news to most of us; consider the rhythms of life – they are not randomised. The opening and closing of leaves, the release of a plant's perfume, herd migration, the growth of beard hair, body temperature, birth, menstruation, menopause, seasonally affected disorder (SAD), all are linked to time. The modern world impacts on our biology through technological advance. Electricity allows us to turn night into day at the flick of a switch and foreign travel is so quick we can fall asleep in winter and hours later wake in summer. Before 'clock' time was constructed people followed the laws prescribed by nature, and the motion of the planets. Nature's clocks no longer control us but are in competition with the ones on our wrists. Much of life's rhythms are under the control of the brain. Our body clock is hidden within the electrical activity of a cluster of cells called the suprachiasmatic nuclei. To complicate the issue, our environment interacts with our 'clock' genes which have now been localised.[2] Hundreds of years ago the Chinese observed the ebbs and flows of human physiology with regard to the day night cycle and even those of the seasons. Their observations can now be confirmed.

The famous symbol used to represent *Yin-Yang* illustrates a situation of homeostasis whereby *Yin* and *Yang* are present in equal quantities. The *Yin-Yang* symbol shows that the dark and light shaded areas can wax and wane and that at no point is either *Yin* or *Yang* absolute. The small dots within the larger shaded areas indicate that even at a maximum there is a seed of the opposite; it is said that all things hold the *Yin* within themselves and the *Yang* cradled in their arms. Even at the dead of midnight, therein lies the seed of daytime because time never stands still and the Earth keeps turning; there is no real present because as soon as the now exists it is gone in an instant.



Yin-Yang symbol

Yin-Yang theory can be applied universally to natural phenomena; it does not only apply to medicine. *Yin-Yang* theory describes the fundamental laws of the

universe. It is these laws, which can be described in terms of *Yin* and *Yang* that result in the symmetry of life, the universe and everything. These natural laws are of course the laws of physics.

Yin-Yang is an expression of the dynamic interplay between opposites to achieve homeostasis. Fundamentally, it describes energy and matter; the more ethereal aspect, energy, pertains to *Yang* whereas the denser aspect, matter, pertains to *Yin*. As previously established, energy and matter are essentially the same thing, although differently manifest. *Yin* and *Yang* therefore describe different manifestations of the same thing, at opposite ends of the spectrum if you like.

If we consider the building block of matter, the aforementioned atom, we can understand more about *Yin-Yang* and their inter-relationships. Remember that the model of an atom consists of a nucleus containing protons and neutrons with electrons orbiting around it. The number of protons and electrons is equal so their opposite electrical charges cancel out; *Yin* and *Yang* are balanced. It is worth mentioning here that hot (*Yang*) and cold (*Yin*), and positive (*Yang*) and negative (*Yin*) do not actually exist in this context but are just descriptive terms, so therefore they are equal but opposite, neither superior to the other.

The denser, more substantial part of the atom is its nucleus; electrons form only a small fraction of the total mass of an atom. So in this case, the nucleus is *Yin*, and the lighter fraction, the electron, is *Yang*. Electrons are mobile whereas the nucleus is not; activity pertains to *Yang* and inactivity to *Yin*. With reference to time, we now disregard the sundial and instead use the second as defined by the more reliable oscillation of a caesium atom.

Yin and *Yang* serve only one purpose in Chinese medicine. They give us a model by which to differentiate the aetiology and pathology of disease and consequently to formulate an appropriate treatment plan according to the individual symptom presentation of a given patient.

In order to apply *Yin-Yang* clinically we must, of course, learn something about its correspondences and any rules that apply.

If we look at the Chinese characters for the words *Yin* and *Yang*, and also at its symbolic representation, this will serve as a good starting point for its understanding.

The character for *Yin* represents the shady side of a mountain.

Character for *Yin*

The character for *Yang* represents the sunny side of a mountain.

陽

Character for *Yang*

In order to understand how *Yin-Yang* can be experienced it will be useful to conduct a thought experiment. In your mind's eye imagine yourself sitting on a mountain, first on one side, then on the other. How does it feel fundamentally different?

How we experience the mountain will differ depending upon which side we stand. These differences can tell us our first *Yin-Yang* correspondences (Table 13.1).

The presentation of signs and symptoms can be translated into the language of *Yin-Yang* to help us understand their root. Should there be an attempt by some external influence to disturb the internal environment of the body then several processes will occur in an attempt to affect homeostasis. These signs of change are indicative of imbalance and can occur as a result of two situations:

1. Moderate but persistent external influences
2. Extreme external influences

To help illustrate change as a result of these influences, another thought experiment is useful. We can again use the model of the imaginary mountainside. Firstly, picture ourselves on the *Yang* side,

Table 13.1

Yin	Yang
Darkness	Brightness
Cold	Heat
Rest	Activity
Wetness	Dryness

where it is sunny and warm. While you are standing on this mountainside, unfortunately, a landslide occurs and you get trapped, unable to descend. Being the ill-prepared mountaineer type that you are, you are not equipped with cool drinks, sunscreen or sun hat. There is no stream or lake anywhere in sight where you may bathe to cool off or take a refreshing drink. After a time your body will be nudged out of homeostasis and will warn you that you need to address this problem before you get ill. These observations are broadly representative of what Chinese medical practitioners call *Yang* disease. Simply put, all it means is that the body is starting to overheat and certain signs and symptoms will be apparent indicative of the imbalance. Table 13.2 will give you an idea of the kind of observations you might make.

Now let us imagine ourselves on the *Yin* side of the mountain where it is cold and snowy. Again, being rather unfortunate while on the mountain, an avalanche occurs and you are trapped, once again unable to descend. As ever, rather unprepared, you do not have a thermos flask filled with nice warm soup, a hat, woolly jumper, scarf or gloves. This does not agree with your body and it will show signs of complaint as it moves away from homeostasis. These signs are broadly representative of *Yin*, or cold type disease (Table 13.3).

In this way, any symptom can be transposed into the *Yin-Yang* system of categorisation. Clearly, this is a simplified version to aid understanding. Every symptom that a patient may present with and every organ system is questioned, in detail, to come to a *Yin/Yang* diagnosis. It should also be noted that it is not uncommon for patients to have a mixture of signs and symptoms if they have several conditions or multiple organ pathologies. In order to gain a more thorough understanding pertinent to substance misuse, a little more explanation is necessary.

Table 13.2

Yang Symptoms
Sensation of heat or fever
Restlessness
Thick, sticky secretions
Thirst
Sweating
Hot, red skin or rashes
Inflammation
Anxiety
Insomnia
Constipation
Concentrated urine
Rapid pulse

Table 13.3

Yin Symptoms
Chills and shivering
Lethargy
Clear, watery secretions
No thirst
No sweating
Cold, pale skin
Oedema
Sedate
Sleepy
Loose stool
Abundant urine
Slow pulse

Yin and *Yang* describe opposites

It can now be seen that essentially *Yin* and *Yang* are complementary opposites; this is fundamental to nature. This opposition is not however absolute, it

is a relative opposition. Something can only be defined as either *Yin* or *Yang* with respect to a given reference point. With regard to the human body that reference point is homeostasis. Should there exist much deviation from this point signs and symptoms will manifest.

For example: *Yin* pertains to cold and *Yang* to hot. But by what definition? Is 20°C hot or is 50°C hot? And if 50° is hot is 49°? The answer is it depends entirely on the point of view of the observer; it is relative. In the body we at least have some idea of an average normal body temperature, 37°C (degrees Celcius). This figure indicates *Yin* and *Yang* in harmony; any colder or hotter and there is a degree of imbalance.

So, if *Yin* and *Yang* are relative there can be no absolutes; *Yin* and *Yang* are in a state of dynamic equilibrium. For example, in chemistry, some types of reaction are reversible, i.e. the products C and D are produced by the reaction of A and B but also the reaction of C and D will produce A and B. So which is the product and which is the reactant, is, in a sense, hypothetical.

$$\mathbf{A + B \leftrightarrow C + D}$$

In these types of reaction a position of equilibrium is reached; the quantities of the products balance each other but the chemical reactions on either side of the equation do not stop occurring. The balance is only apparent; the equilibrium is dynamic.

Viewing the universe as a closed system, where no substances can escape, an intermediate position is reached; *Yin* and *Yang* are balanced. This principle was stated in the Western world in 1888 by Henri Le Chatelier. He stated that when any system at equilibrium is subjected to change the system will adjust in such a way as to minimize or accommodate the effect of the change. For example, if you apply heat to a system the reaction will shift in an endothermic direction, i.e. one that absorbs heat.

This theory of equilibrium is important in human biology because biological reactions tend to be reversible. One should remember, however, that the body is not a closed system. We can, for example, put nutrition into the system and reaction products can be removed. It is this that allows reversible reactions to continue moving in a specific and desired direction.

The temperature of the body is a useful example here too. Although our temperature is around 37°C it will not be absolutely stable; it will adjust according to changes to the system, for example, through exercise or climatic factors. If we exercise and get hot, our body will go through several changes to bring about homeostasis again, for example we sweat.

Mutual consumption

Yin and *Yang* are in a constant state of flux; remember, homeostasis is a dynamic process. *Yin* and *Yang* consume each other, so an excess of either one will induce a decrease in the other. For example, if we have a bout of intense exercise and increase our *Yang* it will induce a decrease of our *Yin* or body fluids thus leaving us dehydrated (due to sweating). Similarly if we stay out in the cold (*Yin*) too

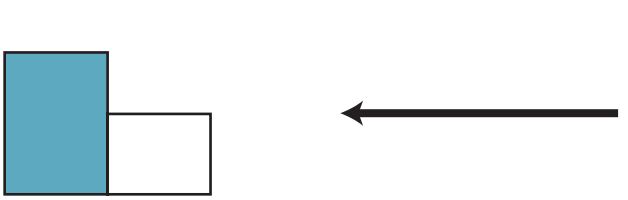
long it will induce a decrease in our *Yang* energy, our circulation will be impaired and our extremities turn blue.

The ideal situation for health is a balance of *Yin* and *Yang*, as denoted by the Tai Chi symbol. In disease, there is an imbalance. We use the following bar diagrams to illustrate the possible imbalances of *Yin* and *Yang*; these are easier to draw and understand than altering the circular Tai Chi symbol to reflect imbalance:

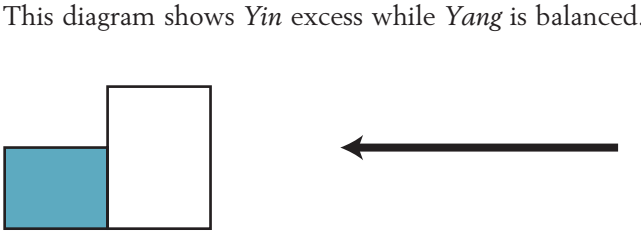
This diagram shows *Yin* and *Yang* in perfect balance, the horizontal arrow indicating their ideal level, that of homeostasis.

This diagram shows *Yin* deficiency while *Yang* is balanced.

This diagram shows *Yang* deficiency while *Yin* is balanced.



This diagram shows *Yin* excess while *Yang* is balanced.



This diagram shows *Yang* excess while *Yin* is balanced.

Table 13.4

1. Excess of Yin
2. Excess of Yang
3. Deficiency of Yin
4. Deficiency of Yang

Table 13.5

1. Increase Yin
2. Increase Yang
3. Reduce Yin
4. Reduce Yang

So, simplistically, four types of imbalance can exist, as shown in Table 13.4.

So let us consider how signs and symptoms might manifest in each of the diagrams of imbalance. First, consider the picture where *Yin* is balanced but *Yang* is excess. A patient with this picture will experience the symptoms outlined for *Yang* in Table 13.2. These symptoms could be described as Full-Heat because the hot symptoms are due to excess.

Now consider the picture where *Yang* is balanced but *Yin* is in excess. A patient with this picture will experience the symptoms outlined for *Yin* in Table 13.3. These symptoms could be described as Full-Cold because the cold symptoms are due to excess.

Next consider the picture where *Yang* is balanced but *Yin* is deficient. A patient with this picture will also experience the symptoms outlined for *Yang* in Table 13.2. The difference being that, this time, the symptoms are described as Empty-Heat because they arise due to a deficiency of the cold aspect. This means that in terms of relativity, what the body manifests is more of the hot, *Yang* aspect than of the cooler, *Yin* aspect. The *Yang* is therefore only in apparent excess.

Finally, consider the picture where *Yin* is balanced but *Yang* is deficient. In this case, the patient will also manifest with the symptoms outlined for *Yin* in Table 13.3. These symptoms are described as Empty-Cold because they arise due to the deficiency of *Yang* as there exists a relative excess of *Yin*. The *Yin* is therefore only in apparent excess.

So it can be seen that symptoms can sometimes be misleading. Very similar symptoms can actually have a different root and hence should be treated as such. Practitioners of Chinese medicine learn how to question the body in great detail using several diagnostic tools that allow them to differentiate the true root of disease without jumping to wrong conclusions. In reality, a much extended version of this *Yin-Yang* model is used. These methods are out of the scope of this text but with regard to substance misuse turn out to be unnecessary in any case. This is due to the fact that addictive behaviour is rooted in the same imbalance regardless of the drug of choice.

In a nutshell the various treatment approaches can be outlined in Table 13.5.

Yin-Yang and the duality of the autonomic nervous system

As previously described the autonomic nervous system is responsible for the control of homeostasis. It achieves this by constant monitoring and change of all body functions. There are two divisions which, as described by *Yin-Yang* theory,

work in complementary opposition, the sympathetic and parasympathetic divisions. Table 13.6 illustrates this opposition.

Yin-Yang and the neurotransmitters

As aforementioned, it should be noted that neurotransmitters are also broadly considered to have either excitatory or inhibitory actions. As such, they can also be viewed from the perspective of the duality represented by *Yin-Yang* theory. Some pertinent examples are shown in Table 13.7. It should be noted that

Table 13.6

Sympathetic nervous system (Yang)	Parasympathetic nervous system (Yin)
Increased heart rate	Decreased heart rate
Increased blood pressure	Decreased blood pressure
Increased sweating	Decreased sweating
Rapid breathing	Slow breathing
Diarrhoea	Constipation
Muscle tension	Muscle relaxation
Goose bumps	No goose bumps
Behavioural arousal	Behavioural inhibition
Stress	Relaxation

Table 13.7

Yang neurotransmitters	Yin neurotransmitters
Dopamine – anticipation, excitement, arousal, craving	Serotonin – increases satisfaction, maintains self control, reduces depression, reduces craving, reduces anxiety and promotes sleep
Glutamate – excitatory, implicated in seizures and fits. Associated with memory	GABA – reduces stress, anxiety and pain
Norepinephrine – transmitter of sympathetic nervous system hence of stress and fight or flight response	Acetylcholine – transmitter of parasympathetic nervous system, facilitates relaxation
Substance P – relays pain messages. Associated with stress and anxiety	Endorphin – restricts transmission of pain, reduces craving and depression

neurotransmitters can have different actions in different parts of the nervous system and so this list refers to functions relevant to the substance-misusing client group.

Yin-Yang and the brain

The limbic system is the part of the brain where addictive chemicals exert the bulk of their influence. Although some neuroscientists include the frontal cortex as part of the limbic system it is, for our purposes, clearer to consider it as separate. It is involved in reward but it very much takes on the role of executive function.

The limbic system motivates reward seeking and so can be considered *Yang* in nature. It is activated by several situations including: the pharmacological effects of drugs, withdrawals, memory and the presence of possible reward-causing craving. Activity here is fuelled by the actions of the *Yang* neurotransmitter, dopamine.

So let us recap. The limbic system is the emotional part of the brain. It is here that the pleasure centre resides along with a whole host of other modules whose collective purpose it is to initiate instinctive survival behaviours such as reward seeking. The frontal cortex is the part of the brain that can restrain the excitement of the limbic system and so can be considered *Yin* in nature. This aspect of frontal cortical activity is fuelled by the *Yin* neurotransmitter, serotonin.

What is necessary for optimal brain function with regard to impulse and impulse control is, as ever, balance. Harmony is necessary between the limbic system and frontal cortex, dopamine and serotonin, and *Yin* and *Yang* (Fig. 13.1).

Survival mechanisms

Normally, this dynamic interplay of neural mechanisms governs our survival behaviours. This can be illustrated using hunger for food as an example (Fig. 13.2).

Yin, *Yang* and addictive behaviour

With respect to addictive behaviour, two themes dominate. In the absence of the drug or behaviour individuals crave what they are lacking and are motivated to seek out their drug(s) of choice. Drug withdrawal is also an important feature although not definitive of addiction per se. It is quite possible to experience withdrawal symptoms from drugs that are not addictive in the behavioural sense.

In terms of how the repercussions of drug use feel to a patient the following list is fairly representative:

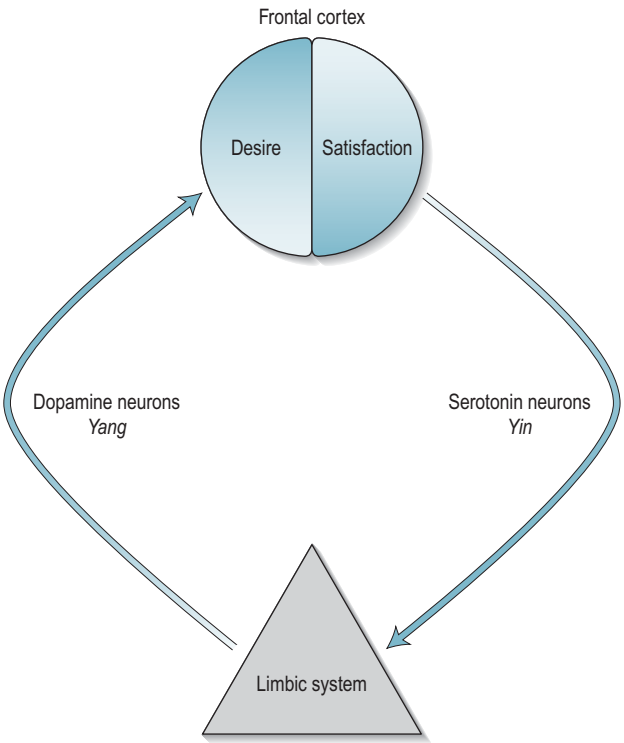


Fig. 13.1 Homeostasis of impulse control.

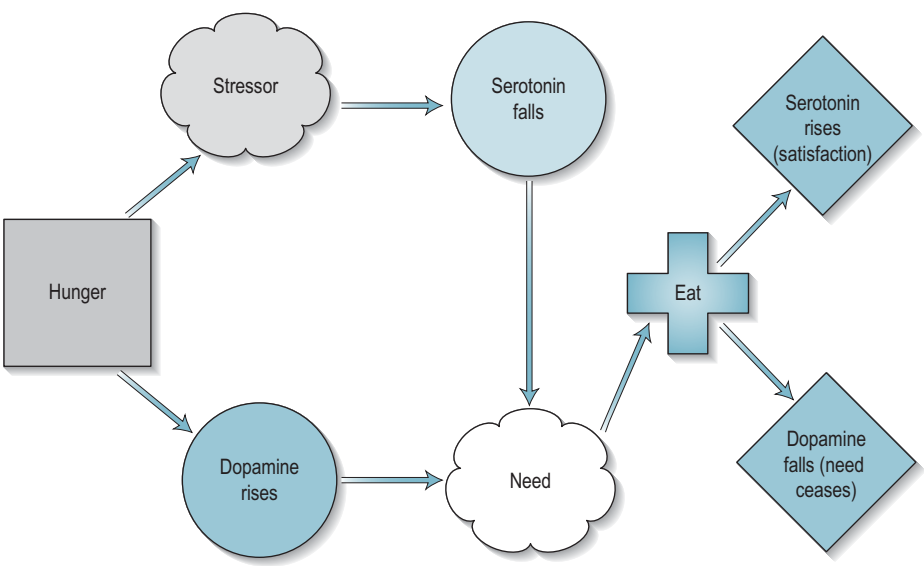


Fig. 13.2 Mechanisms of survival behaviours.

1. *Stimulants*. Depression, insomnia, anxiety, restlessness, paranoia, craving, lack of motivation for all else but drugs, lack of self control
2. *Depressants*. Depression, insomnia, anxiety, restlessness, paranoia, craving, lack of motivation for all else but drugs, lack of self control

As can be seen from the list the manifestations of addiction are actually rather similar, regardless of the chosen substance. What can differ is some of the physical withdrawal effects; these tend to be the opposite of those of the chosen chemical.

The reason for the similarity lies in the fact that addictive chemicals, although having some quite diverse physical effects, have the same action in terms of their effect on the reward circuitry. The commonalities lie in their effects upon dopamine levels in the limbic system and the resultant inhibition of the frontal cortex.

From the perspective of *Yin* and *Yang* the lists of the key signs and symptoms of addiction are pretty clearly *Yang* in nature. This is because all drugs or addicting behaviours increase the *Yang* neurotransmitter dopamine. The difference lies in how the excess heat is caused and is dependent on the category of drugs chosen. This corresponds with the different ways with which drugs cause the increase in dopamine as outlined in the chapter on the addictive chemicals. An analogy is again useful to help understand how this arises.

Consider the following illustration.

In the cauldron model of addictive behaviour, the cauldron is used to represent the human body. The flames are used to represent the *Yang* aspect of brain activity. The fluid in the pot is used to represent the *Yin* aspect of brain activity. Should the brain 'overheat', lots of activity becomes apparent at the fluid's surface – it bubbles wildly and steam is given off; this is a model for the signs of addictive behaviour, that of insomnia, anxiety, restlessness, etc.

Let us consider two time frames:

1. A person has recently taken the drug and is experiencing its effect
2. The brain has adapted to the presence of the drug; it has been metabolised and is being excreted.

Stimulants

In the first time frame, stimulants provide the user with an initial rush of energy and euphoria, increasing alertness, concentration and endurance. Clearly this represents an increase in the *Yang* aspect, a stoking up of the fire. In the second time frame, one would expect that the *Yang* manifestations lessen but as can be observed this is not true in terms of the brain and behaviour, only with some of the physical effects. The patient manifests with all the *Yang* symptoms mentioned above. This is because according to the rule of mutual consumption, the *Yin* aspect has been consumed. By analogy, excess fire dries up the water.

Depressants

In the first time frame, depressants provide the user with relief from anxiety, insomnia, increasing calmness and relaxation. It would appear therefore that these drugs increase *Yin*. However, this is not the case; the apparent cooling effect is purely illusory. What in reality these drugs do is mask the *Yang* excess. This becomes clear in the second time frame, when the drug wears off. The user is now left with the same, and usually worse symptoms of agitation. Depressants are analogous to putting a lid on the cooking pot. It is now impossible to see all the agitation and steam. This is the desired effect to a user – no symptoms of agitation. The problem is because the heat cannot escape as it builds – a pressure cooker has been created. Imagine trying this at home: if you put a lid on a pot it comes to the boil much quicker; if you then slide the lid off it would be most unwise to have your face above the pot as all the heat (symptoms) escape. Often, as tolerance builds to a drug, valium for example, the symptoms may recur and so a heavier lid is prescribed or self administered. So again, in time, as heat builds the water evaporates as steam (when allowed to escape).

To summarise, stimulants create heat by stoking the fire; depressants create heat by suppressing the heat and creating a pressure cooker. The net result is the same: addictive behaviour manifesting as craving, restlessness, insomnia, agitation, paranoia, psychosis, etc. In both cases a user will ultimately suffer the pattern of *Yin* deficiency causing an uncontrolled flaring up and down of *Yang*. Consider a candle just about to run out of paraffin wax (*Yin*), the flame (*Yang*) flickers up and down uncontrollably.

The treatment principle, therefore, in Chinese medical terminology is to increase the *Yin*. How this relates to key neurotransmitters will be addressed below. Auricular acupuncture addresses this issue of *Yin* deficiency, thereby increasing the ability of the individual to exhibit restraint, and supporting overall improvements in well-being.

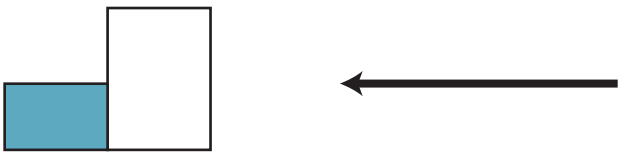
Yin-Yang and the psychoactive chemicals

The key to understanding the addictive nature of all the substances of abuse is not through knowledge of their diversity but through comprehension of their similarity. Clearly the similarity lies in the fact that although these drugs cross the spectrum of pharmaceutical manipulation of the nervous system they all converge at the same point: addiction. The neurobiological process of addiction as outlined previously is predominantly rooted in the cross talk between the neurotransmitters, dopamine and serotonin, and two key areas of their activity, the limbic system and frontal cortex. The diversity of pharmacological action of the drugs is such that the means with which their impact on these key neurotransmitters varies but the net result is the same. So let us clarify again what happens to the addicted brain:

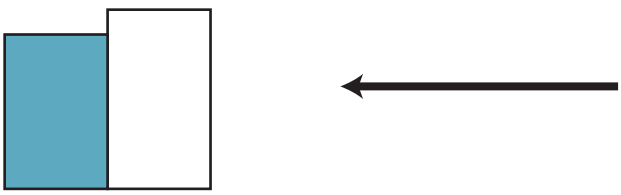
1. Serotonin signals satiation. This is the mechanism of liking. When serotonin levels fall dopamine is raised as a consequence.
2. Dopamine drives craving, anticipation and the memory of pleasure. This is the mechanism of wanting.
3. Underactive serotonin systems mean that natural behaviours do not supply much reward or pleasure.
4. Underactive dopamine systems mean that natural behaviours are not recorded as satisfying and so are not sought and anticipated in normal ways.
5. Drugs (or strongly emotional behaviours) overpower normal rewards with regard to their ability to force a rise in dopamine significantly and so carry high value.
6. These behaviours are now strongly burned into memory systems.
7. The overpoweringly high neurotransmitter levels cause a resetting of the liking and wanting thermostats.
8. The dopamine system is subnormal but sensitised by memory to addictive behaviours that have proved themselves to be highly rewarding.
9. Withdrawals cause a reduction in serotonin and a hypersensitivity of dopamine neurons and so are felt more strongly than is 'real'. This causes a rise in dopamine and consequently craving.
10. The memory of pleasure triggers hypersensitivity of dopamine neurons to further drive cravings of drug use. There is again some rise in dopamine levels.
11. Although both serotonin and dopamine are subnormal due to the biochemical pathways of serotonin synthesis there exists a relative excess of dopamine at all times.
12. In short, what exists is uncontrolled fluctuations in dopamine relative to serotonin.

These relationships can be expressed in the language of *Yin* and *Yang* as follows:

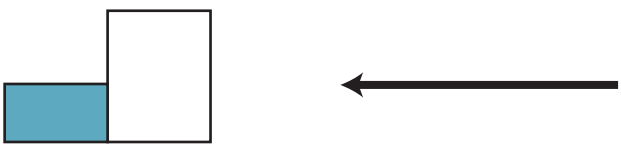
1. While on an addictive drug, *Yang* (dopamine) rises uncontrollably.



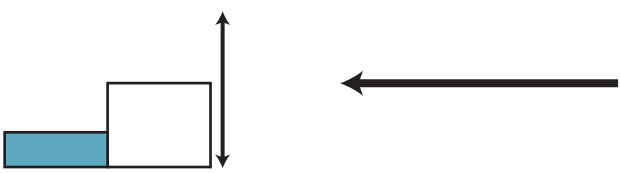
2. In an attempt to redress the balance *Yin* (serotonin) will rise, if sufficient satiation will occur. Satiation is of course not the reality of an addict, due to imbalances in the serotonin circuitry. It can never rise strongly enough to match dopamine manipulated by drugs.



3. The drug-induced rise in dopamine results in the depletion of the serotonin.



4. The down-regulation of dopamine also causes it to deplete to subnormal but it is easily retriggered by memory or renewed drug intake. In the presence of insufficient *Yin* (serotonin), *Yang* (dopamine) flares uncontrollably.



How does acupuncture affect this situation?

This section summaries the hypothesised mechanisms of ear acupuncture and synthesises it with *Yin-Yang* theory.

1. Needling stimulates nerves in the ear.
2. This stimulates the raphe nuclei in the brainstem.
3. This causes an increase in production of serotonin (*Yin*).
4. Sympathetic nervous output (*Yang*) influenced by the amygdala and the locus coeruleus is reduced by the increased inhibitory input from the serotonin.
5. Serotonin helps reduce pain through its action on nociceptors.
6. Endorphins (also *Yin*) are also released. This helps control fear, pain and anxiety.

So, the action of acupuncture upon reinforcing *Yin* reduces the uncontrolled flaring of *Yang*.

Yin-Yang and the stages of change

It must be accepted that in order to succeed in the task of tackling addiction, one must change. It is our belief that for change to occur, behaviour must carry with it an emotional charge. It is not sufficient for most to be informed that a behaviour is unhealthy or expensive. Attempting to talk to the conscious brain in the initial stages will not be effective because the disorder lies in the subconscious part of the brain. Recognition of a fact has to be heartfelt. One's emotions or beliefs related to a behaviour must be consciously experienced, challenged and ultimately changed. The transtheoretical model of change used by many addiction counsellors and psychologists seeks to explain why it might be that patients either succeed or fail. It is this model to which motivational interviewing techniques are applied. It is a model that helps us to understand why patients sometimes appear to be fixed within a given pattern of behaviours. The model is based upon years of research and has come to find that individuals appear to flow through a series of stages when adopting new behaviours and that there exist certain predictors of progression through the stages of change.[3]

These stages of change are:

1. Precontemplation: in this phase individuals exhibit no intent to change their behaviour. They may be described as being in denial or unmotivated. The individual is unaware that a behavioural modification could improve their life.
2. Contemplation: in this phase individuals have recognised that they have a problem. They state their intent to change but are likely to delay or postpone any action.
3. Action: in this phase the individual makes perceptible attempts to modify their behaviour. They are motivated to change.
4. Maintenance: this phase is used to consolidate gains initiated during the action phase and prevent relapse.

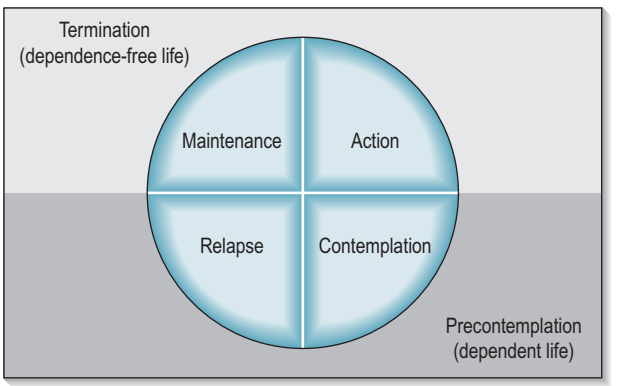


Fig. 13.3 The cycle of change.

5. Relapse: if this occurs the cycle restarts at either precontemplation or contemplation.
6. Termination: in this phase, former behaviours are known to be undesirable.

See Figure 13.3.

In an ideal world, progression through these phases over time is in a linear fashion. In reality this is very rarely the case. It is far more common for patients to make several unsuccessful attempts, sometimes moving forward and sometimes taking a retrograde step or two. It is also not uncommon for events to occur in a circular fashion, an individual moving through all the steps but then relapsing and ending up back where they started. Rotation through the cycle can take up to seven cycles.[4] This should not be seen as out-and-out failure. Everything that one has done in the past got the patient to where they are today and so any experience, positive or otherwise, can be learned from.

The principles of cognitive behavioural therapy are often applied to help the patient move round this cycle of change. The patient must be helped to:

1. Spot errors in their thinking and understand their thought processes related to the problem
2. Identify and measure their emotional reactions to the problem
3. Identify how thoughts and feelings interact to produce the behavioural patterns
4. Challenge their thought patterns and implement alternative behaviours

Individuals can be helped to move round the cycle of change but ultimately they need to think, and particularly feel, all its components. Assisting in this process is the role of a skilled professional and not the role of those unqualified to do so.

Most professionals working in the field will have many times come across individuals for whom change seems impossible. They seem 'stuck'. It would appear obvious that in order to remove 'stuckness' one needs to initiate movement. In Chinese medical terms, movement is energetic and therefore *Yang* in nature. Herein lies the problem. How can patients be expected to move if they do not have the fuel (*Yin*) reserves to do so? As we have established previously, the predominant problem is that addicted patients are termed *Yin* deficient. The problem lies not therefore in an inability to move which is illusory, but in that the patient lacks the fuel to provide movement. By analogy, you can push a car all you like but it will not keep moving until you put some petrol in the tank. While talk therapies (pushing) are of course a vital component it seems that something else is often needed. Acupuncture appears to fill that gap. Through supporting the *Yin* aspect of a person their 'petrol' reserves are built up which provides the potential for change. Remember that the agent for change often lies in the ability to reflect upon one's internal state with reference to controlling and understanding emotionally driven, compulsive behaviours. This ability to show restraint is driven by the serotonin (*Yin*) projections into the frontal cortex. It is an increase in the production of serotonin that acupuncture is thought to effect through its actions in the raphe nucleus, as shall be fully discussed in the final chapter.

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CHAPTER 14

Auricular acupuncture mechanisms

'If the only tool you have is a hammer, you tend to treat the world like a nail.'

(Anonymous)

Historical background

For most scientifically-minded individuals, it is difficult to imagine how needling a given site on the body can affect the function of an area anatomically distant from the needle site. It feels instinctively ridiculous. There exists, however, a rapidly expanding evidence base to support the clinical application of acupuncture. The research to date very strongly suggests that acupuncture mechanisms are linked to its effects at the neurophysiological level.

Hundreds of years ago the Chinese discovered that acupuncture benefited many conditions. Since neither they, nor anyone else at that time, had the scientific understanding to explain its possible modes of action they created a theory that worked for them practically. This was the theory of *Qi* energy and acupuncture meridians. Human knowledge has subsequently greatly expanded and so outdated concepts are replaced by that of current scientific reason. This is in no way a criticism. The pioneers of acupuncture created an incredible system of medicine purely by strict application of the scientific method: observation, reason and experiment. It is the nature of science to evolve and improve upon knowledge that already exists. It is unscientific to stop asking questions. In the spirit of this advancing knowledge, much of the research into the physiology of acupuncture is conducted in the Far East and seeks to support the development of Chinese medicine, thus bringing an ancient therapy into the modern world. Traditional Chinese medicine (TCM) is fast becoming contemporary Chinese medicine (CCM) and this can only be a positive step forward.

Auricular acupuncture is rooted in ancient China and was first mentioned in a rudimentary way in writing in the *Yellow Emperors Classic of Internal Medicine* (*Huang Di Nei Jing*), dating from c. 500 BCE. Between 500 BCE and 100 CE, ancient Egypt, Greece and Rome had also adopted the clinical use of auricular acupuncture, which was recorded by both Hippocrates and Galen, whose theories dominated Western medical science for over 1300 years.

Auricular acupuncture, as practised today, is largely influenced by the work of a Frenchman, Paul Nogier. In 1957, Nogier developed a more complete theory which became so respected that it was adopted by the Chinese themselves, becoming integrated into their existing model which previously consisted of seemingly random scattered points useful for the treatment of various conditions. Nogier's theory proposed that auricular acupuncture points be arranged on the auricle in such a way as to correspond to an inverted fetus in utero, with the head represented in the region of the ear lobe and the limbs towards the top of the ear. This theory for the arrangement of the acupuncture points on the ear was based upon the proposition that the points were mapped as a homunculus (little man) in the same way that a neurological homunculus has been demonstrated for some areas of the cerebral cortex. A distorted human figure can be superimposed on diagrams of the brain to reflect the relative space our body parts occupy on the somatosensory cortex and motor cortex (Fig. 14.1). There is as yet no research to substantiate the connection between Nogier's homunculus (Fig. 14.2) and the organisation of neurons in the brain. While being an incredibly ingenious piece of work, with no evidence to support it, the proposition does seem to require a leap of faith and so is not a model that we subscribe to, but may perhaps form the basis for some fascinating future research projects.

The use of auricular acupuncture for addiction is a much more recent phenomenon. In 1973, Dr Wen, a neurosurgical consultant in Hong Kong, started investigating the potential for acupuncture to be used as an analgesic for operative and postoperative pain. At that time in Hong Kong a massive 15% of the population were opiate addicts. As a consequence, during the course of Wen's investigations, several patients volunteered the information that following

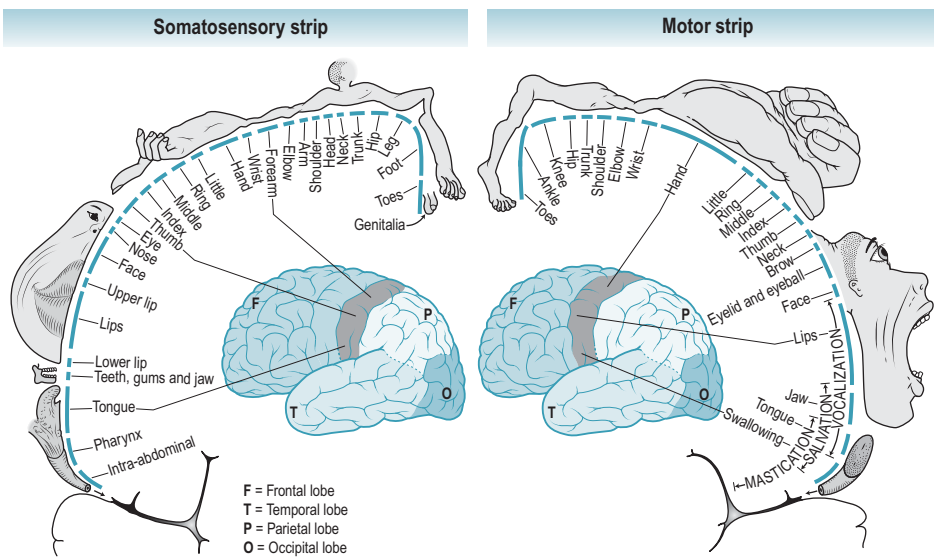

Fig. 14.1 The homunculus in the brain. F = frontal lobe, O = occipital lobe, P = parietal lobe, T = temporal lobe.

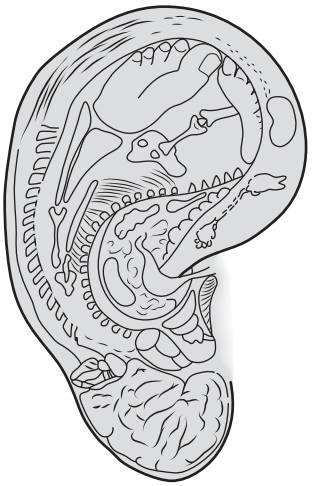

Fig. 14.2 Auricular homunculus.

acupuncture their opiate withdrawals improved. Concomitant to this Wen found many addicts willing to try acupuncture as a treatment for their drug dependency. Wen and his co-researcher Cheung reported on their first 40 patients in the *Asian Journal of Medicine* in 1973.[1] A single case was also described in detail by Sainsbury in the *Medical Journal of Australia* in 1974, in which the results were witnessed by independent psychiatrists.[2]

In Hong Kong in 1973, the presence of addicts in surgical wards was deeply resented and so the patients received no other therapeutic interventions commonplace today, such as counselling, behavioural therapy or medication. Despite this the majority of Dr Wen's patients improved, 39 out of 40 patients abstaining from drug use without the need for medication.[1]

Several years later, in the mid-1970s, at the Lincoln Hospital in the Bronx, New York, Michael Smith was searching for an alternative to methadone treatment for heroin addicts and became interested in Wen's findings. Smith gradually modified Wen's protocol with the addition of several other points chosen empirically according to the clinical presentation of addicted patients. Another key modification by Smith was to discontinue the use of electroacupuncture in favour of manual needle manipulation, which he felt provided more consistent clinical outcomes. In personal conversation with Smith, he has suggested that he is not particularly in favour of research, believing that patients tell you what you want to hear. We would agree that in some cases this is true, whereas in other cases, such as with incarcerated populations, the opposite may actually be true. For these reasons, more research using biochemical markers or neuroimaging techniques is desirable to eliminate such factors. However, a survey conducted at Lincoln Hospital in 1982 is of interest. Patients reported 90% relief of symptoms in acute withdrawal following acupuncture. Ninety per cent of all detoxification intake clients returned for further acupuncture treatment with no ancillary

incentives such as other medications, welfare credit or probation merits. An estimated 60% of all acupuncture clients receiving the full series of treatments remained drug free for at least several months.[3]

In 1989, a single blind placebo control trial was conducted at Hennepin County Detoxification Centre. After 6 months, none of the patients given the true treatments had been readmitted and 26% had not consumed any alcohol in that time. In the control group, 39 of the 40 patients had used alcohol and/or been readmitted.[4] The research highlighted the fact that this could mean potential cost savings if acupuncture was to be implemented.

In the US, several states have implemented the use of auricular acupuncture in drug courts whereby acupuncture is offered to offenders as an alternative to a custodial sentence. Studies at Multnomah County and American University in Washington DC show the re-arrest rate for those who did not receive acupuncture to be almost four times higher than those who received acupuncture treatment.[5]

The SMART (Substance Misuse Academy Registered Training) view

While undoubtedly Dr Nogier produced some truly innovative work on auricular acupuncture, there exist to our minds some conceptual difficulties. One of the main problems is that Nogier proposed several different patterns of somatotopic distribution on the same regions of the ear, and the Chinese proposed a further different map. This begs the question, how could the body possibly know which map, if any, is correct and which we have chosen to subscribe to?

Nogier noticed that the innervation of the ear corresponded to the three primary tissue types found in a developing embryo: ectoderm, mesoderm and endoderm. Following fertilisation of the human egg by a sperm the cell starts to divide. As it divides and grows the ball of cells differentiates into three distinct layers of tissue and it is from these three layers that the organs are formed:

1. The endoderm becomes the digestive tract, respiratory system and abdominal organs. Nogier states that these areas are represented in the central cave of the ear called the concha. This area is innervated by the tenth cranial nerve, a branch of the autonomic vagus nerve.
2. The mesoderm becomes muscle, connective tissue, joints, bones, blood cells, circulatory system, lymphatic system, adrenal cortex and urogenital organs. Nogier states these areas were represented on the antihelix, scaphoid fossa, triangular fossa and some areas of the helix. This area is innervated by the fifth cranial nerve, the somatic trigeminal nerve.
3. The ectoderm becomes the outer skin, cornea, eye lens, nose epithelium, teeth, peripheral nerves, spinal cord, brain, pituitary, pineal and adrenal medulla. Nogier states these areas are represented on the ear lobe and helix tail. This area is innervated by the cerebral cervical plexus nerves.

The areas of innervation mentioned above are not in dispute, but the flow of information from these areas to specific organs or tissues simply because they developed from the same embryological basis has not yet been substantiated and frankly seems somewhat far fetched. What could, however, be important is the innervation itself. With regard to the location of the points used for addiction, the somatic trigeminal nerve and autonomic vagus nerve are stimulated by needling and it would appear that it is the physiological response to this stimulation that accounts for the benefits to the patient.

Nogier described his alternative maps as phases. The phases allude to the different phases of light as it is separated when diffracted through a glass prism. It is suggested that the existence of more than one point at the same location is due to the notion that each type of primary embryological tissue has a certain resonance frequency. The alternate maps are related to differing activation of the frequency resonance of the corresponding tissue of the body. These frequencies were determined by holding different coloured transparency slides over the ear and monitoring for changes in amplitude of the pulse at the radial artery. In reality, a pulse change is inevitable and is most unlikely to have anything to do with the coloured slides. Any autonomic change caused by human interaction will affect the pulse. Treading on a toe, shouting 'boo' or touching someone's hair, for example, would have the same effect. All of these ideas are interesting, but remain hypothetical without scientific verification.

Resonance describes the tendency of an object to oscillate at maximum amplitude at a certain frequency. Human tissue does not, however, resonate due to low intensity light falling on it. It is possible to make some of the atoms in human tissue resonate but it is not straightforward, requiring the radio frequency pulses of a magnetic resonance imaging (MRI) machine to trigger atomic resonance or the application of ultrasound to trigger mechanical resonance. There is some scientific evidence to show that light can increase the production of cellular energy by stimulation of mitochondria, but this is a very different phenomenon to those suggested by Nogier. Nogier even went so far as to apply a plastic container of diseased organs to the skin of the arm. A change in the electrical conductivity of the ear was said to indicate the intolerance of the body to that particular tissue. This reaction was meant to happen only if the patient had the same imbalance as the organ in the container. Nogier would do the same experiment with a vial containing a virus or bacteria to assess what organism might be responsible for disease. He would then apply a container of homeopathic medicine (water!), trying several until the right supposed remedy was chosen by a change on the ear or pulse. Our view is that these far-fetched ideas eliminate any possible credibility that Nogier might have previously held.

Nogier also frequently referred to 'reticular energy' and to the *chakra* energy of Ayurvedic medicine. Without clear definition these concepts, too, appear unscientific. Although many still refer to Nogier's work, his reference to esoteric concepts has now led many practitioners to subscribe to the Chinese charts of auricular points, which although based on the work of Nogier are not identical. It is to the Chinese charts and point naming system that Smith subscribed when

developing the substance misuse protocol. We are of the mind that esoteric concepts are not helpful to the integration of acupuncture into scientific medicine. To that end we also choose to shy away from the traditional Chinese or Nogier point-naming system, as it serves only to confuse those with Western medical training and certainly does not increase the understanding of the practitioner seeking to work in the field of addiction.

With regard to the theory of the homunculus superimposed onto the ear we struggle to make sense of it. It seems to have developed largely because an embryo bears some visual resemblance to a human ear. This is not a satisfactory basis for a system of medicine. Sensory information gathered by the nerves of the auricle are merely ultimately relayed to the area of the somatosensory cortex related to the auricle itself and not other areas of the body. It seems unlikely, therefore, that the connections suggested by the homunculus theory can be correct. The broader acupuncture effects are more likely to be the result of humoral mediation, whereby the circulation of neurotransmitters and hormones carry the effects of sensory information to more widespread areas of the body.

Some research has shown that acupoints in the ear are selective in function. Asamoto and Takeshige (1992) stimulated points in the inner cave of the ear which correspond to the theoretical representation of the gastrointestinal tract.[6] The stimulation caused activation of part of the hypothalamus associated with satiation of appetite. Stimulation of more peripheral regions of the ear did not activate the hypothalamus. This was taken as proof of the existence and selectivity of the stomach point. We would suggest that this is not the case without more specific research. Would it not be more accurate to state that this point was the hypothalamus point since it did not affect the stomach itself? It is more likely that because the periphery and inner ear are innervated differently, stimulation of the areas causes a different response. It is quite possible and likely that stimulation anywhere in the inner cave of the ear causes the same hypothalamic change. The Chinese 'lung' point, also in the concha, being innervated by the vagus nerve may, for example, have the same effect.

Until much more research is gathered, our preference is to relate the function of the acupoints to the observed behavioural responses of an addicted patient. This does not dismiss the more commonly used names out of hand, but merely allows the point functions and names to be integrated into the language and paradigm familiar to that of a substance misuse worker. It is also our preference not to refer to ear points affecting the flow of *Qi* energy in the meridians. Our interpretation of *Qi* has been clearly outlined earlier in the text, which expands on our view that meridians do not exist at all but that the mechanisms of acupuncture – whether auricular or somatic – are neurophysiological. Whether these 'points' have direct influence on the specific brain modules will require neuroimaging research. It is our view that the apparent selectivity of points relates to the underlying nerve distribution of the area and not to the flow of *Qi* in meridians. It is therefore likely that there are actually far fewer 'points' than is commonly accepted, but rather that a handful of areas have a limited sphere of action.

Point naming

Previously, the points used to treat addiction, as empirically shown by Smith, have taken the Chinese names ascribed to them. The problem with this system is that the words used are either in the Chinese language or use names relating their function to traditional Chinese medical organ designations. For practitioners in the West these terms are confusing, either because they do not speak Chinese or do not understand the multitude of physiological functions that the Chinese traditionally attached to organ complexes. It is also the case that these traditional names can provoke fear in patients when they hear that their 'liver' or 'kidneys' are being treated. According to the Chinese organ designations these ear points are capable of affecting an enormous array of conditions. Whether true or not, this naming system does not support the understanding of SMART practitioners and so is not particularly useful. To this end, we have chosen names that relate to addiction much more closely. The names we have chosen do not relate to specific point function because, as with the existing names, this is currently unprovable. They relate to the needs and clinical presentation of addicted persons and use the mnemonic SMART purely for the ease of memorisation, as shown in Table 14.1. These names do not imply any specificity of point function, but give a sense of the overall behavioural picture. For those who do not find mnemonics useful, a simple numerical system is also used. It is likely that the 'points' are actually much more diffuse areas that can be used to provide neural stimulation. At this time, however, no controlled research has been carried out comparing various adjustments in needle positioning and so, since these points have shown themselves to be beneficial, the locations should be upheld.

Table 14.1

Traditional Chinese name	SMART name
Sympathetic	**S**edation
Shenmen	**M**otivation
Kidney	**A**nxiety
Liver	**R**esolve
Upper Lung	**T**emptation
Lower Lung	**T**emptation

Auricular points and diagnosis

Unlike the somatic (body) acupuncture points, those of the ear are said to become detectable only if there is a pathological condition in the corresponding part of the body that the auricular acupuncture point represents. It is also considered by many that the precise location of the auricular acupoint may move slightly from day to day, as it reflects the different stages of the underlying disorder.[7] It has been observed that in some cases there is increased sensitivity to pain on palpation of certain points, corresponding to pathology in the related organ or body structure.

We are very cautious about such diagnostic claims, which seem to be rooted in the observation of the phenomenon of referred pain. Referred pains are sensations experienced in an area different to the actual pathological site.

Commonly, these sensations arise from the irritation of a nerve root, although the pain is felt in the region of the body served by the nerve in question. For example, a herniated intervertebral lumbar disc may refer pain to the thigh, or even the foot. In this case there is no pathology of the foot and treatment of the disc problem will alleviate the symptoms. Internal organs may also cause referred pains to the body's periphery. This occurs when nerves from the internal organ, such as the gall bladder, converge with the nerves conducting information from the periphery, usually the right shoulder. The nerve from the gall bladder and the nerve from the shoulder may synapse in the spinal cord and input from either is interpreted in the same way. As the brain is much more used to input from the neurons in the shoulder rather than the gall bladder, it may interpret gall bladder pathology as a shoulder problem. Needling at the shoulder may reduce the pain via spinal gating mechanisms, but clearly successful treatment will not involve simply treatment of the shoulder tip, but will require the addressing of the underlying condition of the gall bladder. This phenomenon occurs in many conditions. The difficulty is that the nerves that innervate the ear do not synapse with nerves that innervate, say, the foot. Pain referred to the ear must be limited to the regions innervated by the same nerves, in this case, several cranial nerves. Auricular acupuncture cannot be related to these changes at the dermatomal level in the spinal cord because the ear is supplied by cranial nerves which directly penetrate the brain without spinal cord involvement. This implies that higher brain centres must also be involved. So to clarify, pain can refer to the ear but it is limited to the following conditions:

1. Trigeminal neuralgia
2. Gastro-oesophageal reflux disease
3. Temperomandibular joint disease
4. Muscle spasm in the head or neck
5. Throat problems
6. Dental or oral disorders
7. Cancer of the pyriform sinus, larynx, pharynx, oesophagus, nasopharynx, epiglottis, lungs, tonsils or tongue
8. Aneurysm

With this list in mind, it is obvious why we do not support short courses of auricular diagnosis that purport to diagnose disease. A thorough and rounded medical education is essential so that potentially fatal conditions are not missed. Even if it is true that organ pathology causes increased tenderness in an area on the ear, it is of no diagnostic importance. Whether one subscribes to Western or TCM diagnostic methods, a tender area gives no indication whatsoever as to what any pathology, or its severity, might be. In our view this could easily lead to unqualified practitioners making potentially dangerous errors of judgement. The same is true of assessing electrical resistance and conductance properties of areas on the skin of the ear that are also often used to indicate organ pathology.

The research regarding these phenomena is variable, and so we view it as unreliable. A recent double blind research project conducted in 2007 has highlighted the fact that the commonly proposed somatotopic relation in which patients report musculoskeletal pain and tender points located on the external ears according to auricular maps are inaccurate. According to auricular acupuncture map theory it is proposed that tender zones in the ear correspond with regions in which patients report musculoskeletal pain. No statistically significant agreements were found.[8] McCarrol and Rowley showed that low skin resistance was related only to lingering over the same point.[9] Nordergraaf and Silage also concluded that the value of resistance was so closely related to pressure placed on the electrode that the results were invalidated.[10] It is unlikely that spring-loaded 'constant pressure' rods eliminate this phenomenon. Other factors, such as the emotional state of the patient, sympathetic nervous discharge, skin moisture, temperature, dirt, vascularity and the thickness and pathology of the underlying skin, add too many variables for reliable information to be gathered.

Research has been conducted to attempt to confirm that organ pathology can be detected by conductive spots on the ear. In one such study, 95 patients were tested for conductive points before, during and after subtotal gastrectomy operations. During the trauma of the operation the number of conductive points increases, but these points are not confined to a fixed area, nor do they reflect in their distribution in the ear a pattern that can be described as the image of an inverted fetus.[11] The unlikelihood of the homuncular map is also confirmed by research that highlighted the therapeutic effect of auricular acupuncture in back pain patients. Auricular acupuncture in the concha of the ear led to pain relief within 20 minutes and an elevation of beta-endorphin in the cerebrospinal fluid. No points to treat back pain are located in the concha. These are traditionally said to be located on the crus of the antihelix. Points located in the concha are said to be those only of thoracic organs. This means the concha seems to treat pain, not bad backs specifically. This implies that acupuncture effects are neurotransmitter mediated rather than by a mysterious meridian or distinct neural connection between body structures and the ear. Many of the points used in auricular acupuncture do not make any sense whatsoever in clinical application without an understanding of Chinese medicine, and in truth, probably do not exist at all. For this reason we use point names more likely to have meaning to our student groups.

Many theories exist as to the mechanisms of acupuncture, but the majority of evidence clearly supports the neuroendocrine hypothesis and so that is the model to which we subscribe. To that end this chapter will explain the mechanisms of acupuncture not in accordance with unbelievable energetic principles, but based on neural models of action.

The neurophysiological basis of auricular acupuncture

We do not align ourselves to the view that unconventional energetic principles are at the root of any benefits attributed to acupuncture. We subscribe to the

neurophysiological paradigm because it has some basis in reality and evidence-based practice. We do attempt to translate some traditional Chinese medical concepts such as *Yin-Yang* theory, but only where they serve as a model for understanding as opposed to a proposed reality. There is no arrogance meant by this approach, but merely the suggestion that science is about asking questions in the search for truth. It is hoped that this chapter will help serve this process by exploration of the current state of knowledge and proposing future research directions.

Acupuncture provides sensory information to nerves lying in the periphery. This stimulation provides a cascade of neural responses that can affect the person in a multitude of ways. It is in the brain that emotional and behavioural responses to sensory stimulation are integrated. This means that sensory input can create a response at a much more profound level than just the sensation of touch itself. Sensory input, in effect, diffuses throughout the brain. For example, a kiss is much more powerful than merely a sensation on the lips. At whatever level a person is affected, neurochemical change forms its basis. Research into the neuromodulatory effects of acupuncture is far reaching and so rather than examine it in its entirety, this text will address only those aspects pertinent to the field of substance misuse.

The modern view of the action of somatic (body) acupuncture is that it relates to the dermatomal distribution of nerves. This is proven by the fact that the severing of a nerve innervating a given region results in the acupuncture stimulation of points in that region which are supplied by that nerve having no effect whatsoever.[11] However, clinical experience implies that the actions of acupuncture cannot simply be related to this spinal segmental concept. It is clear, for example, that points on the head, face and of course the ear, are effective but yet are not supplied by any segmental spinal nerve. Ear acupuncture must therefore work through a different mechanism.

The innervation of the ear is provided by the cranial nerves. Cranial nerves differ from spinal nerves in that rather than emerging from the spinal cord they emerge directly from the brain. This means that any acupuncture effect must be mediated by areas of the brain itself such as the brainstem and limbic system. So, it seems acupuncture has two modes of action. Somatic acupuncture interferes with ascending (afferent) nerve impulses whereby point stimulation carries information to the spinal cord where the signal then ascends through the medulla and periaqueductal grey. From here the signal reaches the posterior and lateral hypothalamus and thalamus. Neurons from the thalamus then stimulate the pituitary, resulting in the secretion of beta endorphins.

Ear acupuncture would seem to work as a consequence of descending (efferent) impulses from the brain. Since the innervation of the ear is supplied by cranial nerves, the role of the central nervous system, and specifically the brainstem, will be the focus of this part of the chapter.

Perhaps the most interesting fact about the cranial nerves that supply the ear is that they all possess nuclei in a part of the brainstem called the reticular formation. The brainstem represents the lower part of the brain that adjoins the spinal cord. It controls autonomic function and relays information between the brain and spinal cord. We consider that acupuncture stimulation causes

information to be conveyed to the reticular formation. Changes in the levels of neurotransmitters at the reticular formation can therefore alter the activity of much of the nervous system. Harnessed correctly, it is felt that acupuncture stimulation could provide a method with which to provide potentially widespread therapeutic effects without side-effects.

Remember, the points shown to support addicted patients lie in the regions of the ear innervated by the somatic trigeminal and autonomic vagus nerves, and stimulation of these nerves directly affects the brainstem.

The reticular formation

The reticular formation is involved in a multitude of physiological functions and is an evolutionarily, very ancient part of the brain structure. Along with the limbic system it is considered one of the most important brain regions concerning human behaviour. In fact, antipsychotic drugs provide much of their effect at the reticular formation. Included in its roles are an involvement in pain sensitisation, alertness, fatigue, sleep and motivation. It is also felt to be related to character traits such as introversion and extroversion. Introverted individuals are in possession of a more easily stimulated reticular formation and so are less likely to seek out stimulation, while extroverts actively seek out stimulation because their reticular formation is somewhat underactive. It could be hypothesised that addicted patients are in possession of an underactive reticular formation and so therefore crave stimulation. Most importantly the sagittal division of the reticular formation forms the raphe nuclei.

The raphe nucleus

The raphe nucleus is considered to be part of the reticular formation and is located in the brainstem. It is responsible for the release of serotonin to other parts of the brain. Selective serotonin reuptake inhibitor (SSRI) drugs, for example, are thought to act on the raphe nucleus. It has been shown in several research studies that acupuncture accelerates the synthesis and release of serotonin.[12] As we have already seen, depletion of serotonin levels in the brain is implicated in the development of several conditions such as depression, increased suicide risk, violent behaviour, insomnia, obesity, chronic pain, inhibition of gastric secretion, decreased smooth muscle tone, vasoconstriction contributing to peripheral neuropathy and, of course, addiction.

The raphe nucleus is itself made up of several substructures. In terms of importance to the physiology of auricular acupuncture, the raphe magnus and raphe dorsalis are of particular note. The raphe magnus has an important role to play in the modulation of pain. It is thought, therefore, to participate in the mechanisms with which acupuncture can provide analgesic effects. In fact, the raphe magnus sends projections directly to the spinal cord to relieve pain. In primates and especially humans, the raphe dorsalis is particularly well developed. It is the largest serotonergic nucleus and its primary role is to provide

serotonergic innervation to the forebrain. It is here, in the raphe dorsalis, that SSRI drugs are believed to work. It is easy to hypothesise therefore that acupuncture, through stimulation of this nucleus, can therefore improve the ability of the individual to resist the temptation of drugs and behave in a more socially appropriate manner, and this is borne out by clinical observation. This nucleus has also been implicated in the manifestation of opiate withdrawals. It has been shown that electrical stimulation of the raphe dorsalis can produce alleviation of morphine withdrawals in rats.[13] The raphe dorsalis also sends projections to the locus coeruleus where many of the excitatory autonomic symptoms of drug withdrawals originate. This structure also projects to the amygdala, a key part of the limbic system involved in the formation and storage of memories associated with emotional events such as the pleasure associated with drug taking and the fear of withdrawals. Addicted or depressed individuals show increased amygdala activity due to the lack of serotonin-mediated inhibitory input. The amygdala also innervates the locus coeruleus allowing emotional pain and physical stressors of withdrawal to trigger noradrenergic (norepinephrine) (fight-or-flight) responses. This is, in part, why anxiety is such a common feature of our patient group. With regard to the pain often experienced in drug withdrawal, the raphe nuclei project serotonin down to the spinal cord where they can suppress the activity of nociceptive neurons, so reducing uncomfortable sensations.

The substantia nigra

The substantia nigra is also of importance with regard to ear acupuncture. It is here that the dopamine is produced that plays a key role in reward motivation and habituation in addictive processes. When serotonin levels are increased the knock-on effect is an inhibition of inhibitory gamma-aminobutyric acid (GABA), resulting in more dopamine production. Remember a rise in dopamine does not only motivate one to seek reward but also facilitates learning. Acupuncture is now remembered as a natural reward. Neurons from the substantia nigra project to the striatum where dopamine is released. The striatum has several functions, including involvement in cognitive processes, those of executive function involving initiating appropriate actions and inhibiting inappropriate actions. Executive function is controlled in part by dopaminergic projections from the striatum to the frontal cortex. This area is therefore also implicated in addiction and is associated with reward. Dopamine released in this area also inhibits pain.

The role of dopamine

As will be remembered, dopamine levels are raised by all addictive chemicals, albeit through different mechanisms. This accounts for at least some of the pleasurable sensations attached to the anticipation of them and their ability to cause the behavioural modification and distortion of reward perception characteristic of addiction. If dopamine is raised concurrent to pleasure sensations then the memory of the causative agent of the pleasure is implanted in memory. The

increase in dopamine resulting from drug taking ultimately causes a reduction in normal dopamine signalling and so normally rewarding behaviours become less important.

Increased serotonin levels in the raphe nucleus subsequently raise dopamine levels in the hypothalamus. This increase can trigger the reward cascade (albeit far more gently than drugs) and so acupuncture is inherently rewarding and carries with it motivational stimulus. It is felt that acupuncture can start to rebalance the reward cascade, thus reducing dysphoria, depression, craving and withdrawals (Fig. 14.3). The difference between a natural reward like acupuncture and drugs, for example, is that once the signalling has been achieved, the signal stops. This is not the case for addictive chemicals; the signal is well in excess of normal values.

The locus coeruleus

The locus coeruleus primarily consists of noradrenaline (norepinephrine) neurons. This region of the brain is responsible for the stress and panic associated with addictive behaviour, particularly the manifestation of withdrawals. Remember, if the brain is not getting adequate stimulation of the pleasure centre it assumes a

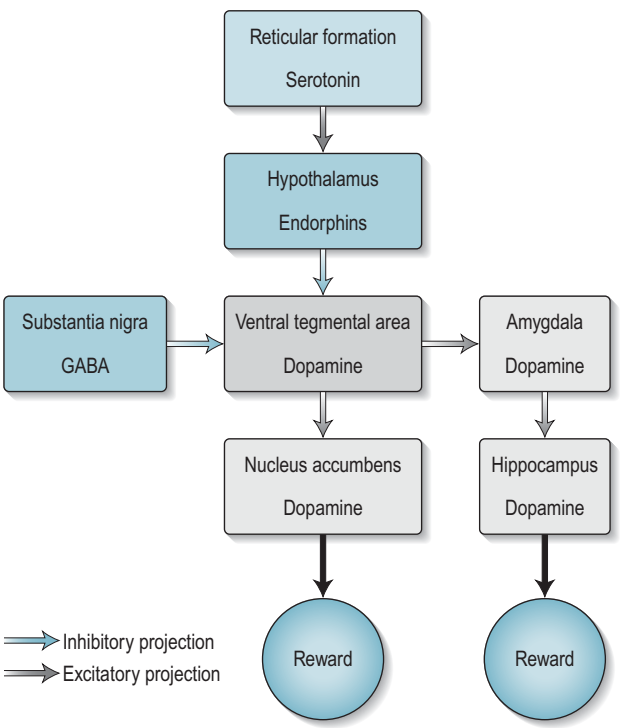

Fig. 14.3 The reward cascade.

potential life-threatening situation and so activates the locus coeruleus. This module has a very large part to play with regard to homeostasis and receives input from the hypothalamus, the link between the nervous system and the hormonal system. Pathology of the locus coeruleus is related to clinical depression, post traumatic stress disorder, panic disorder and anxiety conditions. It is also intimately involved in the sleep–wake cycle. Research has shown that acupuncture decreases available noradrenaline in the brain thus inhibiting the sympathetic activity of body systems.[14] This area is also quieted by inhibitory input from serotonergic neurons emerging from the raphe dorsalis.

The role of endorphins

Endorphins are the body's endogenous opiates. When endorphin activity is stimulated – either naturally or by chemical means – individuals experience relief of pain and sensations of improved well-being. It is important to note that, in the reward cascade, endorphin release (specifically met-enkephalin) inhibits the inhibitory neurotransmitter GABA, and consequently dopamine is also released. Individuals who have become addicted to drugs such as heroin have abnormally stimulated their opiate receptors and so through the process of down-regulation, have a less active opiate system. This means that when the use of the drug is discontinued they experience unpleasant sensations. It has been shown in numerous research studies that acupuncture increases the amount of endogenous opiates and this answers the question as to why acupuncture is so effective at providing relief from pain and drug withdrawal. It appears that the release of endorphins is caused by acupuncture-related activation of a structure known as the periaqueductal grey (PAG), another region of the reticular formation which is key to the control of pain, fear and anxiety. Neurons, if stimulated here, activate neurons in the raphe nucleus, which project down into the dorsal horn of the spinal cord and prevent pain sensation. So neurons from the PAG synapse in the raphe nucleus have the knock-on effect of serotonin release. The PAG sends signals to the raphe magnus when stimulated by opiates. It has been shown that acupuncture analgesia is largely mediated by the release of endogenous opiates by the PAG. This is proven due to the fact that the acupuncture effect can be antagonised by naloxone, an opiate antagonist.[15] From the PAG, neurons project to the hypothalamus, the intralaminar nuclei of the thalamus and to portions of the limbic system such as the amygdala. The activity of these higher brain centres is the mechanism with which sensation may alter physiological function and provide emotional content.

The thalamus

The thalamus is essentially a relay station for information passing between sensory systems and the cortex, translating the information as it passes. The thalamus is also important with reference to the regulation of sleep and wakefulness. The thalamus receives input from numerous regions including the PAG,

but that of the caudate nucleus is also of note. The thalamus contains numerous opiate receptors but also receives ascending serotonergic fibres from the raphe dorsalis. It is thought that the thalamus contributes to obsessive compulsive disorder because dysfunction of the caudate nucleus causes excessive signalling between the thalamus and orbitofrontal cortex, leading to distortions in decision-making processes with regard to satiation. The development of Korsakoff's syndrome is also partly due to thalamic lesions. Modification of thalamic activity by acupuncture is thought to affect its processing of noxious stimuli.

One region of the thalamus, the habenula, relays information between the brainstem and limbic system, thereby having an important role to play in the release of neurotransmitters related to sleep disorders, mood and behaviour.

The hypothalamus

As aforementioned, the hypothalamus links the nervous system to the hormonal system of the body and is also a site for the action of endorphins. It is here that circadian rhythms and other homeostatic processes are controlled. Through its effect on the hypothalamus, acupuncture can regulate various metabolic and autonomic activities. It is the hypothalamus that all limbic structures attempt to influence and the region of the brain that allows for physiological change in response to mood and emotion. Stimuli carried by the vagus nerve influence the hypothalamus via the brainstem. It has been suggested that it is through the influence of acupuncture on the hypothalamus that most aspects of the body's homeostasis, such as body temperature, can be influenced.

The amygdala

Both serotonergic neurons from the raphe nucleus and opiate neurons from the PAG innervate the amygdala. Inputs from both these neurotransmitters serve to calm the emotional impact of pain, fear and anxiety.

The somatosensory cortex

This area of the brain receives information about touch and pressure from the skin and body. It is this part of the brain that truly does represent a homunculus. This model indicates the relative amount of cortex devoted to each region of the body and their topographical relations. The amount of cortex devoted to a given region of the body surface is proportional to the amount of use and sensitivity of that region. Before the information is conveyed to the somatosensory cortex, nerve impulses first pass through the brainstem, passing through the thalamus. There are actually two distinct sensory areas on the cortex. Interestingly, the second somatic sensory area, SII, projects to the limbic system, including the hippocampus and amygdala. It is thought that impulses from SII back to

the thalamus and PAG, initiated by the acupuncture stimulus, maintain the endorphin-raising effects of acupuncture.[11]

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CHAPTER 15

An evaluation of auricular acupuncture with high security, substance-misusing male prisoners

Michael Wheatley

Background

From a general literature review using conventional databases, only two published studies were found on auricular acupuncture with incarcerated populations. In one, Geijer compared treatment outcomes in 65 imprisoned opiate-dependent subjects and randomly assigned these people to either methadone detoxification with auricular acupuncture or methadone detoxification alone.[1] Significantly fewer withdrawal symptoms (stomach cramps, diarrhoea, headache and depression) were reported by the acupuncture group, who also recorded smoking fewer cigarettes (98% compared with 35% in the methadone only group). Geijer's study suggested auricular acupuncture helped alleviate withdrawal discomfort. The second study, by Berman et al,[2] tested the validity of auricular acupuncture with prisoners for alleviating symptoms of psychological and physical discomfort and reducing the incidence of drug use. Prisoners were randomly assigned to a treatment group that used the five common auricular acupuncture points or a control group using non-specific points located on the outer edge of the ear. Berman et al found that drug use occurred in the treatment group but not in the control group.[2] However, confidence in the auricular acupuncture treatment group increased over time whilst in the control group it decreased. Both groups reported reduced symptoms of discomfort and improved night-time sleeping. This study had several limitations. During both treatments, music was played and some participants also listened to guided relaxation tapes. It is therefore difficult to isolate a treatment effect to a specific intervention.

An unpublished evaluation of drug and alcohol services in three high security prisons in England reported interesting findings associated with auricular acupuncture.[3] The study reported staff saying prisoners slept better, were more relaxed, less stressed and wanted more treatments. The authors reported that: 'They [prisoners] want to come and it's [auricular acupuncture] enjoyable and something different. Prisoners don't feel like they are in prison for those forty

minutes of treatment. . . .'[3] The study also reported better alliances between prisoners and staff, finding that: 'the barriers had totally gone, they don't see the uniform now . . . not so much Prison Officers but someone who can help them . . . and that is a good thing because it spreads throughout the whole establishment and gives for a nice calm and relaxing atmosphere.'[3]

More generally, the World Health Organization has acknowledged that a therapeutic effect for acupuncture has been shown for opium, cocaine and heroin dependence (although not with incarcerated populations) for which further evidence was needed.[4]

Prison populations are increasing and many policy makers believe around 65% of the population are problematic drug users. This means that potentially over 50 000 problematic drug users are in the prison system at any one time. From the evidence, auricular acupuncture has shown promise with substance-misusing populations and could be a useful intervention in prisons. No study had been conducted on this intervention in high-security prisons in England.

The research presented in this chapter attempted to clarify the promise of the intervention and to contribute to the literature on auricular acupuncture by asking if the SMART-UK-trained auricular acupuncture intervention contributed to a promotion of general health and well-being when compared to standard institutional care. Implementation issues that might affect auricular acupuncture outcomes were also studied. The study was undertaken by the Directorate of High Security Prisons and the Institute of Criminology, University of Cambridge.

Methodology

The study was conducted in six high security prisons with male prisoners. Three of the prisons were classified as 'local', holding prisoners directly from court either on remand or convicted awaiting sentence or sentenced prisoners pending allocation to lower security training prisons. The remaining three prisons were classified as 'dispersal' prisons, which accommodated prisoners sentenced to a minimum of 4 years in custody. The primary functions of a dispersal prison are to settle long-term inmates into their sentence and institutional life, stifle risk of escape by circulating high-risk prisoners around the prison estate and address risk and needs associated with reoffending.

At each site, an auricular acupuncture coordinator and two SMART-UK-certified practitioners (standardised insertion and acupuncture point location techniques were confirmed by SMART UK) were recruited to deliver eight treatments of 40 minutes over a 4-week duration.

Participants were recruited using a leaflet and poster campaign supported by the issue of a 'Notice to Staff' and a 'Notice to Prisoners'. On receipt of an expression of interest to participate, potential participants were issued with a questionnaire gathering general background information such as age, substances taken, substance misuse services being engaged with and health distress symptoms, the Alcohol Dependency Scale[5] and the Drug Abuse Screening Test.[6] All

respondents completed the screening questionnaires with the support of the ear acupuncture team either individually or in a group. An informed consent form was also issued and signed by respondents.

Potential participants had to meet six inclusion criteria:

1. Be aged 18 or over
2. Sign the informed consent form and express a willingness to participate
3. Be available to participate and have no planned moves within 8 weeks
4. Function at an intellectual level to enable the completion of assessment materials
5. Have self reported problematic drug use, problematic alcohol use, or both, corroborated by a dependency score on the relevant questionnaires
6. Declare three or more health-related (distress) symptoms

Three exclusion criteria were established:

1. Not to be receiving auricular acupuncture currently or have had it within the last 30 days
2. Not be receiving anti-psychotic, anti-depressant, sedative, stimulant or other mood altering medications
3. Not be currently located in a segregation unit or close supervision centre where security risks would prevent programme participation

Respondents who met the inclusion criteria and avoided exclusion formed a stratified sample. This sample became the participant group and were randomly assigned (using computer software) to one of two experimental conditions; a treatment group (TG: received auricular acupuncture immediately) or a control group (CG: intention-to-treat, who would receive auricular acupuncture within 4 weeks, after the TG had completed treatment). Assigning subjects randomly to the treatment or control groups ensures that systematic or researcher bias does not affect the assignment of participants to groups. Respondents who expressed an interest to participate but did not meet the inclusion/exclusion criteria were placed on a waiting list and were to be offered auricular acupuncture at some future point.

Programme participants were given instructions verbally about the auricular acupuncture treatment protocols including requirements for completion of assessment measures.

The TG received standard institutional care plus the SMART-UK-trained five-point auricular acupuncture intervention. The treatment protocol was standardised: each treatment session lasted 50 minutes – 5 minutes for needle insertion, 40 minutes for treatment and 5 minutes for needle removal and disposal. Participants chose to either lie on a floor mat or sit on a comfortable chair. Participants and practitioners were encouraged to relax and remain silent. No music or audio input was allowed. The CG received only standard care whilst the TG had auricular acupuncture. This Intention-to-Treat design has several advantages because it helps control for spontaneous remissions, provides clinically useful information and offers an ethical design framework.

Participants who did not attend three out of eight treatment sessions or at least one session per week were coded as dropouts (and allowed to continue with treatment) and their data excluded from analysis. Participants who were unexpectedly transferred or released during the study period were coded as withdrawals. Their data was excluded from analysis.

Four questionnaires were used to measure outcomes during the study period:

1. The Health Distress Index (HDI-40R)[7]
2. The Acupuncture Treatment Assessment Scale (ATAS)[2]
3. The Stress Arousal Questionnaire (SAC)[8]
4. The Treatment Credibility Scale (TCS)[9]

The HDI-40R was administered four times (weekly) during the study period and measured sleep disturbance, somatic pain, visceral distress, illness condition, anxiety, depression and positive well-being. The ATAS measured the dimensions of worry, muscle tension, drug craving, physical and psychological well-being. The SAC measured the general sense of well-being and arousal. The TCS measured perceived credibility of the intervention by analysing degrees of confidence about auricular acupuncture helping drug or alcohol problems and general health symptoms, whether participants would recommend auricular acupuncture to a friend and extent of logical understanding that the intervention would help substance and general health problems.

The HDI-40R was administered to both experimental groups at weekly intervals during the study period. The ATAS and SAC were administered to the TG only at each treatment session before needle insertion and after needle withdrawal. The TCS was administered pre and post study to all participants. This data formed the basis of the quantitative data analysis. Following treatment completion, participants were interviewed via focus groups to ascertain the social reality of the intervention as they experienced it. Answers to specific open questions and guided discussions formed the basis of the qualitative data analysis. This was undertaken within 6 weeks of completing treatment.

The study was therefore a combined multi-modal approach utilising quantitative and qualitative methods. Quantitative data (the questionnaires) were analysed using SPSS software. Qualitative data (interviews with participants) were analysed using NVivo software.

Results

Figure 15.1 details the selection process and progress of participants in the study.

A total of 4193 prisoners were incarcerated within the six high-security prisons; 265 prisoners were excluded from the study for security reasons (isolated or segregated), leaving 3928 prisoners who received an information

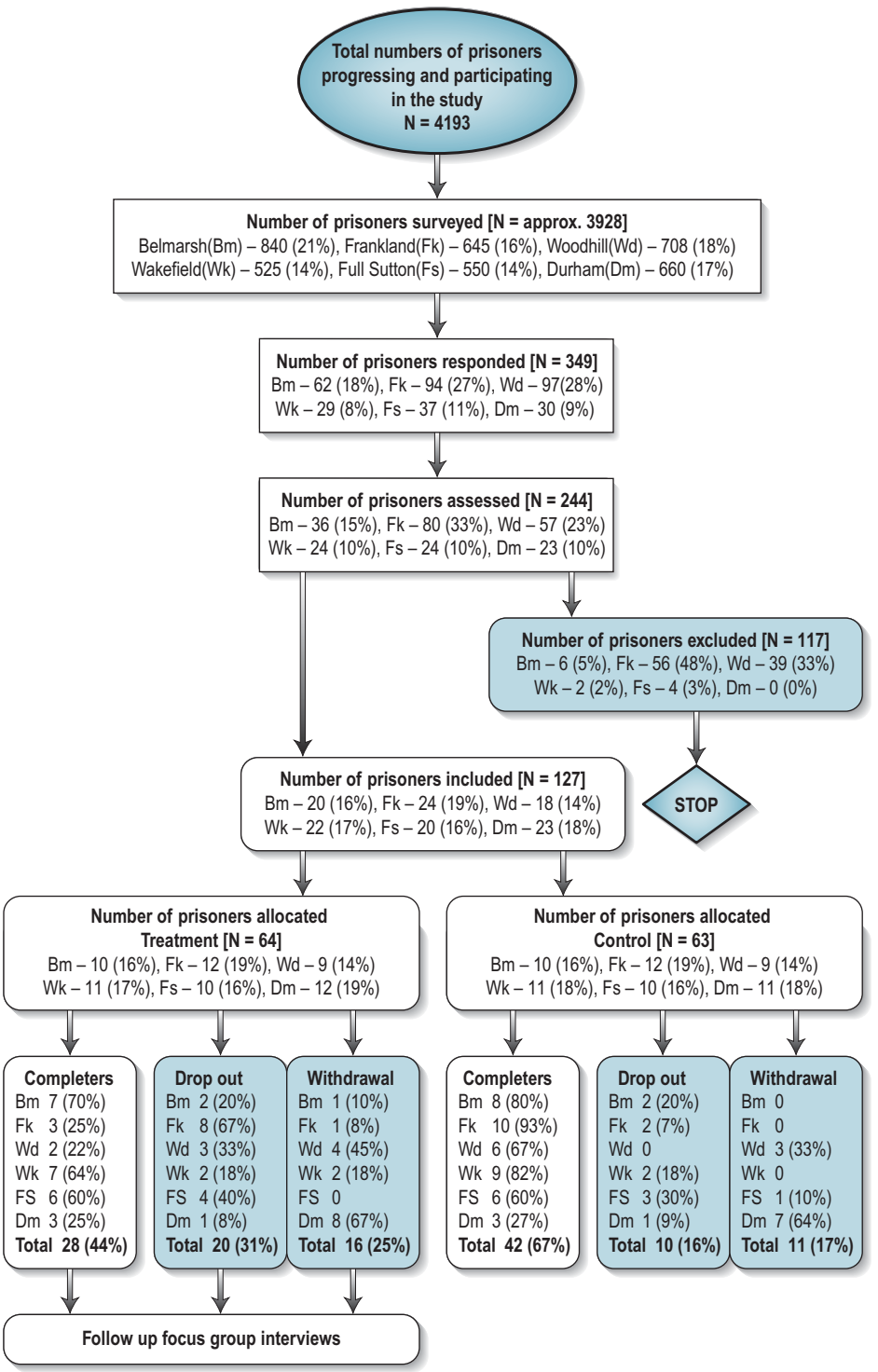

Fig. 15.1 Flow chart throughput data – prisoners progressing and participating in the study. Bm = Belmarsh, Fk = Frankland, Wd = Woodhill, Wk = Wakefield, Fs = Full Sutton, Dm = Durham.

leaflet inviting them to participate in the study. In all, 349 (9%) prisoners responded and deemed themselves eligible for the study; of these, 244 completed screening questionnaires.

A total of 127 inmates of those completing screening questionnaires was selected for participation and met the inclusion criteria; 64 were randomly allocated to a TG and 63 allocated to the CG. The rest were allocated to a waiting list for treatment at another time. A total of 44% of the TG completed the study compared with 67% of the CG.

Taking into consideration age, sentence status, time in prison, substance of preference, health distress symptoms, level of problematic alcohol and drug use, there were no statistically significant differences between the TG and the CG enrolled in this study.

From the focus group interviews, the following treatment effects were identified.

Sleep promotion: one respondent typically described:

'It sorted me sleep out and all that. I was having really bad sleep. Now I am sleeping like a baby, belters. I was sleeping bad, tossing and turning and waking up at daft times in the morning and all that. I was not getting a full night sleep. Now I am and sometimes sleep through until the door opens and all that. I am more relaxed and getting some good sleeps in.'

Improved relaxation: this appeared to reduce stress, worry and anxiety. One participant described:

'I am getting some better sleep but with me it was like being more chilled and relaxed. Now I don't really get stressed. It's mad but it's true. Now I am like dead chilled. I am canny happy and that. It's done something to me like. I got no stress, not as stressed as I used to be. More relaxed. Even when I get on the phone and before I used to come off fuming and all that, now I am dead chilled. And when you are in here you cannot sort things out; you have to wait a week or so until a visit to get things sorted. You have to jump on the phone for ten seconds and that. But since I got acupuncture I am more relaxed and when I heard things were happening outside and that, I thought I will let them sort it out and that. Not really bothered. That's what its done for me. It's crazy but that's what it's done for me! It's good.'

Renewed vigour: this involved increased levels of energy following acupuncture. The following quote describes a typical response:

'You feel relaxed but you want to get up and do, you feel like I must sort that out tonight and I get going to do that.'

Better coping skills: all sites described behaviour that implied a better way of coping with interpersonal and institutional situations both within and outside prison:

'It [acupuncture] helps you deal with the reality of the situation you are in and the people around you, especially because some people are not in single cells and you in with up to two other people that you never seen before in your life. In normal circumstances, not being racist, you would not really be

talking to that person, not saying that you are better than that or they are better than you; so you are all being forced to get along, in that same room with the same toilet! This acupuncture makes you more calm, I just thought that I got to get along with them, as long as he don't punch my face or push me off my chair, I will just get on with it – get on with the situation and be more humble and calm. More like an adult.'

Reduced cravings for nicotine: many participants reported, unintentionally, that their smoking patterns had changed during and after the treatments and nicotine intake had reduced:

'I think it has changed my lifestyle. It certainly gave me a healthier outlook. It's given me a course to eat and taste the food. I got a better taste bud now and I believe stems back to the fact I am practically a non-smoker now. Where I used to be a heavy smoker, I don't have the craving there. I have cut two ounces down to an ounce and this week I haven't even bought any because I still got tobacco from last week. I want to come back to acupuncture to continue the way I am feeling now. I feel tip top. For 50 years old, I feel fit and got no health problems at all.'

Amended cognitions: some participants reported an increased awareness of the impact of external events on their thinking and controlling their thinking in a productive, more positive way:

'I had no headaches and I don't stress or worry that much again. It's like a medication for me. I just started my life all over on a different track. I don't worry about it no more. I used to worry about me wife. Now I think and I say, 'I in prison, nothing I can do. If she want to stay she stay, and if she go she go'. Before the acupuncture I never used to think like this. I think evil things. I thought I would do this and do that. Now since acupuncture I start to think differently.'

General health improvements: participants reported some health improvements, sometimes associated with the reduction in smoking. Responses include:

'I thought that me chest started to clear up. Also coughing out lots of liquid from me lungs. And smoking, I cut down on me smoking as well which was a good thing.'

'The thing that made me believe in it [acupuncture] more than anything was when I came out of hospital and I could not get warm. I was on drugs for thinning my blood. I was constantly cold. I wore sweatshirts. I was sleeping in sweatshirts and tracksuit bottoms to keep warm. That first afternoon in here [acupuncture room] I was amazed. It was the first time that I felt warm. And that was even then causing me to think is it all up here [points to head], am I believing its done that or had it done that?'

Analysis of the questionnaires administered weekly (HDI-40R), per treatment session (both pre- and post- [ATAS and SAC]) and before and after the study (TCS), gave the following findings.

Using a repeated measure analysis of variance (ANOVA) on the HDI-40R subscales, the following statistically significant results were found. There was a positive improvement in well-being and a reduction in total health distress scores in the treatment group. Figure 15.2 illustrates the trend in positive well-being for the experimental groups.

The treatment group saw an improvement whilst the control group reported a decline. Figure 15.3 describes the total distress scores for both groups.

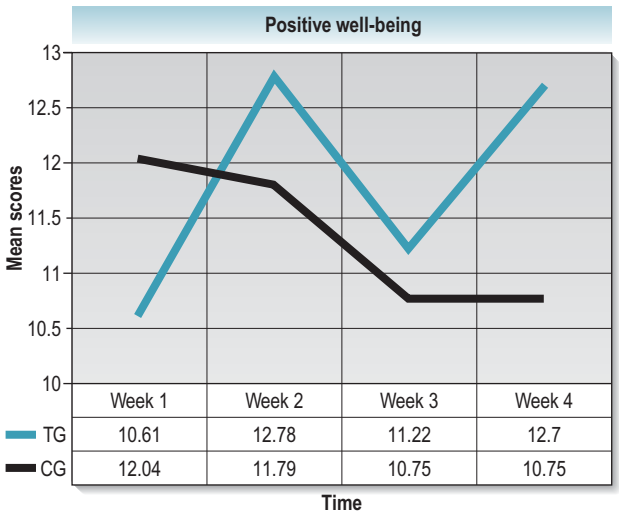

Fig. 15.2 Changes over time on the Positive Well-Being Scale. TG = treatment group, CG = control group.

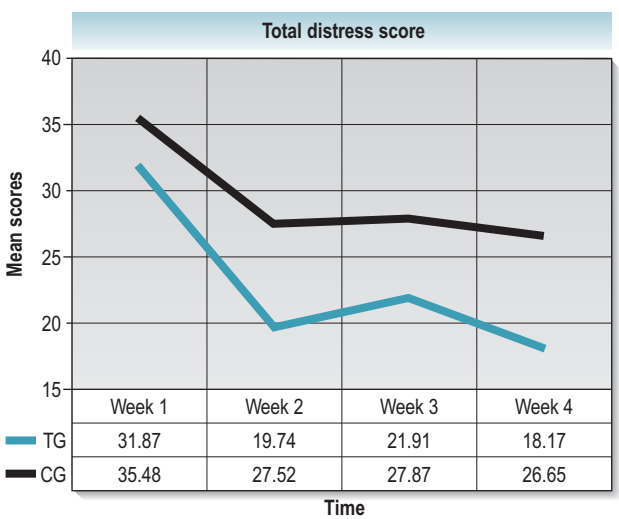

Fig. 15.3 Changes over time on the Total Distress Scale. TG = treatment group, CG = control group.

Whilst the trend in both groups shows a decline, only the treatment group was statistically significant. No statistically significant effects were found in the treatment group for the other six sub-scales of the HD-40R. No significant effects were found in the control group at all.

Paired-sample *t*-tests were used to evaluate the impact of the auricular acupuncture on worry, muscle tension, drug craving, physical well-being and psychological well-being, sub-scales of the ATAS. There was a statistically significant reduction in worry (all sessions), muscle tension (all sessions), drug craving (first seven sessions), promotion of physical well-being (all but session three) and increased psychological well-being (all but session three).

Using the SAC, a paired-sample *t*-test was conducted to evaluate the impact of auricular acupuncture on mean stress scores. There was a statistically significant decrease in stress scores for sessions 1, 4, 5, 6 and 7.

From the TCS the treatment group reported a statistically significant increase in confidence that auricular acupuncture could help address drug and alcohol issues and general health problems. TG members reported being willing to recommend auricular acupuncture to a friend and said that the intervention was logical to understand in addressing substance problems as well as general health distress. No significant findings were reported by the CG.

Implications

Theory

The results of this study support previous research findings on auricular acupuncture with prison populations where subjective symptoms of physical and psychological discomfort were reduced.[2] Results were congruent with previous findings on reduced anxiety,[10,11] reduced drug craving,[12,13] and reduced muscle tension.[1,12,14] This supports the suggestion by Lipton et al that auricular acupuncture might affect aspects of emotional and physical health related to prolonged use of any substance.[15]

Marlatt and Gordon identified precursors to relapse into substance misuse.[16] The three primary precursors were negative emotional states, negative physical states and interpersonal conflict. The study findings indicate the potential role auricular acupuncture can play in the management of high-risk situations and urges/cravings that might help eliminate the precipitating factors of relapse. This is possibly a fresh conceptualisation of the role of auricular acupuncture in relapse prevention management. It may even have a contribution to make in smoking cessation programmes.

The findings also contribute to the debate around the number of treatments required and duration of intervention needed to produce a treatment effect. This study supports treatment effects being generated following twice-weekly interventions over a 4-week period lasting 40 minutes per session. Previous studies have also found this (T. Oleson, personal communication, 2004).[17]

Research

This study was innovative as it was conducted within high security prisons and concentrated primarily on evaluating symptomatic relief. There now needs to be a concentration on replicating the findings to validate and confirm the findings.

A multi-method approach to research is advocated. Subjective accounts are often regarded by some as stories or anecdotes and relegated to minor findings when compared to 'gold standard' randomised controlled trails and quantitative analysis. However, a qualitative approach uses the same rules of science – to gather and analyse data systematically, to minimise bias and to achieve accurate, valid, credible data which is useable, to answer questions, predict effects and plan for the future,[18] and therefore should be supported.

The overall strengths of the study were challenged by several limitations in research design. As drop-outs and withdrawals did not complete questionnaires an attrition bias may have occurred which limits the ability to quantify the treatment effect in all participants thereby possibly over-inflating estimates of general treatment effects. All measures were self-report and future studies will benefit from objective measures being introduced such as urinalysis programmes to measure levels of abstinence during treatment intervention. Follow-up data was not obtained to measure the sustained effect of auricular acupuncture. This should be built into future research studies. Finally, this study did not address the issue of placebo effect. The nature of placebo effect is difficult to specify and future research should look to evaluate if the placebo can enhance and prolong active treatment effects,[19] and whether auricular acupuncture can harness specific placebo effects for reducing health distress associated with substance misuse.

Practice

The study produced a number of implementation issues that should be addressed as they may affect auricular acupuncture outcomes. These include:

- *Room setting*. Four requirements became apparent: enough space to be treated either sitting or lying, warm temperatures, comfortable facilities and room cleanliness. Where these conditions were not met, drop out rates were highest.
- *Distracting noise*. Minimising noise irritations was deemed necessary as this prevents disturbance which interferes with the treatment process. Again, high levels of reported noise led to attrition.
- *Practitioner suspicion*. Participants reported high levels of anxiety associated with practitioners, especially because the treatment was invasive, by piercing the skin of the ear and of personal space. Two suggestions materialised to address this issue: first, ensure all practitioners are well trained, have a thorough knowledge of auricular acupuncture and how it works, have good needle insertion techniques, excellent treatment skills that promotes a strong therapeutic alliance and have personal experience of auricular acupuncture. Regular supervision to ensure

competence in these areas is essential. Second, provide an information booklet explaining how auricular acupuncture works and the potential benefits to ensure consistent and sound understanding of the treatment.

- *Organisational support*. Participants commented that a consistent supportive approach from the organisation to the client and practitioner was essential and beneficial in alleviating anxiety, promoting credibility and increasing confidence of continuation of treatment.

Conclusion

This study presents the findings of one small, randomised controlled trial on auricular acupuncture with male substance misusers within a number of high security prisons in England. Study participants reported sleep promotion, improved relaxation, renewed vigour (energy levels), better coping skills, reduced cravings for drugs (including nicotine), amended cognitions (enhanced thinking skills), promoted physical and psychological well-being and general health improvements. Findings support no negative side-effects of this treatment other than transitory discomfort associated with needle insertion.

Auricular acupuncture may have a part to play in prison induction programmes, relapse prevention management strategies and smoking cessation interventions. Auricular acupuncture is a low cost treatment modality (approximately 50 pence per treatment), non-verbal, non-confrontational, not dependent on high levels of motivation for participation, is easy to access training to facilitate and can be practised by any staff discipline. Being non-verbal and non-confrontational makes it an attractive intervention for clients who are reluctant to enter traditional talk-based substance misuse programmes, but who may well graduate into these services following treatment. Auricular acupuncture can promote engagement in substance misuse treatment services and contribute towards overall recovery and rehabilitation.

Further research is needed, with bigger numbers of participants, to replicate the findings, overcome some of the study limitations and utilise modern technologies to strengthen the correlation between treatment effects and auricular acupuncture. Meanwhile, auricular acupuncture remains supported by governors within high security prisons, has been promoted from a fringe activity to a mainstream substance misuse intervention and continues to show great promise as an adjunctive complementary intervention within drug and alcohol services.

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CHAPTER 16

Diversity in practice

Sue Cox: SMART course tutor

One important lesson that we have learnt during practice and our teaching is that nothing at all is done in isolation. Everything that we do links us to other people. Even making a cup of tea, we are connecting with the person that picked the tea, the person that made the cup, the person that moulded the plastic for the kettle, the truck driver who drove the sugar beet and his wife who made him his sandwiches.

Nothing is more true and more apparent than when working and listening to our wonderful members, and if we could include every single one of them and their story we would heartily do so. Perhaps this is the seed of an idea for the next book!

This selection of contributions reflects experiences and stories from a broad spectrum of members from across the range of services at varying geographical points. They illustrate very well the kind of services that are being run and the response that introducing auricular acupuncture illicits in professionals involved with vulnerable patient groups.

Auricular acupuncture in Westgate Unit, HMP Frankland, DSPD (dangerous and severe personality disorder) unit

Caroline Doyle

The Westgate Unit at HMP Frankland is an 80-bed purpose built DSPD (dangerous and severe personality disorder) unit. The main aim of the unit is to manage and treat male prisoners whose risk of serious offending is linked to severe personality disorder. The main outcomes of the DSPD programme are:

- Better public protection
- New treatment services improving mental health outcomes and reducing risk
- Understanding of what works in the treatment of those whose severe personality disorder presents a high risk of serious offending

Prisoners are referred from the whole prison service to the Westgate Unit and are accepted for assessment to establish if they meet DSPD criteria.

The Westgate Unit ethos is to use the multidisciplinary team of staff to deliver all interventions. This team is made up of prison officers, psychologists, nurses, PE staff, educational staff and horticulture staff, supported by administration staff and operational support grades.

All activities and interventions within the unit are classed as treatment, as prisoners are given the opportunity to transfer the skills learnt in formal treatment sessions to everyday activities. All staff involved in the assessment process and delivery of treatment on the unit attend a competency-based selection centre. This will highlight areas of strength and development for staff motivated to work closely and therapeutically with prisoners.

The admission criteria to DSPD services are:

- The prisoners are more likely than not to commit an offence that might be expected to lead to serious physical or psychological harm from which the victim would find it difficult or impossible to recover.
- They have a severe disorder of personality.
- There is a link between the disorder and the risk of offending.

Prisoners referred to the Westgate Unit have varying levels of motivation, which affects their level of engagement and participation. Prisoners often have complex and difficult social histories that are complicated by substance misuse. Many prisoners have histories or underlying mental illnesses, which complicate the prisoner's level of need.

Prisoners accepted to the Westgate Unit complete an individualised and in-depth assessment that aims to assess levels of risk and severity of personality disorder a prisoner presents. An individualised treatment analysis indicates which interventions are required to reduce this risk and a treatment plan is formulated. Throughout the treatment interventions, change in risk is measured using psychometric risk tools and risk management tools.

The treatment framework aims to:

- Address offending behaviour through the reduction of risk, by targeting criminogenic factors and meeting mental health needs
- Be based on treatment models, grounded in evidence, susceptible to rigorous validation and external evaluation
- Provide individualised treatment plans that are tailored and flexible, with regular progress reviews

The treatment framework at Westgate Unit has two main aims. The first is to reduce and manage the risk that offenders pose to the public. The second is to enhance the life skills and values of offenders so that they can develop new pro-social ways of living. The treatment models are based on specific treatment programmes, as well as pro-social modelling and complementary regime activities.

Overall treatment aims are to: motivate and engage the prisoner within treatment, address the symptoms of personality disorder, modulate the temperament

aspect of personality, increase social, occupational and relational functioning, modify the schema dimension of personality, as well as targeting offending behaviour.

Chromis programme

The Westgate Unit is piloting the Chromis programme, which is specifically designed for violent offenders whose level or combination of psychopathic traits affects their ability to engage in treatment and behavioural change. The Westgate Unit has developed a LINKS team, which helps prisoners maintain family and community ties while they are in prison. This can help the rehabilitation process and discourage re-offending.

The LINKS team fosters positive links with the prisoner and family or significant person in their life as this will allow that person(s) to feel, and be, more involved in the prisoner's sentence and therefore creates a mutual support mechanism between themselves and the prisoner.

Substance misuse work

Given the high prevalence of substance misuse within the DSPD population, Westgate substance misuse team delivered various interventions such as: assessment of need (including drug, alcohol and solvents), a substance awareness course, substance surgeries (drop-ins), individual support (two to one), auricular acupuncture, stress and relaxation.

Auricular acupuncture

The introduction of auricular acupuncture was a contentious issue for the Westgate management team as it was a risk to introduce a new complementary activity to a group of prisoners that might, in the eyes of the media, be viewed as being untreatable and too dangerous to release from prison. Luckily, one of the management team had been trained by SMART UK and was a strong advocate for auricular acupuncture, having introduced auricular acupuncture into two previous establishments and seen the benefits of the results.

Working in a high-security establishment to introduce auricular acupuncture was a challenge as it is imperative that there is no compromise to the security of the establishment. The team developed local protocols and procedures including security risk management protocols and health and safety risk assessments. Every piece of auricular acupuncture equipment had to be logged and accounted for at all times.

The team wanted to promote the benefits of auricular acupuncture to staff and prisoners and held small focus groups, educating them about the history and origins of acupuncture. The success and interest following these focus groups allowed the Westgate management team to support 20 staff in SMART-UK training.

These staff members were enthusiastic and motivated by the training and delivered auricular acupuncture in a variety of settings. Initially, the traditional group room setting was utilised to provide treatment but staff quickly adapted areas to allow prisoners to have individual or group acupuncture sessions.

The benefits staff observed from acupuncture were almost instantaneous. Prisoners reported they were sleeping better, they felt more relaxed and refreshed in the mornings and able to concentrate in their sessions.

Many prisoners were sceptical about the benefits of acupuncture and watched from afar while prisoners attended regular sessions. The substance misuse team remained enthusiastic and promoted the theories of auricular acupuncture to both prisoners and other staff. In a short space of time the prisoner numbers expanded for each session and acupuncture became an almost daily session for many prisoners. The substance misuse team began using acupressure beads as a maintenance aid for prisoners who were not able to access sessions due to the high attendance numbers.

The introduction of auricular acupuncture prompted many staff to look at alternative therapies, both in their dealings with prisoners and in their own personal lives. Staff have since introduced yoga and tai chi, coupled with stress and relaxation packages; prisoners now have an option of looking beyond conventional treatment options.

Many of the prisoners on the Westgate Unit have led chaotic and disruptive lifestyles. Complementary activities such as auricular acupuncture have allowed them to look at other ways of managing their personal issues and the automatic responses they have to situations.

Many prisoners have personality disorder traits that make them mistrustful and paranoid about clinical interventions offered to them. The auricular acupuncturists alleviate these concerns through educating and providing the prisoner with easy-to-read literature.

Auricular acupuncture sessions afford prisoners quiet time to reflect on their daily activities and lifestyles on the Westgate Unit. Prisoners have developed close therapeutic relationships with staff and nurtured a feeling of respect and trust.

The close contact of administering acupuncture needles was an initial concern for both staff and prisoners. Health and hygiene was at the forefront of the staff's minds. These issues were quickly managed through the introduction of guidelines and protocols based on good practice.

The benefits prisoners felt and their keenness to attend regular sessions ensured staff felt their input into prisoner care was rewarded. Many staff have reported they have developed relationships with prisoners who have difficulties with interpersonal skills.

Auricular acupuncture has been available to prisoners on the Westgate Unit for approximately 2 years and everyone remains as optimistic and motivated by its positive effects and benefits to prisoners' behaviours and attitudes.

The Westgate Unit staff is highly motivated and strives for exceptionally high standards of care, always looking for areas of good practice and improving prisoner care and welfare. The Westgate research team is looking at feedback information from prisoners on the usefulness and benefits of acupuncture in relation to prisoners feeling less anxious and stressed in a DSPD unit.

Overall the clinical effectiveness of auricular acupuncture can be seen through the improved sleep patterns, higher levels of participation and concentration in daily activities and a reduction in anxious behaviours in prisoners.

A fairy tale of Manchester (some reflections on ear acupuncture)

Chris Nortley, NHS Psychiatric Nurse and fully qualified acupuncturist

We crucified the Christ; we've casseroled the Easter Bunny and now it's your turn Father Xmas.

Early on in my career I heard some other acupuncturists saying that, when you are well, every day should feel like Christmas Day. For the patients I had begun to see in Manchester at that time there were no Christmas Days; even Christmas Day itself was not like Christmas Day any more. The magic had gone. It was as though they were no longer able to be in rhythm with the natural highs and lows intrinsic to ordinary living. In a vain attempt to accentuate and prolong the pleasure and minimise or eradicate any suffering, we have all become used to stimulating ourselves with a barrage of alcohol and drugs, TVs and PCs, holidays and compulsive shopping, chocolate and cosmetics; and in our desperation to stay antidepressed, we kill everything that's either naturally uplifting or naturally still and calming, and when gaps appear in our synthetic euphoria we fall apart.

By the time we are hooked on whatever we're hooked on – it does not matter what is on the hook, whether it is heroin, diazepam, fluoxetine or chocolate biscuits – it has become the thing that keeps us from drowning in existential terror. By this time, to get off the hook, change has to occur at a very fundamental level. It is my contention that five-point ear acupuncture affords us something that can effect that change.

A critical concept inherent in traditional Chinese medical philosophy is that the only thing you can be sure of is 'change'. It is implicit in China's most ancient text, the *I Ching* ('The Book of Changes'). The *Yin* and *Yang* lines of this oracle constantly move and transform into one another, reflecting the ebb and flow of natural cycles in a constant rhythm of change . . . from morning into afternoon into evening then night and back to morning . . . from breathing in, to becoming filled with fresh air and then exhaling fully only for inspiration to follow.

Always changing. That is nature. So, in the darkest hour of the night, at the deepest, most *Yin* point of midwinter, in your dark night of the soul when there seems nothing left but oblivion, if you only knew it, the seed of change is already twinkling, growing through *Yang* towards daylight and spring. When you are hooked on to an unnatural high like a drug, however, you do not see Father Christmas popping down your chimney. You feel you have got to hang on to the hook or fall into the abyss. It is not so; *Yin* and *Yang* are not just black and white!

The potential to change is what five-point acupuncture can initiate. The change is there anyway, clamouring to happen; the acupuncture just gives you the wherewithal by instituting a return to natural rhythm.

I've worked as an acupuncturist in an NHS psychiatric hospital in inner city North Manchester for 8 years, developing a service offering acupuncture to people with mental illness alongside, and integrated with, modern orthodox psychiatry.

The clinic is very innovative, very busy, very successful and very popular. We have three full-time staff: a traditional acupuncturist, a medical acupuncturist and a senior support worker. In addition, our consultant psychiatrist responsible medical officer (RMO) provides one session of medical acupuncture per week. We see around 150 patients per week. Clinical audit indicates that at any one time 10% of our patients are hospital inpatients; 38% have a history of inpatient care; 27% have a psychotic illness, 25% have been victims of serious assault; 11% have perpetrated serious assault; 17% have been victims of abuse; 39% have a history of serious self-harm.

As a traditional acupuncturist, I know that the strength and beauty of Chinese medicine lies in the artistry of discerning the subtle energetic imbalance of any individual and in translating that into a treatment unique to that individual at that time. Historically, we developed our service in accordance with this understanding and found it a wonderful complement to our approach to psychiatry. The particular blend of Western and Eastern styles we developed seemed to work well.

By contrast, when we were first introduced to five-point ear acupuncture as a standard, fixed procedure administered to every patient regardless of the person or their individual problems, it appeared immediately at odds with our brand of individualistic acu-psychiatry. It was sheer clinical pragmatism that ultimately turned us on to the role of five-point acupuncture in the process of helping someone return to health and, once begun, this procedure very quickly became an established and essential component of our clinical practice.

Our psychiatrist had been faced with an increasing number of patients presenting in the outpatient clinic in states of extreme agitation and distress, who were not responding at all to increased levels of typical medication. He suggested trying traditional acupuncture. We found, however, that many of these patients, men and women of various ages and backgrounds, as well as being beyond medicinal help and certainly beyond the point where talking therapies could help, were also beyond consenting for traditional acupuncture. This type of treatment necessitates a fairly lengthy consultation and physical examination and undressing towards undergoing a precise and intricate procedure. Some of these people were just too acutely distressed to take the first step. They could not begin to assimilate the proposal of body acupuncture no matter how I packaged it. It was out of desperation, then, that we began to try five-point acupuncture as an alternative.

This little procedure felt odd; there was no obvious artistry; no thinking through pathological processes and their resolution. There was even no real need to establish rapport or enter a relationship with the patient other than to simply perform the procedure of inserting the needles.

Paradoxically, however, the beauty of this treatment lay in its very simplicity. It did not require any talking; it was exceptionally quick and easy to administer; it did not require the person to undress; it provoked less sensation and stimulation; it was less distracting for the person. Not only did we find that this procedure was eminently acceptable to these people but, time and again, we saw it effecting change within a matter of a few treatments; the person becoming calmer, more present, back in reality, more able to talk, and often even able to avoid a hospital admission.

Somehow the treatment was felt instantly to create stillness and space; to stop the carousel; to interrupt the chaos; and allow relief and calmness and perspective to return. It is right there and then that a person can change; can turn the corner towards health again; can return towards a semblance of ordinary life; just simply turning *Yang* to *Yin*, *Yin* to *Yang* again.

Five-point acupuncture quickly became part of our repertoire. Research at the time was indicating some success in its use in smoking cessation. So, at the start of 1999 we offered it as a treatment to any staff from our hospital to give up smoking. We treated 75 staff and achieved around a 60% quit rate. The *Manchester Evening News* ran an article on the project and we were subsequently inundated with GP referrals for members of the public wanting help. Consequently, every lunchtime for about 12 months, we were open to the public so that they could have acupuncture to stop smoking. Ultimately, our clinical director said that the project was so successful that it was detracting from the main remit of the service and had to stop! He was right, of course, and we did wind down the project but we were left with no doubts at all that the treatment worked.

However, it was the referrals that came continually from within psychiatry, who we treated over time, that gave us more understanding of ear acupuncture as something more than just a prescriptive treatment for a particular condition. For example, a 38-year-old man came for treatment. He was referred by his psychiatrist to give up smoking. He had been seeing the psychiatrist for treatment of unremitting panic attacks in the context of agoraphobia. A couple of years previously he had been driving along a stretch of motorway known locally as 'death valley' and, hemmed in by large lorries, had experienced a massive panic attack; he had thought he was having a heart attack and presented to hospital. The panic attacks, undoubtedly the surfacing of various sources of worry, anxiety and life stresses all in a moment, persisted and turned his life upside down. From that time onwards he could not drive anymore (American cars had been his passion); he had become too frightened even to go out alone; he had just really retreated from any potential trigger situations.

He came for his first appointment with his wife. Ordinarily we would have used traditional acupuncture to address these symptoms but as he had actually been referred to stop smoking, we started with five-point ear acupuncture and after a while he stopped smoking. He said the acupuncture also made him feel a little better and so he continued to come for treatment and continued to tell us that he felt less anxious and less depressed and that he was experiencing fewer feelings of panic, and then that he was getting out of the house more and then

driving again; he ultimately said that he felt well enough to drive the family away for a holiday and had a great time. He had got it back; he had changed. He'd turned the corner and was actually driving back up life's highway in a Cadillac and all he had had was this simple five-point ear acupuncture treatment.

For some people, acupuncture seems to be the agent that best catalyses change, effecting the turn around, the return. That is the singular and most important thing. Once someone has turned around, there are all sorts of therapies and life-styles that can help towards recovery, whether it is psychotherapy, counselling, group work, traditional acupuncture, religion, or something else. Acupuncture is just good at triggering that initial change at that critical level and opening the perspective. It is also useful in maintaining this perspective. Continuation of treatment helps a person to be relaxed and open and receptive enough to assimilate what is going on during the process of recovery; enabling them to maximise the benefits of whatever therapy they are using. So we simply find it worthwhile to provide acupuncture for the duration of the acute stage or throughout a detox and to continue treatment in a supportive role through rehabilitation and 'maintenance' (the 'getting on with life' bit).

Around the same time, a 30-year-old man was brought into the clinic having been admitted to one of our acute admission wards the previous night. He had been admitted via the casualty department in a terrible state following a serious suicide attempt. The massive daily amount of heroin and crack cocaine he had been taking had lost him his successful city-centre business, his family and ultimately his ability to live; he had nothing left but debt and guilt, and addiction and resentment. Luckily he had not succeeded in killing himself and had elected to try acupuncture to assist his detox. He began treatment that day and attended twice a day for the first week and then daily for the following week. The only prescribed drug he had had whilst in hospital was one dose of thioridazine on admission. He had suffered no withdrawal effects and commented that this was the 'cleanest' detox he'd experienced.

My clinical experience with five-point acupuncture continually convinced me of its effectiveness. However, research into acupuncture as an aid to substance detoxification was equivocal at the time. The question of research into acupuncture is critical. Acupuncture is inherently difficult to research with conventional methodology. It defies placebo trials as, quite simply, if you are having needles stuck in you, you know it is happening and if you are the one doing the needling, you know you are doing it. It does not lend itself to blind trials. This does not mean for one moment that it does not work! It means that orthodox research design is unable to discern what is going on during acupuncture. This is just a matter of developing different, more subtle research design and having more accessible technology.

In the meantime, we are bombarded daily with indicators of its clinical efficacy. For example, most of the people who come along to detox in our clinic do not elect to come; they have not chosen acupuncture from a range of options; they have not been attracted by its eastern promise; they have been 'sent' by their GP or psychiatrist. They do not even expect acupuncture to work and by and large

they let you know, in the vernacular, what they think about it. So time and again, you see the most hardened hoody melt into a state of calm and peace and sleep during treatment, and afterwards, excitedly relate to you that 'something has happened to them' and that they feel better, more grounded, more tranquil but more 'alive'.

As a practitioner you definitely come to feel, as a result of accumulated clinical experience, that the effect of acupuncture is unequivocal. It involves something which is difficult for a practitioner or a patient to explain; and it is difficult for research to demonstrate definitively, but it is indeed unequivocal. Of course, not everybody improves dramatically with treatment. Every day we see people either improve or hold their own or struggle; that is just clinical reality common to any treatment modality. However, every so often someone who has undergone treatment, just an ordinary person off the street in Manchester, will say something poignant about what has happened to them, in their own words, something that hints at the essence of what's happened to them. It reflects the ancient Chinese Taoist concept of *wu wei*. *Wu wei* meant 'no action' or 'least action' and implied letting the *Tao* just happen or 'letting nature take its course' or 'going with the flow'. When you are ill or addicted, you are no longer naturally flowing, you are stuck, you are on a hook. As an acupuncture practitioner, you make an intervention to help someone in this state, to re-establish their flow. *Wu wei* infers performing the least treatment possible to let nature resume its course and allow the person to return to health, to lightly touch the very heart of the matter and allow things to right themselves.

For example, a 54-year-old man we had treated fortnightly over about 3 years had successfully stayed off alcohol. One lunchtime he came into the clinic in a distraught state. He had had a lapse; he had had a drink, driven his car, bumped another car and the whole thing had ended up in the local newspapers. I had rarely seen anyone as agitated and in such resignation. He said 'It's done something to me! I can't go on like this! . . . Can't sleep . . . can't eat . . . it's with me all the time! . . . Everybody knows now! . . . How can I work again? . . . How can I live?' Words cannot console someone in this state, they are beyond 'talking therapy' and medication would only temporarily subdue the distress. So he had five-point acupuncture. On removing the needles after 1 hour he said 'It's gone! . . . The whole feeling is gone! Everything is still again . . . everything is sorted . . . I'm OK!' This is *wu wei* in clinical practice, a minimal action that reconnected this man with the stillness in his heart and let the chaos settle and opened his perspective, allowing him to resume his living.

I initially commented that, as a traditional acupuncturist, I thought that five-point ear acupuncture was too prescriptive to work well; it was not individualistic, it had no intricacy or subtlety or artistry. To be honest I was wrong and had wholly missed the point. Five-point formula does have a beauty in its simplicity and its internal strength. Although devised in modern times it is rooted in traditional Chinese medicine and withstands the philosophical scrutiny of that tradition. If you analyse the formula in terms of any Chinese

medical model, whether five-element or *Yin Yang* or whatever theory, it holds up; it is a perfect microcosm in itself. It does not require any more points to be added and it would not work with any less. The five individual points resonate together in a perfect whole. Its resilience and robustness do become quite intriguing in terms of the energetic dynamics that pervade Chinese medicine. However, similarly, in terms of modern Western medicine where we need to demonstrate the physiological substrates of behavioural change; as research gathers pace it is clarifying how acupuncture is working at a biochemical level by effecting a resurgence of particular endogenous neuropeptide substances, which become redundant when individuals misuse substances exogenously. Withdrawal symptoms are consequently negated in a gradual return to chemical equilibrium.

The concept of gradual return is important. As I have suggested, this treatment can work as a stand-alone intervention with spectacular effect. More often though, it serves its purpose best within a repertoire of other therapeutic options, providing a role both in interrupting acute and chronic pathological patterns and subsequently in a continual complimentary and supportive role throughout a process of rehabilitation and recovery.

In addition, this practice is so easy to learn, so easy to perform, it is cheap to run, it assimilates easily into any clinical setting and governance structure, it is eminently safe, and people love experiencing it!

All these things of course make five-point acupuncture an extremely attractive proposition. Its real beauty, however, lies in its clinical application. There is a loveliness in the innovation that it can inspire just at the level of humans helping each other.

One 60-year-old woman came in for treatment with her care workers. She wanted to give up smoking and had tried everything else. Acupuncture, as is often the case, was her last hope. She suffered from Huntington's chorea and the exaggerated involuntary movements she was subjected to meant that her cigarette smoking was becoming increasingly dangerous. She had accidentally burned her clothes, her furniture and carpets and was considered so much at risk by her care team that she would have to move from her flat, which she loved, into residential care. She came for treatment over 2 weeks and gave up smoking without a problem and was able to continue living in her flat.

This woman, like many others, could not wait for research to demonstrate beyond all doubt that acupuncture works. She needed to give it a go and like the others, it worked for her.

As I have already noted, more appropriate research is developing rapidly as experimental design becomes more imaginative and technology more sensitive. You can now have acupuncture whilst undergoing functional magnetic resonance imaging (MRI) scanning and demonstrate actual changes occurring within the brain. This is the level of scientific evidence we have come to require in the West before we will accept that all the recovery that goes on every day in our clinic, for example, is not solely due to coincidence or to magic.

The evidence is on its way, but for the moment there is definitely magic here and for some of us in Manchester, Father Christmas is off the hook.

The Bridge Programme

Lee Ball

> *'If you treat an individual as he is, he will stay as he is, but if you treat him as if he were what he ought to be and could be, he will become what he ought to be and could be.'*
> (Johann Wolfgang von Goethe)

The Bridge Programme is a new initiative by the Salvation Army in Cardiff. Its aim is to tackle the substance misuse issues of homeless individuals seeking control over their dependency prior to being resettled in the community.

Humankind's capacity to be our own worst enemy is symptomatic of the human condition. Who better to kick us when we are down, to twist the knife and then tell us we will never get back up? This situation is compounded by the fact that our modern Western media and society is saturated with stigmatising labels and value-laden judgements, which in turn disempower the individual and set up self-fulfilling prophecies.

There are few things guaranteed in life. You are born, you die and somewhere in between things change. The certainty that things change is the crux of the debate of the human condition. Things can change. People can change. The role of the support worker is to reinforce this certainty.

After working with homeless substance misusers for the past year on the Bridge Programme, you come to realise the fragility of life. To appreciate how quickly things can change for the worse, quite how easy it would have been to make one wrong move and it could have been you, but how with unconditional positive regard things can change for the better.

Many of the service users start on the programme with damaged lives, with society telling them on many levels that they are a public enemy. We see trends of vilification throughout British culture. Many of the representations dominant within the mass media are unfortunately often racist, homophobic and sexist. The repeated use of the label 'junkies' and the way substance misusers are negatively stereotyped, is another expression of the lack of compassion extended to vulnerable groups.

To pre-empt the human condition is a positive force. Such interventions are more difficult when homeless people find it difficult to enter health treatment, and in particular, mental health treatment. This is even more problematic if they present with substance misuse issues. Services often play a chicken and egg game with the apparent intention of passing responsibility. This means that some of the most damaged members of society find themselves alienated, without access to the support they so desperately need.

Having direct access to therapeutic treatment is crucial for service users with substance misuse issues. It is also important that service users feel they have some control and can have input into such treatment services. The central ethos of The Bridge Programme is that it is a client-led service. This principle forms the cornerstone of all of our working practice and is intrinsic to the way in which the programme evolves. Service users are encouraged to set their own methadone

reducing rates, to shape the content of the therapeutic day programme and constantly feedback on how improvements can be made to the treatment they receive. The acupuncture we offer integrates very well within this framework, as it is a voluntary component of the broader package of support available.

There are a number of reasons to explain why the majority of the service users we work with so highly appreciate acupuncture. Importantly, it is immediate. After initially explaining the nature of the treatment and obtaining consent, the service users do not then wait weeks for appointments with lengthy assessment procedures. Another important factor is the therapeutic quality that comes from such a one-to-one interaction, where you are physically demonstrating to that individual they are worthy of time, care and a holistic sense of well-being.

The experience of receiving acupuncture can be transforming, helping individuals to reshape their traditional frames of experience. This is something that is obviously pertinent to substance misuse and eliciting change. As a service user put it, 'I have never felt anything like that in my life. It was like there were waves of energy flowing through my whole body. It was better than any drink or drug I have taken'.

Whilst acupressure beads may not provide the full impact of needles, the role they play is just as significant. They provide the service users with an intervention that they can control, with one stating, 'Whenever I get stressed now, I give the beads in my ears a little rub and it helps to calm me down'. For all these reasons, we have come to recognise and value the difference made by incorporating acupuncture into the programme.

The very nature of acupuncture being an adjunctive treatment means that it co-exists. It co-exists with their therapeutic programme. It co-exists with their substitute medication. It co-exists with their choices. It is this sense of personal responsibility and in turn, personal autonomy, that allows the individual to claw back a true sense of self, to say enough is enough, on their own terms.

We live in a world that dictates the necessity to turn its back. We have a medical profession that dictates the monopoly on treatment with its questionable benevolent altruism. To have success stories society dictates the need for the unsuccessful as its yardstick. Yet, against all odds, we are privileged to meet those with the courage of introspection, to look inside and face what will always be their own worst enemy, with the drive to change, to not become the label but for the label to embody their true being.

Addaction

Karl Sheldon, Team Leader, Stimulant Service, Addaction Middlesbrough

My first experience of auricular acupuncture came about approximately 2 years ago when I travelled to the deep south (being a Smoggy [a colloquial term for someone from the Teeside area] that's anywhere past Manchester) and met up with Sue, Kim and Lou from SMART UK to begin my training into the mystical art. Even before the training began I was bowled over by the passion, knowledge,

motivation and enthusiasm of these people. Once they started talking to us I was hooked.

Due to the tropical heat of the south, I overdid the communal wine and entered my second day with a head full of African drums. After one treatment I felt relaxed, yet energised, and the storm in my head had passed. 'Nice one' I thought, 'this is going to be good'.

I find it difficult to express the true power of this treatment and it is not overstating the point to say that auricular acupuncture has, is, and will, continue to be a vital part of our treatment package for problematic stimulant drug users. On a daily basis we see clients coming in for treatments, stressed, unable to sleep, unable to function and scared of what the next hour will bring, never mind the next day or week. After every session they leave more relaxed, focused and you can see the tension decrease. This has had a direct influence on their sleep, eating patterns and gives these individuals the knowledge that they can get through their craving episodes. You need a break from the stress to focus the mind, strengthen your resolve and keep yourself active and this treatment helps to do all of this and more.

We are an outreach service and this treatment has been an essential ingredient when working with individuals and their families in their own homes. We always offer this treatment to clients, families, carers and friends because as we all know, many of the symptoms seen in problematic users are seen within the close circle of individuals involved. Stress affects us all.

Sue, Kim, Lou and all connected with SMART UK are true friends and totally inspirational. God bless and take care.

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