The Psychology and Neuroanatomy of Functional Pain

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Abstract

Symptoms which are experienced in the absence of a clear biomedical diagnosis, after appropriate investigation are commonly labelled as 'functional'. A theoretical model encompassing functional pain and conversion disorder within a framework of 'auto-suggestive disorder' provides the starting point for the studies reported here.

Direct hypnotic suggestion of increasingly painful heat was used to produce an experience of truly 'functional' pain in a group of highly hypnotisable participants, judged to be similar to an experience of 'real' physically-induced pain. This result was supported using functional imaging, demonstrating similar patterns of neural activation in response to physically-induced and hypnotically-induced pain. This study is the first to demonstrate specific neural activity associated with a functional pain experience in healthy controls.

Hypnotic and non-hypnotic suggestion was used to modulate the pain experienced by a group of fibromyalgia patients, a condition considered by many to be a functional disorder. Manipulation of such pain in this way enabled the direct observation of the neural activity underlying fibromyalgia pain, circumventing the 'baseline problem' common to neuroimaging investigations of chronic pain. The results linked specific regional activity in areas of the pain matrix with the modulation of fibromyalgia pain.

The hypnotic susceptibility of a cohort of fibromyalgia patients was assessed and compared with a group of control participants. No significant differences in hypnotic susceptibility scores were observed, failing to confirm the auto-suggestive disorder hypothesis that these patients should score higher than controls.

The findings presented here do not directly support the classification of functional pain conditions as auto-suggestive disorders. However, they do demonstrate for the first time the neural activity associated with the production of a truly functional pain. They provide support for the existence of a central pattern generator for pain, a mechanism capable of generating the experience of pain in the absence of nociceptive input.

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Chapter 1 – Introduction

1.0 Background & statement of problem

Functional pain (pain in the absence of obvious pathology) accounts for a large proportion of healthcare spending and is associated with significant disability. Unfortunately little is known about the aetiology and functional anatomy of chronic functional pain. There is some evidence, however, that hypnosis can be useful in the study of functional pain (Hilgard, Morgan, Lange et al, 1974) and that hypnosis is an effective treatment for acute and chronic pain (Montgomery, DuHamel & Redd, 2000; Patterson & Jensen, 2003). Clinical applications provide further information regarding the utility of hypnotic interventions: notable recent developments into the study of the effectiveness of hypnotic therapies include a favourable analysis of hypnosis as an adjunct to cognitive behavioural therapy (CBT) in the treatment of irritable bowel syndrome (IBS: Gonsalkorale, Miller, Afzal, Whorwell, 2003).

Hypnotic suggestion can be used to produce negative hallucinations such as blindness (Sackeim, Nordlie & Gur, 1979), deafness (Crawford, Macdonald, Hilgard, 1977) or limb paralysis (Oakley, Ward, Halligan, Frackowiak, 2003). Modelling negative functional symptoms in this way provides us with valuable evidence regarding the 'natural' (non-hypnotic) onset of these conditions. In the same way, the hypnotic reduction of pain can also be thought of as a type of negative hallucination. Consider the case of hypnotic analgesia being used to 'mask' the pain produced by having a hand immersed in ice-cold water (Hilgard & Hilgard, 1994). It is likely that information about the noxious stimulus is being transmitted from the site of the insult, but this information is not reaching conscious awareness. Study of the hypnotic modulation of pain has been useful in helping to understand central mechanisms responsible for pain perception (e.g. Rainville, Duncan, Price, Carrier, Bushnell, 1997).

Hypnotic suggestion can also produce positive hallucinations, inducing percepts of objects, situations or phenomena that are not actually present. Examples include the fly or insect hallucination items common to many hypnotic susceptibility scales (e.g. Harvard Group Scale of Hypnotic Susceptibility: Shor & Orne, 1962; Stanford Hypnotic Susceptibility Scale: Weitzenhoffer & Hilgard, 1962), or the taste or auditory hallucination items on the Stanford scale. Hypnotic suggestion has also been used to produce hallucinated experiences of pain which lead to physiological responses similar to 'real' pains (Hilgard, Morgan, Lange, Lenox, Macdonald, Marshall, Sachs, 1974; Dudley, Holmes, Martin, Ripley, 1966; Barber & Hahn, 1964). This work forms a key component of the background to the studies presented here.

This thesis investigates the phenomenon of suggested pain within the broader framework of functional pain. A conceptual model is developed drawing on the work by Oakley (1999b) which itself places conversion disorder within an explanatory framework encompassing hypnotic suggestion. As well as using hypnosis here as a cognitive tool to produce analogues of functional pain I also describe a functional imaging study in which hypnotic suggestion is used to modulate the pain associated with fibromyalgia, a functional somatic syndrome. In this introductory chapter I will outline some of the important concepts regarding hypnosis, pain, and functional symptoms which are built upon in the remainder of the thesis.

1.1 Pain

"An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"

International Association for the Study of Pain (IASP) Definition (Merskey et al, 1994)

1.1.1 Definitions of pain

Pain is often taken as a paradigm case for philosophers as an example of a phenomenological experience. Unfortunately this has not translated into a solid understanding of the nature of pain. Hardcastle (1999, p95) illustrates this by tabulating the philosophical positions of a number of prominent thinkers. Her analysis shows that pain is conceptualised as anything from being intrinsic to the body part (Armstrong, 1981), to being a perception (Tye, 1995), or a mysterious subjective experience (McGinn, 1983); some even argue that pain is a special case which should not be included in any general theory of consciousness (Hardcastle, 1997).

The IASP definition of pain views it as being 'always subjective' and also acknowledges the multidimensional nature of the experience. This definition of pain has been vigorously debated (Cunningham, 1999; Derbyshire, 1999; Hardcastle, 1999) but remains the foundation for contemporary pain research. The current definition reflects twentieth century models of pain (section 1.1.2) and at the very least this is a considerable advance on Cartesian pain theory which leads pain to be tautologically defined based on the stimulus: pain is defined in terms of a stimulus that is deemed to be painful because it causes pain. *"Pain is present where there are 'pain behaviours' or 'pain stimuli' or, more simply, pain is present when there is pain"* (Derbyshire, 1999).

1.1.2 Models of Pain

This section is not intended to be an exhaustive account of pain theory (see Melzack & Wall (1996) for a more detailed account), but aims to give a brief overview of the most influential models.

1.1.2.1 Specificity theory

The traditional view of pain is encompassed by 'specificity theory'. This view proposes that a pain-specific system carries messages from pain receptors in the periphery to a pain centre in the brain. Specificity theory has been presented in a number of different guises and has adapted over the centuries to account for advances in physiological data. Descartes (1664) saw the pain system as a channel from the skin directly to the brain. He

drew parallels between the system and bell-ringing in a church: a rope is pulled at the bottom of the tower and the bell rings high above.

Figure 1.1: From Descartes analysis of pain 'If for example fire (A) comes near the foot (B), the minute particles of this fire, which as you know move with great velocity, have the power to set in motion the spot of the skin of the foot which they touch, and by this means pulling upon the delicate thread (cc) which is attached to the spot of the skin, they open up at the same instant the pore (d e) against which the delicate thread ends, just as pulling at one end of a rope one makes to strike at the same instant a bell which hangs at the other end'. Reproduced from Melzack & Wall, 1996.

Different types of nerve fibres do transmit different types of information from the periphery to the brain, but this information alone cannot account for the variety of *feeling* associated with pain. Melzack and Wall (1996) usefully draw a distinction between *physiological specialisation* and *psychological specificity*. There is plenty of good evidence for the former: components of the sensory system are highly specialised. However, psychological specificity implies that components of the sensory system subserve only certain qualities of the psychological experience of pain, and there is little evidence for this, particularly with regard to the peripheral components of the pain system. There are different types of sensory fibres which carry information from the periphery, commonly grouped into A-beta, A-delta and C fibres as well as sub-types of each of these. But each type of fibre does not lead to a particular sensation. It is through a synthesis of complex afferent transmissions, sent as a distributed pattern across different types of fibres, that sensations are generated when unravelled centrally (Melzack & Wall, 1996).

Another problem faced by specificity theory is the situational variability of pain, of which there are many examples. An oft-cited example is Beecher's (1959) report of soldiers wounded during the Second World War. He noted that despite severe wounds only one out of three soldiers complained of enough pain to require morphine when carried into combat hospitals. The condition of shock cannot be used to explain the low pain reports as the men apparently complained vigorously in response to an inept vein puncture. Beecher cites their relief at having escaped alive from the battlefield as a possible cause of their lack of pain. Comparable results were obtained with a study of Israeli soldiers during the Yom Kippur war (Carlen, Wall, Nadvorna, Steinbach, 1978). Similarly, an analysis of patients in an accident and emergency ward of a city hospital revealed considerable variability in reports of pain to serious injuries; some patients said that they did not feel pain until minutes, sometimes hours, after the injury (Melzack, Wall, Ty, 1982).

Phantom limb pain presents another challenge to specificity theory. Nearly all amputees experience some form of phantom limb sensation (Melzack & Wall, 1996). One investigation found that 72 percent of amputees had phantom limb pain eight days after amputations, with this proportion falling to 60% seven years after amputation (Jensen, Krebs, Nielson, Rasmussen, 1983, 1985; Krebs, Jensen, Kroner, Nielsen, Jorgensen, 1984). The experience of phantom limb pain contradicts specificity theory; if pain depends on a continuous system of nerve firing from the periphery to the brain how can pain be experienced in a limb which is no longer there? Specificity theory remains commonplace in lay conceptions of the pain system and can explain a lot of 'everyday' pains. However, these challenges have led to a search for models which can account better for the complexity of the human pain experience.

1.1.2.2 Gate-control theory

In an attempt to account for some of problems with previous pain theories, including the variable relationship between injury and pain and the multidimensional nature of pain (see section 1.1.3), Melzack and Wall (1965) proposed the Gate-Control theory. Instead of specificity theory's one-to-one relationship between an injury and subsequent pain experience, the gate-control theory allows for modulation of the experience through the influence of psychological factors. More specifically the theory states that nerve impulses due to injury can be influenced at the level of the dorsal horn of the spinal cord by ascending and descending systems – transmission of the nerve impulses can be facilitated or inhibited by top-down control from the brain and by additional inputs from the periphery.

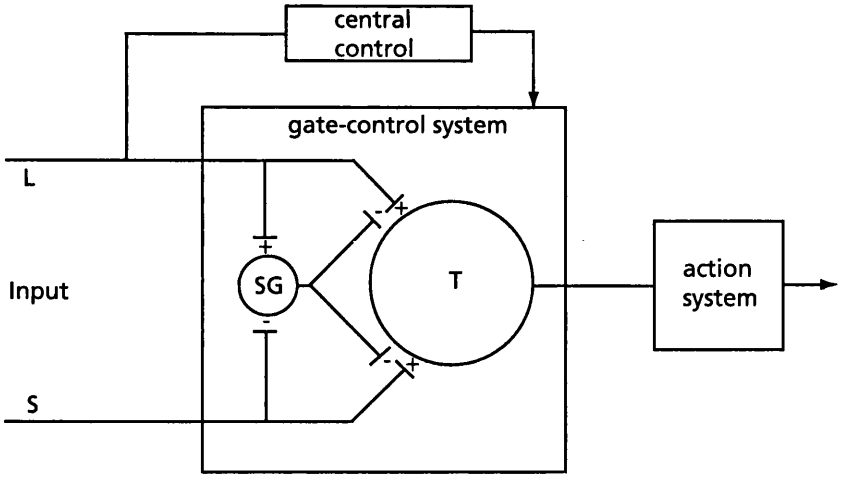


Figure 1.2: Schematic diagram of the gate-control theory of pain illustrating pathways for ascending and descending excitation and inhibition: L, the large diameter fibres; S, the small-diameter fibres. The fibres project to the substantia gelatinosa (SG) and first central transmission (T) cells. The inhibitory effect exerted by SG on the afferent fibre terminals is increased by activity in L fibres and decreased by activity in S fibres. The central control trigger is represented by a line running from the large fibre system to the central control mechanisms; these mechanisms, in turn, project back to the gate control system. The T cells project to the action system +, excitation; -, inhibition. (Adapted from Melzack & Wall, 1965)

Gate-control theory has catalysed a revolution in the study of pain, but one of its shortcomings is a certain lack of clarity surrounding how psychological factors influence the experience of pain. The theory accommodates physiological mechanisms of pain excitation and inhibition extremely well, but does not seem particularly well suited for data at the psychological level of description. *"Though theories of this ilk can account for several "low level" puzzling cases involving pain ... they are notoriously indistinct when it comes to discussing central gating mechanisms"* (Hardcastle, 1999, p96).

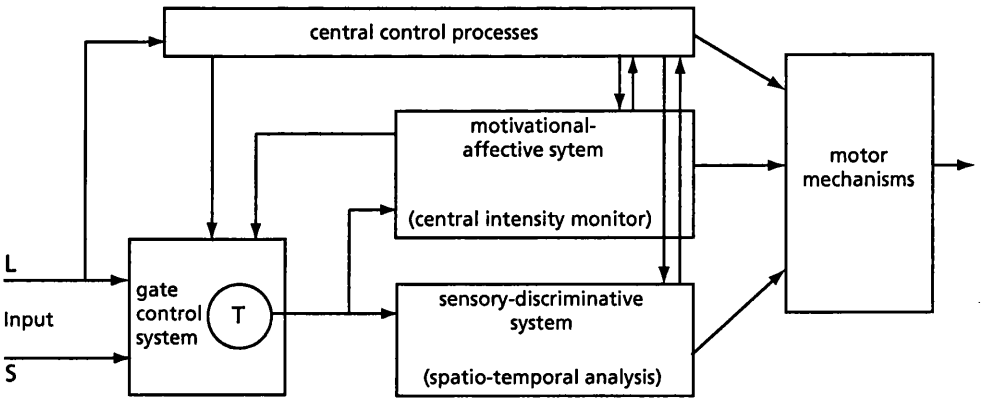


Figure 1.3: Conceptual model of the sensory, motivational and central control determinants of pain. Mechanism of action often does not advance beyond this level of description. (Adapted from Melzack & Casey, 1968)

1.1.2.3 Biopsychosocial theory

The biopsychosocial theory of pain (Waddell, 1987) extends the gate-control theory by placing more emphasis on the psychological and social aspects of the pain experience. Essentially, the biopsychosocial model is an attempt by Waddell to halt what he sees as the over-application of the disease model in medicine. He emphasises that human illness is distinct from human disease, and that a more holistic approach which takes into account individual feelings about an illness will be more effective. Reflecting this approach, a biopsychosocial analysis of back pain by Waddell, Aylward and Sawney (2002) examines trends in the epidemiology of back pain. They provide evidence supporting the view that significant increases in complaints of back pain between 1970 and 1990 are associated with social and welfare changes rather than any pathological change in the spine or variation in medical treatment. Practically, the biopsychosocial model is useful in that it provides a sound theoretical base for a variety of pain treatment modalities including cognitive therapies.

Recently the biopsychosocial model has been criticised on the grounds that the theoretical advances it offers have not been followed up by equally impressive improvements in pain control (Derbyshire, 2004). Derbyshire notes that while the biopsychosocial model is an advance in that it recognises components of the pain experience (social, psychological) not considered in depth in other models this approach may in fact be detrimental to certain patients *"Advocating a view of pain that places a premium on experience currently serves to produce medical diagnoses for a vastly expanding number of people without any hope of an effective treatment"*. But despite the criticisms levelled at it the biopsychosocial perspective, as it is perhaps better termed, remains an influential attempt to acknowledge the multiple moderators of the experience of pain. Future directions of this perspective are hinted at by Derbyshire (2004) with the recognition that some pains weigh more heavily on the 'bio' component whereas others load strongly on the 'psycho[logical]' or 'social' dimensions.

1.1.2.4 Central representation and incongruent information pain theory

Recent work, originally concerned with phantom limb pain, has led to new theoretical propositions regarding the origins of certain types of pain. Ramachandran (1993) demonstrated that the part of the cortical somatotopic map (the body surface is represented as a 'map' on the somatosensory cortex) corresponding to an amputated body part can be activated by sensory input from a closely located region. For example, the face and the hand regions are located closely together on the somatotopic map, after amputation of the arm sensory input from the face can activate the hand area of the map (Ramachandran, 1998). Harris (1999) describes how moving a hand generates a motor intention and motor commands which are monitored by proprioceptive and

visual feedback to the sensorimotor cortex. In phantom limb patients there may be motor intention and commands to move the limb, but no visual or proprioceptive feedback, leading to an overflexed position of the phantom limb and pathological cramping pain. Ramachandran and Rogers-Ramachandran (2000) used mirror visual feedback (using mirrors to allow amputees to 'see' an image of the phantom limb) to give congruent visual feedback which enabled amputees to relax and move their phantom limb, and found that the procedure relieved phantom pain.

This increasingly accepted explanation of phantom limb pain is extended to account for repetitive strain injury (RSI), which occurs after low-amplitude finger flexing (commonly typing on a keyboard) with little proprioceptive or visual feedback, and there is some indication that exercises to restore the cortical maps may relieve RSI pain (Byl & Melnick, 1997). This explanatory framework has more recently been extended to investigate complex regional pain syndrome type 1 (CRPS type 1), a painful condition characterised by sensory disturbances such as burning pain and allodynia and which can occur spontaneously or following trauma; the severe pain of CRPS is out of proportion to the original pathology. McCabe, Haigh, Ring, Halligan, Wall and Blake (2003) used mirror visual feedback to allow patients to have the feeling of moving a painful limb painlessly by viewing movement of a non-painful limb in a mirror. They found significant pain reduction, especially so in patients in the early stages of CRPS. They conclude that their results present an insight into the nature of CRPS and other 'inappropriate' pain conditions. Interestingly McCabe, Haigh, Halligan and Blake (2005) also present qualitative data indicating that it is possible to use incongruous mirror visual feedback to produce a sensation of discomfort in healthy volunteers. The relationship between cortical reorganisation, incongruent feedback, and the functional disorders as classified by Wessely, Nimnuan & Sharpe (1999: see section 1.1.5) remains uncertain and will not be considered further here (initial indications are that pain due to sensory-motor incongruence most closely relates to pain conditions such as repetitive strain injury and complex regional pain syndrome type 1 [CRPS] rather than the cluster of syndromes identified by Wessely et al [1999]: this area of 'functional' pain definitely deserves more research). The relationship between cortical reorganisation, incongruent feedback, and the functional disorders as classified by Wessely, Nimnuan & Sharpe (1999: see section 1.1.5) remains uncertain and will not be considered further here.

1.1.3 The dimensions of pain

Although pain is now considered to be a multidimensional experience early research treated pain as a single dimension varying only in magnitude. Evaluating pain in this way provoked much useful research, but this uni-dimensional view is somewhat like examining sound only in terms of volume, and consequently much valuable information is lost.

Broadly, the modern shift from uni- to multidimensional descriptions of pain began when Melzack and Casey (1968) proposed that there were three dimensions: sensory, affective, and cognitive-evaluative. Melzack designed the McGill Pain Questionnaire (MPQ) to elucidate these dimensions and to allow clinicians to assess their patients' pain. Patients select words from a list which best describe their pain. These give rise to a score on three dimensions. The three overall classes were: Sensory words which describe pain in terms of temporal, spatial, pressure, and thermal qualities; Affective words which describe tension, fear and autonomic qualities; and Evaluative words which describe the overall intensity of the pain experience (Melzack, 1975). The design of the MPQ allows any pain experience to be rated on twenty qualities, although it is most commonly scored only on the sensory, affective and evaluative dimensions.

References to the sensory and affective dimensions of pain are now commonplace. These dimensions make intuitive sense and have been partially validated by pharmacological interventions which can be used to manipulate them independently. Gracely, McGrath and Dubner (1978), for example, used diazepam to manipulate the affective dimension of pain semi-independently of the sensory dimension. This result has been replicated by Thomas, Eriksson and Lundeberg (1991) who compared diazepam to acupuncture in a group of patients with cervical osteoarthritis, again diazepam differentially influenced the affective more than the sensory component of pain. In an extension to their investigations with diazepam Gracely, Dubner and McGrath (1979) administered the opioid Fentanyl to ten subjects and administered a painful electric shock to the tooth-pulp via an electrode. They found that sensory intensity responses were significantly reduced after fentanyl but not after a placebo. They also found that a placebo saline control injection could reduce the unpleasantness but not the sensory magnitude of the stimulus.

Functional imaging of pain (reviewed in detail in chapter 4), in particular Rainville et al's (1997) work has delineated more clearly sensory and affective systems which subserve the experience of pain. This is supported by surgical work with chronic pain patients indicating that destruction of certain neural architecture, for example parts of the cingulate cortex (cingulotomy) or somatosensory cortex can alter the quality of the pain felt. Cingulotomy patients are reported to be still aware of the sensory qualities of their pain but no longer find it bothersome. Foltz and White (1962) note that one of their cingulotomy patients *"ceased her continual whining complaints ... and began to move about again"*.

Activity in the somatosensory cortices is thought to underlie the sensory-discriminative dimension of pain. Ploner, Freund and Schnitzler (1999) discuss a patient with stroke damage to somatosensory cortex, noting that when a hot laser stimulus was delivered to the affected arm the patient did not report an experience of pain but described an ill-localised and ill-defined unpleasant feeling. The interpretation of this result was that

the affective dimension of pain was present in the absence of the sensory dimension. This lesion research is supported by another functional imaging study utilising hypnotic suggestion. Hofbauer, Rainville, Duncan and Bushnell (2001) used hypnotic suggestion to modulate the intensity of a painful (hot water) stimulus. Although affect co-varied with pain intensity, regression techniques were used to determine which cortical areas were involved in which dimension of pain. Once again pain affect was found to vary with activity in the anterior cingulate. Pain intensity was associated with significant activity in primary somatosensory cortex with a trend towards the same relationship in secondary somatosensory cortex.

1.1.4 Acute vs. chronic pain

The primary distinction between acute and chronic pain is a temporal one. Pain is variously described as chronic if it persists for longer than six months (Turk & Rudy, 1992) or three months (Merskey, 1986), but this simple definition is often complicated by discussion of the source of the pain within the same linguistic framework. Acute pains tend to be stimulus-driven and some long-lasting pains, such as chronic arthritis, demonstrate pathology sufficient to produce the pain observed. However, many chronic pains are not accompanied by pathological changes considered responsible for the pain (e.g. Waddell, 1987) and these pains are believed to be maintained or underpinned by psychological factors (Turk, 1999). Discussion of pains in the absence of pathology might be best served by categorisation along an organic/functional dimension. However, the boundaries between acute/chronic and organic/functional have become blurred and, as a result, many pains labelled in the literature as 'chronic' are assumed to possess a greater psychological component (Birket-Smith, 2001; Turk, 1999).

Experimental studies have shown that psychological factors which play an important role in the perception of pain include anxiety (Hall & Stride, 1954); stress and aversive life events (Harris, 1974); feelings of control (Bowers, 1968); availability of social support (Flor, Kerns, Turk, 1987) and attentional focus (Hall & Stride, 1954). But knowledge of these influences does not explain exactly why some pains become chronic. Turk (1999) emphasises that pain can be viewed from a physical, psychosocial or behavioural standpoint and that all of these factors can influence what a patient feels. From a behavioural perspective pain behaviours can be increased, maintained, or decreased through contingent reinforcement. Sedentary behaviour can be strongly reinforced by the non-occurrence of pain. This, coupled with the idea of stimulus generalisation, may lead a patient to do less and less to avoid what they perceive as pain-provoking situations. This in turn leads to physical deconditioning, leading to more activities becoming pain-provoking.

In an examination of social factors on back pain across Europe Waddell, Aylward & Sawney (2002) suggest that since there is no *a priori* reason to expect variations in the biological basis of this complaint then the large differences in self reported low back pain between these countries are best explained in terms of psychological and particularly social factors (see Raspe, 1993). Derbyshire (2004) cites the rapid rise in chronic pain complaints (an increase from 20 million working days lost in the UK in 1955 to 100 million days lost in 1995 [Waddell, 1996]) as an implication of a social rather than physiological cause.

Cognitive factors are also known to play a large role in pain perception. One area of research interest has been the interplay between depression and pain. Rates of depression are higher amongst chronic pain patients and even mild symptoms of depression are associated with twice the normal level of chronic painful conditions (Ohayon and Schatzberg, 2003). Pain patients with depression report more severe pain (Birket-Smith, 2001; Dworkin et al, 1986) and are more likely to develop physical symptoms than those without (Hotopf, Mayou, Wadsworth, Wessely, 1998). Whether there is a causal link between pain and depression, or whether the two are simply comorbid remains questionable. There is evidence supporting both perspectives (Fishbain, Cutler, Rosomoff et al, 1997; Gureje, Simon, Von Korff, 2001; Hendler, 1984), although two recent prospective studies have demonstrated depression to be a strong independent predictor of disabling neck/back pain (Carroll, Cassidy, Côté, 2004; Carrington Reid, Williams, Concato et al, 2003).

As outlined at the beginning of this section a distinction can be made here between chronic pains which, at least initially, have a clear pathological cause and those in which local pathology is not identified. Arthritis of the knee is a good example of the former. Following knee replacement surgery 90% of patients reports either no pain or mild pain and their walking is no longer functionally impaired (Garcia, Bewley, Redden, 2003). Conversely, functional pains (to be considered in detail in the next section) have no obvious pathology, at least not sufficient to account for the pain experienced (Waddell, 1987; Barsky & Borus, 1999; Wesseley, Nimnuan, Sharpe, 1999). Much of the time, however, the distinction is often not explicit. Chronic conditions such as non-specific low back pain (NSLBP) may often be preceded by back injury which has healed but in which the pain persists; where no pathology can be found to account for ongoing pain the possibility is raised that it is both chronic and functional (although there is always the residual possibility that there is a subtle underlying pathology that simply has evaded detection).

1.1.5 Functional pain

"Emotion compels communication, and communication requires a language. While some persons suffering emotional tension and distress can express their discomfort verbally, others find it more natural and fulfilling to express dysphoria in somatic complaints, abnormal posture or gait, invalid life style, and/or diminished activity levels. In such cases the expressed pain is not about tissue trauma: rather tissue trauma is a metaphor for threat to the self as a psychological entity. In short, pain is a language and not a symptom for some chronic pain patients."

(Chapman, 1996)

When symptoms are experienced in the absence of a clear biomedical diagnosis, despite appropriate investigation, they are commonly labelled as 'functional' (Sharpe, Mayou, Bass, 1995; Barsky & Borus, 1999). Historically, medically unexplained symptoms have been labelled as somatisation, somatoform disorders, hysterical, psychogenic, medically unexplained symptoms, or as functional disorders[1] (Wessely, Nimnuan, Sharpe, 1999). Despite very similar accepted meanings the popularity of the various terms waxes and wanes over time with particular labels becoming more fashionable as older terms amass more negative connotations.

On a theoretical level the existence of truly functional disorders remain contentious. Many scientists and doctors do not accept that symptoms can occur in the absence of pathology. In a thorough review of the psychology, biology and philosophy of pain Hardcastle (1999) concludes that *"whatever distinctions we make with respect to pain, the psychogenic/organic one should not be it."* From a strictly materialist standpoint she is, of course, correct. Mental events have a physiological substrate and so can be described in physiological terms. In support of Hardcastle and others' views it is often the case that improvements in medical science do mean that some pain syndromes find a physiological explanation. Melzack & Wall (1996) venture that *"It often happens that, when a new syndrome is discovered, the cause is found not long after."* They cite the example of 'painful legs and moving toes' syndrome (Spillane, Nathan, Kelly, Marsden, 1971) which was later found to be due to nerve-root lesions which generate nerve impulses which spread in the spinal cord and are the basis of pain and motor outflow (Nathan, 1978).

Of course caution should be exercised when labelling a disorder as mentally induced, and we must recognise that mistakes have been made in the past. A prime case is that

[1] The term 'functional pain' will be used throughout this thesis to refer to pain which, after appropriate investigation, is deemed not to have a physical cause. It is worth reflecting briefly upon the history of terminology used to describe pain of this sort. Trimble (1982) traces the use of the word 'functional' in relation to nervous diseases back to 1831 and describes its change in meaning over time from physiological to psychological dysfunction.

of ulcers. Received wisdom was that duodenal ulcers were caused by stress until Warren and Marshall proved that they were a consequence of infection with the bacterium Heliobacter pylori by studying 100 duodenal ulcer patients and demonstrating their presence every patient, and by swallowing a culture of the bacterium and suffering acute symptoms (Marshall, 1983; Marshall & Warren, 1984). But recognising that disorders may have a physical basis is not the same as disproving the existence of functional disorders. The nervous disorder hysteria can be traced back to the second century and although physiological aetiology has frequently been proposed it has not been demonstrated. Over time the term hysteria has come to imply illness without disease, specifically illness of the nervous system (Slavney, 1990).

We must bear in mind that as well as using the physical level we can also make sense of our world by describing features of our psychological life. Are we afraid because we saw a lion or because of activity in our amygdala? Although both are technically correct we can choose the level of description at which to discuss the problem (Fear-amygdala relationship: Adolphs, Tranel, Damasio, Damasio, 1994). We should be aware that not everything can be described in physical terms: *"every day of our lives we are reminded that not everything can be reduced to the physical, and nor can the social be understood as natural. The world contains a myriad of things that are not physical entities: racism, Nato, the debate between rationalism and empiricism, a sense of duty ... the social world is no less real for being subjective: its entities interact with the physical world, and cause changes in the physical world"* (Malik, 2000). But there seems to be a resistance within the field of pain research to anything other than a model recognising the primacy of biological factors. *"While psychological processes contribute to pain they are only part of the activity in a complex nervous system. All too often, the diagnosis of neurosis as the cause of pain hides our ignorance of many aspects of pain mechanisms"* (Melzack & Wall, 1996). This kind of argument is less apparent, however, in other fields of psychological research. For example, psychogenic amnesia, sometimes referred to as dissociative amnesia or psychogenic fugue, is a recognised condition in the study of memory (Markowitsch, 2003) and psychogenic seizures are clearly differentiated from epileptic seizures (although the former are diagnosed by exclusion of the latter: Kuyk, Van Dyck, Spinhoven, 1996; Kuyk, Lietjen, Meinhardi, Spinhoven, Van Dyck, 1997). Psychogenic gagging is also an acknowledged problem in dentistry (Saunders & Cameron, 1997).

Still the idea of psychogenic pain remains controversial. Hardcastle (1999) states that *"In all likelihood, all pains are physical in origin"*, not simply on the basis of the physicalist argument that all mental events ultimately have a physical basis, but on empirical grounds: in Hardcastle's view the diagnosis of 'psychogenic' is too easy an option and we should look harder for a peripheral cause for pain. This brings us to a discussion of explanatory theory. Lambie (2001) presents the example of nausea as a symptom for which the explanatory account can vary from psychogenic to somatogenic.

Sometimes noxious food can cause nausea. Other times nausea can be caused by beliefs and thoughts such as 'I will die if I get on that plane' or 'what if they ask me a tough question?' Lambie gives an account of physiological processes which underlie nausea and clarifies the point: *"In both psychogenic and somatogenic nausea, saying the cause is mental or physical means, in the present context, 'the best explanation of the nausea, all things considered, is that it was caused by [mental event x/somatic event x]'"*[2]. Blushing is another good example of a bodily response which can be activated physically (e.g. a homeostatic response to maintain consistent body temperature) or psychologically (as a consequence of embarrassment). The implication of examples such as these is that we must be prepared to accept multiple levels of description; what Rose (1997) terms 'epistemological pluralism', in order to understand complex human phenomena. Evidence of possible psychogenic or functional pains will be considered later in this chapter (section 1.2.4) and in chapter 4.

The approach taken here will be to use a framework which combines discussion involving biological, psychological and social factors. An awareness of the interplay between these should ultimately increase explanatory power. This is an approach becoming adopted more widely, notably by researchers working within the field of cognitive neuropsychiatry: *"The remit of CNP [cognitive neuropsychiatry], however, goes beyond the largely modular systems considered so far by cognitive neuropsychology. Psychiatric disorders, even when there is good evidence of demonstrable brain disease (that is, neuropsychiatric disorders), extend to include belief formation, attribution, insight, willed actions, and the conception of self and others. CNP enters this 'twilight zone' populated by concepts such as feelings, assumptions, self-deception, and social and cultural processes. It embraces the challenge by incorporating into its explanatory models the influences of these concepts on cognitive processes. By embracing their influence, it is hoped that neuroscience will be invigorated by a richer understanding of normal psychology"* (Halligan & David, 2001).

1.1.5.1 What are the functional disorders?

The term functional somatic syndromes encompasses a wide range of disorders including multiple chemical sensitivity, repetitive stress injury, chronic whiplash, side effects of silicone breast implants, Gulf War syndrome, chronic mononucleosis and symptoms resulting from video display terminals (Barsky & Borus, 1999). They also include three other syndromes – chronic fatigue syndrome (CFS), fibromyalgia (FM), and irritable bowel syndrome (IBS) – but acknowledge that doubt exists concerning the presence of demonstrable pathophysiology. Wessely, Nimnuan and Sharpe (1999) go

[2] Interestingly, there is recent evidence that hypnotic suggestion can be used to induce a sensation of nausea in healthy volunteers (Houghton, Fell, Meier-Augenstein, Kemp, Cooper, Lawrie, Whorwell, Morris, 2001)

further, arguing that functional somatic syndromes (including CFS, FM & IBS) overlap substantially, and that similarities between them outweigh the differences.

Functional pain disorders such as fibromyalgia, chronic temporomandibular joint disorder, non-specific low back pain, or irritable bowel syndrome present a real challenge to researchers and clinicians alike. These disorders often occur in the absence of observable physical disease, do not respond well to traditional medications or treatments and are a considerable drain on resources available for health care provision. (Gran, 2003; Delvaux, 2003). Functional pain disorders are a huge problem for our medical and welfare systems. Fibromyalgia, characterised by musculoskeletal pain, fatigue, poor sleep and tenderness upon palpation at 'tender points', affects about 3-5% of the population (Gran, 2003). Irritable bowel syndrome (IBS) accounts for 20-50% of referrals to gastroenterology clinics (Delvaux, 2003). Depending on criteria used to assess IBS, prevalence is estimated to be between 2-25% in the UK (Wells, Hahn, Whorwell, 1997). Incidence of both conditions (and traditionally functional symptoms in general) is higher among women, and the course of the disease is characteristically unpredictable (Delvaux, 2003; Gran, 2003). Importantly, response to orthodox pharmaceutical treatment is highly variable (Delvaux, 2003; Klein, 1988). One study of functional chest pain found that 75% of patients had symptoms 10 years after presentation (Potts & Bass, 1995). It is increasingly recognised that sociological and psychological factors are important in the development of these conditions (Gran, 2003). Recent evaluations of the yearly healthcare costs generated by patients with IBS put the figure between €206.90 and €822.95 per patient (Wells, Hahn Whorwell, 1997; Talley, Gabriel, Harmsen, et al, 1995). Despite considerable variability in reported costs it is evident that the large patient population makes this a significant problem. Assuming a prevalence of 10% of the adult population and a per-patient cost of €1000 one review estimated the costs of IBS to Western Europe at €23.38 billion (Delvaux, 2003).

Some researchers oppose this distinction of functional pain. Hardcastle, in *the Myth of Pain*, spends a long time explaining that medical science isn't perfect and demonstrating that pain disorders we previously thought to be psychogenic are now found to have an organic cause. *"In short, we have found precious little evidence that pains differ from one another in a fundamental or significant way. In all likelihood, all pains are physical in origin. At least that is where the data currently point"* (Hardcastle, 1999, p31). However, in this stage of her book she restricts the evidence-base for her argument to DSM-recognised pain disorders; disorders for which scientists are earlier criticised for not investigating enough. Unsurprisingly this does not leave much evidence to consider and the conclusions cannot be considered definitive. Hardcastle's is not an isolated viewpoint though. Gamsa (1994) concludes a review of pain literature stating that *"the body of psychological research into pain has failed to yield compelling evidence for a direct*

causal relationship between psychological factors and pain in the general population of pain patients".

Equally though, the body of biological research into functional pain has not identified a direct causal mechanism between pathology and pain for this large population of patients. At the risk of trying to prove a negative, high profile research does not seem to be demonstrating non-psychological cause for the functional disorders. In the case of fibromyalgia elevated spinal fluid substance P and low serum growth hormone levels have been observed (Bennett, Cook, Clark, Burckhardt, Campbell, 1997; Russell, Orr, Littman, Vipraio, Alboukrek, Michalek, Lopez, MacKillip, 1994) but it is not clear whether these are causes or consequences of the pain disorder. In a controlled study of multiple chemical sensitivity it was determined that patients did not differ significantly from controls on a battery of immunologic measures but that they did report more frequently seeking care for medically unexplained physical symptoms (Simon, Daniell, Stockbridge, Claypoole, Rosenstock, 1993). Walker, Roy-Burne, Katon et al (1990) compared a sample of irritable bowel syndrome patients with a cohort of inflammatory bowel disease patients on measures of psychiatric illness and found significantly higher levels of medically unexplained symptoms in the IBS group as well as significantly higher levels of psychiatric disorders pre-dating the illness. Finally, Gold, Bowden, Sixby et al (1990) demonstrated no correlation between presence of the Epstein-Barr virus (EBV) and symptom improvement in a sample of patients with chronic fatigue syndrome. In the absence of definitive physical causal frameworks it seems prudent to investigate the possibility of psychological pain generation.

Complementing an investigation of the psychological generation of pain is the opportunity to measure, using functional imaging techniques, the neural correlates of such experiences. In the absence of gross structural changes responsible for symptom generation, attention is turning to alterations in function within systems responsible for the experience of those symptoms. In the case of fibromyalgia, with the absence of reliable physiological or chemical diagnostic markers, such an approach is starting to yield explanations which describe the condition as a product of abberant activity within the pain network (Gracely et al, 2002; Yunnus, 1992). Functional imaging techniques offer the opportunity to categorise (and maybe to diagnose and validate) the functional disorders in terms of altered patterns of neural activity. The results of this approach are considered further in a review of the functional imaging literature in chapter 4.

To summarise our analysis of functional disorders: recognition of an explanatory framework involving biological, psychological and social factors, in the absence of clearly defined pathology, leaves open the possibility of psychological mechanisms as causal agents in the generation of symptoms, including pain. In the following sections we will analyse the role of hypnosis in the study of truly functional pain, and the proposed link between suggestion and suggestibility and other psychogenic disorders.

1.2 Hypnosis

"Hypnosis is a social interaction in which one person, the hypnotist, gives suggestions to another person, the subject, for imaginative experiences involving alterations in perception, memory, and the voluntary control of action. In the classic instance, these suggested experiences are accompanied by a degree of subjective conviction bordering on delusion, and an experience of involuntariness bordering on compulsion."

Kihlstrom (2004)

1.2.1 The state non-state debate

The study of hypnosis has traditionally been divided over the issue of whether hypnosis is an altered state of consciousness. On the one hand hypnotic suggestion has been shown to produce changes in sensation and perception which are outside normal everyday experience; and participants who strongly experience the effects of hypnotic suggestion often report that the experience of being hypnotised is not a normal one. On the other hand there is good evidence that suggestion, in the absence of a hypnotic induction, can produce alterations in sensation and perception and that the addition of a hypnotic induction does not increase responsivity to suggestion by more than a few points on standard scales (Kirsch & Braffman, 2001). If the effects of suggestion can be experienced in the absence of hypnosis, the argument goes, why posit the need for a special state?

A key factor in the debate is that a 'state of consciousness' is often left undefined. Unconsciousness, due to intoxication or head injury for example, and sleep are taken to be a different state from waking consciousness, but what about moods such as happiness and sadness which can also affect perceptions? Ultimately, states of consciousness will be defined in terms of altered brain function. A recent model which encompasses altered states due to daydreaming, drugs, meditation and hypnosis posits that transient deregulation of the prefrontal cortex underlies our subjective experience of altered states (Dietrich, 2003). In the case of hypnosis neurophysiological accounts of altered brain function are beginning to clarify the processes underlying differential responses to suggestion (Gruzelier, 1998; Crawford & Gruzelier, 1992).

It is not the purpose of this thesis to discuss or to investigate the nature of hypnosis; indeed a theme throughout this work is the use of hypnosis as a cognitive tool to produce the effects of interest (discussed in more detail in the next section), which are then examined using different methodologies. However since a significant part of the work reported here concerns the results of functional neuroimaging investigations it is worth reflecting briefly upon some of the specific neuroanatomic systems believed to underpin the effects of hypnosis.

The status of hypnosis as an altered state of consciousness or otherwise is one which remains both current and unresolved (for an up-to-date analysis of the major issues see the most recent issue of *Contemporary Hypnosis*, Vol 22, No.1, 2005). One primary concern is whether hypnosis produces an 'altered background state of consciousness'. The question being asked is whether hypnosis, in the absence of specific suggestions, produces alterations in consciousness and whether such an alteration produces measurable differences in neural functioning. Contemporary models of functioning in hypnosis are beginning to explore these issues. Rainville & Price (2003) discuss possible neurochemical and neuroanatomical contributions to altered states of consciousness, including regions such as the brain stem, thalamus and anterior cingulate cortex (ACC). Further, they find that components commonly attributed to the hypnotic state, such as relaxation and absorption, reveal themselves in different patterns of activity within these regions.

Kihlstrom (2005) proposes that progress in the neural delineation of hypnosis is most likely to be made through a focus on the physiological correlates of specific hypnotic suggestions. In this analysis Kihlstrom is only partially correct. Examination of the effects of suggestion does offer greater scope for experimental manipulation than examination of hypnotic states alone (although neuroimaging investigation of the correlates of different aspects of the hypnotic induction is already underway – D.A. Oakley, 2005, personal communication), but because the effects of a suggestion are typically observed in a hypnotic context it will be necessary to examine the relative effects of hypnosis (trance) and suggestion.

One of the most promising avenues of neuroimaging research on hypnosis is one which combines both of the above approaches. It is the interactions between hypnotic state and response to suggestion or performance on other tasks which will yield answers to questions concerning the nature of hypnotic phenomenon. By separating 'trance' from 'suggestion' and having participants respond to the same suggestion before and after a hypnotic induction it will be possible to assess the interaction between response to suggestion and hypnosis. Although they do not examine the effects of suggestion Egner, Jamieson & Gruzelier (2005) present one of the first of this new generation of studies by using fMRI to investigate high and low hypnotisable participants' performance on a Stroop task before and after a hypnotic induction. In this way they were able to assess empirically the relative merits of theories of hypnosis which characterise it as a state of focussed attention (e.g. Barber, 1960) or an opposing characterisation of hypnosis as a state which compromises attentional control systems (e.g. Hilgard, 1965, Gruzelier, 1990). An observed interaction in high hypnotisable participants in a high conflict (more difficult) Stroop condition provides support for the compromised attentional control model of hypnosis and is an encouraging demonstration of the likely course of neuroimaging investigations of hypnosis.

Appropriate neuroimaging studies of hypnosis which provide information on the neuroanatomical basis of hypnosis are relatively sparse, but there are some indications that regions involved in attention and executive control are involved. Rainville and colleagues (2002, 2003) identify activity in the anterior cingulate as a correlate of increased absorption in hypnosis, and the opposite pattern of activity in the ACC as a correlate of increasing relaxation. Similar patterns of activity were also observed in the brain stem and thalamus. Maquet et al (1999) compared responses to requests to imagine a pleasant autobiographical scene in and out of hypnosis to identify a network of brain regions associated with the hypnotic state. Their task selection (revivification of pleasant autobiographical memories) makes it difficult to pick apart activations likely due to mental imagery and memory and those related to hypnosis but it seems likely that right-sided ACC activation and ventro lateral prefrontal cortex (VLPFC) activation are significantly associated with the presence of a hypnotic state.

Despite obvious methodological differences between these briefly reviewed studies it seems apparent that regions such as the anterior cingulate cortex, and areas of the prefrontal cortex are likely to play important roles in hypnosis. The ACC is known to be involved in conflict monitoring (Kerns et al, 2004) and the prefrontal cortex is known to be involved in supervisory or executive control systems (D'Esposito et al, 1995). Both of these processes have been implicated in hypnosis (Jamieson & Sheehan, 2004; Brown & Oakley 2004).

1.2.2 Demand characteristics

A common criticism of hypnosis research relates to the demand characteristics of the experimental situation. Martin Orne, in exploring the role of uncontrolled task-orienting cues noted that participants in psychology experiments often express the desire to be a "good subject" and wished the experiment to be a success (Orne, 1962). Orne realised that this state of affairs, motivated by participants beliefs, expectations and intentions could lead to systematic error which would severely hamper the interpretability of data collected. One method to counter this, particularly favoured by social psychologists, was to use deceptive paradigms in order to minimise participants awareness of the research hypothesis and therefore remove one source of systematic bias (Elms, 1982).

The mobilisation of demand characteristics as an explanation of the effect of a hypnotic suggestion questions the validity of the hypnotic manipulation. For those interested in demonstrating the true (as opposed to feigned) nature of hypnotic effects the demand characteristics of the situation must be minimised or in some way controlled. In hypnosis research deception can be difficult, since the true nature of the experiment is often directly communicated by the suggestions used (e.g. the demands of a hypnotic

analgesia experiment are communicated fairly clearly to the participant by suggestions for numbness or other pain reduction). Orne developed experimental methodologies which allowed investigators to gauge the demands of an experimental situation. Particularly useful was his real-simulator design, whereby experimental participants of low hypnotic susceptibility were tested by an experimenter blind as to their level of susceptibility. These low hypnotisable's, but not the high hypnotisable's, were told to act as if they were highly hypnotisable. Additionally, the simulators are told that the experimenter would terminate the study if he suspected simulation. The logic of the real-simulator paradigm indicates that any differences between the performance of the reals and simulators can be attributed to the differences in hypnotic susceptibility (a genuine effect), whereas if the results are identical experimental demands cannot be ruled out as a critical factor. Unfortunately real-simulator paradigms, although a valuable tool for unpicking experimental demands, come with attendant methodological difficulties. Foremost is the need for at least two experimenters, one blind to the hypnotic susceptibility of the subject.

Since a major criticism of hypnosis research is the reliance on subjective report that a participant is experiencing sensory or perceptual change in response to a suggestion any methodology which allows investigators to bypass or confirm this subjective report is of immense value. Consequently, varying modalities of functional neuroimaging technique used to validate the effectiveness of hypnotic suggestion have generated much interest within the hypnosis community (e.g. Electroencephalography: Spiegel, Cutcomb, Ren, Pribram, 1985; Positron Emission Tomography: Rainville et al, 1997). Some of the work presented in this thesis involves the use of functional neuroimaging to independently and objectively verify and elucidate the nature of the experiences of participants.

1.2.3 Measurement of hypnotic susceptibility

Measurement of hypnotic susceptibility forms a key component of modern hypnosis research. Hypnotic susceptibility, the ability to respond successfully to suggestions following a hypnotic induction (thereby differentiated from non-hypnotic suggestibility), is regarded as an individual difference measure reflecting a personality trait. Hypnotic susceptibility has been demonstrated to be relatively stable over time (Morgan, Johnson & Hilgard, 1974) and is a capacity which is normally distributed across the population (Hilgard, 1965).

Arguably the first modern hypnotic susceptibility scales developed by Weitzenhoffer & Hilgard at Stanford University in the late 1950's. The key scale is the Stanford Hypnotic Susceptibility Scale: Form C (Weitzenhoffer & Hilgard, 1962) which begins with a waking suggestion, followed by an induction procedure which is then followed by 10 test suggestions, including 5 motor challenge items. The Harvard Group Scale of Hypnotic

Susceptibility: Form A (Shor & Orne, 1962) is a modification of the Stanford:A scale for use in a group setting. A number of suggestions are modified for group administration, and a key change from the Stanford is that the scale is scored by the participants themselves.

Although the Stanford and Harvard scales are the most widely applied a number of other scales are in common use, typically for clinical or teaching rather than research purposes (although there are notable exceptions, e.g. the CURSS). These 'other' scales include the Stanford Clinical Scale (Morgan & Hilgard, 1978/79), the Barber Suggestibility Scale (BSS: Barber, 1965), the Creative Imagination Scale (CIS: Wilson & Barber, 1978), the Carleton University Responsiveness to Suggestibility Scale (CURSS: Spanos, 1983) and the Hypnotic Induction Profile (HIP: Spiegel & Spiegel, 1978). Different scales have varying strengths and weaknesses. From a practical point of view the Stanford scales are lengthy to administer, especially when compared to the group scales such as the Harvard or shorter scales such as the CIS which can be administered in group or individual settings. However, they are widely considered to be the gold standard and new scales are typically compared against the Stanford. Other scales are more flexible. The BSS and CIS can be administered with or without an induction and both are relatively short. The BSS is more authoritarian whereas the CIS is more permissively worded. Whereas most of the other scales measure observable behaviour, the CURSS benefits from taking an index of whether or not responses to suggestions were experienced as involuntary. Involuntariness, thought to characterise a classic response to suggestion (Weitzenhoffer, 1953), can also be measured on other scales such as the Harvard with the inclusion of a measure of the subjective strength of each suggestion. Involuntariness measures typically allow for a more fine-grained assessment of the success of the participant in responding to a suggestion, rather than the blunt pass/fail of behavioural assessment.

One key factor in hypnotic susceptibility testing concerns the correlations of participants scores on different scales. Weitzenhoffer (2002) notes that the Stanford scales have been used as a benchmark against which new scales have been tested, but points out that the correlations between scales, although significant, are often only moderately in size. This does not necessarily imply that different scales are measuring different constructs (at some level hypnotic suggestibility is common to all the scales), but indicates that other factors such as the type of items (motor, challenge, cognitive) which are loaded differently on each scale are likely to affect inter-scale correlations. For example, the Stanford:C scale is loaded with more cognitive items than the Stanford: A/B scales, and is typically considered to be 'harder', Fellows (1988) notes that it is often used as a follow-up scale for highly susceptible subjects. Group scales could fairly be considered to be subject to more variability than individually administered scales, and for this reason they are often used by researchers as an initial screening instrument, with

scores later confirmed on a individually administered test. As an alternative to testing twice with standardised scales, a common practice is to screen with a group scales, then confirm in individual subjects that they are able to experience a particular test suggestion important for that particular experiment (e.g. Szechtman et al, 1998). The latter is the approach adopted for the purposes of this thesis.

1.2.4 The use of hypnosis as a cognitive tool

Hypnosis is becoming increasingly recognised as a valuable tool in cognitive research. Its use is extending beyond asking questions about what hypnosis is to exploring other issues such as volition (Blakemore, Oakley & Frith, 2003), the automaticity of the Stroop effect (Raz, Shapiro, Fan & Posner, 2002) and auditory hallucinations (Szechtman, Woody, Bowers & Nahimas, 1998). Its great utility lies in the fact that hypnotic suggestion allows researchers to make cognitive manipulations that would not otherwise be possible. In recent functional imaging experiments hypnotic suggestion can be seen to act as a catalyst, generating a phenomenon to be studied and, with an adequate control condition, being partialled out in the analysis (although different analyses of the same data can also reveal information about hypnosis itself [Rainville, Hofbauer, Bushnell, Duncan, Price, 2002]). An early example of this use is Szechtman et al's (1998) study of hypnotically-induced auditory hallucinations. The control over hallucinations offered by the use of hypnotic suggestion allowed for the relatively straightforward study of the phenomenon in the functional imaging environment. Functional imaging of auditory hallucinations had previously been difficult, relying on less predictable naturally occurring hallucinations (Cleghorn, Garnett, Nahmias et al, 1990). Bär, Gaser, Nenadic & Sauer (2002) provide another example of the unreliability of nonhypnotic experimental options in investigating clinical symptoms. They studied naturally occurring somatosensory hallucinations using functional magnetic resonance imaging (fMRI), requiring a schizophrenic patient to press a button to signal whenever she felt the painful sensations in her legs and abdomen. This experimental design required long runs of functional imaging and only yielded relatively short periods of useful data. Significant activation was observed in the medial parietal cortex but it is not clear that these data are easily interpretable. The authors acknowledge that there are *"several constraints in interpretation arising from the nature of the study"*.

1.2.5 Hypnosis in pain research

One particularly productive area of hypnosis research has concerned pain. Analgesia is one of the most obviously remarkable phenomena which hypnotic suggestion can be used to produce, and it has generated a lot of research interest (Hilgard & Hilgard, 1994; Miller, Barabasz, Barabasz, 1991; Eastwood, Gaskovski, Bowers, 1998; De Pascalis,

Magurano, Bellusci, 1999; Hargadon, Bowers, Woody, 1995; Montgomery, DuHamel, Redd, 2000). A key question in hypnotic analgesia research has concerned whether the effects are genuine. One main criticism concerns the demand characteristics associated with hypnosis. In many psychological experiments it is not particularly clear what the experimenters goals are, but when a participant is given direct suggestions of analgesia the intended effect is quite obvious and any results obtained could be due to the fact that participants are simply reporting what they believe the experimenter wants to hear, not what they actually felt (Orne, 1962). In an attempt to combat these criticisms sophisticated experimental designs have been developed. In real/simulator experimental designs high and low hypnotisable participants are hypnotised by an experimenter naïve to the hypnotisability of the participants; the low hypnotisable, but not the high hypnotisable, participants are given instructions to behave as they think a high hypnotisable would. Real/simulator experiments on hypnotic analgesia have demonstrated that low hypnotisable participants, told to simulate, will tolerate more pain following appropriate instructions. This leads some to believe that the effects associated with hypnotic suggestion, even in so called high hypnotizables, may be the product of simulation or reporting bias (Spanos, 1986; Wagstaff, 1981).

Intuitively it seems unlikely that all participants will try so hard to please an experimenter, especially if they will experience more pain as a result. There is good evidence to suggest that demand characteristics cannot fully account for hypnotic analgesia. Lang, Benotsch, Fick et al (2000) compared hypnotic relaxation with conditions of structured attention and standard care in 241 patients undergoing percutaneous vascular and renal procedures. Patients in the hypnosis group were significantly less anxious and reported significantly less pain than patients in the standard care group. It is difficult to ascribe the result to demand characteristics in this case because similar demands existed in the structured attention condition, from which the hypnosis condition differed only slightly. The authors note that the greater haemodynamic stability observed in the hypnosis group would be difficult to explain based on a biased response. Recent meta-analyses have confirmed that hypnotic suggestion for analgesia is an effective method of pain relief. These analyses have considered data from clinical and non-clinical studies and confirm, among other things, that patients treated with hypnosis demonstrate greater analgesic response than 75% of patients in a standard or no-treatment control group (Hawkins, 2001; Montgomery, DuHamel & Redd, 2000) and that hypnosis is an effective adjunct to surgery (Montgomery, David, Winkel, et al 2002).

Finally, strong evidence concerning the 'genuine' nature of hypnotically suggested effects comes from functional neuroimaging studies. In an experiment which will be discussed in more detail in chapter 4, Rainville, Duncan, Price, Carrier & Bushnell (1997) used hypnosis as a cognitive tool to modulate the unpleasantness of a painfully hot stimulus

independently of its intensity. By doing so in a positron emission tomography (PET) environment they were able to reveal that the anterior cingulate cortex but not the somatosensory cortex, both areas of the 'pain matrix', is linked with the encoding of perceived unpleasantness; this result helped to confirm hypotheses generated by earlier clinical lesion studies (e.g. Foltz & White, 1962). In an extension of the hypnotically-modulated-unpleasantness experiment, members of the same team report that the intensity of pain can be modulated with hypnotic suggestion (Hofbauer, Rainville, Duncan & Bushnell, 2001). The result, activations in primary somatosensory cortex, underscores the idea that the dimensions of pain can be influenced independently using hypnotic suggestion. A number of other similar neuroimaging studies, reviewed later, have produced similar patterns of results (Faymonville, Laureys, Degueldre et al, 2000; Crawford, Gur, Skolnik, et al, 1993). The fact that the reported changes in pain experience are associated with congruent changes in appropriate brain areas is at least *prima facie* evidence that participants are reporting an experiential change rather than simply complying verbally with the perceived experimental demands.

1.2.6 Using hypnosis to induce pain

Complementing the large literature concerning hypnotic analgesia and the down-modulation of pain with hypnotic suggestion there are a small number of reports of hypnotic induction of pain. These investigations were published mainly in the 1960's and early 1970's and were largely concerned with the physiological concomitants of physically-induced and hypnotically suggested experiences of pain. As they are of considerable relevance to the work described here each will be reviewed in detail.

1.2.6.1 Barber & Hahn (1964)

In this experiment Barber & Hahn report that they intended to investigate the physiological effects produced by imagining pain and to contrast these with measures relating to experienced pain. They took measurements in- and outside the hypnotic context (i.e. before and after a hypnotic induction). One hundred and forty seven female students were administered the Barber Suggestibility Scale (Barber & Calverley, 1963), fifty-two of them scored highly (six or above out of eight) and were invited to take part in an experiment described as a "physiologic study with the polygraph." Forty-eight participants agreed to participate and were randomly assigned into one of four groups A (pain stimulation), B (innocuous stimulation), C (waking imagined pain) and H (hypnotic imagined pain). Each participant in this between-groups study was tested individually.

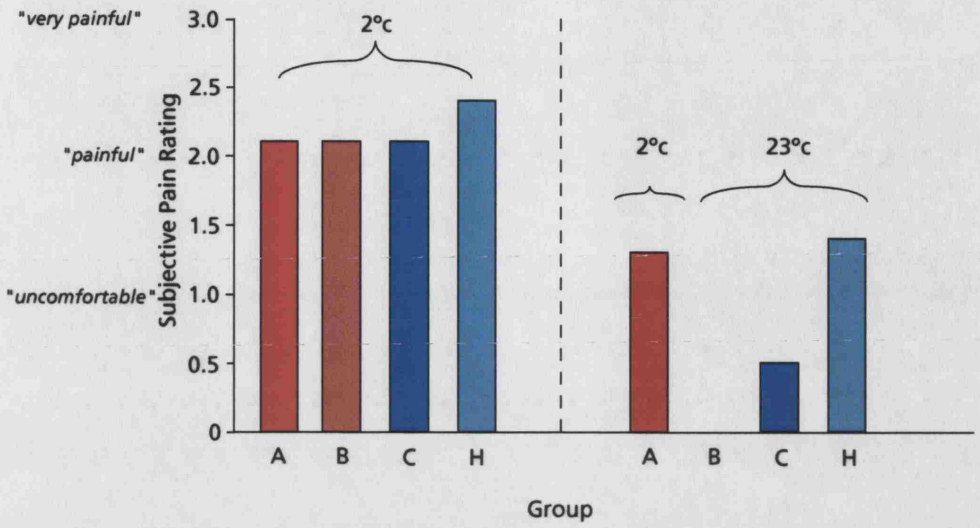
In the first twenty minutes of each test, participants in groups A, B, and C were asked to sit quietly for 20 minutes. Participants in group H were given a standardised

hypnotic procedure including *"eye fixation on a light blinking in synchrony with a metronome, repetitive suggestions of eye closure, relaxation, drowsiness, sleep, and deep hypnosis, suggestions intended to produce positive motivation to respond maximally on the forthcoming tasks, and suggestions that it was easy to respond to further suggestions"*. In this first phase of the experiment participants in group H did not receive any further suggestions. Participants in all groups were then told that they would soon be asked to immerse their left hand, up to the wrist, in cold water (2°c) and not to remove their hand until instructed to do so (Phase I: Anticipation). One minute was allowed to elapse then the instruction to immerse their hand was given (Phase II: Stimulus). Measures of skin resistance, heart rate and frontalis muscle tension were recorded continuously.

Following this first pain experience participants in group C (waking imagined pain) and group H (hypnotic imagined pain) were then given the following instructions:

"In a little while I am going to ask you to place your left hand in a different bucket of water. This water will be slightly cool but not cold, not at all as cold as the water your hand was in previously. When your hand is in this slightly cool water I want you to try to the very best of your ability to imagine vividly and to think continuously that it is as cold as ice and that it is as uncomfortable and as painful as the previous water. Try very hard to vividly imagine, to re-create, and to experience again the same sensations and the same feelings as you had previously. With a few exceptions other subjects participating in this experiment were able to do very well on the test; they were able to think about and to imagine vividly and to feel again their previous sensations. I want you to try hard to make this experiment a success. If you really try during the time your hand will be in the water to think and to imagine that it is the same ice-cold water you had previously, the polygraph record will show that you succeeded and the experiment will be scientifically important. In one minute I will ask you to put your hand in the water. During the time your hand is in the water, keep trying very hard to feel again your previous feelings and sensations."

Participants in groups A and B were told that they would be asked to place their hand in "cold water" for a further minute (Phase III: Anticipation). Again, one minute was allowed to elapse and the instruction to put the hand in the water was given (Phase IV: Stimulus). In this second-round of stimulation only group A (pain stimulation) was given water at a painfully cold temperature (2°c). Groups B (innocuous stimulation), C (waking imagined pain) and H (hypnotic imagined pain) immersed their hand in water at room temperature (23 ± 1 °c) for one minute. Again physiological measures were taken. After both pain experiences participants were asked to rate each experience on an ordinal scale using the terms pleasant, normal, cool, cold, numb, uncomfortable, painful and very painful. Only the final three terms contributed to a subjective three-point 'pain score'.



Figue 1.4: Subjective pain ratings displayed by group. The first four bars represent ratings taken after the first half of the experiment, when all groups were exposed to the same noxious cold (2°c) stimulus. The last three bars represent the pain ratings taken after the second half of the experiment, where each group was given different instructions. Water temperatures that each group received are displayed. Group A = pain stimulation, Group B = innocuous stimulation, Group C = waking imagined pain, Group H = hypnotic imagined pain.

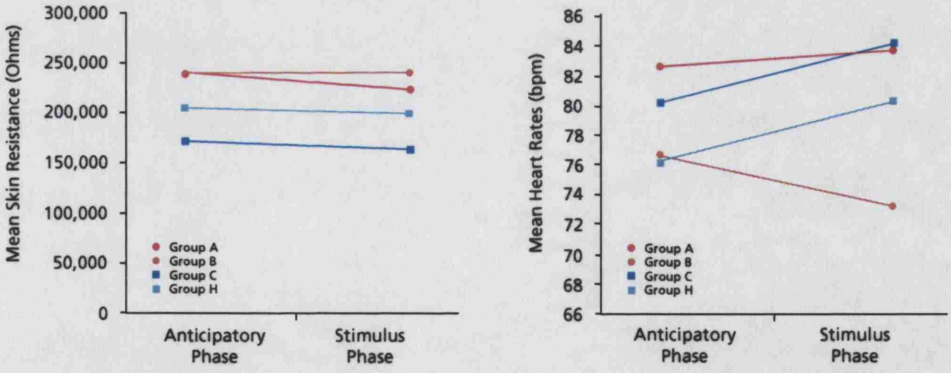


Figure 1.5: Skin resistance and heart rates shown by group for phases III (anticipatory) and IV (stimulus) only. Group A = pain stimulation, Group B = innocuous stimulation, Group C = waking imagined pain, Group H = hypnotic imagined pain.

Results of subjective pain scores for phase II (immersion in cold [2°c] water) are presented in figure 1.4. There were no significant differences between groups. Participants in all groups showed a decrease in skin resistance and increase in heart rate from phase I (anticipation) to phase II (stimulation). These data indicate that 'hypnotised' or 'awake' participants, who have not received any specific suggestions of decreased pain, do not differ on subjective or physiologic responses to a noxious

stimulus. Results of subjective pain scores for phase IV are presented in figure 1.4. Participants in group A, the only group to be given a noxious stimulus, rated the experience between "uncomfortable" and "painful". Participants in group C (waking imagined pain) rated the experience as less than "uncomfortable", while those in group H (hypnotic imagined pain) rated the sensation between "uncomfortable" and "painful". Scores from participants in groups A and H did not differ significantly from one another, but were both significantly higher than scores from group C. Thus instructions to imagine pain, when delivered in a hypnotic context, can elicit a subjective report of pain as strong as that produced by a matched noxious physical stimulus. Physiological data from phase IV are presented in figure 1.5. Mean heart rate in groups A, C and H differed significantly from mean heart rate in group B (innocuous stimuli). There was a trend towards lower skin resistance in groups A, B and H compared to group C, but no significant difference. For measures of frontalis muscle tension groups A, B and H did not differ significantly from one another, but did differ significantly from group C.

A difficulty presented by this study concerns the task demands or demand characteristics of the situation. It is not clear that the experimenters made it plain to participants that they were interested in whatever the participants experienced in response to the instructions. Instead, very strong task motivational instructions were given including *"I want you to try hard to make this experiment a success"*. Additionally, the physiological data presented by Barber & Hahn is ambiguous. Heart rate was greater in the 'pain' groups than in the innocuous stimuli group, as was muscle tension. Significant differences were not observed in relation to skin resistance. These data are consistent with the author's interpretation that instructions to imagine pain are sufficient to produce some of the physiological effects characteristic of noxious stimulation. However, since participants in group C (innocuous stimulation in phase IV) were told that they would be experiencing painfully cold stimulation it is plausible that they relaxed upon realising that the water was at room temperature. This factor could account for the significant group differences (groups A, B & H vs. group C) on the physiological measures. Overall, the subjective ratings observed in phase IV of this experiment indicate that it is possible to elicit changes in experiences of pain through instructions to imagine a painful stimulus delivered in a hypnotic context, and that 'waking' instructions are less effective. Adequate data is not available to determine if waking instructions produced pain experience ratings that were significantly greater than zero.

1.2.6.2 Dudley, Holmes, Martin & Ripley (1964), Dudley, Holmes, Martin, Ripley (1966), Dudley, Homes & Ripley (1967)

Data concerning similar experimental methods, and from what appear to be the same pool of participants, are published across these three papers and will be reported here collectively. Eleven participants took part in a series of experiments examining the effects of hypnotically induced pain, emotion and exercise upon respiratory function. Before the hypnosis experiments ten of the participants were stimulated with a metal headband with 14 adjustable rubber-tipped screws around the circumference. The device was worn for fifteen minutes and produced an intense pressure headache. During this time effects upon respiration were measured. At a later date and after the induction of hypnosis it was suggested to participants that they would *"relive the headscrew situation and the pain you just experienced"*, at intervals of two to four minutes it was suggested that the pain was getting *"worse and worse"* or *"more and more unbearable"*; suggestions were continued for ten to fifteen minutes. Physiological measurements were made of respiratory rate, fractional concentration of carbon dioxide, oxygen consumption, blood pressure, pulse rate and skin temperature.

In response to actual headband stimulation there were significant increases of oxygen consumption and blood pressure, and a significant decrease in fractional concentration of alveolar CO_2. The respiratory response of the participants to the hypnotic suggestion of the headband experience was similar to that of the actual experience; except that changes in blood pressure were not reproduced, and pulse rate increased significantly. Graphical representations of the reported data (Dudley et al, 1966) are given in Figure 1.6.

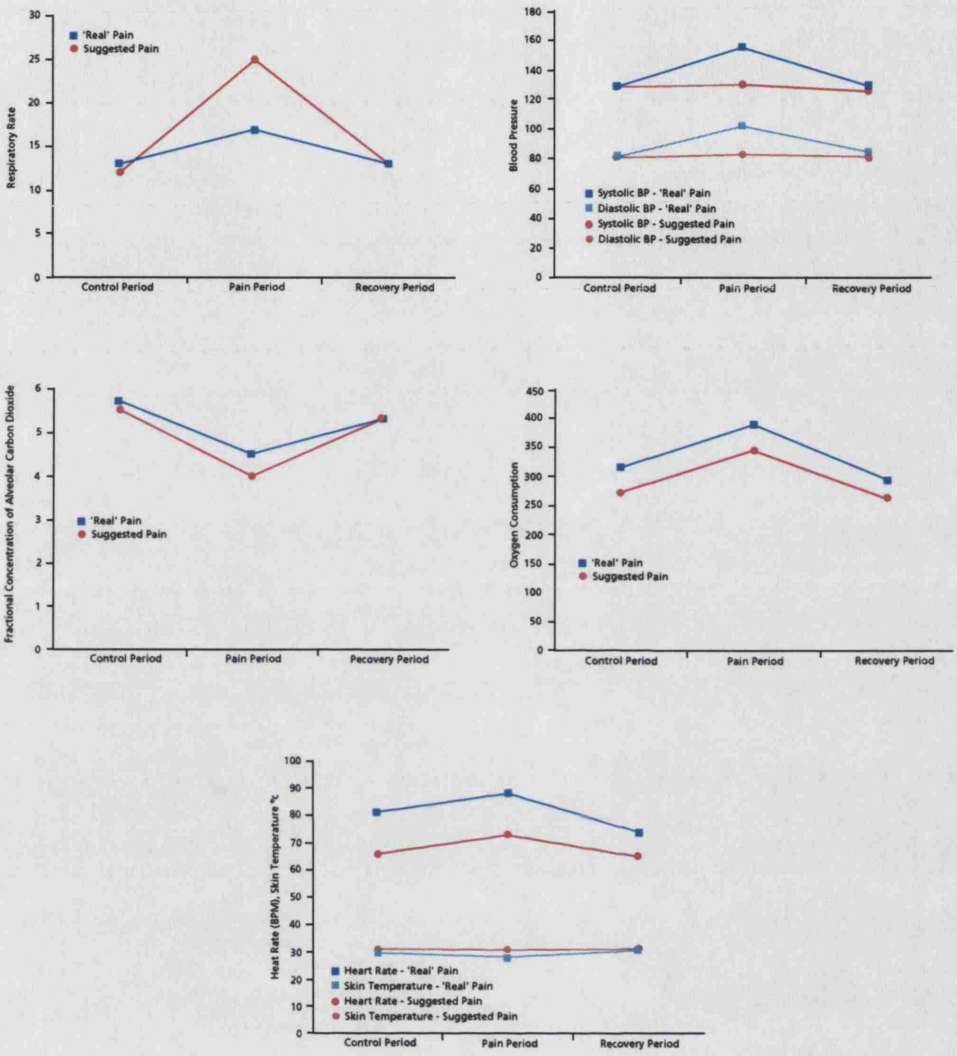


Figure 1.6: Graphs showing physiological responses to 'real' and suggested pain.

Dudley and colleagues also report on the subjects 'psychologic' responses to the painful stimuli, unfortunately not in a manner that allows for statistical analysis. They state that four subjects had good reproduction of the head pain and emotions, six had good reproduction of emotions but only fair reproduction of head pain, and one had poor reproduction of both emotions and head pain. From the table of comments given by the subjects (Figure 1.6) it seems apparent that the actual head pain was experienced as being more intense and unpleasant than the suggested pain with less variability in response.

Subject	Immediately After Suggested Headache	Immediately After Actual Headache
1	"I wanted to terminate it. I'd had enough. The painful sensation was a real threat. I was fighting the head pain and was angry with you."	"I wished it were over. I would have done anything to stop it."
2	"I felt uncomfortable. I had a headache but I couldn't feel the headscrew."	"I felt like getting out of the situation somehow."
3	"I relived the pain, but it didn't bother me a bit. I'm immune to pain. I can grin and bear that headband."	"It didn't bother me a bit"
4	(Migrane headache) "I actually developed a headache and was very happy to get it over with. It was frontal and more on the left side. Great relief afterwards."	"Oh boy! My migrane headaches are excruciating. I often get them when I'm trying to find out whether I can handle situations."
5	"I was uncomfortable. I resented it. After it was over, it took me a while to realise it was just an experiment, I didn't deserve it."	"I just wanted to get out. I felt very tense and restless."
6	"I was trying to hang on until the end of the pain which was much like the actual headscrew application."	"During the final period I had panic. The foremost thought in my mind was 'God Almighty, I've got to get this over with.'"
7	"I could kind of feel it. As you reinforced it, I could feel it more and more."	"It seemed almost unbearable. It was the worst pain I ever had. I just wanted to get out."
8	"Some head pain was experienced. My stomach got upset as it did with the actual head screw. I clenched my fist and had nasal hyperfunction and dryness of the mouth."	"I really had a terrible headache. The thought passed my mind to tear it off."
9	"I had an uncomfortable feeling with tension in my neck. I squirmed and felt it might be something outside."	"There was some basic challenge to overcome it (the head pain). I had a choking sensation with panic. I just wanted to get out."
10	"The pain was hard to bear. It was difficult to tolerate the discomfort much longer."	"It was unbearable. What the hell am I doing here?"
11	"It was the most real situation of all. I pictured myself with the headscrew. The pain was almost unbearable. The nose clip was also painful."	"It was extremely painful. I tried to concentrate on something else. I wished it were over."

Figure 1.7: Comments elicited from subjects after 'actual' and suggested pain.

Hypnotic susceptibility, unfortunately not measured here, may play a key role in the response of subjects. Dudley reports that the desire of the subject to cooperate was a key factor in the production of emotional and physiologic change *"The subjects who appeared to be most interested and cooperative had the best reproduction of all parameters of reaction"* (Dudley et al, 1966). Dudley, Holmes and Ripley (1967), reporting on a similar experiment, state that physiological response was directly related to the depth of trance and vividness of reliving suggested events. However, hypnotic susceptibility in this case was assessed subjectively by the experimenter. Interestingly, Dudley comments on the "noxious" nature of the situation in which he placed the participants, causing them anxiety about unknown factors in the experiment and making them angry at the experimenter *"for placing him in a situation from which he could not gracefully escape."*

1.2.6.3 Hilgard, Morgan, Lange, Lenox, Macdonald, Marshall, Sachs (1974)

Hilgard and colleagues investigated physiological responses to hallucinated pain to provide a control condition for investigations into physiological responses to cold-pressor pain: vasomotor responses to the immersion of the hand and forearm in cold water cannot be separated from the physiological responses to pain, by recording vasomotor responses to hallucinated pain it becomes possible to partial out the response to the cold water independently of pain. Twelve highly hypnotisable subjects who had previously shown the ability to reduce pain almost completely with hypnotic analgesia and could produce pain through hallucination in a manner convincing to themselves were selected for the study. Subjects went through several cycles of experiencing actual cold-pressor pain to familiarise them with the rising pain felt under normal circumstances. In the hallucinated pain portion of the experiment participants were hypnotised; with these highly hypnotisable and highly practised participants the induction consisted of a count to 10, with some self deepening if required. Participants hallucinated that their hand and arm were dropped into the water, while in actual fact they remained in a cradle above it. Verbal pain reports were called for every 5s.

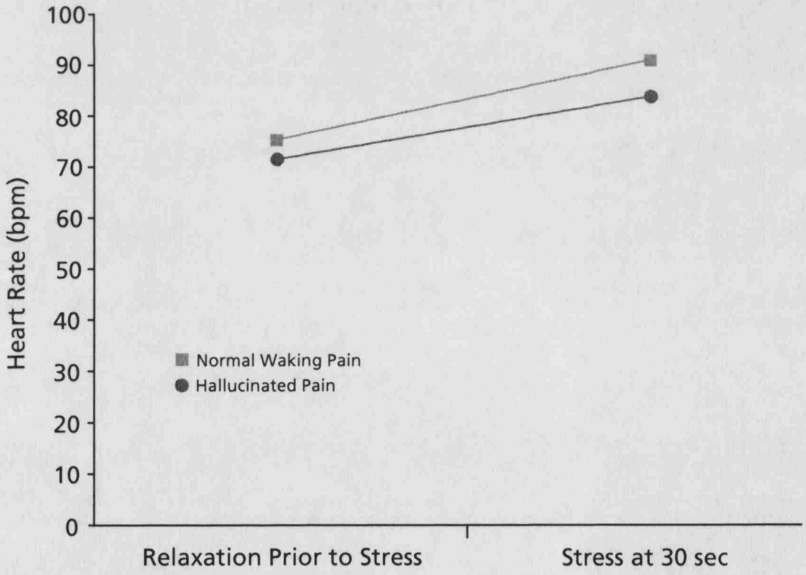


Figure 1.8: Heart rate prior to and during experience of actual and hallucinated pain.

Heart rate from before the pain and 30s into the pain hallucination are presented in figure 1.8. In both the normal waking pain and hallucinated pain conditions significant increases in heart rate are observed over baseline. On the basis of this result Hilgard and colleagues conclude that the heart rate rise is *"a function of* felt *pain, and not merely a consequence of physiological stress."* Unfortunately subjective pain measures from the participants are not reported.

1.2.6.4 Schweiger & Parducci (1981)

Building on the previously reviewed work, Schweiger and Parducci (1981) investigated the nocebo effect; the psychological induction of pain in the absence of both noxious stimulation and hypnotic suggestion. Dudley et al (1967) had previously used non-hypnotic suggestion to produce an experience of pain. However, Schweiger & Parducci note that the context in which Dudley's experiment was conducted carried with it relatively strong demand characteristics which they tried to avoid.

Thirty four participants were randomly assigned to two conditions, involving either 'strong' or 'weak' instructions. The experiment was carried out individually in a room designed to establish a stressful atmosphere; it was small, semi-soundproofed and contained a dental chair. Other instruments were prominently displayed including a shock inducer, power supply, noise generator, polygraph and a brightness comparator. The authors report that the room was intentionally designed to be intimidating. In both experimental conditions subjects were seated in the dental chair and electrodes were affixed to the subjects temples and right hand. Practice trials were given on the brightness comparator – a perceptual task used as 'cover' in this experiment. Participants in the 'strong' instructions group were told that the experiment was a study concerning the aetiology of headaches and ways of dealing with them without drugs. It was explained that the electroencephalograph would deliver a low-voltage current through the temples and that although it would be too mild to be felt on the skin it had produced mild headaches in past studies, headaches which disappeared as soon as the current was turned off. The subject's task was to match the brightness of a the ring and disc components of the brightness comparator, which they were told might prevent headaches, reduce their intensity or have no effect at all. Subjects were to report the intensity of any headaches on another dial after each trial (Dial range 0-100: 0 = no headache, 100 = unbearable headache). Participants in the 'weak' instructions group were informed that the purpose of the study was to investigate the effect of a low voltage current upon brightness matching. Subjects were assured that the current would be too weak to be felt on the skin even though some people develop a mild headache as a side effect. The investigators increased the volume of a white noise generator during the course of the experiment in an attempt to increase the perceived stress of the situation.

Twenty-four participants, approximately two thirds of the total, reported headaches during the experiment. The number reporting headaches in each condition did not differ significantly, nor did the intensity of the headaches differ across conditions (Weak =14.5/100; Strong = 16.3/100). Participants confirmed that they felt headaches, even when informed that no current had been delivered. The pain itself was typically described as tightness and a throbbing pressure. Addressing the issue of compliance the authors note that their study differed from those of Hilgard, Dudley and Barber in that there was nothing in the instructions to suggest that the experimenters wanted

subjects to report headaches. In fact, in the 'strong' instructions condition subjects were informed that the perceptual task might prevent headaches. They also rule out the possibility that the white noise or eyestrain produced the headaches, no subjects reported these as factors in their headache. One factor which the authors draw attention to are the anxiety measures; all but two of the participants who reported headaches reported anxiety before the first trial. 'Psychologic stress' was thus hypothesised to be the cause of pain.

1.2.7 Discussion

The terms which are used to describe the induced pains in the aforementioned series of experiments are varied, but are the pain induction methods used different enough to justify the terminology? Hilgard et al (1974) refer to their hypnotically-induced pain as *hallucinated.* They do not report the exact methods used, just that twelve subjects were selected for the ability to reduce (cold-pressor) pain almost completely and also for the ability to *"produce it through hallucination in a manner convincing to themselves"*. Dudley et al (1963/1966/1967) refer to their use of direct hypnotic suggestion. Participants were hypnotised and asked to *"relive the headscrew [painful stimulus] situation and the pain you experienced"*. This was reinforced with suggestions that the pain was getting *"more and more unbearable"* or *"worse and worse"*. In describing their experiment Barber and Hahn (1964) summarise their hypotheses as concerning *imagined* pain. They measured the physiological responses in subjects required to imagine painfully cold water, in and outside the hypnotic context (one group received the instructions 'cold', another group received the same instructions after a hypnotic induction). The exact nature wording of the instruction was given earlier (section 1.2.6.1) and can be viewed as a suggestion, to be delivered in and out of the hypnotic context. Subjects are asked directly to imagine, but also to *"re-create and to* experience *again the same sensations and the same feelings you had previously"* (my emphasis). Schweiger & Parducci's (1981) instructions served to modulate participant's expectations about what would happen during the experiment. They cannot easily be classified as traditional indirect suggestions, and certainly did not involve the repeated and continuous verbal suggestion observed in the other designs.

Of the experiments described, the work of Dudley and colleagues most clearly fits the category of direct suggestion in a hypnotic context. Hilgard was a classic 'state theorist' and his descriptions of hypnotic procedure are often taken as standard procedure. Although his method is not clearly described it is likely that his suggestions were also direct (see Hilgard, 1977). One of the most difficult of the procedures to categorise is that of Barber & Hahn (1964). Is a hypnotic suggestion more than an instruction to imagine a state of affairs which is not real? Terminology aside, these studies appear to demonstrate that pain can be experienced in the absence of a physical stimulus. Confirmation of these results would provide an interesting challenge to our theories

of pain: although the variable link between injury and pain is accounted for by current models, the psychological generation of pain has not been widely considered.

1.3 Model

A description relating the effects of hypnotic suggestion to the symptoms of conversion disorder is outlined and a model linking both is assessed. A template of the model is applied to functional pain disorders and advantages and disadvantages of the formulation are discussed. A plan for investigation is proposed.

1.3.1 Conversion disorder

Kihlstrom (1992) characterises conversion disorder (often referred to as conversion hysteria or hysteria) as a dissociation of lower level implicit information processes from higher level explicit information processes. Essentially, symptoms are believed to be psychologically produced but patients, who are genuinely experiencing them are not consciously aware of their generation (Oakley, Ward, Halligan, Frackowiak, 2003). Conversion disorder falls under the classification of 'somatoform disorders' (DSM-IV, 1994) and the ICD-10 classification system defines somatisation as *"repeated presentation of physical symptoms, together with persistent requests for medical investigations, in spite of repeated negative findings and reassurances by doctors that the symptoms have no physical basis"* (WHO, 1992). Somatoform pain disorder is classified separately although this distinction was only introduced in DSM-III (1980). Pain and non-pain somatisation overlap considerably and a number of authors have questioned the validity of the current distinction between the two (Bishop & Torch, 1979; Watson & Tilleskjor, 1983; Oakley, 1999b). Conversion disorder symptoms can be split into three subcategories: motor symptoms or deficits, sensory symptoms or deficits, and seizures or convulsions. Examples of motor symptoms include paralyses or local weakness, imbalance and difficulty swallowing. Typical sensory conversion symptoms include loss of sensitivity to pain or touch, deafness and blindness. Seizures as a symptom of conversion disorder are often referred to as pseudoseizures, psychogenic seizures or non-epileptic seizures. These can appear very similar to epileptic seizures but are not accompanied by the same characteristic patterns of brain activity.

Hypnosis has long been associated with conversion disorder, with similarities between the effects of hypnotic suggestions and the symptoms of conversion disorder recognised by Janet nearly a century ago (Janet, 1907). Parallels have been drawn throughout the twentieth century by Chertok (1975), Frankel (1978), Gill & Brenman (1959) and Hilgard (1977). Sackeim, Nordlie & Gur (1979) note commonalities between hysterical and hypnotic blindness, offering a model to account for the visually controlled behaviour of hysterically blind patients. As well as reflecting upon similarities there is also a tradition of using hypnotic suggestion to model certain other disorders. Oakley (1999b) notes that an important advantage of using hypnosis in this way is that appropriate 'symptoms' can be compared with conversion symptoms, making the most

of selective creation and removal. A wide range of conversion symptoms have been modelled with appropriate hypnotic suggestion including: analgesia (Hilgard, Morgan & Macdonald, 1975), tunnel vision (Blum, 1975; Miller & Leibowitz, 1976), monocular blindness (Pattie, 1935), binocular blindness (James, 1890/1950; Loomis, Harvey & Hobart, 1936; Ludholm & Lowenbach, 1942-1943). There is little apparent experimental literature on hypnotic induction of seizures but Schwartz, Bickford & Rasmussen (1955) found that by using direct hypnotic suggestion they were able to initiate and stop seizures in non-epileptic seizure patients but not in epileptic patients. Some evidence exists that hypnotisability, dissociation and non-epileptic seizures are related (Kuyk et al, 1995; Kuyk, Van Dyck & Spinhoven, 1996), although this is not a universally recognised result (Litwin & Cardena, 1993).

Drawing on this evidence Oakley (1999b) developed a theory linking hypnotically-produced effects and conversion symptoms. The theory itself draws on a model of consciousness (Oakley, 1999a: Figure 1.9) which ties the idea of a central executive structure (or supervisory attentional system) to levels of self awareness. Only when information reaches the highest level of self awareness do we become 'conscious' of it, and importantly the choice of which material is represented in this highest level is determined by the central executive structure – outside of self awareness (consciousness). Oakley describes the production of hypnotic phenomena as the result of a 'contract' between the hypnotist and the central executive structure; a situation which allows the manipulation of the contents in the self awareness system which in turn produces changes in subjective experience. The model gives a good account of hypnotic phenomena, in particular the involuntary quality of suggested effects (and conversion symptoms), and describes the mechanism by which the state-like effects of a hypnotic induction might function. A cognitive account of the model has recently been given by Brown and Oakley (2004).

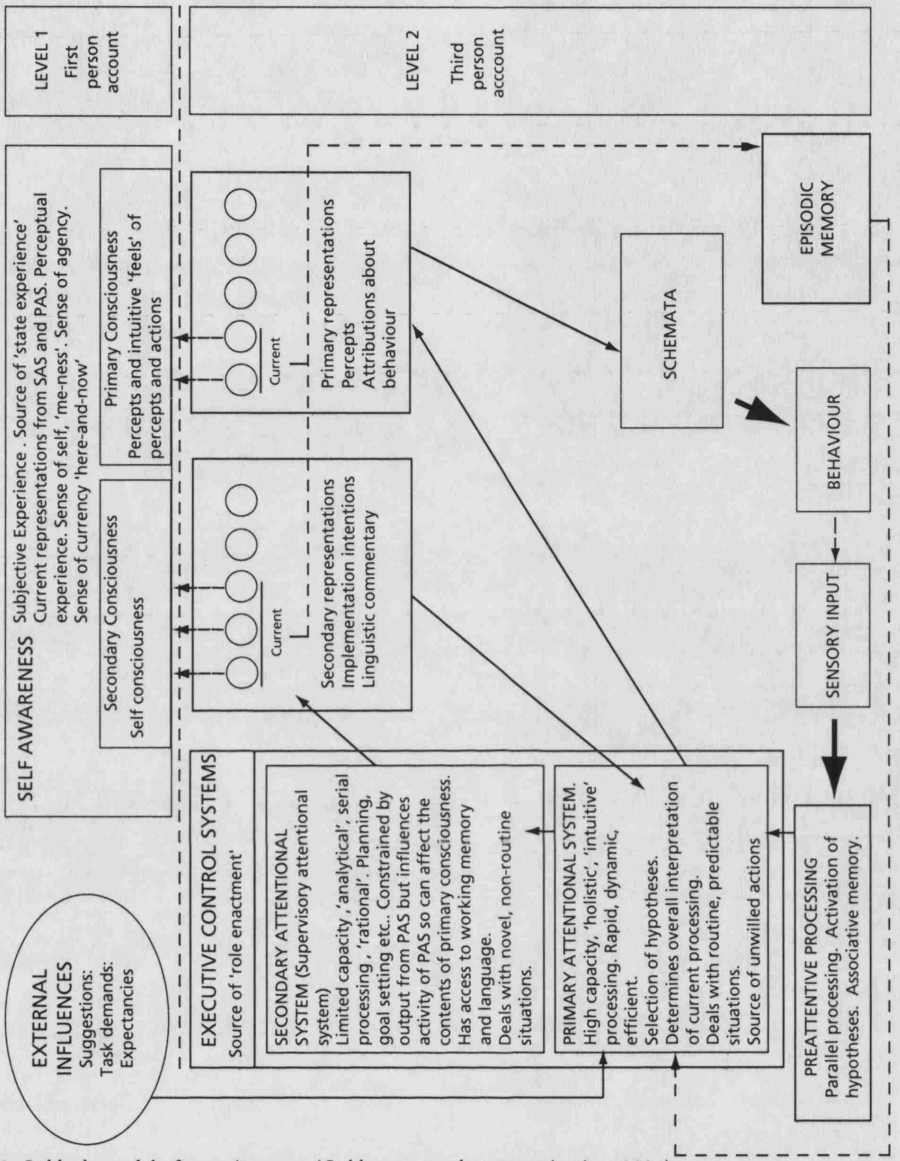


Figure 1.9: Oakley's model of consciousness (Oakley personal communication, 2004).

Oakley's theory draws attention to the similarities between suggested effects and conversion symptoms, in particular the way in which they are perceived as involuntary, the lack of concern expressed concerning the symptoms/effects, the display of 'implicit knowledge' and the apparently compliant nature. Differences between suggested effects and conversion symptoms are also acknowledged. One key factor which distinguishes conversion symptoms from hypnotically suggested effects is the duration of the effects: hypnotic effects are normally confined to the context in which they are suggested whereas conversion symptoms persist over much broader time scales and situations. Also, hypnotically suggested effects are normally suggested by another individual whereas conversion symptoms, if an auto-suggestive disorder as Oakley proposes, are thought to be self-suggested.

1.3.1.1 Mechanisms of suggestion

Following Oakley's (1999a) model of hypnosis and consciousness as an exemplar it is possible to provide an account, both psychological and neurophysiological, of how verbal suggestions can produce changes in subjective experience. Verbal suggestions are initially processed in the auditory cortex, and then processed in a more distributed manner in left frontal regions (encompassing classic Broca's & Wernicke's areas). Oakley hypothesises that suggestions act at the level of the supervisory attentional system (Norman & Shallice, 1986). Executive functions have been demonstrated to have a neuroanatomic basis in the dorsolateral prefrontal cortex (DLPFC) using a variety of tasks (D'Esposito *et al.*, 1995; Owen *et al.*, 1996; Salmon *et al.*, 1996; Collette *et al.*, 1999), although extensive parietal, premotor, cingulate, occipital and cerebellar activation has also been observed in relation to these tasks (Garavan, et al, 2000).

On a psychological level, the central executive is said to make decisions about the contents of conscious awareness. Representations blocked from consciousness are not thought to be underscored by patterns of neural activity associated with consciously available representations. For instance in the case of pain Rainville et al (1997) demonstrated that subjective pain unpleasantness correlated with activity in a region of the anterior cingulate cortex. In terms of the present model, when unpleasantness was manipulated by suggestion (via the central executive), activity in specific networks (the pain matrix: see chapter 4) was concurrently modulated.

Whereas pain reduction can be thought of as a negative hallucination (the reduction of perception), positive hallucinations present a more complex picture for analysis. The central executive structure this time must represent information which is not present in the environment at the level of conscious awareness. Production of the hallucinatory percepts is hypothesised to depend upon the modality of the suggested hallucination; visual hallucination would be expected to engage areas of the visual cortex (e.g. Kosslyn et al, 2000), with the information that the percept is self-generated not being available to subjective awareness.

1.3.2 Testing the connections between conversion symptoms and suggested effects

Extending beyond theories drawing similarities between conversion symptoms and suggested effects there have been a number of recent investigations aimed at empirically testing the proposed links between hypnotisability and conversion disorder.

1.3.2.1 Hypnotic susceptibility of patients with conversion disorder

Roelofs, Hoogduin, Keijsers, Näring, Moene and Sandijck (2002) tested two of the major assumptions associated with the 'autohypnosis' family of theories regarding conversion disorder; the idea that spontaneous self-hypnosis leading to a dissociation of sensory or motor function might generate conversion symptoms. The first prediction of this view is that patients with conversion disorder are highly hypnotically susceptible, the second is that hypnotic susceptibility will be related to dissociative symptomatology. In a controlled study Roelofs et al (2002) tested the hypnotic susceptibility of 50 conversion patients and also tested an age and sex matched group of patients with affective disorders. They found that patients with conversion disorder scored significantly higher on the Stanford Scale of Hypnotic Susceptibility: Form C than the matched patients in the control group, and also that they scored higher than a matched non-psychiatric control group; however the mean score of the conversion group still fell within the 'medium' range of scores on the Stanford.

This result is in agreement with earlier studies. Kuyk, Spinhoven and van Dyck (1999) found higher levels of hypnotic susceptibility a sample of 20 patients with pseudoepileptic seizures than in a sample of 17 patients with real epileptic seizures. Bliss (1984) also found high levels of hypnotic susceptibility in 18 patients with conversion symptoms. However Roelofs et al (2002) point out that theirs is the only controlled study to assess the hypnotisability of conversion patients, highlighting relatively serious methodological shortcomings in earlier work. Roelofs and colleagues also found that the number of pseudoneurological symptoms in conversion patients, as measured by the SCID-I (First, Spitzer, Gibbon, Williams, 1996), is significantly correlated with hypnotic susceptibility. They interpret this finding as meaning that high hypnotisability could be a risk factor for the development of conversion symptoms. In contrast to these generally positive findings, Goldstein, Drew, Millers, O'Malley and Oakley (2000) using the Creative Imagination Scale (Wilson & Barber, 1978) as a measure of hypnotisability found no difference in suggestibility between 20 patients with pseudoseizures and a non-clinical control group.

1.3.2.2 Functional imaging of hypnotic and conversion symptoms

Additional evidence comparing hypnotically suggested effects with symptoms of conversion disorder comes from a series of brain imaging studies. These investigations have examined the neural activations underlying attempted movement of a limb paralysed either as a conversion symptom or as a result of direct hypnotic suggestion. Marshall, Halligan, Fink, Wade & Frackowiak (1997) investigated the functional neuroanatomy of a forty-five year old woman with a left-sided paralysis which met

DSM-IV criteria for conversion disorder. Positron emission tomography (PET) scans were taken in conditions of preparing to move, and moving, the right (good) and left (paralysed) legs to the beat of a metronome. Both legs were strapped to restrain any actual movement. Preparation and movement of the right leg was underscored by activation in predicted motor and premotor areas (Fink, Frackowiak, Pietrzyk, Passingham, 1997). Preparing to move the paralysed leg also produced normal activations. However, activations underlying attempting to move the paralysed leg compared to baseline were found in the right anterior cingulate. When attempting to move the paralysed leg was contrasted with attempting to move the good leg additional activation was found in the orbitofrontal cortex. The authors proposed that activations in the orbitofrontal and anterior cingulate cortices act to inhibit the willed action.

Halligan, Athwal, Oakley & Frackowiak (2000) used the Marshall et al (1997) study as a model and investigated the neural correlates of a hypnotically generated paralysis using the same PET techniques. A highly hypnotisable participant was hypnotised and given suggestions for left leg paralysis. Scans were taken for each leg in conditions of rest (no move), preparing to move, and attempting to move. Again both legs were restrained to control for absence of movement in the conditions involving the paralysed leg. Contrasts were made to reveal relative activations when the participant attempted to move the paralysed leg that did not occur when attempting to move the right (unparalysed) leg. Activations were observed in the anterior cingulate and orbitofrontal cortex and interpreted as representing neural activity responsible for inhibiting the participants voluntary attempt to move his left leg.

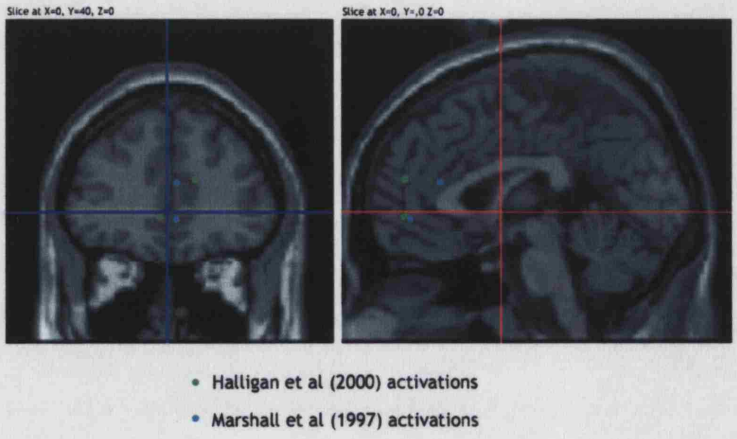


Figure 1.10: Activations from Halligan et al (2000) and Marshall et al (1997) produced by the contrast ([attempt to move left leg – prepare to move left leg] – [attempt to move right leg – prepare to move right leg]).

As can be seen from figure 1.10 (above), the similarities in patterns of results of both studies are striking. The figure shows activations from both studies produced by the contrast ([attempt to move left leg – prepare to move left leg] – [attempt to move right leg – prepare to move right leg]), producing a difference image showing activations specific to the attempt to move the paralysed leg (see chapter 4 for a more detailed description of functional imaging contrasts). Activations from both studies do not overlap exactly but this is most parsimoniously explained by slight differences in neural architecture across individuals which is not corrected for perfectly by the spatial normalisation stage of functional imaging analysis. Taken together, these studies indicate that paralysis, whether produced by conversion disorder or hypnotic suggestion, is mediated by similar brain processes; indicating further that hypnotically-suggested effects might be good analogues for other functional disturbances.

A number of recent neuroimaging studies have examined regional cerebral blood flow (rCBF) associated with functional somatosensory deficits (Mailis-Gagnon, Giannoylis, Downar, Kwan, Mikulis, Crawley, Nicholson, Davis, 2003; Vuilleumier, Chicherio, Assal, Schwartz, Slossman, Landis, 2001). Mailis-Gagnon and colleagues (2003) found that unperceived stimuli failed to activate areas that were activated with perceived touch and pain and found deactivations in primary and secondary somatosensory cortex, posterior parietal cortex and prefrontal cortices. Vuilleumier et al (2001) observed hypoactivations of thalamus and basal ganglia contralateral to limbs affected by unilateral sensorimotor loss. These experiments have not yet been replicated using hypnotic analogue 'symptoms' but more than twenty years ago hypnotic analgesia was cited as an example of conversion reactions of analgesia (Hilgard, Morgan & Macdonald, 1975; Sackeim et al, 1979) and demonstration in functional imaging would serve as a useful test of the model as well as providing valuable information concerning central causes of somatosensory deficits.

1.3.3 Testing the extent of the model: is functional pain covered?

As we have seen, Oakley's model accounts well for symptoms of conversion disorder such as paralysis. But he goes further by proposing that symptoms originally considered 'hysterical' should now be subsumed under the label of 'auto-suggestive disorder'. This new classification would encompass not only 'classic' conversion symptoms such as paralysis and blindness but would also cover conditions such as psychogenic amnesia and, importantly for this thesis, pain. This reintegration of psychogenic pain with conversion symptoms finds support from other authors who have questioned the distinction between pain and non-pain somatisation disorder (Bishop & Torch, 1979; Watson & Tilleskjor, 1983).

Walters (1961) has been cited as proposing a dissociation between the diagnoses of hysteria and hysterical pain *"theories of hysteria do not appear to account for the production of... pain"* (Birket-Smith, 2001). However, a closer examination reveals that he makes this distinction on the grounds that patients with what he describes as 'psychogenic regional pain' also suffer from other depressive, and in some cases psychotic, states; also that contemporary (mid-20th-century) theories of hysteria could not account for the pains. On this basis he believed that a diagnosis of hysteria did not accurately reflect the psychological background of the patients and confused theoretical understanding of the condition. If we look at Walters' definition of psychogenic regional pain, however, we see that it closely reflects what has been referred to earlier in this thesis as functional pain. Specifically, Walters states that psychogenic regional pain is characterised by having no underlying peripheral cause and is psychogenic in its evocation, which he clarifies as relating to a mental or emotional disorder.

Increasingly, the differential diagnosis of various functional somatic syndromes are being viewed as artefacts of medical diagnostic procedure; a diagnosis of fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome or pain disorder may depend more on which specialist a patient sees than what symptoms they have (Wesseley et al, 1999; Hazemeijer & Rasker, 2003). Wessely et al (1999) present a review suggesting that patients suffering from the functional somatic syndromes do not differ as substantially from one another as the variety of diagnoses from different specialities suggests. They provide evidence demonstrating that core diagnostic features of the different syndromes overlap substantially and that co-morbidity among the somatic syndromes is high.

Differences between the common functional pain syndromes and conversion symptoms exist too. Functional pain patients may differ from conversion disorder patients on measures of concern. Whereas conversion patients are classically unconcerned about their symptoms functional pain patients are concerned and seek diagnosis and reassurance, often from multiple specialists. Emotional distress is reportedly higher in patients with IBS compared with a matched sample of patients with inflammatory bowel disease (Walker et al, 1990) but it is not known whether this distress is symptom specific or a characteristic of these individuals. The usefulness of the concept of *la belle indifférence* has been questioned by a number of authors (Bishop & Torch, 1979; Lewis & Berman, 1965; Pincus & Tucker, 1978; Rangell, 1959) which may serve to ameliorate this possible distinction between traditional conversion symptoms and functional pain.

Bringing together the strands of research investigating hypnotically-induced pain and following Oakley's model (classifying pain disorders as auto-suggestive disorders) yields a number of predictions:

First, it should be possible to model functional pain disorders using hypnotic suggestion.

Second, brain activity underlying the hypnotically-suggested symptoms should mirror closely the 'genuine' symptom.

Third, if it is correct to equate functional pain patients with conversion disorder patients then sufferers of functional pain should display scores that are above the norm on measures of hypnotic susceptibility.

Finally, as with conversion symptoms, it should be possible to modulate or ameliorate the pain symptoms with hypnosis.

Chapter 2 – Investigating the subjective experience of hypnotically-induced pain

2.0 Introduction

This first experiment was designed primarily to assess whether it was possible to induce a sensation of pain using direct suggestion. Methods of pain induction in earlier studies (see chapter 1, section 1.2.4) were varied, and previously described differences in terminology make interpretation difficult (section 1.2.5). Also, relatively informal attempts were made at assessing the subjective experience of hypnotically-induced pain, a shortcoming to be rectified in this trial. This study was designed to assess a number of factors. Firstly, can a sensation of pain be produced by direct hypnotic suggestion? Secondly, how similar are hypnotically-induced pains to physically-induced pains? (are hypnotically-induced pains experienced 'as real' or are they somehow different?). A key factor distinguishing this experiment from previous investigations was a focus on the subjective experience of pain instead of its physiological concomitants.

2.0.1 Physically-induced pain

Methodologies employed in previous investigations of hypnotically-induced pain have varied considerably but all have involved matching a suggested pain to a physical stimulus such as Dudley et al's (1964/1966/1967) hypnotically suggested reliving of a previously experienced painful headband event. A physically-induced pain was included in this investigation in order to contextualise the hypnotically-induced pain experience and to provide an easily understandable benchmark. Commonly used noxious stimuli in modern pain research includes electrical, heat and cold stimulation. It is now recognised that an ideal laboratory pain stimulus would be one which could reproduce more dimensions of pain than just intensity. A real-world pain has more aspects to it than intensity and unpleasantness – a sufficiently serious injury can force the sufferer to evaluate what this injury means to them and what effects it will have on their life. In the laboratory, however, a stimulus this severe cannot be ethically delivered, and subjects are aware of this. No matter how menacing the equipment may appear, subjects may realistically assume that in the laboratory nothing will be done which will cause any lasting harm. On these grounds laboratory research has been the target of criticism:

Results from half the sample of participants included in this study were published in a paper by Whalley & Oakley (2003).

"what is being measured is pain without suffering that can be instantly abolished" (Wall, 1999, p78); practical solutions to these criticisms have been less forthcoming though.

2.0.2 Hypnotic suggestion for pain

Earlier investigations into the psychological induction of pain used a variety of methods from direct hypnotic suggestion, to instructions to imagine a sensation, to manipulation of expectation. Direct hypnotic suggestion including imagery was chosen for this first study. Imagery has been shown not to be an essential component of hypnotic analgesia suggestions (Hargadon, Woody, Bowers, 1995) and its role in suggested pain is unknown. Imagery is commonly used in clinical practice, however, and was used here with the intention of maximising the chance of obtaining an effect. The suggestions given in the hypnotically induced (HI) pain condition were matched as closely as possible to an actual physically induced (PI) pain experience to allow a more direct examination of the subjective similarity of the PI and the HI pain experiences.

2.0.3 Measurement of subjective pain experience

A relatively large number of subjective pain assessment techniques were chosen for use in this first study with the intention of assessing their merits for use later. The literature on pain assessment was reviewed and discrete numerical or verbal category scales, and bounded continuous-measure scales (Gracely & Naliboff, 1996) were identified as being among the most used. One particular scale, the McGill Pain Questionnaire (Melzack, 1975), has also been prominent in the literature. A further technique, multidimensional scaling, is less commonly used but its properties are reviewed here.

2.0.3.1 Bounded continuous scales

Visual analogue scales (VAS) are a widely used pain assessment tool. In their most common form they consist of a 100mm line with descriptors at each end such as "no pain" and "worst pain imaginable". To indicate the magnitude of pain they feel, subjects or patients mark the line at an appropriate place. The scales are scored by direct measurement on a scale of 0-100. Price, McGrath, Rafii and Buckingham (1983) asked chronic pain patients and healthy volunteers to rate the intensity and unpleasantness of a number of heat stimuli using VAS scales, the pain patients also rated the lowest, usual and highest levels of their pain over the previous week. It was found that the VAS's gave valid and reliable assessments of the sensory and affective dimensions of both experimental and clinical pains. It was further concluded that, unlike discrete category scales (e.g. simple 0-10 scale), this data was on a ratio rather than interval scale, allowing

for meaningful comparisons across and between subjects (and for the use of parametric statistical tests).

2.0.3.2 The McGill Pain Questionnaire

The McGill Pain Questionnaire (MPQ: Melzack, 1975) has been described as the 'gold standard' of pain research tools and its use has been strongly advocated (e.g. Melzack & Wall, 1996; Melzack & Katz, 1994). Despite being validated for use in the clinic and laboratory (Melzack, 1983) the questionnaire remains rather unwieldy (although a short-form version is available), requiring patients to use unfamiliar language (e.g. pain descriptors such as 'lancinating'), and appears to be less commonly used in recent pain research. It was used here because of its reputation as a key pain measurement tool.

2.0.3.3 Multidimensional scaling

The aim of multidimensional scaling (MDS) is to give a visual representation of the similarities between a set of stimuli. Similar stimuli are placed close together in an r-dimensional space (most commonly two dimensions) with increasing dissimilarity being represented by greater and greater distance between items. It allows experimenters to explore patterns of interrelations in data where underlying dimensions are unclear (Shepard, Romney, Nerlove, 1972; Schiffman, Reynolds, Young, 1981). One of the advantages of MDS is that it does not contaminate the data with the experimenter's preconceptions. In particular, it does not provide a structure for the participants to work within as the McGill Pain Questionnaire does (the MPQ forces uses to pick 'pain descriptors' from a list which are then summed to provide dimensional pain scores). With MDS participants are simply asked to make judgements as to how similar they believe pairs or lists of stimuli are. The solution which MDS provides is a reflection of how the subjects perceive and classify the stimuli.

2.1 Method

2.1.1 Participants

Participants were 23 students (15 Female, 8 Male) recruited from University College London. Mean age was 22.5 (Range 18-54). Participants were recruited from an existing database of highly-hypnotisable individuals (Scoring >8 on the Harvard Scale of Hypnotic Susceptibility (Shor & Orne, 1962)). Their mean Harvard score was 9.91. This study was approved by the Joint UCL/UCLH Committees on the Ethics of Human Research and informed consent was obtained from all participants. Participants were

tested individually. The experiment took about one hour, and participants were paid £6 for their time.

2.1.2 Hypnotic induction

Participants were seated in a chair in front of the apparatus; the hypnotic induction and suggestions were presented from a compact-disc player via a loudspeaker. This procedure was adopted to allow for the standardisation of the instructions. Before beginning the experiment participants were briefed about the hypnotic procedure and given the opportunity to ask questions.

The hypnotic induction began with instructions for the participant to close their eyes and continued with instructions to imagine a colour representing tension, and imagine breathing out air tinted with that colour; then to replace this tense breath with air tinged with a calming colour. This was followed by progressive muscle relaxation and then a deepening procedure involving the participant in imagery of descending steps within a garden. The induction finished with instructions to go to a 'special place' of their own choosing where the participant would be relaxed and comfortable (a full copy of the induction is given in Appendix 2.1).

2.1.3 Pain induction techniques

Subjects received two pain experiences, one to each hand, in the course of the experiment. They remained hypnotised and had their eyes closed throughout the procedure. In both instances of pain they were instructed that when their hand became painful they should return it to their lap, at which point the pain would be removed. The order of presentation of the pain induction technique was counterbalanced, as was the instruction for which hand to use first.

2.1.3.1 Physically induced pain

In the physically induced pain condition subjects were asked to place their hand palm-down on to a table surface in front of them. A 100W infra-red lamp was then shone on to the back of the hand from a distance of 12cm.

2.1.3.2 Hypnotically induced pain

In the hypnotically-induced pain condition participants were instructed to place their hand on a table in front of them and to focus their attention on that hand. Suggestions were given that a powerful lamp was shining on to it, and that their hand was becoming increasingly hot until it became painful. These suggestions were repeated for a

maximum of three minutes. (complete suggestions and timing are given in Appendix 2.2)

2.1.4 Measures

2.1.4.1 Post-experimental questionnaire + visual analogue scales

A simple questionnaire was initially used to assess whether the participant had felt a sensation of heat and a sensation of pain. Descriptions of these aspects of the experience, particularly what participants had felt to be the cause of the pain, were also elicited whenever they were reported. 100mm visual analogue scales were used to assess: (i) the similarity of the hypnotically-induced (HI) to the physically-induced (PI) pain, (ii) the intensity of the HI and PI pains, and (iii) the unpleasantness of the HI and PI pains (The intensity scale was bounded by the terms "no pain at all"-"most intense pain imaginable", and the unpleasantness scale "not at all unpleasant"-"most unpleasant pain imaginable"). These measures were designed to investigate the dimensions of pain mentioned most often in the pain literature, namely its sensory and affective dimensions. (post-experimental questionnaire given in Appendix 2.3).

2.1.4.2 Multidimensional scaling

A rank-ordering task was given to produce similarity data for a multidimensional scaling analysis. Twelve cards, each representing a different but relatively common pain experience (pinprick, toothache, sore throat, cramp, backache, headache, hitting thumb with hammer, stomachache, electric shock, stubbed toe) and including the PI and HI pain experiences, were presented to the participant. One of these cards, termed the 'reference card' was placed on the participants' left-hand side. Their task was to rank the pain experiences identified on the remaining eleven cards in order of similarity to the one on the reference card. This task was repeated until each of the twelve cards had been used as a reference card. The result of this reference ranking procedure is a matrix of similarity data which, unlike many other forms of data collection, is claimed to be relatively free of experimenter bias (Schiffman, Reynolds, Young, 1981). Similarity data collected from each of the participants was transformed into a square asymmetric dissimilarity matrix (a 12 x 12 matrix of numbers representing the inverse of how similar each participant had rated each of the stimuli). These were combined and analysed using an INDSCAL model within SPSS 11 (SPSS INC, 2000).

2.1.4.3 McGill Pain Questionnaire

Participants completed a McGill Pain Questionnaire (MPQ: Melzack, 1975) for each of the pains (HI & PI). The McGill gives a range of scores, allowing analysis of the different dimensions of the pain experience. From the pain descriptors list the McGill gives a Sensory Pain Rating Index [S(PRI)] – an index of how many words were chosen describing the sensory aspect of the pain experience (out of 42). An Affective Pain Rating Index [A(PRI)] – an index of how many words were chosen describing the sensory aspect of the pain experience (out of 14). An Evaluative Pain Rating Index [E(PRI)] – an index of how many words were chosen describing the sensory aspect of the pain experience (out of 5). A Miscellaneous Pain Rating Index [M(PRI)] – an index of how many words were chosen describing the sensory aspect of the pain experience (out of 17). The number of words chosen (total out of 20) is also taken as a measure of the strength of the pain. An ordinal scale is also used to assess how strong the pain was 'at it's worst' (out of 5: 0=nothing, 1=mild, 2=discomforting, 3=distressing, 4=horrible, 5=excruciating) (a long-form MPQ is given in Appendix 2.4).

2.1.4.4 Pain Beliefs Questionnaire

In order to investigate whether participants who could feel the HI pain differed from those who couldn't all participants were assessed with a Pain Beliefs Questionnaire (Edwards, 1992). The PBQ assesses the strength of an individual's belief that pain is (a) the product of purely physical processes, (b) the product of psychological processes (the PBQ is given in Appendix 2.6).

2.1.4.5 Time taken to move hand

A manually operated stopwatch was used by the experimenter to record the time taken by each participant to move their hand following the start of each pain induction.

2.2 Results

2.2.1 Post-experimental questionnaire and visual analogue scales

Table 2.1 shows how many participants felt heat and pain in both the hypnotically- and physically-induced pain conditions.

HI - feel heat	HI - feel pain	PI - feel heat	PI - feel pain
91.30%	60.90%	100%	91.30%
(21/23)	(14/23)	(23/23)	(21/23)

Table 2.1: Percentages (and numbers) of participants to feel each sensation.

Table 2.2 shows pain data for only those participants who experienced pain in each condition (HI and PI).

	HI Pain	PI Pain	
Pain Intensity VAS	32.36 (18.72)	37.79 (18.99)	$t(13)=1.021$ $p=0.326$
Pain Unpleasantness VAS	35.00 (18.46)	30.07 (18.13)	$t(13)=0.872$ $p=0.399$
McGill PRI Sensory (x/42)	18.43 (6.47)	15.00 (9.95)	$t(13)=1.311$ $p=0.213$
McGill PRI Affective (x/14)	01.07 (2.37)	01.36 (3.88)	$t(13)=0.363$ $p=0.723$
McGill PRI Evaluative (x/5)	02.50 (2.24)	02.36 (1.95)	$t(13)=0.208$ $p=0.838$
McGill PRI Misc (x/17)	05.43 (4.15)	04.29 (4.12)	$t(13)=0.808$ $p=0.433$
McGill No. of Words Chosen (x/78)	07.86 (3.90)	06.64 (4.34)	$t(13)=1.469$ $p=0.166$
McGill "At its worst"	02.86 (1.03)	02.64 (0.93)	$t(13)=1.000$ $p=0.336$

Table 2.2: Pain data for HI and PI conditions from the 14 participants who felt pain in both conditions. Means (and standard deviations) are reported for each measure. The fourth column reports the result of a paired samples t-test comparing means of the previous two columns.

Paired samples t-tests were performed on each dependent variable to assess whether HI and PI pain differed on any of the measures (VAS's of intensity and unpleasantness; McGill sensory, affective, evaluative, miscellaneous, number of words chosen, pain at its worst). No significant differences were found for any variable (see table 2.2). Figure 2.1 (below) shows the VAS intensity and unpleasantness ratings for the HI and PI pain

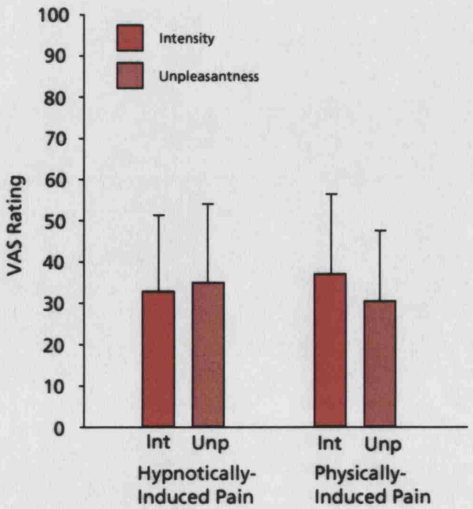


Figure 2.1: Intensity and unpleasantness VAS rating for hypnotically-induced (HI) and physically-induced (PI) pain.

2.2.2 McGill Pain Questionnaire

In order to assess the utility of the McGill Pain Questionnaire in comparison with the widely-used VAS measures of pain intensity and unpleasantness correlations between the two types of measure were examined. Table 2.3 shows the correlations between pain measures for the hypnotically-induced pain experiences. There are significant correlations between scores on the intensity and unpleasantness VAS', the McGill Sensory and McGill Affective scales, and between the intensity VAS and the McGill 'pain at it's worst' measure. There are no significant correlations between the VAS' and McGill sensory, affective, evaluative or miscellaneous measures.

		VAS Intensity	VAS Unpleasant	McGill Sensory	McGill Affective	McGill Evaluative	McGill Misc	McGill 0-5 Rating
VAS Intensity	Correlation Significance	1.00 .	0.788** 0.001	0.074 0.802	0.383 0.177	0.147 0.615	-0.148 0.614	0.595* 0.025
VAS Unpleasant	Correlation Significance	.788** 0.001	1.00 .	0.181 0.536	0.417 0.138	0.171 0.559	0.100 0.735	0.503 0.067
McGill Sensory	Correlation Significance	0.074 0.802	0.181 0.536	1.00 .	0.586* 0.028	0.143 0.625	0.291 0.313	-0.071 0.809
McGill Affective	Correlation Significance	0.383 0.177	0.417 0.138	0.586* 0.028	1.00 .	-0.282 0.328	0.404 0.152	0.352 0.217
McGill Evaluative	Correlation Significance	0.147 0.615	0.171 0.559	0.143 0.625	-0.282 0.328	1.00 .	0.149 0.612	-0.100 0.734
McGill Misc	Correlation Significance	-0.148 0.614	0.100 0.735	0.291 0.313	0.404 0.152	0.149 0.612	1.00 .	0.232 0.424
McGill 0-5 Rating	Correlation Significance	0.595* 0.025	0.503 0.067	-0.071 0.809	0.352 0.217	-0.100 0.734	0.232 0.424	1.00 .

Table 2.3: Correlations between VAS and McGill Measures of the hypnotically-induced experience of pain. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

Table 2.4 shows the correlations between pain measures for the physically-induced pain experiences. There are significant correlations between the VAS measures of pain unpleasantness and intensity, between McGill measures of the sensory and affective and miscellaneous dimensions of the pain experience, and between VAS intensity and the McGill 'pain at it's worst' measure. However, there are no statistically significant correlations between VAS' and McGill sensory, affective, evaluative or miscellaneous measures of the pain experience.

		VAS Intensity	VAS Unpleasant	McGill Sensory	McGill Affective	McGill Evaluative	McGill Misc	McGill 0-5 Rating
VAS Intensity	Correlation	1.00	0.824**	-0.227	-0.314	-0.275	-0.146	0.523*
	Significance	.	0.000	0.435	0.275	0.342	0.619	0.015
VAS Unpleasant	Correlation	0.824**	1.00	-0.248	-0.346	-0.116	-0.029	0.418
	Significance	0.000	.	0.393	0.225	0.692	0.921	0.060
McGill Sensory	Correlation	-0.227	-0.248	1.00	0.746**	0.159	0.606*	0.021
	Significance	0.435	0.393	.	0.002	0.587	0.022	0.928
McGill Affective	Correlation	-0.314	-0.346	0.746**	1.00	0.359	0.802**	-0.174
	Significance	0.275	0.225	0.002	.	0.207	0.001	0.451
McGill Evaluative	Correlation	-0.275	-0.116	0.159	0.359	1.00	0.264	-0.77
	Significance	0.342	0.692	0.587	0.207	.	0.361	0.739
McGill Misc	Correlation	-0.146	-0.029	0.606*	0.802**	0.264	1.00	-0.147
	Significance	0.619	0.921	0.022	0.001	0.361	.	0.525
McGill 0-5 Rating	Correlation	0.523*	0.418	0.021	-0.174	-0.77	-0.147	1.00
	Significance	0.015	0.060	0.928	0.451	0.739	0.525	.

Table 2.4: Correlations between VAS and McGill Measures of the physically-induced experience of pain. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

2.2.3 Assessment of interaction by group

To assess whether experiencing PI pain before HI pain, or the other way around, influenced the subsequent pain experience the VAS measures of pain intensity and unpleasantness were compared. Scores are displayed in table 2.5. The number of participants from each order group (HI first or PI first) able to experience HI pain was not significantly different (U=58, p=0.561).

	PI First (N=6)	HI First (N=8)
PI Intensity VAS	40.16 (24.69)	36.00 (15.02)
PI Unpleasantness VAS	32.83 (22.90)	28.00 (14.99)
HI Intensity VAS	31.67 (15.36)	32.88 (21.95)
HI Unpleasantness VAS	28.50 (13.77)	39.88 (20.84)

Table 2.5: Intensity and unpleasantness scores for HI and PI pain, analysed according to which was experienced first.

Independent samples t-tests were conducted to examine any differences on the VAS scores between the two conditions. No significant differences were found (PI intensity $t(12)$=0.393 p=0.701; PI unpleasantness $t(12)$=0.479 p=0.641; HI intensity $t(12)$=-0.115, p=0.910; HI unpleasantness $t(12)$= -1.156, p=0.270).

2.2.4 Time taken to move hand

Participants were instructed to move their hand back to their lap when it became painful. Of the fourteen participants who experienced both the HI and PI pain, all fourteen moved their hand in the PI condition and the time taken to move the hand was 42.24s (StDev 33.58s).

Of the fourteen participants who reported experiencing HI pain only six participants moved their hands (for these 6 participants the average time-to-move = 100.63s, StDev 33.97s). Debriefing indicated that two participants chose not move their hand because they were interested in the sensation.

2.2.5 Pain Beliefs Questionnaire

Scores on the Organic and Psychological subscales of the Pain Beliefs Questionnaire are presented by group (Participants who did feel HI pain vs. participants who didn't feel HI pain) in Table 2.6.

	Organic	Psychological
Did feel HI pain	3.33 (0.50)	4.64 (0.76)
Did not feel HI pain	3.36 (0.54)	4.33 (0.77)

Table 2.6: Scores on the PBQ sub-scales presented by group.

Independent samples t-tests were conducted to examine any differences in PBQ sub-scale scores between the two groups. No significant differences were found for the organic ($t(21)=0.139, p=0.890$) or psychological ($t(21)=-0.945, p=0.355$) sub-scales.

Harvard Scale of Hypnotic Susceptibility scores were examined by group to assess whether hypnotic susceptibility had any bearing upon whether participants felt HI pain. Table 2.7, below, shows the Harvard scores of both groups.

	N	Harvard Score
Did feel HI pain	14	9.857 (0.864)
Did not feel HI pain	9	10.00 (0.866)

Table 2.7: Mean (and standard deviation) of Harvard scores by group.

An independent samples t-test was conducted to examine mean differences in Harvard score by group. No significant difference was found $t(21)=-0.387$ $p=0.703$.

2.2.6 Differential pass-rates

Table 2.8 (below) compares pass-rates for the direct suggestion of pain, used here, with pass rates for items on the Harvard Group Scale of Hypnotic Susceptibility: Form A (Shor & Orne, 1962). Participant groups are comparable, only data from participants scoring >8/12 on the Harvard are presented here. These data indicate that for highly-hypnotizable participants the direct suggestion of pain is roughly equivalent to the cognitive items on the Harvard in terms of item difficulty. The direct suggestion of heat is more equivalent to the motor or challenge items i.e. passed by most of this highly hypnotisable sample.

Suggestion	Pass-rate
Direct suggestion of pain	60.90%
Direct suggestion of heat	91.30%
Harvard: Eye closure	97.14%
Harvard: Finger lock	95.71%
Harvard: Head fall	94.29%
Harvard: Hand lowering	94.29%
Harvard: Arm rigidity	91.43%
Harvard: Magnetic hands	91.43%
Harvard: Communication inhibition	90.00%
Harvard: Arm immobilisation	90.00%
Harvard: Eyes glued shut	80.00%
Harvard: Amnesia	51.43%
Harvard: Post-hypnotic suggestion	31.43%
Harvard: Fly hallucination	27.14%

Table 2.8: Pass rates for direct suggestions of pain compared with Harvard pass rates.

2.2.7 Multidimensional scaling analysis

Raw similarity data collected from each participant (participant ratings of how similar each item was to each other item) was transformed into square asymmetric dissimilarity matrices for analysis in SPSS (a matrix of data containing the inverse of all the similarity ratings). Data were analysed using an INDSCAL model. Data from all subjects was analysed collectively; for participants who had not felt the HI pain appropriate columns and rows of data were blank and treated by the MDS algorithm as missing data (this is standard practice, MDS procedures tolerate missing data well). Data points for the 'cramp' pain were also removed from the final analysis as they contributed large amounts of 'stress' to the model (see below). Feedback indicated that for this item only there was a sex difference: female participants were more likely to interpret this item as referring to stomach cramp where male participants viewed it as muscle cramp.

The INDSCAL analysis yielded a two dimensional solution shown in figure 2.2. The stress of this solution, which is an inverse measure of the correspondence between the input data and the distances among points on the MDS map, was 0.299 (Stress levels

below 0.35 are considered to be an acceptable fit: Borgatti, 1997). The root square value, which is the proportion of variance of the scaled data in the set which is accounted for by the MDS solution, was 0.603

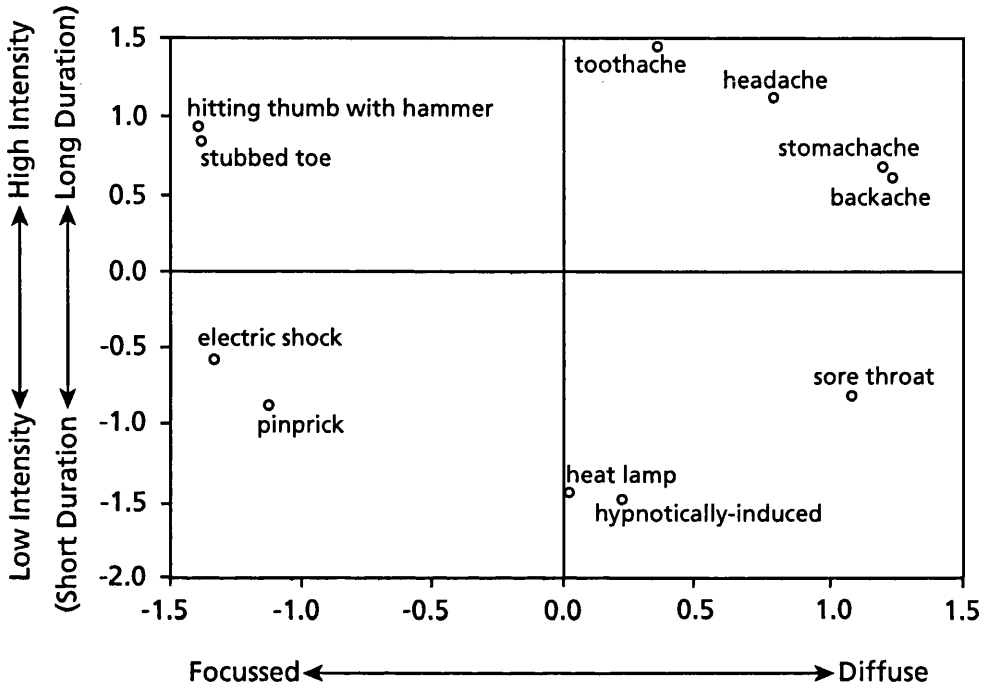


Figure 2.2: Derived stimulus configuration from Multidimensional Scaling analysis.

MDS analysis was also used to check for any group differences between those participants who felt HI pain and those who could not. The INDSCAL analysis assumes that participants are making decisions based upon the dimensions revealed but provides a description of how heavily each participants ratings weighted upon each dimension. Figure 2.3 shows a plot of derived subject weights with distinction made between those participants who felt HI pain and those who did not. The two groups overlap considerably, not clustering into separate group, indicating similarity in the systems by which participants rated the similarity of the pains.

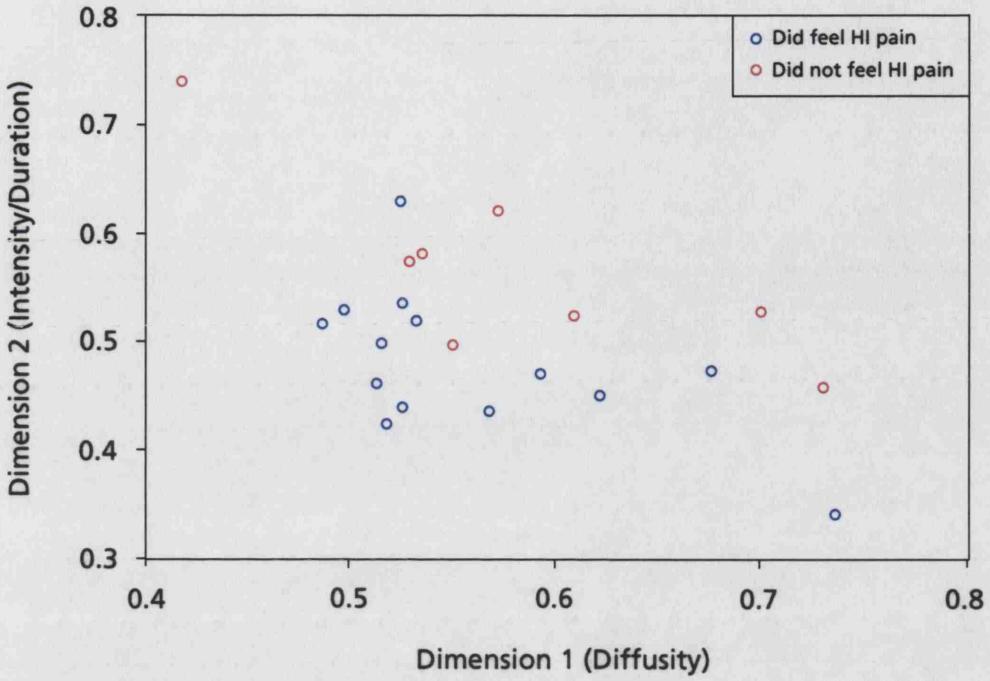


Figure 2.3: Derived subject weights from Multidimensional Scaling analysis.

2.3 Discussion

Clearly it is possible to induce a sensation of pain via direct hypnotic suggestion in highly hypnotisable participants, and that the intensity and unpleasantness of these experiences are rated as non-zero. In fact, more than half of the sample (60%) were able to experience pain in response to suggestion, and 91% were able to experience the sensation of heat. No order effects were detected, demonstrating that having experienced a PI pain just previously does not affect a participant's ability to experience HI pain. This finding indicates that the hypnotic generation of a pain experience is based upon long-term rather than short-term memories of pain.

Examination of the subjective experience of pain was the main aim of this investigation. As such, a wide variety of subjective pain measures were taken. Table 2.2 and figure 2.1 show the reported intensity and unpleasantness of the HI and PI pains as recorded by VAS measurements. Of the fourteen participants who felt both the HI and PI pains the intensity and unpleasantness of the HI pain did not differ significantly from that of the PI, this lack of significant difference is partially explained by the large inter-individual differences; one participant rated the HI pain as four times more intense than the PI, while another participant rated the PI as twice as intense as the HI. Intensity and unpleasantness measures for both the HI and PI pain both correlate highly. The relatively low intensity and unpleasantness scores observed in both the HI and PI

conditions is likely due to the instruction given to participants to move their hand when it became painful; an instruction not to move the hand until the pain became intolerable may have led to higher sensory and affective scores.

The McGill Pain Questionnaire revealed itself to be a disappointing tool for pain assessment. Aside from a long administration, the scores obtained for each subscale (sensory, affective, evaluative, miscellaneous) do not correlate well with the standard VAS assessments of the components of the pain experience. Tables 2.3 and 2.4 demonstrate that correlations between the measures are generally low; although internal consistency (intercorrelations within measurement method) for VAS and McGill assessment is satisfactory. The McGill 'pain at it's worst' measure, a simple selection from a 0-5 pain scale, correlates well with VAS measure of intensity, indicating that the participants could make consistent judgements about their pain. A likely reason for the lack of relationship between McGill and VAS measures lies in the nature of the McGill procedure: the scores on sensory, affective, evaluative and miscellaneous scales are determined according to how many words a participant picks from a list. For the PI pain, participants only picked an average of seven words from a total possible of 78; for HI pain participants only picked an average of eight words. It might reasonably be suspected that such a low proportion of words selected could undermine the effectiveness of the McGill; this result highlights a possible reason why the McGill is currently less frequently used in experimental pain research.

To make an assessment of hypnotic 'item difficulty' the pass rate of the direct suggestion for pain was compared with the pass rate for items on the Harvard Group Scale of Hypnotic Susceptibility: Form A (Shor & Orne, 1962; Table 2.8). Harvard data for subjects scoring as highly susceptible (>8/12 on the objective scale of the Harvard) was taken for comparison from the UCL Hypnosis Unit database. The data indicate that, in highly hypnotisable participants, the ability to experience heat as a result of direct suggestion is common and that the 'item difficulty' of this suggestion is low; comparable with ideo-motor or challenge items on the Harvard. However, the ability to experience pain as a result of direct suggestion is much rarer, with an item-difficulty much more similar to the 'cognitive' items on the Harvard scale, such as the suggestion for post-hypnotic amnesia. Although an exact comparison is not possible it seems likely that the ability to experience suggested warmth, as assessed by this experiment, is in a similar range to that assessed by Gheorghiu, Polczyk and Kappeller (2003) on their 'warmth suggestibility scale'; they report that on average participants, not selected for hypnotic susceptibility, reported feeling heat in response to about half of the challenges/ suggestions.

The multidimensional scaling analysis revealed an interesting pattern of data. Figure 2.2 shows the two dimensional solution that was generated. As the VAS data would predict, the points for HI and PI pain are clustered close together, indicating a high

degree of similarity. The two dimensional model presented here accounts for 60% of the variance in the raw similarity data. The analysis revealed a stable stimulus configuration; the location of stimulus points is very similar to the pattern described in Whalley and Oakley (2003), which reported a preliminary analysis of only six participants who had felt the HI pain.

Like factor analysis, the dimensions in an MDS solution are label-free and open to interpretation. The dimensions are extracted in order of importance. Dimension 1 in the solution shown here is the x-axis, which I have interpreted as the perceived focus/diffusity of the pain experience. Pains such as a pinprick or stubbed toe, which are highly localisable, are located towards the focussed end of the dimension. Vaguer pains, including the aches, are at the diffuse end of the dimension. Dimension 2 is harder to interpret. In Whalley & Oakley (2003) this dimension was interpreted as reflecting the duration of the pain, with HI and heat lamp pain perceived as short-duration pains. This interpretation accounts well for the 'ache' pains which are all relatively long duration, but does not account well for the pains 'stubbed toe' and 'hit thumb with hammer', which although considered longer lasting than 'pinprick', cannot easily be considered long-duration pains. It may be equally valid to interpret dimension 2 as reflecting the intensity of the pain experiences. VAS measures of the intensity and unpleasantness of the HI and heat lamp pain placed them both as mild to moderate experiences of pain. Although we have no data reflecting these participants intensity ratings of the other stimuli used in the MDS analysis a dimension of intensity reflects a reasonable fit with the data.

One major shortcoming of this method of analysis is that participants are required to make similarity judgements concerning two types of pain: pains they have just experienced, and pains which they are being asked to recall from past experience. Commonly felt pains were chosen to ensure that most participants had experienced each stimulus type, but we must accept that the position of the HI and PI pains relative to the other stimuli may be, at least partially, an artefact of the data collection method. The influence of recall in this investigation, however, cannot be fully assessed.

Three measures were used to assess whether there was a difference between participants who could feel HI pain and those who could not. The Pain Beliefs Questionnaire revealed no significant differences, on beliefs regarding the organic vs. psychological nature of pain experiences, between the two groups. Assessment of Harvard scores of hypnotic susceptibility did not reveal any differences between groups, although the range in this group was small. Finally, a derived subjects weights analysis was performed. Figure 2.3 is a plot showing how strongly each participant weighted each of the dimensions as they made their similarity judgements; some participants decisions were based more on the perceived intensity of each stimulus, so were based more on the focus/diffusity of the stimulus. Participants who did feel the HI pain do not form a

separate cluster from those who did not on this plot, indicating that how participants rated the variety of pains was not related to whether or not they could experience the HI pain.

As this was an initial test regarding the possibility of inducing pain via suggestion, strong direct suggestion including imagery was chosen to maximise the chance of obtaining an effect. Imagery has been shown not to be an essential component of hypnotic analgesia suggestions (Hargadon, Bowers, Woody, 1995), and investigation of the specific contribution of imagery to the production of suggested pain is likely an interesting field of further research. Qualitative feedback from the participants indicated that imagery played a part in their experiences; one participant, a theatre technician, visualised a '2,500 Watt spot lamp burning my hand', others described very focused pain experiences such as laser beams directed at the hand.

In summary, the results of this investigation allow us to conclude that it is possible to induce a sensation of pain via direct hypnotic suggestion in highly hypnotisable participants, and that the intensity and unpleasantness of the HI pain is rated as being similar to a matched PI pain experience. A multidimensional scaling analysis further confirmed the perceived similarity of the two pain experiences.

This study is an important first step towards understanding functional pain, but leaves a number of issues unanswered such as: can only highly hypnotisable participants experience pain in response to suggestion, and were participants responding to demand characteristics? Participants with a range of hypnotic susceptibility were not tested here and the issue of demand characteristics is not addressed: the possibility remains that participants are simply reporting pain without experiencing an accompanying sensation. Finally, a criticism sometimes levelled at hypnosis research is that participants are 'simply imagining' (rather than 'experiencing') the suggested effect. Later studies will address these concerns, including a comparison of suggested and imagined pains.

Chapter 3 – Investigating similarities and differences between hypnotically-induced and imagined pain

3.0 Introduction

"Close your eyes now and imagine that someone has just kicked you, very hard, in the left shin (about a foot above your foot) with a steel-toed boot. Imagine the excruciating pain in as much detail as you can; imagine it bringing tears to your eyes, imagine you almost faint, so nauseatingly sharp and overpowering is the jolt of pain you feel. You just imagined it vividly; did you feel any pain? Might you justly complain to me that following my directions has caused you some pain? I find that people have quite different responses to this exercise, but no one yet has reported that the exercise caused any actual pain. Some find it disturbing, and others find it a rather enjoyable exercise of the mind, certainly not as unpleasant as the gentlest pinch on the arm that you would call a pain. Now suppose that you dreamed the same shin-kicking scene. Such a dream can be so shocking that it wakes you up; you might even find you were hugging your shin and whimpering, with real tears in the corners of your eyes. But there would be no inflammation, no welt, no bruise, and as soon as you were sufficiently awake and well oriented to make a confident judgement, you would say that there was no trace of pain left over in your shin – if there ever was any in the first place. Are dreamed pains real pains, or a sort of imagined pains? Or something in between? What about pains induced by hypnotic suggestion?"

(Dennett, 1991)

Dennett does not provide direct answers to his questions, and he presents us with more. If his instructions are taken as reasonable directions for imagining pain then it is difficult to see a clear distinction between imagination and suggestion; some hypnosis researchers would consider these relatively direct suggestions for the experience of pain, although hypnotic suggestions might continue for longer. Does the difference between imagining and experiencing depend upon the length of the instructions? Or on another factor such as the precise language used?

The experiment detailed in the previous chapter was designed to assess whether it is possible for healthy control participants to experience pain as a result of direct suggestion, in some ways a replication and extension of work conducted thirty years previously (Barber et al, 1964; Dudley et al, 1964, 1966, 1967; Hilgard et al, 1974). The results were consistent with the possibility that for highly hypnotisable participants it is possible to experience a sensation of pain in response to direct suggestion. This

follow-up investigation takes the notion of suggested pain further and tests more hypotheses related to the model proposed in chapter 1. Firstly it is important to verify the proportion of the population capable of experiencing pain in the absence of a noxious stimulus, and the characteristics of such a group. If only highly hypnotisable persons are capable of experiencing hypnotically-induced pain, support is provided for the prediction of the model that patients suffering from functional somatic syndromes will score highly on scales of hypnotic susceptibility. Additionally, this investigation also sought to examine differences and similarities in outcome between instructions to imagine, and suggestions to experience pain, both delivered in the hypnotic context. Measures were taken of intensity, unpleasantness, externality and clarity of the suggested and imagined experiences.

3.0.1 Hypnotically-induced and imagined experiences

A typical response to a description of hypnotic experience is that the participant has simply imagined the effect without any necessary concomitant change in sensation. Partly in response to comments of this nature, this experiment aimed to test hypotheses regarding the imagination of experiences during hypnosis. Very little rigorous work has explicitly investigated how people imagine while hypnotised, but it is often claimed on the basis of subjective evidence that suggested hypnotic experiences are more vivid than day-to-day imagination; hypnotic effects have been termed *"believed-in imaginings"* (Sarbin, 1997) reflecting the greater subjective reality of the experience. Most psychological research into imagination has been conducted in the visual modality, a fact reinforced by synonyms of imagery mostly referring to visual phenomenon, e.g. "picturing", "visualising", "having a mental image". However, non-visual forms of quasi-perceptual experience have been deemed to be just as common and important and there is a small but significant literature on 'kinaesthetic imagery' and 'haptic imagery' (Thomas, 2001). Shepard and Metzlers' (1971) work on mental rotation is a key example of work on mental imagery. What they demonstrated was a linear relationship between the angle a participant is asked to 'mentally rotate' an image and the time taken to complete the mental rotation. More recently though, a number of studies have used functional imaging to investigate the neural basis of other modalities of hypnotically-induced and imagined events, and this body of work can inform our hypotheses regarding imagined and suggested pain. Only aspects of the studies relating to imagination and suggestion will be reviewed here in detail; other methodological aspects of these studies will be covered in more detail in chapter 4.

Kosslyn, Thompson, Costantini-Ferrando, et al (2000) demonstrated convincingly that hypnotically-suggested effects are not only perceived, by highly hypnotisable subjects, as 'real' but are underscored by congruent neural activity. Kosslyn et al investigated visual hallucinations using highly-hypnotisable subjects in the positron emission tomography

(PET) environment. They asked hypnotised participants to see a colour picture in greyscale ("drain the colour from it"), or to see a greyscale picture in colour ("add colour to it"). Scans were also taken in the absence of suggestions for colour change; in this condition participants colour perception was unaffected. The results indicated that when hypnotic suggestions were given to perceive a greyscale stimulus in colour relevant left hemisphere colour perception regions (including fusiform gyrus [V4]) were significantly activated. This contrasts with the results of a previous neuroimaging experiment investigating imagination of colour which concluded that V1 and V4 activations (considered to be strongly associated with colour perception) were observed during perception, but not imagination, of colour (Howard, ffythche, Barnes, et al, 1998).

Szechtman, Woody, Bowers and Nahimas (1998) conducted a PET study to contrast neural activation in conditions of 'real', hallucinated and imagined sounds in hypnotised participants. They demonstrated similar patterns of brain activity in the 'real' and hallucinated conditions but these activations were much greater in intensity and differed in location from the activations observed in the imagined condition. Additionally, ratings of clarity and externality of the hallucinated sound correlated significantly with regional cerebral blood flow (rCBF) in the right anterior cingulate cortex (ACC), leading the authors to link activity in the right ACC with attribution of an internally-generated percept to an external source. This investigation strongly demonstrates differences between hypnotically-suggested experiences and events imagined within the hypnotic context.

Levy, Henkin, Lin, Hutter and Schellinger (1999a) used functional magnetic resonance imaging (fMRI) to investigate the neural correlates of actually experienced and imagined odours. In the scanner participants were either given the smell of bananas or peppermint, or asked to imagine these odours. The main finding was that it was possible for participants to imagine odours and that imagination of them produced activation in the same brain areas as actual perception of these odours, albeit at a lower intensity of approximately 30% of the strength produced by the actual odour. This figure is in agreement with studies of imagined motor movement which find similar but significantly weaker activations in the imagined compared to the actual movement conditions (Roth, Decety, Raybaudi, et al, 1996; Nair, Purcott, Fuchs et al, 2003).

The only published work experimentally investigating the imagination of pain was conducted by Veerasarn and Stohler (1992). Their experiment investigated the EEG correlates of pain (induced by intramuscular infusion of hypertonic saline into the masseter [jaw] muscle) which were compared with the correlates of imagined pain experiences. The precise instructions given to induce 'sham' [imagined] pain consisted of instructions to recall the earlier experimental pain or a past painful experience (in the cases where sham pain preceded experimental pain). In a previous study the authors

determined that the infusion of hypertonic saline produced statistically significant changes in subjective pain experience (average rating 5.2/10 ± 2.2), no subjective ratings were taken of the imagined pain intensity. Unfortunately in the case of experimental pain the authors found that their EEG data were heavily contaminated with motor and muscle movement, severely limiting the conclusions they could draw. Statistically significant increases in fast frequencies were observed in response to imagined pain when compared with appropriate baseline data, but these measures of imagined pain did not differ significantly from equivalent measures of experimental pain. The authors interpret this data with respect to Lang's (1978) theory of emotional imagery, whereby *"image processing can produce physiological responses in the same fashion as actual perception"*, but the noted methodological difficulties make it difficult to accept this interpretation uncritically. The functional imaging experiments presented above do not provide unequivocal support for this position either, although individual studies in a particular modality (e.g. Olfactory: Levy et al, 1999a) do tend to substantiate Lang's argument

Fundamentally there is confusion regarding the concept of 'imagined pain'. The term has been used interchangeably to describe the product of cognitive processes which have also been termed 'memory for pain' (Erskine, Morley, Pearce, 1990; Veerasarn & Stohler, 1992), 'suggested pain' (Barber & Hahn, 1964), and 'anticipation of pain' (Hugdahl, Rosén, Ersland, et al, 2001). Although the same terminology of 'imagining pain' was used, it is unclear that participants in Barber & Hahn's (1964) investigation would have had a similar experience to those in Veerasan & Stohler's (1992) study. Full publication of the language used in this experiment will hopefully clarify the anticipated distinction between imagined and suggested pain.

3.0.2 Hypothesis

It was hypothesised that the ability to perceive hypnotically suggested pain would vary as a function of hypnotic susceptibility, with highly hypnotisable participants being more capable of experiencing a change in sensation; the same prediction was made for hypnotically suggested heat. Analysis of previous literature does not challenge the view that all participants, regardless of hypnotic susceptibility, should be able to imagine the sensations of heat and pain: Veerasarn and Stohler (1992) did not select participants for a particular ability to imagine pain, and Dennett (1991) gives no indication that sections of his audience find the imagination of pain impossible. In line with the results of Szechtman et al (1998) it was further predicted that hypnotically suggested pain and heat would be experienced as being more intense, unpleasant, externally-generated and clear than imagined pain and heat.

3.1 Method

3.1.1 Participants

Participants were 52 students (10 male) from University College London who had previously been screened on the Harvard Group Scale of Hypnotic Susceptibility: Form A (Shor & Orne, 1962). Mean age was 20 (Range 18-24). Mean hypnotic susceptibility, as measured by the Harvard, was 6.59 (SD=2.53) with a range from 2 to 12. The mean Harvard score of this sample did not differ significantly from the mean of all scores stored on the Hypnosis Unit database (HU database: mean=6.41, SD=2.87; $t(634)=0.444$, $p=0.657$).

3.1.2 Procedure

The experiment was run in groups of 6-10 participants. Participants were selected from a pool previously screened on the Harvard Group Scale of Hypnotic Susceptibility (HGSHS:A). Upon arrival participants were seated around a large table, given information about the procedure, and signed consent forms. A briefing concerning the nature of hypnosis was given, and participants were given the chance to ask questions. In order to set the context and ensure that all participants were attuned to potential differences between imagined events and experienced ones it was explained to them that for this experiment it was very important to understand the difference between experiencing and imagining. To aid this understanding participants were asked to close their eyes and listen to a short piece of music. Participants were then asked to open their eyes and were told they had just experienced a piece of music. They were then asked to close their eyes once more and to imagine the piece of music they had just heard. It was reinforced that participants had just experienced and imagined music (The precise text of the introductory briefing and instructions regarding experiencing and imagining can be found in Appendix 3.1).

3.1.2.1 Hypnosis scripts

The order in which participants were asked to experience or imagine painful heat was counterbalanced across groups. Both sets of instructions followed a hypnotic induction which, as described in the previous chapter, consisted of instructions to concentrate on slow and steady breathing, muscle relaxation, deepening and a special place procedure (Precise wording can be found in Appendix 3.2).

In both the 'experience' and 'imagine' conditions imagery was presented of lying in the shade on a hot sunny day with only the dominant hand exposed to the sun and reference was made to the heat from the sun becoming painful heat. The instructions

presented in both conditions were very similar, with only particular words changed. For instance, in the 'experience' condition the instruction was given that *"The temperature in your hand is continuing to rise as the sun shines down onto the back of your hand ... the penetrating heat getting hotter and hotter"* whereas in the 'imagine' condition this was changed to *"Think about the temperature in your hand continuing to rise, think about the sun shining down onto the back of your hand ... imagining the penetrating heat getting hotter and hotter"*. The script for each condition lasted for approximately two minutes before instructions were given that the hand was feeling completely back to normal. Between presentation of scripts to experience or imagine pain participants were given instructions to relax and rest in their special place for a few minutes (Complete scripts for both conditions can be found in Appendix 3.2).

3.1.2.2 Measures

After the ending of hypnosis participants were asked to complete a set of response booklets (given in Appendix 3.3). A cover sheet reminded participants to be aware whether a question was asking about experienced or imagined pain. One questionnaire booklet related to the experienced pain and another related to the imagined pain, questions in each booklet were the same. Initially the booklet enquired into whether heat and pain had been experienced/imagined, and if so, whether the heat had caused the pain. If the participant responded positively they were required to report the intensity, unpleasantness, externality and clarity of the heat and pain on separate visual analogue scales. The terms used to bound the scales are shown Appendix 3.3.

3.2 Results

Groups (order of script presentation: 'experience' or 'imagine' instructions given first) did not differ with respect to age ($t(49)=1.559, p=0.125$) or hypnotic susceptibility ($t(50)=0.275, p=0.784$). The proportion of participants experiencing pain and heat in response to suggestion did not differ significantly by group [order of presentation] ($t(50)=1.787, p=0.109$; $t(50)=1.298, p=0.200$). The proportion of participants imagining pain and heat in response to instructions did not differ significantly by group [order of presentation] ($t(50)=0.035, p=0.972$; $t(50)=0.743, p=0.461$). For all subsequent analyses data from both presentation orders has been pooled.

The number of participants able to experience or imagine the suggested sensations is given in table 3.1.

	Percentage	n/N
Experienced Heat	55.77%	29/52
Experienced Pain	17.31%	9/52
Imagined Heat	65.38%	34/52
Imagined Pain	28.85%	15/52

Table 3.1: Percentages and raw scores of participants able to experience or imagine the suggested sensations.

The distribution of ability to experience and imagine heat and pain is presented by hypnotic susceptibility score in figure 3.1. Hypnotic susceptibility correlated significantly with ability to experience pain (r=+.434, p=0.001), ability to experience heat (r=+.347, p=0.012) and ability to imagine pain (r=+.386, p=0.005), but was not significantly correlated with ability to imagine heat (r=+.203, p=0.149).

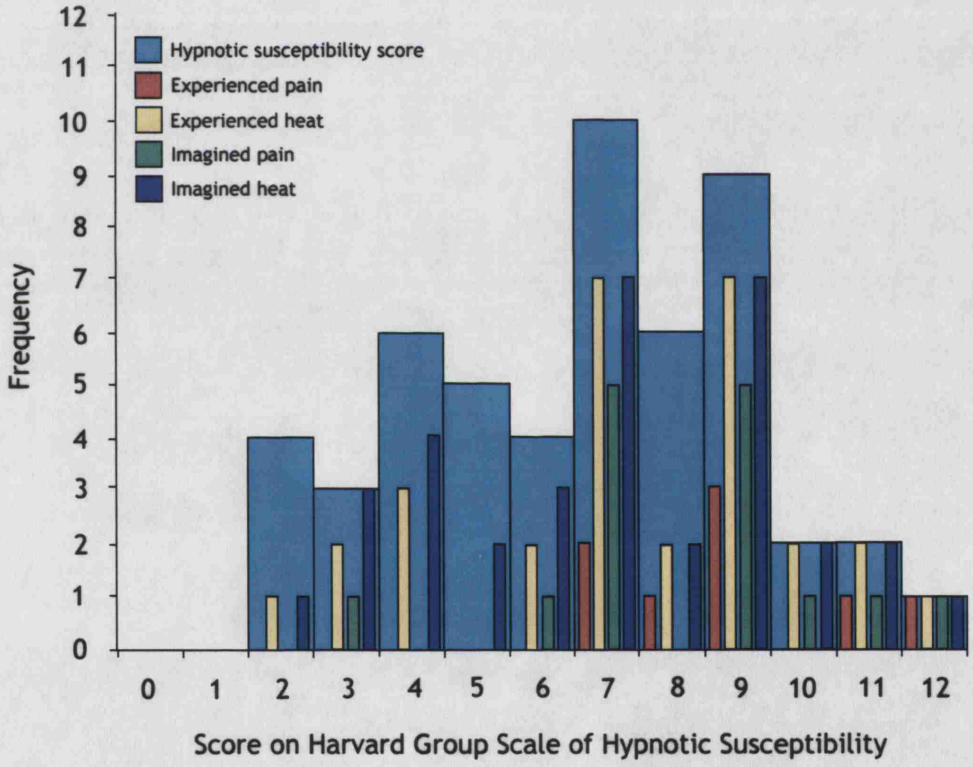


Figure 3.1: Distribution of the ability to hypnotically experience and imagine heat and pain across levels of hypnotic susceptibility.

Of the nine participants who were able to experience a sensation of pain, seven of them responded that the cause of the pain was heat. Of the fifteen participants who were able to imagine pain, twelve of them responded that the cause of the pain was heat. Seven participants were able to experience and imagine a painful sensation, when these participants were asked to rate the similarity of the experienced to the imagined pain on

a 100mm VAS (0 = not at all similar, 100 = exactly the same) the mean similarity rating was 44.71 (SD = 29.83: Range = 22 – 100).

Data from the main VAS measures of each experience are given in Table 3.2 and also represented in Figure 3.2.

	N	Intensity	Unpleasantness	Externality	Clarity
Experienced Pain	9	51.78 (19.98)	48.67 (21.18)	45.22 (26.63)	51.67 (20.72)
Experienced Heat	29	40.07 (22.38)	32.31 (28.34)	38.31 (27.12)	51.07 (25.66)
Imagined Pain	15	35.56 (25.35)	37.25 (27.12)	36.94 (32.19)	37.50 (23.95)
Imagined Heat	34	37.56 (24.40)	27.06 (26.76)	31.71 (23.80)	45.12 (25.05)

Table 3.2: VAS data [means (and standard deviations)] for each of the experienced and imagined conditions.

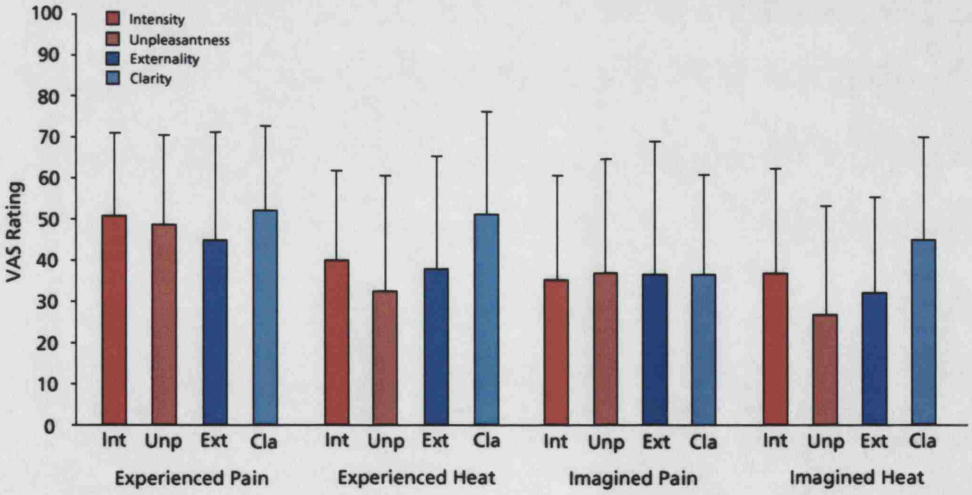


Figure 3.2: Intensity, unpleasantness, externality and clarity VAS scores for hypnotically experienced and imagined heat and pain.

Independent samples t-tests were used to asses the differences between 'experienced' and 'imagined' data for each of the VAS measures. T-scores and p-values are presented in table 3.3. No significant differences were found for any of the measures, although measures of pain intensity and pain clarity approached significance.

Pain Intensity	$t(23)=1.648$ $p=0.056$
Pain Unpleasantness	$t(23)=1.087$ $p=0.144$
Pain Externality	$t(23)=0.655$ $p=0.259$
Pain Clarity	$t(23)=1.565$ $p=0.065$
Heat Intensity	$t(61)=0.423$ $p=0.337$
Heat Unpleasantness	$t(61)=0.756$ $p=0.226$
Heat Externality	$t(61)=1.030$ $p=0.153$
Heat Clarity	$t(61)=0.929$ $p=0.178$

Table 3.3: Independent samples t-tests results for the Experienced vs. Imagined data for each of the VAS measures (All one tailed).

3.3 Discussion

The results presented in figure 3.1 and the significant correlations observed support the hypothesis, indicating that the ability to experience pain in response to direct suggestion is related to hypnotic susceptibility. No participant scoring below 7 on the Harvard scale of hypnotic susceptibility reported experiencing pain in response to the suggestion. The ability to experience heat in response to direct suggestion is also found to be related to hypnotic susceptibility but is less skewed towards the high end of the scale. This compares favourably with Gheorghiu, Polczyk & Kappeller's (2003) results which indicate that the ability to experience warmth in response to indirect suggestion is related to ability to relax.

The distribution observed in figure 3.1 seems to contradict the results of Schweiger and Parducci (1981) who found that approximately two thirds of their (hypnotically unselected) sample reported headaches in response to the indirect suggestion that an electric current might produce them. Procedural differences between the two studies, however, account well for this difference. In the present study direct hypnotic suggestions were given for a hallucinatory experience, participants were aware (to an unknown extent) that whatever they experienced was self-generated. In Schweiger and Parducci's design participants were strongly and deceptively led to expect that any pain would be other-generated, that is, an artefact of the machinery being used in the experiment (an indirect suggestion). It is possible that participants found this a more plausible mechanism for sensory change than the direct suggestions used in the present study. Further investigation is necessary to demonstrate whether the experience of a headache as described in Schweiger & Parducci's experiment is correlated with suggestibility (hypnotic and non-hypnotic).

Instructions to imagine pain, delivered inside the hypnotic context, produced an interesting pattern of results. Two thirds of the sample reported being able to imagine a sensation of heat, and this ability was not related to hypnotic susceptibility. However,

only twenty-eight percent of the sample reported being able to imagine a sensation of pain. This result is at odds with what Dennett (1991) discusses in relation to the imagination of pain. His implication is that most, if not all, participants who undergo his demonstration seem to be able to imagine pain, but that none experience it in any particularly convincing way. This view also seems implicit in other available research on imagination. In research on visual imagination, for example, it is taken as given that everyone, possibly bar those with mental deficits, possesses the capacity to imagine a scene. In Szechtman et al's work (1998) no special instructions were given to help participants 'successfully imagine' the sound of a voice. Participants were told that a tape recorder would not be played and that they were to imagine *"as vividly as possible, hearing the same man's voice repeating the same phrase over and over again"*. Unfortunately Szechtman and colleagues do not report clarity and externality data for the imagined condition but it seems likely that they would have mentioned if some participants had not been capable of imagining the voice. In the work reported by Levy, Henkin, Lin, Hutter and Schellinger (1999a) all participants are reported to have been capable of successfully imagining odours, and in an additional paper Levy, Henkin, Lin, Finley and Schellinger (1999b) it is concluded that taste sensations can also be successfully imagined and result in similar profiles of neural activation to actual taste experiences.

Two explanations seem to account plausibly for the results observed here: a small proportion of participants reporting being able to imagine a sensation of pain. One possibility is that imagination of pain may not be the same as imagination in other modalities. Lang's theory of emotional imagery (1979) though, with some supporting empirical evidence, indicates that individuals can successfully imagine emotional situations. He documents efferent outflow (heart rate, galvanic skin response) which correlates with engagement with imagery and notes that there are individual differences in this ability, although his studies do not specifically extend to pain. A second, more likely, possibility is due to the experiment being conducted in the hypnotic context and the two conditions differing only in terms of subtle linguistic differences between two hypnotic suggestions (in one it was suggested that hypnotised participants would *experience* a change in sensation, in the other subjects were instructed to *imagine* a change in sensation). It is possible that participants were confused by the presentation, in quick succession, of two similar sets of instructions to imagine/experience heat-related pain in a hand. The design of the experiment made it difficult to specify exactly what participants were engaging with at each stage of the study. Particularly difficult was the fact that participants were required to rate 'imagined' and 'felt' pains using the same types of scales (VAS's to rate intensity and unpleasantness). No distinction was made between these, possibly indicating to participants that the same type of experience was expected of them. A key question to ask, but not answered by this study, is whether an 'imagined' experience of intensity X is the same as an 'hallucinated' experience of

intensity X or the same as a 'truly felt' experience of the same intensity. Future research would benefit from using a between-subjects approach to avoid confusion about differences between imagined and experienced percepts, and needs to address which modalities are employed in the imagination of pain (e.g. visual, affective, sensory). Further studies may investigate the imagination of pain both inside and outside the hypnotic context using shorter instructional sets to imagine. Contrasts with physically-induced pain would allow comparison of the strength of imagined percept with those acquired in other modalities.

No significant differences were found between imagined and experienced heat and pain on the measures of intensity, unpleasantness, externality or clarity. However, in line with the hypothesis, contrasts of pain intensity and clarity approached significance with experienced pain being rated more strongly than imagined pain. Mean scores for all measures, although not significantly different, trended in the predicted direction; with experienced pain/heat being rated stronger than its imagined counterpart. The pattern observed here compares favourably with the small body of research investigating the intensity of imagined percepts. Levy, Henkin, Lin, Hutter and Schellinger (1999a) asked participants to imagine and actually smell a peppermint odour. They found that participants rated the intensity of the imagined odour at 40/100 (±6), significantly different from the rated intensity of the actual odour at 78/100 (±4). Of course the Levy et al (1999a) study differs from the present one in that it compares an actually experienced percept with the same percept, imagined in a non-hypnotic context. It must also be noted that the instructions/suggestions given to imagine pain in the present experiment are substantially longer than those observed in other studies of imagination (e.g. Szechtman et al, 1998; Levy et al, 1999a). Such lengthy presentation of the imagination instructions might increase the intensity and clarity of the imagined percept thereby reducing the difference between the imagined and experienced percepts.

The results of this study tentatively conclude that hypnotically experienced pain is different from an imagined percept of pain. The linguistic differences in hypnotic suggestions given (with the focus on 'experience' or 'imagine') did result in different numbers of participants reporting imagined or experienced heat or pain although the rated intensity, unpleasantness, externality or clarity did not differ significantly according to whether the sensation was experienced or imagined. This leaves some important questions relating to the imagination of pain unanswered; particularly the grey area between instructions to 'imagine' and suggestions to 'experience'.

Chapter 4 – A review of functional neuroimaging

4.0 Introduction

Functional neuroimaging investigations form an important component of this thesis. Within hypnosis research this remains a novel investigative tool, one which provides a useful path to objective rather than subjective verification of the veracity of hypnotically suggested experiences. Localisation of function within the brain is by no means a new approach to understanding human behaviour, for over a century lesion studies or direct cortical stimulation have provided us with information regarding brain function. Other approaches aimed at understanding brain function must also be acknowledged. Lang (1978) described electroencephalography (EEG) as a *"tool with which to pry open the mental citadel"*, and newer technologies such as transcranial magnetic stimulation (TMS) and magnetoencephalography (MEG) present new opportunities for broadening our knowledge of brain-behaviour relationships, particularly when disparate techniques are integrated (e.g. Egner, Jamieson, Gruzelier, 2004; Savoy, 2001). The present review of functional imaging techniques is by no means comprehensive (see Savoy 2001 for a more detailed analysis of the issues covered here) but attempts to flag some of the issues of importance in the critique of the experimental designs and analyses used in this thesis.

This chapter reviews a large volume of material, beginning with a précis of some of the important issues facing researchers using functional imaging, then continuing with an evaluation of the main findings of hypnosis and pain studies conducted in the neuroimaging environment. Imaging studies of 'functional' pain conditions are then reviewed before a final consideration of studies concerned with both hypnosis and pain.

4.1 Theory: Functional neuroimaging

4.1.1 Principles of functional neuroimaging

Functional imaging heralds a huge advance in the field of cognitive neuroscience, offering a non-invasive method of studying human brain functioning. Functional imaging techniques such as Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI) do not measure brain activity directly but instead gather data concerning blood flow and oxygenation (collectively termed 'haemodynamics') within the brain. The assumption is made that blood flow within the brain correlates with neural activity.

With PET, a radioactive substance is administered into the bloodstream of the participant. Initially inhalation of radioactive oxygen was a popular technique but has come to be replaced by intravenous injection of radioactive water. The participant's head is positioned inside an array of detectors which measure gamma emission. Radiation can be localised in three dimensions and, since the radioactive substance is carried in the blood, higher measurement of radioactive emission over time is indicative of greater blood flow to a particular region. Functional Magnetic Resonance Imaging (fMRI) works on different principles to PET, but holds similar assumptions about the relation between blood flow and neural activity. fMRI takes advantage of the magnetic properties of iron in haemoglobin in the blood. Oxygenated blood (oxyhaemoglobin) has different magnetic properties from deoxygenated blood (deoxyhaemoglobin) and these differences are reflected in the blood oxygen level dependent (BOLD) signal (Ogawa et al, 1990).

Both techniques have advantages and disadvantages. PET is silent, ideal in this respect for hypnosis. In PET there are gaps of around ten minutes between each acquisition to allow levels of radioactive emission to decay to background levels. Although this means that PET studies often take longer than investigations in fMRI it does allow comfortable time to administer suggestions in hypnosis studies. With PET the amount of radiation which can be administered to each participant is carefully limited so that only a certain number of scans can be conducted on each individual, this can limit the power of studies but can be accounted for by adding additional subjects. One limiting factor in PET is cost. Maintaining a cyclotron nearby to manufacture radioactive isotopes makes PET a much more expensive option than fMRI. fMRI, in contrast, provides a relatively cheap way to collect a lot of data. Compared to 12 scans over two hours for PET, fMRI can collect many magnitudes more volumes (three dimensional representations of brain activity). In addition, the same subject can be studied over time, coming back for multiple scans. fMRI has disadvantages such as the noise which can present difficulties, especially for hypnosis studies, with participants being forced to wear ear protection. fMRI is also a more claustrophobia-inducing technique than PET, a problem becoming worse as the bore of the more advanced magnets is becoming smaller to allow increases in power.

The basic design of a functional imaging experiment relies on subtraction methodology. This involves measuring regional cerebral blood flow (rCBF) in two conditions (task and control) which ideally differ in only one component, and subtracting control from task (cancelling out activations common to both) leaving only rCBF activations from the component of the task which was not common to the control condition. A simple example for a pain study would be to deliver a painfully hot stimulus in the task condition and to deliver a warm stimulus in the control condition. Subtraction of control (warm) from task (painfully hot) leaves activation related to the experience of

pain (excluding localisation and temporal components of the pain experience common to both conditions).

4.1.2 Analysis of functional imaging data

There are a number of steps involved in the analysis of functional imaging data which allow the raw images from the scanner to be transformed into statistical parametric maps (SPMs) which show increases or decreases in relative brain activation between two conditions. The following description of analysis procedure will focus mainly on fMRI analysis but most steps also apply to PET data.

4.1.2.1 Motion correction

In fMRI the functional data (measurement of BOLD signal) is collected in blocks of data acquisition, normally over the course of an hour or more. Participant's heads are restrained in the scanner to minimise head movement but the methods used are not perfect. A common method of head restraint in fMRI is to surround the head with foam pads or a pillow, tightly packed within the head coil. It has been noted that, counter-intuitively, the less restrictive the head restraint the better (less) the head movement (Derbyshire, personal communication).

Analysis of functional data is essentially multiple voxel-by-voxel t-tests comparing signal level during different tasks. Voxels are determined by their position in 3D space, and in order for the procedure to be truly testing a voxel in one condition against the same voxel in another condition the images must be re-aligned to correct for any motion occurring during the scan. Voxel size is dependent upon a number of factors and a trade-off between voxel size, signal to noise ratio and temporal resolution is achieved with the choice of a particular imaging protocol. With current (2004) fMRI technology voxel sizes of roughly $3mm^3$ are the norm.

4.1.2.2 Co-registration then normalisation

Every individual differs in their brain anatomy and this feature must be corrected for in group analysis. The technique used to account for anatomic differences is to 'normalise' participants brains into a standard anatomical space. Originally this was done by normalising into Talairach space (Talairach and Tournoux, 1988), a 3D space described in great detail, based upon the anatomy of a deceased French woman. More recently another system has come into more common usage, the MNI space, based upon averaged structural MRI scans of more than a hundred normal volunteers at the Montreal Neurological Institute. This space is considered to be more representative of the average person's brain and currently coordinates are most commonly reported in

MNI space. Algorithms are available to translate coordinates from Talairach to MNI space and vice versa.

Functional imaging analysis software (e.g. SPM, BrainVoyager) will normalise MRI data to a given template. With high-resolution (typically 256 voxels^3) structural MRI scans this task is relatively easy as the features of each individual brain are relatively obvious and the software accurately detects them, making for successful normalisation. Functional MRI data are acquired at much lower spatial resolution than structural scans (typically 64 voxels^3 compared with 256 voxels^3), and the subsequent images are of much lower quality. This makes it more difficult for the software to normalise these images, as there are fewer 'landmarks' to work from. In order to increase the chances of successful normalisation the functional data are co-registered to each subject's high-resolution structural MRI scan. Once the functional data is 'locked on' to the structural scan the normalisation parameters obtained from an 'easy' normalisation of the structural scan can be applied wholesale to the functional data. Coregistration simply overlays the functional data onto the structural data, accounting for any movement in the time between the acquisition of the structural and functional data. Once normalisation has been achieved the functional data from each subject can be overlaid not only on their own structural MRI, but data from multiple subjects can be grouped (increasing the power of the experiment) and the data can be described in a standardised space, allowing comparison of results across studies.

4.1.2.3 Smoothing

Before the voxel-by-voxel t-tests are performed it is necessary to 'smooth' the functional MRI data. Essentially this smoothing procedure is similar to applying a 'blur' effect to the data and it averages the acquired signal over a specified volume of 3D space. Smoothing is commonly held to improve the signal to noise ratio (SNR) of the data. However, Worsley (1997) demonstrates that this explanation is only true if the actual regions of activation have roughly similar extent to the size of the smooth being applied. Smoothing is also applied to normalise the variability in the data, without a smooth the variability of the data is not necessarily normally distributed – a core assumption of statistic parametric mapping. Finally, smoothing blurs across differences in anatomy. This is especially important if the data is intended for a group analysis since individuals vary in brain anatomy. As a result, different amounts of smoothing are commonly applied for data headed for individual as compared to group analysis.

4.1.2.4 Model fitting

Once the data has been pre-processed it can be analysed. A model is fitted, the design of which is determined by the experimental design. In simple PET and fMRI experiments

'block' designs employ subtraction methodology. In these designs data is collected in 'task' and 'control' conditions. For example, in a basic pain experiment a noxious stimulus is applied in the 'task' condition but not in the 'control' condition, all other aspects of the study remain identical. In order to assess brain activity specific to the application of the stimulus data from the control condition is subtracted from that of the task condition. Application of the model simply tells the analysis software which blocks of scans were taken in the task condition and which were obtained in the control condition.

4.1.2.5 Thresholding

Thresholding is a complex issue within the field of functional neuroimaging. The crux of the problem is that analysis of functional imaging data is essentially multiple t-tests, leading to what is termed the 'multiple comparisons problem'. Savoy (2001) likens the issue to concerns about general experimentation in psychology proposed by Meehl (1967). The issue of the statistical power of a particular experiment impacts greatly upon the result of the investigation; a psychological experiment which yields non-significant results with an N of 20 may yield a significant difference with an N of 2000.

Analysis of functional imaging data consists of many thousands of voxel-by-voxel t-tests. In a simple design each voxel in the task condition is compared with its counterpart in the control condition. However, since a level of significance of 95% (0.05) means that the chance of a Type I error is 1 in 20 then if we conduct multiple t-tests we are likely to be presented with many Type I errors. Since we need to test on a voxel-by-voxel basis the solution is to correct in some way for conducting so many tests. A traditional Bonferroni correction requires that the level of significance be divided by the number of tests being conducted (e.g. 100 tests at a 0.05 [95%] significance level would require a corrected threshold of $0.05/100 = 0.0005$). However, since analysis of functional imaging data requires thousands of significance tests this technique leads to a highly conservative threshold.

Thresholds other than 0.05 corrected for the whole brain are essentially considered arbitrary if the experimenter does not hold hypotheses regarding expected activations. If hypotheses are held, as is often the case, it seems reasonable to drop the threshold but it is at this point the arbitrary nature of the solution becomes apparent. A comprehensive analysis of different thresholding techniques is beyond the scope of this thesis, but a few major techniques are highly prevalent in the literature and will be considered here. Small-volume corrections are commonly used to 'correct for' certain predicted brain regions. Masks can be applied which limit the correction to specified areas of the brain (Friston et al, 1994). However, there is no agreement about how small a small volume is, leading to a wide variety of threshold levels via this technique; this raises the concern

that analysis could be driven by subjective factors. Newer techniques show promise in that, if not resolving the problem, they may ameliorate some of the worst symptoms. False discovery rate (FDR; Genovese, Lazar, Nichols, 2001), for example, corrects for the total number of voxels reported active. As the field matures meta-analyses are emerging as a method of clarifying the state of particular research topics. The cost of functional neuroimaging has led to less replication of experiments than is desirable, but as the pool of data grows discoveries are made regarding typical patterns of activation in response to specific tasks. Reviews of this sort, relevant to pain, will be considered in section 4.3.

4.2 Functional neuroimaging of hypnotic phenomenon

An enduring criticism of hypnosis research is that participants could be simply responding to the demand characteristics of an experimental situation without experiencing any concomitant changes in sensation. According to a strong interpretation of this rationale there is not necessarily any difference between high and low susceptible subjects in terms of what they experience, just what they report. EEG investigations have for some time supported the claims of hypnosis researchers regarding the veracity of participants experience (e.g. Spiegel et al, 1985) but functional neuroimaging offers an unprecedented opportunity to understand the brain activity underlying hypnotic phenomenon; to investigate hypnotic experience beyond the level of subjective report.

The number of functional neuroimaging studies involving hypnosis has steadily increased since the early 1990's. However, the quality of the results in a number of investigations have been hampered by the confounding of suggestion and hypnosis (e.g. Faymonville et al, 2000, 2003; Wik et al, 1999), likely due to certain theoretical preconceptions regarding the nature of hypnosis. The traditional 'state' view of hypnosis holds that the induction of hypnosis places the participant in an altered state of consciousness (presumably reflecting or co-varying with altered brain function) which increases responsiveness to suggestion. The non-state view holds that a hypnotic induction does not lead to an altered state of consciousness, but that factors such as expectation and motivation drive responses to suggestion. Regardless of which view one holds a traditional distinction is made between 'trance' (the 'state' of the participant after they have received a hypnotic induction) and the effects of 'suggestion' which are necessarily given to produce the desired effects (suggestion can be further broadly divided into 'direct' and 'indirect' approaches). This trance/suggestion distinction is made in Heap and Aravind (2002), and consequences for our conduct of functional neuroimaging investigations involving hypnosis based on this distinction are discussed in detail in Oakley and Halligan (2002, unpublished manuscript). It is essential for researchers not to confound the two if their results are to be easily interpretable.

Since the experiments presented in this thesis are concerned with the use of hypnosis as a cognitive tool (Rainville et al, 1997; Raz & Shapiro, 2002), and not with the nature of hypnosis itself, it is contended that the reasonable statistical comparison to be made after collection of functional imaging data will be to 'cancel out' the effects of the hypnotic state by contrasting the effects of BOLD due to a particular suggestion with BOLD due to a subject resting while hypnotised (sometimes termed 'neutral hypnosis'). Conversely, if one's aim was to examine the neural correlates of the hypnotic state then the appropriate statistical comparison would be to compare the BOLD as the result of a suggestion presented in- and outside the hypnotic context (while possibly also accounting for differences in task/suggestion performance between the two conditions, depending upon the task performed). As will be seen in the following review of key functional neuroimaging experiments involving hypnosis this proscription has been followed with varying degrees of success.

4.2.1 Hypnosis with PET

A number of studies have been carried out using hypnosis in a PET environment. They have provided evidence, independent of, but in line with, subjective reports which confirm that hypnosis can be used as a cognitive tool to alter sensations and perceptions (Rainville et al, 1997; Raz & Shapiro, 2002). Important methodological aspects and key results of selected example studies will be reviewed here.

4.2.1.1 Kosslyn, Thompson, Costantini-Ferrando, Alpert, Spiegel (2000)

This study was reviewed briefly in the previous chapter and indicated that activity in left hemisphere colour regions (including fusiform gyrus [V4]) correlated significantly with suggestions given to the hypnotised participants to either see a greyscale stimulus in colour (increased activity in V4), or a colour stimulus in greyscale (decreased activity in V4). While this result demonstrates strongly that suggestions given in hypnosis can produce perceptual changes the investigators also attempted to quantify the effect of suggestions given outside the hypnotic context. Appropriately, in the hypnotic context participants were asked to *"alter actively the stimulus, to drain or add colour while focussing on the altered stimulus"*. However, in the non-hypnotic context participants were asked to try to *"remember and visualise the stimulus in its other form"*. This change of suggestion/instruction can essentially be regarded as a different task, making it difficult to draw conclusions from this study regarding the effects of non-hypnotic suggestion on colour perception.

4.2.1.2 Szechtman, Woody, Bowers, Nahimas (1998)

Szechtman et al (1998) conducted what can be considered one of the most methodologically sound functional neuroimaging experiments involving hypnosis. As reviewed briefly in the previous chapter this study investigated the neural activation associated with hypnotically-produced auditory hallucination and compared them with activations observed when the same hypnotised participants heard a real sound or were asked to imagine the same sound. Similarities in activation were observed in the 'real' and hallucinated conditions, but large differences were observed between the former conditions and the 'imagination' condition which resulted in much fewer activations. The investigators also took measures of the externality and clarity of each sound. Collection of data of this sort allows for a correlational analysis of objective (rCBF) and subjective measures of the same phenomenon; providing powerful evidence of a relationship between activity in a particular brain region (physical-level) and a subjective (psychological-level) descriptor of a percept.

4.2.1.3 Halligan, Athwal, Oakley, Frackowiak (2000)

Halligan et al (2000 - reviewed in chapter 1, section 1.3.2.2) used hypnotic suggestion as a cognitive tool to model the clinical symptom of a functional leg paralysis. The neural activations underlying the hypnotically-produced symptom closely match those observed in a prior study on a patient with conversion paralysis (Marshall et al, 1997). The similarity of the activations observed between this pair of studies neatly demonstrates the utility of using hypnotic suggestion to model clinical symptoms.

4.2.2 Hypnosis with fMRI

At the time of writing only two published studies had reported using hypnosis with fMRI. Certain aspects of the PET procedure make it ideally suited for using hypnotised participants, such as adequate time between infusions in which to instigate hypnotic suggestions and to collect subjective reports of suggested experiences. The relative quiet of the PET environment is also an advantage. However, as fMRI becomes more dominant because of its higher spatial and temporal resolution, and lower price, it seems inevitable that hypnotic techniques will have to be adapted to the fMRI environment. Indeed a number of studies have been conducted and are reported to be in the pipeline (e.g. Egner, Jamieson, Gruzelier, 2004; Raz et al, c.f. Raz et al, 2003).

4.2.2.1 Crawford, Horton, Hirsch et al (1998)

Crawford et al (1998) report a study investigating the neural correlates of hypnotic analgesia in fMRI. However, the report is an abstract submitted for conference

proceedings. It contains no solid detail regarding techniques used in the course of the investigation and presents only preliminary analysis of two participants.

4.2.2.2 Rosén, Hugdahl, Ersland et al (2001)

Rosen et al (2001) report an interesting fMRI study on a single patient with phantom limb pain. Hypnotic suggestion was used to allow the patient to imagine making painful and non-painful movements of fingers in the amputated stump. Activations were compared with those resulting from finger tapping in the non-amputated stump. Hypnotic techniques in the fMRI environment were not mentioned in any detail, but some pain-related activations were found when the patient was asked to imagine making painful movements of the fingers in the phantom limb (this paper is reviewed in more detail in section 4.5).

On a practical level it will certainly be interesting to observe the techniques reported by different experimenters used to modify their routines for compatibility with the fMRI environment.

4.3 Functional neuroimaging of pain

The study of pain in the functional imaging environment has progressed significantly since the first early studies (Jones et al, 1991; Talbot et al, 1991). The relatively high level of replication of 'simple' pain studies is a welcome development within the field. This is a factor which allows for meta-review techniques to be used to give us a clearer picture of brain regions which respond to pain (e.g. Peyron, Laurent & Garcia-Larrea, 2000; Porro, 2003). As more results become available these review techniques are also being used to describe patterns of activation in response to sub-types of pain experience (e.g. Visceral vs. somatic pain: Derbyshire, 2003). Brain regions which they report as being consistently activated in response to pain are reported in table 4.1. (Derbyshire, 1999; Peyron, Laurent & García-Larrea, 2000; Porro, 2003).

	S-I	S-II	ACC	Thalamus	Insula	PFC	PAG	SMA	Basal Ganglia	Cerebellum	Striatum	IPC (BA39/40)	OFC	Brainstem	Frontal Cortex	Lentiform Nucleus
Porro (2003) Review of activations in response to acute pain	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑						
Peyron et al (2000) Review of activations in response to acute pain	↑	↑	↑	↑	↑		↑	↑		↑	↑					
Derbyshire (1999) Review of activations in response to acute pain	↑	↑	↑	↑	↑	↑					↑	↑				↑

Table 4.1: Neural activity consistently observed in response to experimental pain stimuli (tonic and phasic). Results from Derbyshire (1999) are only presented for his analysis of experimental pain, not clinical conditions. ↑ and ↓ represent increases and decreases of rCBF or BOLD signal. Abbreviations: S-I - primary somatosensory cortex; S-II – secondary somatosensory cortex; ACC – anterior cingulate cortex; PFC – pre-frontal cortex; PAG – periaqueductal grey; SMA – somatosensory motor area; IPC – inferior parietal cortex; OFC – orbito-frontal cortex.

4.3.1 Dissociating the components of pain

As table 4.1 demonstrates, a network or "neuromatrix" (Melzack, 1999) of activations is observed in response to an acute pain stimulus in normal participants. Not all studies demonstrate all of the activations tabulated here, but these regions are reported to give the most consistent responses. Beyond showing a network of activations, though, a key interest for neuroscientists lies in explaining which components of the network are responsible for different aspects of the pain experience. Specialisation of different brain regions involved in the experience of pain has been apparent for some time. Early examples are patients who underwent cingulotomy operations to relieve chronic unremitting pain conditions; lesions to the cingulate did not relieve the pain entirely, but patients reported finding it less bothersome: an example of modulation of the affective dimension of pain (Foltz & White, 1962). Accepting that there is a pain matrix activated in a specific fashion in response to a stimulus perceived as painful, functional neuroimaging experimenters have manipulated factors affecting components of the pain experience to localise regions underlying these sub-components. Many different components of the pain experience have been studied including anticipation of pain (Ploghaus, Tracey, Gati, Clare, Menon, Matthes, Rawlins; 1999), pain intensity (Derbyshire et al, 1997; Coghill, McHaffie & Yen, 2003), and affective vs. sensory contributions (Rainville, Duncan, Price, et al, 1997; Hofbauer, Rainville, Duncan, et al, 2001).

4.3.1.1 Rainville, Duncan, Price, Carrier, Bushnell (1997)

Of particular relevance to the discussion of the dissociation of components of the complete experience of pain, and to work of this thesis, is a PET investigation conducted using hypnosis as a cognitive tool to modulate the affective dimension of pain. Modulation of the unpleasantness of a painful stimulus independently of its intensity is conventionally very difficult. In most investigations the two subjective ratings given by participants are highly correlated (if not identical: some investigators doubt the ability of experimental participants to introspectively separate the two [Chapman et al, 2001]). Rainville et al (1997), however, circumvented this problem by using hypnotic suggestions to modulate the unpleasantness of a painful (hot water) stimulus independently of its intensity. Using a covariate analysis it was possible to demonstrate blood flow in an area of the anterior cingulate cortex which correlated with subjective ratings of unpleasantness. As can be seen in figure 4.1 the activations observed by Rainville et al confirm, in a relatively non-invasive way, the results of previous lesion studies of the cingulate.

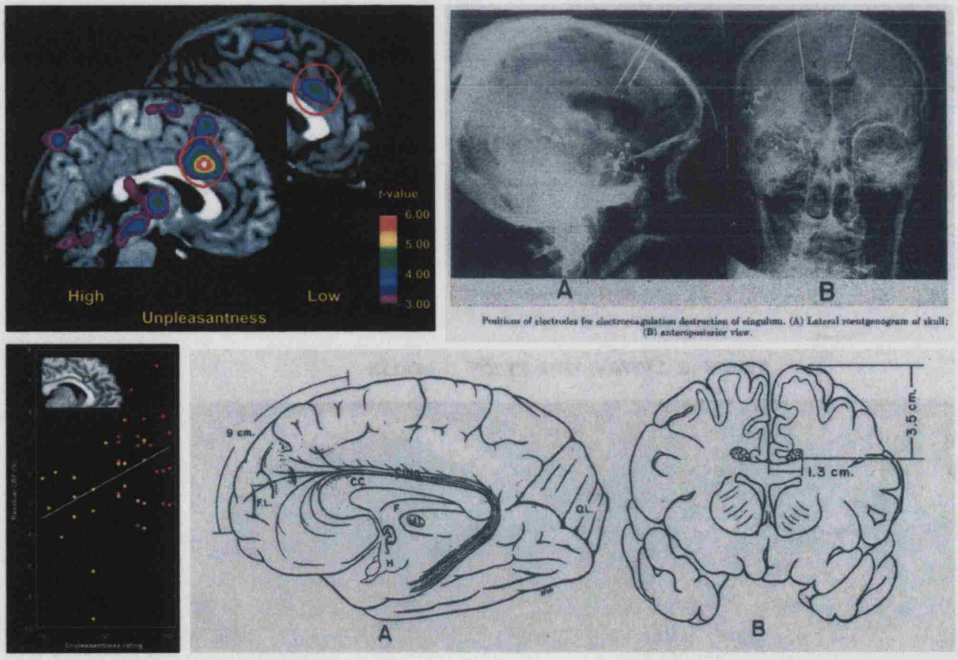


Figure 4.1: Results of Rainville et al (1997: left 2 images) and Foltz and White (1962: right 2 images) demonstrating the location of the region of anterior cingulate cortex involved in processing pain affect. CING = cingulum; C.C. = corpus callosum; F.L. = frontal lobe

Not all components of the pain matrix have been studied or are understood in such great detail as the ACC/affect relationship, and structural and functional analyses of the anterior cingulate indicate that the ACC may serve a number of different

functions including attentional processes (Vogt, Nimchinsky, Vogt, Hof, 1995; Vogt, Berger, Derbyshire, 2003; Peyron, Laurent, Garcia-Larrea, 2000). Proposed functions of other regions include analysis of sensory features of pain in the primary and secondary somatosensory cortex, thalamus and insular regions. The thalamus routes information to other areas of the pain matrix and activity here may represent generalised sensory processing. Motor-related processing is associated with activity in the striatum, cerebellum and supplementary motor area (SMA). Periaqueductal grey (PAG) is discussed with reference to pain control, and activity in the thalamus and anterior cingulate cortex have also been observed to be more active during analgesia procedures. Petrovic (2004) has discussed the midbrain with reference to temporally early rather than late experiences of pain and notes that activity here often correlates with autonomic response. For a more comprehensive review, and fuller discussion, of neural activations in response to pain see Peyron, Laurent & Garcia-Larrea (2000), Porro (2003), Derbyshire (1999) or Coghill, Sang, Maisog and Iadarola (1999). For the present purposes it is sufficient to note that activity in the 'matrix' of brain regions described above is significantly correlated with the experience of pain.

4.4 Functional neuroimaging of functional pain conditions

A number of studies have used neuroimaging techniques to investigate functional pain conditions. Firstly we will examine the general approach within the neuroimaging community towards functional pains such as IBS and fibromyalgia (e.g. Naliboff et al, 2001; Gracely et al, 2002), then we will consider functional imaging analysis of some more unusual functional 'pains' (e.g. Eisenberger et al, 2003; Singer et al, 2004).

4.4.1 Functional neuroimaging of fibromyalgia and irritable bowel syndrome

Although a key aim of neuroimaging researchers investigating functional pain conditions is to examine the neural events underlying the pain condition in question, subtraction methodology presents an obstacle. Functional pain conditions such as fibromyalgia and irritable bowel syndrome are chronic and resistant to treatment. If a drug treatment were given to acutely modulate the pain the logic underlying subtraction methodology would be invalidated. Observed brain activation would be confounded by unknown effects of the drug on rCBF. This barrier to progress has led many researchers to try another approach: namely to 'stress the system' by applying a painful stimulus and observing augmented responses in patients compared to controls.

4.4.1.1 Gracely, Petzke, Wolf, Clauw (2002)

Gracely et al (2002) take advantage of one of the diagnostic criteria of fibromyalgia, widespread tenderness, to investigate augmented pain processing in patients compared with healthy controls. Blunt pressure was applied to the fingernail beds of patients to produce a pain rating of 11/20 (*"moderate pain"*), the same force was applied to control participants, producing a pain rating of 3/20 (*"faint to very weak"*). Control participants were additionally exposed to blocks of pressure which they rated at 11/20. In response to the 'low pressure' condition pain-related activations were observed in the patients but not the controls, although when control participants reported similar levels of subjective pain experience as the patients (extra 'high pressure' condition) a similar pattern of activation was observed. Activations in patients in response to the low pressure stimulus, which were not observed in controls, are presented in table 4.2 at the end of this chapter.

This study confirms that patients with fibromyalgia have augmented pain sensitivity. The authors state that the results are *"not consistent with simple psychological mechanisms of changed labelling behaviour, in which patients establish a more liberal response criteria for reports of pain threshold"* although they note that attentional mechanisms such as hypervigilance could conceivably be responsible for the observed effects. One major problem, which the authors note, is that the study addresses the consequences of fibromyalgia rather than the causes.

4.4.1.2 Cook, Lange, Ciccone, Liu, Steffener, Natelson (2004)

Cook et al (2004) conducted a similar experiment to that of Gracely et al (2002). Cook used a thermal stimulus to investigate augmented pain processing in fibromyalgia patients compared to a matched control group. FM patients demonstrated greater sensitivity to heat stimuli than controls and enhanced pain-related neural activity in response to stimuli which control participants rated as non-painful. Greater pain-related neural activity was observed in FM patients compared to controls in response to matched stimuli. Increased relative activity was observed in prefrontal cortex, SMA, ACC and insula (see also table 4.2). The results again demonstrate augmented pain processing in fibromyalgia.

The authors argue that *"These results support a physiological explanation of FM pain and provide objective evidence of cortical and subcortical amplification of both painful and nonpainful thermal stimuli"*. This claim is reasonable to the extent that it indicates that FM patients are feeling pain and not malingering, but the observed results do not address the causes of fibromyalgia.

4.4.1.3 Gracely, Giesecke, Grant, Petzke, Williams, Clauw (2004)

Gracely et al (2004) adopted an innovative approach to the functional imaging investigation of fibromyalgia. In this experiment they assessed the tendency to catastrophise about pain in a sample of 29 fibromyalgia patients and scanned the patients during delivery of slightly intense pain. Patients more prone to catastrophising did not differ from low-catastrophisers on subjective measures of pain intensity or affect. However, significant correlations were observed between measures of catastrophising and brain activity in the claustrum, medial frontal gyrus, cerebellum, postcentral gyrus (SII), middle frontal gyrus (SMA), anterior cingulate cortex and lentiform nucleus (see table 4.2). The authors conclude that brain activity in areas associated with pain, emotion and motor activity is associated with pain catastrophising and they propose that directed therapeutic modulation of threat perception in patients with clinical pain may be beneficial. Studies of this sort go beyond traditional imaging methodologies and demonstrate altered brain activity concomitant with distorted cognitive processes in functional pain patients.

4.4.1.4 Silverman, Munakata, Ennes, Mandelkern, Hoh, Mayer (1997)

The experimental induction of visceral pain is commonly achieved through the insertion of rubber balloon catheters into the rectum or colon which can be inflated to produce a painful sensation. This technique has been used in a number of functional imaging experiments investigating irritable bowel syndrome (IBS) because of the close relation of the stimulus to the clinical symptoms in question.

IBS patients and healthy controls were tested in conditions of low, moderate and intense balloon inflation. Scans were also taken in an additional condition where it was only simulated that the balloon was being be inflated, which Hardcastle (1999) considers a suggestion for pain. After each trial participants rated the subjective intensity of the painful sensation. The authors do not report subjective intensity data separately for the high pressure (painful stimulus) and low pressure (anticipation of painful stimulus) trials, making it difficult to assess the effectiveness of their suggestion in inducing a sensation of pain in the absence of a stimulus. No pain activations were observed in relation to the simulated delivery trial.

Overall, the majority of functional imaging studies of IBS and fibromyalgia have failed to deliver results which significantly advance our understanding of these conditions. It has confirmed, for example, that fibromyalgia patients are more sensitive to physical pressure and are not malingering, but the studies to date have not been able to inform us about the causes of these patient's discomfort.

4.4.2 Functional imaging of 'other' functional pains

A number of investigators have examined the neural correlates of pains, or at least events with negative emotional valence, in the absence of an identifiable organic cause. The papers reviewed in this section do not fall within Wessely et al's (1999) definition of 'functional somatic syndromes' but serve to illustrate a wider range of 'functional' pains.

4.4.2.1 Bär, Gaser, Nenadic, Sauer (2002)

Experimental literature concerning hallucinated pain is sparse. However, an attempt has been made to investigate hallucinated pain using functional imaging. Bär, Gaser, Nenadic and Sauer (2002) report the results of an attempt to scan 'naturally' occurring hallucinated pain (in contrast to investigations of deliberate induction). Bär et al attempted to scan schizophrenic patients with coenaesthesia. This is a sub-syndrome of schizophrenia with symptoms including tactile hallucinations and often sometimes painful itching and burning sensations. Their experimental design was naturalistic in that functional imaging data was collected from patients in extended blocks. Patients were to press a button upon the occurrence of a hallucination and to release the button when the sensation disappeared. Four patients were scanned in this way but the authors only report data from the single case in which symptom duration allowed for the required analysis. The patient, a 53 year old woman had a history of reporting painful sensations, including itching or stabbing, in her legs as well as other visceral somatic hallucinations. At the time of the study the hallucinatory sensations were sharp and painful. During a functional imaging acquisition period of twenty-eight minutes 26 hallucinatory events were reported with a mean length of 10.4s (SD=6.4). Total hallucination time was not reported.

Unfortunately the results were not reported in a consistent manner. In particular, activations relevant to pain (hallucination vs. rest) were not reported systematically, and no activations were reported to have reached a corrected level of significance. Uncorrected patterns of activation were visually displayed but do not appear to reside in areas commonly activated in response to noxious stimuli. When data from the hallucination condition were contrasted with data collected from the same patient during a scan carried out 3 months later in a condition of non-painful tactile stimulation (when the patient was taking drugs to control hallucinations – a factor which could itself affect interpretation of the results) an activation was reported in the medial parietal cortex significant at a level of $p<0.05$ corrected. The authors are unclear about the functional significance of such an activation in this area, although it is close (slightly posterior) to the primary somatosensory cortex representation of the leg – an area which would be expected to activate in response to pain in the leg. Despite the sensible methodology utilised, this report demonstrates the difficulty of

making a 'suck it and see' approach work. There are considerable practical difficulties of using functional imaging to measure a naturally occurring phenomenon with variable temporal properties: it is difficult to collect enough data to provide adequate statistical power; and there is no guarantee that the patients will hallucinate in the scanner (the present study was conducted on four patients but only one experienced enough hallucinatory sensation to analyse). These uncontrolled factors most strongly account for the lack of significant results observed in this study.

4.4.2.2 Singer, Seymour, O'Doherty, Kaube, Dolan, Frith (2004)

Singer et al (2004) report an interesting study which merits inclusion here under the rubric of functional pain (defined as the experience of pain in the absence of a physical stimulus). In an investigation of the relation between empathy and pain Singer scanned the female partner of a couple while the male partner was present in the MRI room. Scans were taken in conditions of electrical pain being administered to the female partner, and also when the female partner observed a signal indicating that her partner was receiving a similar pain stimulus. Activations in response to an actual pain were observed throughout the pain matrix including insula, S-II, S-I, M-I, ACC, thalamus, brainstem and cerebellum. Activations observed when the participant knew their partner was being shocked included areas of the brain known to be associated with the affective qualities of pain, including ACC, insula, IPC, cerebellum and brainstem (shown in table 4.2). Singer et al also noted that activity in the insula and anterior cingulate cortex correlated significantly with individual difference measures of empathic concern. This study did not directly measure or report the subjective experiences felt by the participants but does support the hypothesis that functional pain experiences are underscored by brain activations in relevant areas of the pain matrix. Experience of another's pain is not a cognitive abstraction but a 'felt' response, since cognitive processing of an event on its own would not be expected to produce such extensive affective response.

4.4.2.3 Eisenberger, Lieberman, Williams (2003)

This study investigated the neural correlates of social exclusion but merits a brief entry here because the semantic description of the feeling of social exclusion as 'hurt feelings', would on the face of it seem to describe a form of painful experience in the absence of a physical stimulus; that is, a functional pain. Utilising fMRI and a computer task with which they could make participants feel excluded, the experimenters correlated subjectively reported distress with rCBF. Activations were reported in the ACC and right ventral prefrontal cortex (RVPFC) which the authors interpret as being *"very similar to those found in studies of physical pain"*. Comparison of Eisenberger et al's results with

reviews of acute pain studies (see table 4.2) immediately demonstrates, however, that the claimed similarity is not present: activations in important areas for pain such as the thalamus and primary somatosensory cortex were not observed.

4.5 Functional neuroimaging studies involving hypnosis and pain

Aside from Rainville et al's (1997) oft-cited work there are a number of other studies which have investigated the use of hypnosis to modulate pain in a neuroimaging environment. Two of the reports in this section concern phantom limb pain. For the purposes of this thesis phantom limb pain is not considered in the same light as the other members of the 'functional somatic syndromes'. Although an unusual pain in that it is perceived by the patient to be located in an absent body part, it is not considered to have a large psychosocial component. This consideration is reflected in the high incidence of the condition amongst amputees and would seem to reflect a common physical or neuropsychological process (Jensen et al, 1983; 1985). Indeed, recent work by Ramachandran has demonstrated cortical reorganisation in phantom limb patients and he hypothesises that phantom pain may be the result of an absence of visual and proprioceptive signals confirming that motor commands to move the limb have been obeyed (Ramachandran & Rogers-Ramachandran, 2000). This level of explanatory framework has been extended to encompass Complex Regional Pain Syndrome (CRPS) with demonstrations of referred sensation (McCabe, Haigh, Halligan, Blake, 2003) and symptom relief with mirror-visual feedback (McCabe, Haigh, Ring et al, 2003). Recent demonstration of sensory disturbances, including induced pain, in fibromyalgia patients through the use of incongruent visual feedback opens the possibility for new explanations of fibromyalgia syndrome (Bodamyali, McCabe, Haigh et al, 2004) and it will be interesting to investigate the possibility of similar induction of pain in healthy controls. However, the relationship between cortical reorganisation, incongruent feedback and the other functional somatic syndromes (as classified by Wessely et al, 1999) remains uncertain and will not be considered further here.

4.5.1 Crawford, Gur, Skolnick, Gur, Benson (1993)

In a very early functional imaging study Crawford et al (1993) investigated the effects on cerebral blood flow of hypnosis, hypnotic suggestions for analgesia, and hypnotic susceptibility during ischemic pain. Interpretation of the results is limited by the ^{133}Xe imaging method, including its lack of penetration to measure CBF in subcortical areas. The authors observed increases in activity in the sensorimotor cortex and orbitofrontal cortex in high hypnotisable subjects during the condition of hypnotic analgesia; they interpret OFC activity as indicative of increased attentional effort during hypnotic

analgesia by the 'executive control system', but more studies will need to be conducted to improve our understanding of hypnotic analgesia. Technical limitations aside though, balanced studies of this sort merit replication using more advanced scanning technologies.

4.5.2 Wik, Fischer, Bragée, Finer, Fredrikson (1999)

Wik et al (1999) report the results of an investigation into hypnotic analgesia with fibromyalgia patients. This work predates investigations along similar lines reported later in this thesis (chapter 8) but it contains serious methodological flaws which hamper interpretation. Eight highly hypnotisable women suffering from fibromyalgia were scanned using PET in two conditions: resting wakefulness and hypnotic analgesia. Rather than have participants close their eyes during both conditions the investigators chose to attempt to *"control for the visual aspect of resting differences"* by showing participants videotapes with scenes of individuals walking in a park. During resting wakefulness patients were told to be comfortable and watch the videotapes. The hypnotic analgesia condition was induced by *"gently talking to the subjects, instructing them to be relaxed and to go into a deep trance, to watch the videotapes and not to feel any pain whatsoever"*. Pain ratings were taken after each scan but testing across conditions only demonstrates a trend towards significance, with a small absolute difference (mean 4.3 ± 2.5 vs. 3.2 ± 2.7, p=0.066). Imaging results are further confounded by the presence of a hypnotic 'state' in only one of the conditions.

Wik et al (1999) report that compared to the resting state, hypnotic analgesia increased rCBF in the thalamus and decreased it in the ACC, both components of the pain matrix (see chapter 4). If we assume that fibromyalgia pain (like acutely induced experimental pain) is associated with increased rCBF activation in areas of the pain matrix then we would expect to see decreased activity in these areas in response to hypnotic analgesia. Therefore the thalamus activation observed here does not fit the pattern of expected results, leaving only the anterior cingulate activation possibly interpretable as a decrease in unpleasantness of the pain in the hypnotic analgesia condition (Rainville et al, 1997). However, there is some indication that baseline thalamic activity decreases in chronic pain conditions, possibly explaining this activation pattern (Gracely et al, 2002; Cook et al, 2004; Hsieh et al, 1995; Mountz et al, 1995; Kwiatek et al, 2000). Activations are presented in table 4.2.

4.5.3 Faymonville, Laureys, Degueldre et al (2000)

In a similar manner to Wik et al (1999) Faymonville et al (2000) conducted a investigation into hypnotic analgesia using a sample of healthy volunteers and a thermal pain stimulus using PET. The investigators design did not include specific suggestions

for analgesia, yet achieved significant reductions in pain intensity and unpleasantness scores compared to rest. This finding contradicts the results of other investigators (Hilgard, 1969; Evans & Paul, 1970) who found that the induction of hypnosis alone, without suggestions for analgesia, is not sufficient to produce decreases in pain sensation. This factor, combined with a hypnotic 'state' being present in only one of the experimental conditions, makes precise interpretation of the results difficult, although activity in the anterior cingulate cortex is reported to mediate hypnotic analgesia.

4.5.4 Willoch, Rosen, Tölle, et al (2000)

Willoch and colleagues used hypnotic suggestion and imagery to modulate phantom limb pain in the PET environment. Eight unilateral arm amputees who had all used hypnosis to treat their phantom limb pain and who were all moderately to highly hypnotisable took part in the study. Hypnosis was used as a cognitive tool, to allow participants to *"resurrect the personal experiences of PL [phantom limb] sensation"*. Scans were taken in four conditions representing typical phantom sensation: comfortable position, comfortable movement, painful position and painful movement. Movements of the phantom were timed to the beat of a metronome and visual analogue scale ratings of pain intensity and unpleasantness were taken after each scan. Participants all rated the painful conditions as more painful than the comfortable conditions. The authors report that participants did not have the feeling that it was *"as if"* they were feeling the suggested sensations, but that they actually experienced vivid and real phantom sensations. VAS ratings for intensity and unpleasantness are shown in figure 4.2

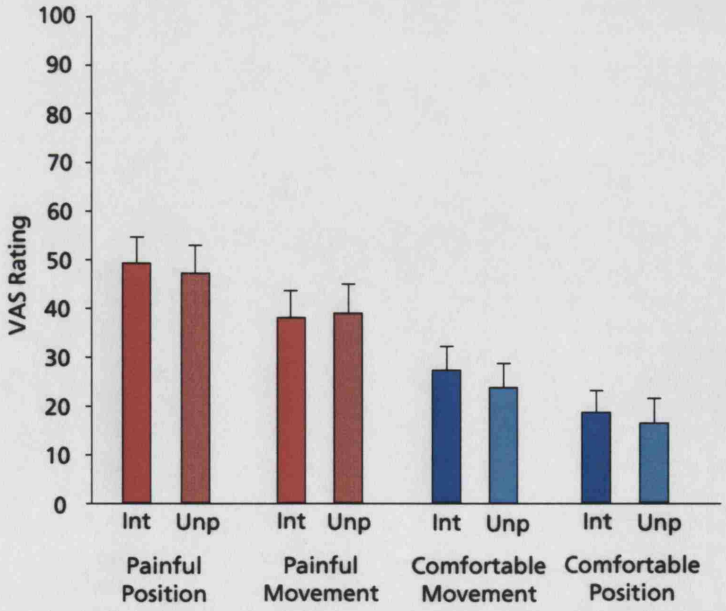


Figure 4.2: Subjective pain ratings given by amputees in each of the 'movement' or 'position' conditions. Int = Intensity, Unp = Unpleasantness.

Activations associated with painful movement included S-I, M-I, SMA, cerebellum, PFC, insula and ACC. Painful position was additionally associated with activity in the lenticular nucleus, thalamus and parietal cortex, but was absent the activation in the cerebellum (all pain related activations from this study are given in table 4.2). This is an example of a functional pain. It demonstrates strong responses in a network of brain regions most consistently activated by pain, but crucially it does so in the absence of peripheral noxious stimulation, and supports the notion of central generation of pain.

4.5.5 Rosen, Hugdahl, Ersland, et al (2001)

This study, described briefly in section 4.4, is essentially a smaller version of the Willoch et al (2000) experiment but conducted in fMRI. The investigators studied the neural activations underlying the conditions of an amputee participant imagining the following within hypnosis: painful finger movement, non-painful finger movement, painful positioning and non-painful positioning. In contrast to the Willoch study, however, the investigators report that the participant did not actually feel any pain during any of the conditions, but that having experienced phantom limb pain *"he could easily imagine pain in the arm stump"*. Appropriately, activations (contrast: [pain]-[no-pain]) were observed in the post-central gyrus, anterior insula and thalamus; an incomplete activation of the pain matrix. No activations were observed in primary somatosensory cortex, and, fitting with the absence of pain sensation (specifically unpleasantness) there was no activity observed in the ACC.

4.6 Discussion

Activations from functional pain studies, and the contrasts that produced them, are presented in table 4.2. A variety of activation patterns are apparent, with many studies demonstrating incomplete activation of the 'pain matrix'. The studies by Gracely et al (2002) and Cook et al (2004) demonstrate greater activation in functional patients than controls in response to an experimental stimulus. This kind of result is normally attributed to factors such as 'hypervigilance' in such patients, but Gracely et al (2004) demonstrate that catastrophising-related brain activity may account for a proportion of it. Experiments such as the latter show potential for better understanding of these disorders. These approaches separate patients and controls on measures of cerebral activity in response to a symptom challenge. With the appropriate choice of functional imaging paradigm they have the potential to inform our operational diagnostic criteria for functional disorders. Wik et al's (1999) results present us with uncertainty, driven by weak experimental control over the patient's pain. However, they do promisingly demonstrate activations previously linked to the cognitive processes underlying

hypnotic analgesia (Crawford et al, 1993) and, of course, pain-related activity (ACC, thalamus).

	S-I	S-II	ACC	Thalamus	Insula	PFC	PAG	SMA	Basal Ganglia	Cerebellum	Striatum	IPC (BA39/40)	OFC	Brainstem	Frontal Cortex	Lentiform Nucleus
Porro (2003) Review of activations in response to acute pain	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑						
Peyron et al (2000) Review of activations in response to acute pain	↑	↑	↑	↑	↑		↑	↑		↑	↑					
Derbyshire (1999) Review of activations in response to acute pain	↑	↑	↑	↑	↑	↑					↑	↑				↑
Gracely et al (2002) Activations observed in fibromyalgia patients but not controls in response to "low-pressure" trials	↑	↑	↑		↑					↑		↑			↓	
Cook et al (2004) Areas of greater pain-related activity in fibromyalgia patients compared to controls		↑	↑					↑		↑						↑
Gracely et al (2004) 'Catastrophising'-related activations		↑	↑			↑				↑		↑			↑	
Wik et al (1999) Hypnotic modulation of fibromyalgia pain. Contrast: [hypnotic analgesia]-[resting wakefulness]			↓	↑								↑	↑			
Willoch et al (2000) Hypnotic modulation of phantom limb pain	↑		↑	↑	↑	↑		↑		↑		↑				↑
Rosen et al (2001) Hypnotic modulation of phantom limb sensation - patient did not feel pain				↑	↑											
Singer et al (2004) 'Empathic pain': activations observed when participant knew partner was receiving electric shock			↑		↑					↑		↑		↑	↑	
Eisenberger (2003) 'Hurt feelings': activations observed in condition of social exclusion			↑			↑										

Table 4.2: Neural activity observed in the context of the experiments, described in this chapter, investigating clinical and experimental functional pain conditions. ↑ and ↓ represent increases and decreases of rCBF or BOLD signal. Abbreviations: S-I - primary somatosensory cortex; S-II – secondary somatosensory cortex; ACC – anterior cingulate cortex; PFC – pre-frontal cortex; PAG – periaqueductal grey; SMA – somatosensory motor area; IPC – inferior parietal cortex; OFC – orbito-frontal cortex.

The studies by Willoch et al (2000) and Rosen et al (2001) are the most successful demonstrations of neural pain activity in the absence of a physical stimulus. Phantom limb patients presented a population familiar with pain (and its subsequent hypnotic

modulation), the results confirm the subjective reality of such pain. An important point, clarified by the consideration of the Willoch and Rosen studies, is that it appears that pain that is 'felt' is driven by full patterns of activity in the pain matrix. Pain that is simply imagined is driven by incomplete activation patterns. This conclusion is further supported by consideration of the Singer et al (2004: empathic pain) and Eisenberger et al (2003: social exclusion) studies. Singer's study, more closely approaching what would be considered a painful experience (and not just negative affect) is underscored by fuller activations in the pain matrix. Comparison of the results described in the studies that follow with those reviewed above should allow assessment of felt pain in response to suggested pain experience and modulation.

Chapter 5 – The functional neuroanatomy of functional pain

5.0 Introduction

The results of the investigations described in chapters 2 and 3, and the review of earlier investigations of hypnotically-induced pain reviewed in chapter 1 all indicate that, at least in highly hypnotisable participants, it is possible to induce a subjectively real experience of pain through hypnotic suggestion. Physiological changes demonstrated in response to hypnotically-induced pains seem to match changes induced by 'actual' pain (e.g. Dudley et al, 1964; Barber & Hahn, 1964), but the relevance of this evidence is rendered doubtful by negative contemporary scientific judgement on the strength of the relationship between physiological and subjective measures of pain (Chapman et al, 2001). Changes in subjective report, especially in the context of hypnosis studies, are also open to criticisms relating to demand characteristics (Orne, 1962). Functional imaging techniques offer the opportunity to objectively validate self-report measures of pain. This experiment was conducted to investigate the neural correlates of a hypnotically-induced experience of pain, and to compare these with activations underlying a corresponding physically-induced and imagined pain experiences. The relatively mature state of pain imaging described in the previous chapter guided the experimental hypotheses.

Components of the present investigation have been considered before, most notably by Willoch et al (2000) who used hypnotic suggestion to generate pain in phantom limb patients. This experiment expands upon those findings, however, by investigating hypnotically-hallucinated pain in a normal (non-patient) population using different methodology (hallucination vs. direct suggestion), different technology (fMRI vs. PET), and by the addition of 'actual' and 'imagined' pain conditions to allow direct within-subject assessment of the similarities and differences between these pain experiences.

This investigation was carried out collaboratively with Dr Stuart Derbyshire at the University of Pittsburgh Magnetic Resonance Research Center. Ethical approval was sought and obtained by Dr Derbyshire. All contact with participants was conducted by MW, who also designed the study. The methodology adopted reflects the balance of competing interests (time in scanner, pain to participants, other constraints) chosen by MW to provide maximal acquisition of meaningful data. All steps of the data analysis were conducted jointly by MW and Dr Derbyshire.

5.0.1 Experimental design: problems and solutions

The fMRI environment presents a number of difficulties for those attempting to use hypnosis. The majority of the problems stem from the noise of the machine. Participants must wear earplugs to protect their hearing and without a good communications system it can be difficult to talk to participants. The Magnetic Resonance Research Centre in Pittsburgh had only very basic communications equipment and it was decided to perform the hypnotic induction by speaking directly to participants when they were lying ready on the scanner-bed wearing earplugs with their head encased in the radio coil. This involved the experimenter (MW) raising his voice somewhat, but as these were experienced, highly hypnotisable subjects who needed little guidance to become hypnotised, this method proved adequate. Once the subject was inserted into the bore of the magnet participants were asked if they could hear the experimenter's voice clearly and all indicated the affirmative with a finger movement before the experiment could proceed.

The main problem facing this investigation of hypnotically-induced pain was fitting the experimental design to the structural and acoustic limitations of fMRI. In Experiment 1 of this thesis (chapter 2) the method chosen to investigate HI pain was direct suggestion of heat and pain. These suggestions were verbally delivered and repeated and emphasised to create and maintain the sensation. This technique required adaptation for use in fMRI and the design described in the section 5.1 is based on Szechtman et al (1998).

5.0.2 Hypothesis

There is good evidence that an experience of acute pain is subserved by activation distributed through the 'pain matrix', as described in section 4.3 and table 4.1. The specific aims of this study were to investigate the haemodynamic correlates of physically-induced (PI), hypnotically-induced (HI), and imagined (IM) pain sensations, all within the hypnotic context. It was hypothesised that PI and HI but to a lesser extent IM pain experiences would result in activations in areas strongly associated with an acute pain, specifically the thalamus, insula, anterior cingulate cortex and primary somatosensory cortex.

5.1 Method

5.1.1 Participants

An initial group of thirty-three participants participated as paid volunteers recruited through advertisements posted at the University of Pittsburgh. The research was

approved by the University of Pittsburgh Institutional Review Board and participants' consent was obtained according to the Declaration of Helinski. Participants were first tested on the Harvard Scale of Hypnotic Susceptibility, Form A (Shor & Orne, 1962). Possible scores on the HGSHS:A range from 0 to 12. Twelve highly susceptible participants (scoring 9+ on the HGSHS:A) were invited to take part in the heat/ pain screening stage of the study. On the basis of this screening eight right handed participants (5 female, 3 male) were selected to complete the final stage of the experiment in the scanner. These final eight participants had a mean age of 25.75 (range 18 to 49) with a mean Harvard score of 11.125 (SD = 0.927).

5.1.2 Screening

The twelve highly hypnotisable participants were screened separately on their ability to hallucinate a painful sensation. In this screening session participants were informed that the purpose of the experiment was simply to investigate pain perception in hypnotised subjects in fMRI. Participants had a heat probe attached to their right hand and it was demonstrated how the device could heat up to become painfully hot (48.5°c). Participants were then hypnotised using standardised instructions for eye closure, controlled breathing, muscle relaxation and a descent image ending in special place imagery (see Appendix 2.1). Participants were then told that *"In a moment I am going to turn on the heat generator. The probe will heat up and cause a painful sensation. I would like you to pay attention to the painful sensation in your right hand. I'm turning the heat generator on now."* After thirty seconds the participant was told that the heat was being turned off and was asked to verbally rate the intensity and unpleasantness of the sensation on 0-10 scales. This procedure was repeated approximately ten times per participant using exactly the same instructions but the heat was only turned on in approximately half of the trials. Participants were selected for scanning if at least two of the no-heat conditions were rated as 2 or more on the intensity scale. Four participants were excluded from further participation as they expressed doubt as to whether the probe had been turned on, leaving eight participants to go on to the scanning stage of the study.

5.1.3 Apparatus and scanning parameters

Scanning took place in a General Electric 3.0 Tesla MRI scanner. PI pain was created using a Medoc TSA-2001 Thermal Sensory Analyser with MR-compatible heat probe. (probe size 3x3cm^2). Brain activation was inferred based on measurement of the blood oxygen level dependent (BOLD) contrast (Ogawa et al, 1990). These measurements were acquired at 3 Tesla using a reverse spiral technique (TE=25ms, TR=1.5s, flip angle=60°, 64x64 matrix) described in detail elsewhere (Noll et al, 1995; Stenger et al, 2000).

5.1.4 Scanning procedure

Participants lay on the scanner-bed wearing earplugs with their eyes closed. Their head was surrounded by a pillow with only their face exposed, and then encased by a radio-frequency (RF) coil. The probe of the thermal stimulator was strapped to the ulnar portion of the right palm and the participant's hand was positioned on their abdomen so that the weight of the hand pressing down on the heat probe ensured a firm and even contact. A standardised hypnotic induction, by then familiar to the participant, was read out and consisted of instructions to focus first on their breathing, then a progressive muscle relaxation, followed by a descent-deepening procedure. Finally subjects were instructed to go to a 'special place' where they would be relaxed and comfortable. The bed was then moved into the scanner and the subject was given instructions that the scanner would make a loud noise but that despite being able to hear it they would not find it bothersome, they were to remain in their special place. A three minute scout scan was then performed to localise the position of the head within the magnetic field

Each participant underwent three 6 minute blocks of functional scanning. Each six minute block was split into 30 second segments with alternating 'task' (pain) and 'rest' conditions. Before the scanning of blocks 1 and 2 participants were instructed *"In a moment the scanner is going to start up again, and again it will make a loud noise. Like before you will find that this noise won't bother or disturb you. During the next block the probe will heat up until it is at a painful temperature. It will become painfully hot. I will warn you when the probe is going to become painfully hot by tapping you once on the left foot. I will inform you of a 30 second resting block by tapping you twice on the left foot."* Scanning then began, the participant's foot was tapped every 30 seconds, alternating between 1 tap and 2 taps. Crucially, actual noxious heat pulse (48.5°c) were delivered following only three of the six single taps. The other three single taps and all six double taps were accompanied by non-noxious heat (37°c).

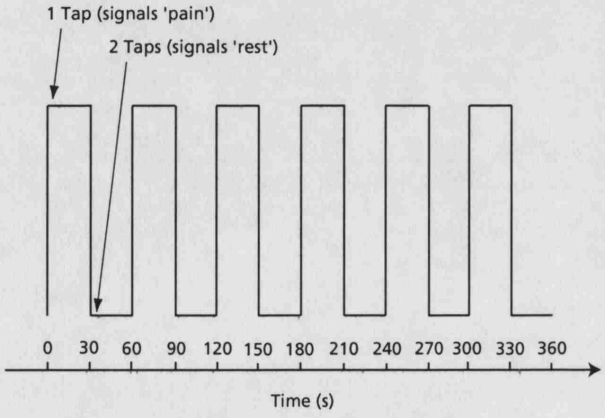


Figure 5.1: Diagram demonstrating the design of functional imaging blocks. The participants foot was tapped either once or twice every 30s to signal that the subsequent 30s would be a 'pain' or 'rest' condition.

After each of the first two blocks the participant was asked to verbally report on a 0-10 scale the intensity of each of the six painful stimuli in the order that they had occurred.

Block 2 was the same as block 1 but with the order of the HI and PI conditions reversed. Presentation of blocks 1 and 2 was counterbalanced across participants. Between blocks it was suggested that the participant return to their special place where they could relax; deepening instructions were also given.

For the third block of functional scanning subjects were given the instruction *"During this block I would like you to just imagine that the probe is heating up. Just to think about it becoming painful. When I tap your foot once I want you to start thinking about the probe becoming painfully hot. When I tap your foot twice I would like you to stop thinking about the probe becoming painfully hot and just to pay attention to your right hand"*. Prior to the beginning of the experiment participants had been explicitly told that in this final block the thermal probe would not be activated and that they were to simply imagine the heat pain as clearly as possible following a single tap. The probe temperature remained at 37.0°c throughout. After the three functional blocks a high-resolution structural scan was taken. After the scan, participants were debriefed and asked about their experience of remaining hypnotised throughout the procedure.

5.1.5 Statistical analysis

Data analysis was performed using SPM2b (Wellcome Trust Centre for the Study of Cognitive Neurology), described in detail elsewhere (Friston et al, 1995). Head movement between scans from every participant was corrected for and functional data for each participant was coregistered with his or her own high resolution structural MRI image and reoriented into the standardized anatomical space of the average brain provided by the Montreal Neurological Institute (MNI). To increase the signal to noise ratio and accommodate variability in functional anatomy, each image was smoothed in X, Y and Z dimensions with a Gaussian filter of 10mm (FWHM). For each participant, a box-car model with a haemodynamic delay function was fitted to each voxel to contrast the effects of interest with a rest, generating a statistical parametric map that was then assessed for significance at the second level for the group analysis. Baseline drifts were removed by applying a high-pass filter and any artefact from the motion correction was removed by applying the correction parameters as covariates of no interest. The random effects implementation corrects for variability between participants so that outlying data cannot drive the result. Brain regions with a large statistic correspond to structures whose BOLD response shares a substantial amount of variance with the conditions of interest. Images were thresholded at an arbitrary $p<0.01$ with an extent threshold of 50 contiguous voxels. Directed searches of activation were conducted on the thalamus, insula, S1, S2 and mid and perigenual anterior cingulate, prefrontal and

inferior parietal cortices. The multiple comparisons problem of simultaneously assessing all the voxel statistics was addressed via correction for the total number of voxels reported active using the false discovery rate (Genovese et al, 2001), or via correction for voxels within a region of interest or spherical volume of 12mm diameter centred upon the search region, or via cluster threshold (Friston et al, 1994). These methods are consistent with those adopted elsewhere (Derbyshire et al., 2002; 1997; Rainville et al., 1997; Faymonville et al., 2003; Derbyshire, 2000) and provide a reasonable balance of protection against false positive without artificially concealing the real profile of activation.

5.2 Results

5.2.1 Behavioural data

Figure 5.2 shows the verbal pain ratings given for HI and PI pain in the screening and scanning sessions. In the screening sessions participants rated the PI pain as significantly more intense than the HI pain (paired samples, $t(7)=3.976$ $p<0.005$ two tailed, 95% CI [-0.405, 1.525]), however, despite the difference in intensity, PI pain was not found to be significantly more unpleasant than HI pain ($t(6)=1.678$ $p<0.144$ two tailed). Intensity and unpleasantness ratings for the physically-induced pain in the screening session were significantly correlated ($r=+.605$ $p<0.001$), as were intensity and unpleasantness ratings for the hypnotically-induced pain ($r=+.770$ $p<0.001$).

Participants rated the perceived intensity of each physically induced (PI) and hypnotically induced (HI) stimulus immediately following each scanning block using a verbal rating scale (0, no pain; 10, maximal pain). Average pain rating following actual delivered stimulation (PI) was 5.7 (range 3-10) and average rating without stimulation (HI) was 2.8 (range 1-9). This difference was statistically significant ($t(82)=6.481$ $p<0.001$, 95% CI [1.93, 3.86]). Intensity of physically-induced pain was not rated significantly differently by the participants between the screening and scanning sessions ($t(7)=0.601$ $p=0.567$ two tailed), nor were the intensity of hypnotically-induced pains rated significantly differently across sessions ($t(7)=1.344$ $p=0.221$ two tailed). Only one subject reported actually experiencing pain (of a low intensity and only on some trials) during the imagined block but all said that they had imagined it clearly. Four of the subjects reported a sensation of increased heat in the imagine condition.

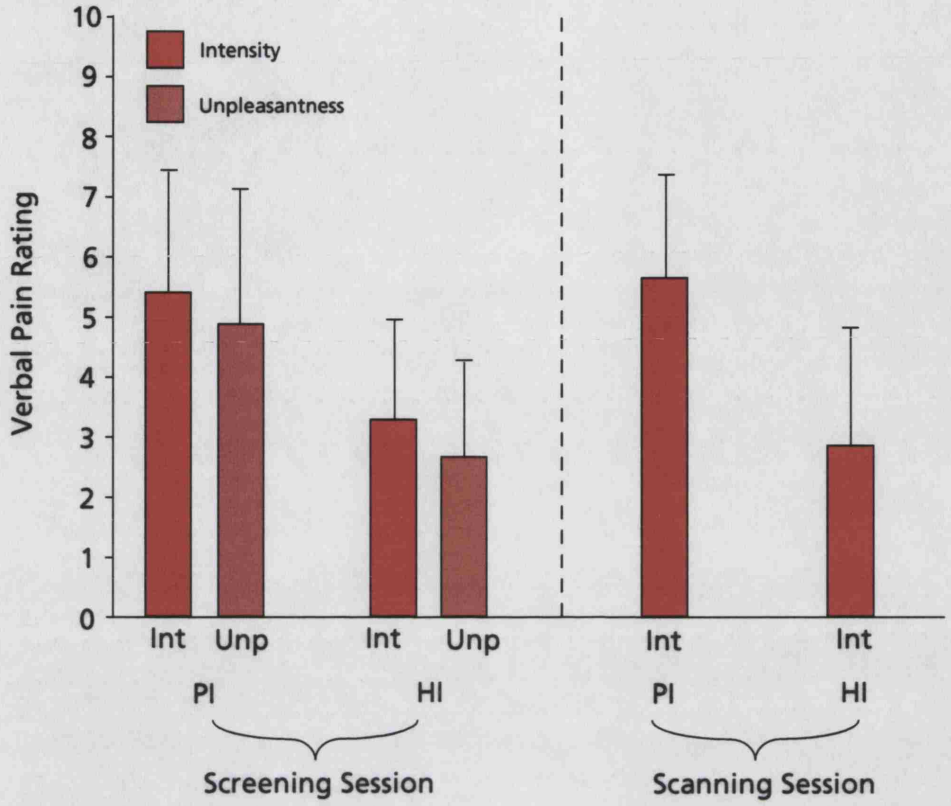


Figure 5.2: Verbal pain ratings taken from participants during the screening and scanning sessions.

5.2.2 Brain activation

The profiles of brain activation dependent upon these perceptual changes in pain intensity are illustrated in figure 5.3 and tabulated in table 5.1. Activation of the thalamus, anterior cingulate cortex (A24'/32'), cerebellum, S2, insula, inferior parietal cortex (BA 39/40) and prefrontal cortex (BA 9/10/46) are common to both physically and hypnotically induced pain although generally with greater intensity and extent during actual stimulation. The imagined condition, in contrast, provided minimal activation in the ACC (A32' extending into medial premotor cortex), insula and S2. Activation in S1 was observed only during HI pain.

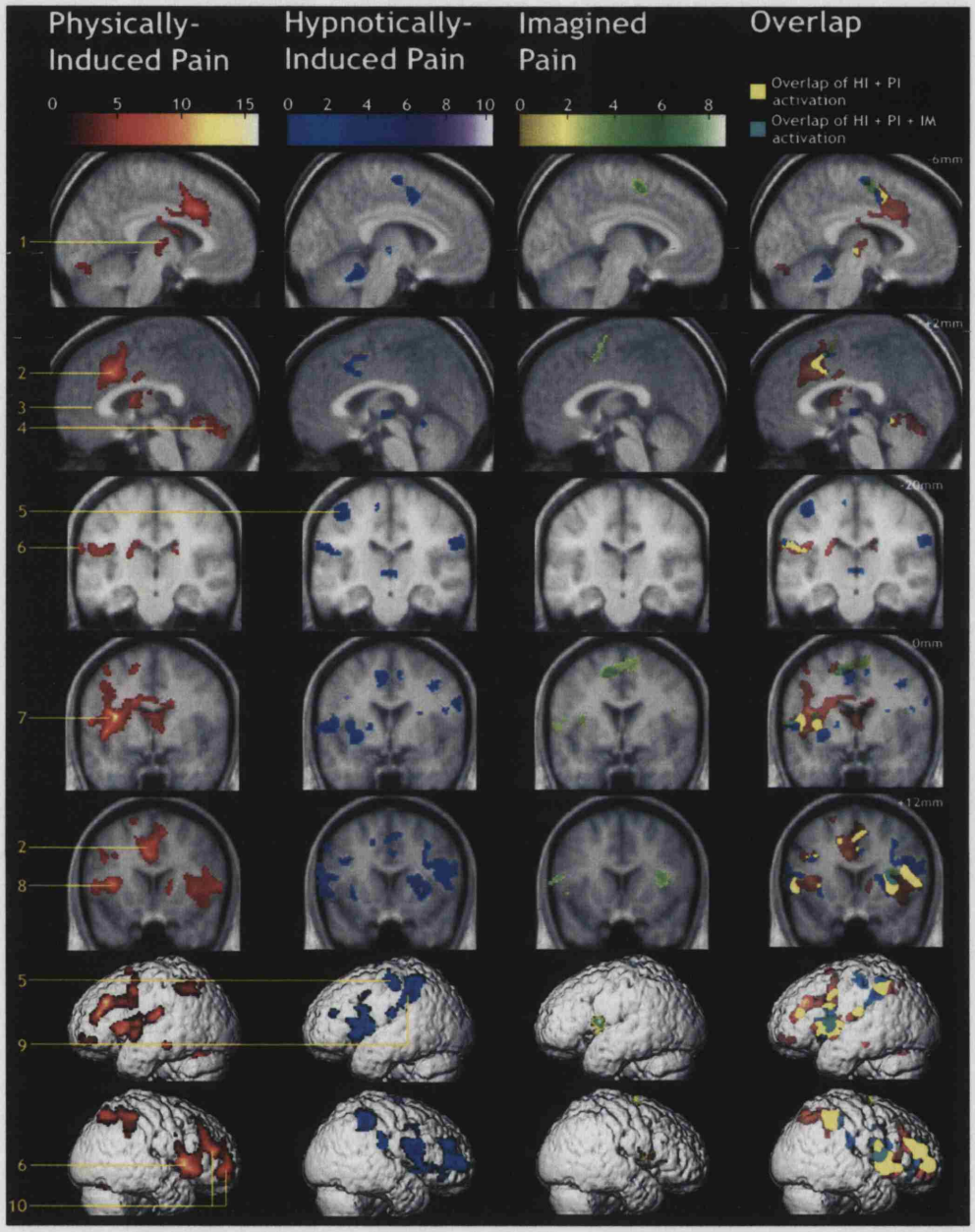


Figure 5.3: Shows activated voxels during physically-induced pain (first column, red-yellow scale), hypnotically-induced pain (second column, blue-purple scale), imagined condition (third column, yellow-green scale), and overlap of activations (fourth column). The effects are shown as SPMs superimposed on an averaged structural MRI derived from the subject's own structural scans. At the top are saggital slices 6mm and 2mm lateral to the midline. Below are coronal slices 20mm posterior (negative), on (0mm), and 12mm anterior (positive) to the anterior commisure. At the bottom are surface projections.

BOLD Increases relative to rest																
(x, y, z coordinates) (region)						(x, y, z coordinates)						(x, y, z coordinates)				
HI	T-Score	$P_{FDRcorr}$	Cluster Size	Pcorr		T-Score	$P_{FDRcorr}$	Cluster Size	Pcorr		T-Score	$P_{FDRcorr}$	Cluster Size	Pcorr
1. Thalamus														
(0,-16,0)	5.7	0.10[b]	74	ns	(-18,-14,10)	7.0	0.04[a]	9590	0.00	No response	-	-	-	-
					(8,0,4)	3.9	0.05[a]	9590	0.00	No response	-	-	-	-
2. ACC														
(-4,4,48)	4.2	ns	417	0.05	(-6,10,46)	6.3	0.06	9590	0.00	No response	-	-	-	-
(6,8,34)	4.3	ns	417	0.05	(8,20,32)	12.0	0.04	9590	0.00	No response	-	-	-	-
3. pACC														
No response	-	-	-	-	No response	-	-	-	-	No response	-	-	-	-
No response	-	-	-	-	No response	-	-	-	-	No response	-	-	-	-
4. Cerebellum														
(-12,-40,-30)	5.3	0.05[b]	187	ns	No response	-	-	-	-	No response	-	-	-	-
(8,46,-10)	5.6	0.05[b]	118	ns	(14,-72,-16)	9.8	0.04	872	0.00	No response	-	-	-	-
5. S1														
(-30,-16,60)	9.7	0.01[b]	332	ns	No response	-	-	-	-	No response	-	-	-	-
No response	-	-	-	-	No response	-	-	-	-	No response	-	-	-	-
6. S2 / Insula														
(-56,16,-2)	9.7	0.01[a]	808	0.00	(-58,-28,-12)	6.7	0.06	110	ns	(-56,8,14)	5.6	0.04[b]	339	ns
No response	-	-	-	-	No response	-	-	-	-	No response	-	-	-	-
7. M. Insula / Putamen														
(-30,0,-6)	5.7	0.05[b]	374	ns	(-38,2,18)	16.1	0.03	9590	0.00	No response	-	-	-	-
(28,10,4)	10.3	0.00[a]	2572	0.00	No response	-	-	-	-	(34,12,16)	4.5	0.05[b]	248	ns
8. A. Insula														
No response	-	-	-	-	(-34,12,8)	9.1	0.04	9590	0.00	No response	-	-	-	-
(40,18,16)	7.4	0.03[a]	2572	0.00	(38,14,6)	5.6	0.05	9590	0.00	No response	-	-	-	-
9. Inf. Parietal Cortex														
(-46, -48,60)	7.5	0.04[a]	1017	0.00	(-32,-52,40)	6.7	0.06	1120	0.00	No response	-	-	-	-
(56,-42,48)	7.0	0.07[a]	606	0.01	(30,-70,56)	5.8	0.07	1452	0.00	No response	-	-	-	-
10. PFC (BA 9/46)														
(-50,42,24)	3.9	ns	56	ns	(-44,34,34)	15.1	0.03	9590	0.00	No response	-	-	-	-
(60,14,20)	8.3	0.01[b]	2572	0.00	No response	-	-	-	-	No response	-	-	-	-
10. PFC (BA 10/46)														
No response	-	-	-	-	(-48,42,18)	10.0	0.04	9590	0.00	No response	-	-	-	-
(40,60,4)	7.7	0.01[b]	2572	0.00	(40,54,-2)	7.2	0.05	9590	0.00	No response	-	-	-	-

Table 5.1: Shows the regions with increased BOLD relative to rest due to HI, PI, and IM conditions separately. The areas are tabulated in terms of brain region, as illustrated in figure 5.3, and their Brodmann's areas (BA). The *x, y, z* coordinates plot each peak (defined as the pixel with the highest T-score within each labelled region) according to the MNI coordinate system (negative is left, posterior and inferior; contralateral listed first for each region). P values based on the false discovery rate (FDR) – see text for details. If a region reached significance for any comparison then the region is tabulated for all comparisons and for both sides except where no voxels reached the display threshold ($p<0.01$ uncorrected) indicated as no response. ACC = anterior cingulate cortex; pACC = perigenual anterior cingulate cortex; S1 = primary sensory cortex; S2 = secondary somatosensory cortex; M. = mid; A. = anterior; P = posterior; Inf. = inferior; PFC = prefrontal cortex.

The differences in activation between these conditions were formally assessed and the results shown in figure 5.4 and tables 5.2 and 5.3. HI pain resulted in marginally greater activity of the mid insula, S1 and orbitofrontal cortex (BA 11/47) while actual noxious stimulation produced greater activity of the thalamus and mid (A24') and perigenual anterior cingulate (A24), prefrontal and inferior parietal cortices. Greater activation throughout the pain matrix was evident for both hypnotically and physically induced pain relative to the imagined condition.

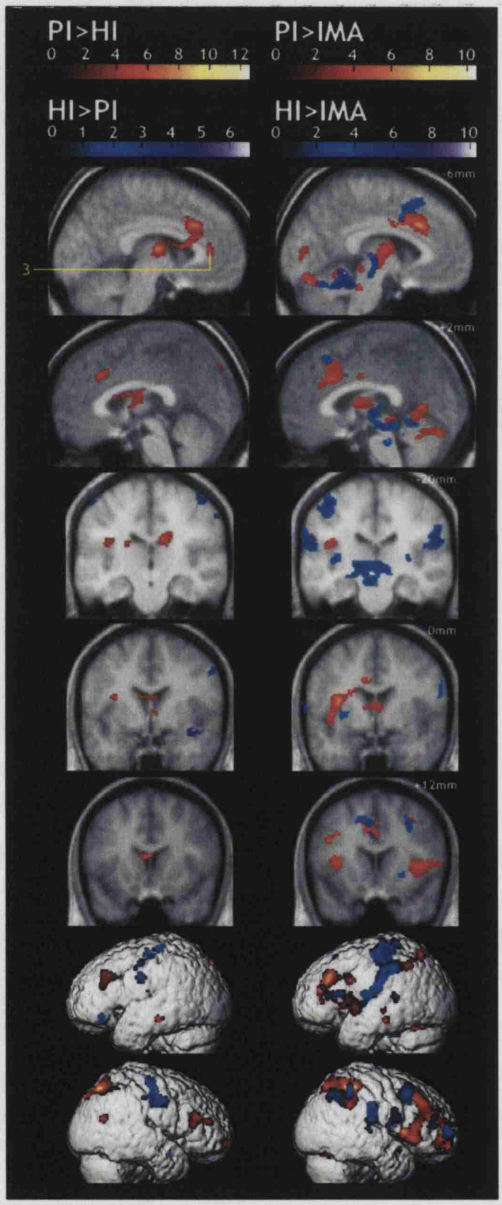


Figure 5.4: Shows the differences between the physically-induced (PI) and hypnotically-induced (HI) conditions to the left and the differences compared with the imagined (IM) condition to the right. The effects are shown as SPMs superimposed on an averaged structural MRI derived from the subject's own structural scans. At the top are saggital slices 6mm and 2mm lateral to the midline. Below are coronal slices 20mm posterior (negative), on (0mm), and 12mm anterior (positive) to the anterior commisure. At the bottom are surface projections.

Differences between HI and PI									
(x, y, z coordinates) (region)					(x, y, z coordinates)				
HI>PI	T-Score	$P_{FDRcorr}$	Cluster Size	Pcorr	**PI>HI**	T-Score	$P_{FDRcorr}$	Cluster Size	Pcorr
1. Thalamus									
No difference	-	-	-	-	(-14,-14,10)	11.05	0.02[a]	1474	0.00
2. mACC									
No difference	-	-	-	-	(-4,26,34)	9.4	0.03[a]	1474	0.00
3. pACC									
No difference	-	-	-	-	(-8,36,12)	8.4	0.03[b]	1474	0.00
4. Cerebellum									
No difference	-	-	-	-	No difference	-	-	-	-
5. S2									
No difference	-	-	-	-	No difference	-	-	-	-
6. M. Insula									
(38,-2,16)	6.6	0.06[b]	84	ns	No difference	-	-	-	-
7. A. Insula									
No difference	-	-	-	-	No difference	-	-	-	-
8. S1									
(50,-14,42)	5.6	ns	410	0.03	No difference	-	-	-	-
9. OFC					PFC				
(-42,34,-12)	6.4	0.05[b]	63	ns	(-42,30,34)	5.1	0.05[b]	160	ns
10. IPC									
No difference	-	-	-	-	(32,-72,54)	12.5	0.00[b]	1149	0.00

Table 5.2: Shows the regions with significantly greater BOLD response during HI compared with PI (HI>PI) or vice versa (PI>HI). The areas are tabulated in terms of the brain regions as illustrated in figure 5.3. OFC = orbitofrontal cortex; IPC = inferior parietal cortex. Other details and abbreviations are as for table 5.1.

Comparisons with imagined									
(x, y, z coordinates) (region)					(x, y, z coordinates)				
HI>Imagined	T-Score	$P_{FDRcorr}$	Cluster Size	Pcorr	**PI>Imagined**	T-Score	$P_{FDRcorr}$	Cluster Size	Pcorr
1. Thalamus									
(-16,-24,-2)	5.6	0.03[b]	2050	0.00	(-12,-10,14)	6.1	0.05[a]	839	0.00
(14,-14,0)	7.2	0.03[b]	2050	0.00					
2. mACC									
(-4,10,46)	5.8	0.04[b]	471	0.02	(-8,24,32)	6.9	0.05[a]	789	0.00
					(10,30,26)	7.1	0.04[a]	789	0.00
3. pACC									
No difference	-	-	-	-	No difference	-	-	-	-
4. Cerebellum									
(-6,-46,-12)	10.3	0.00[b]	2050	0.00	(-26,-60,-24)	7.6	0.01[b]	1023	0.00
					(18,-70,-22)	10.5	0.00[b]	1023	0.00
5. S2					S2 / P. Insula				
(-68,-4,-4)	8.7	0.01[b]	2708	0.00	(-42,-12,18)	6.3	0.04[b]	921	0.00
6. P. Insula					M. Insula				
(-36,-26,8)	6.1	0.03[b]	2708	0.00	(-34,2,16)	10.2	0.01[b]	921	0.00
7. A. Insula									
No difference	-		-	-	(-36,16,12)	4.3	0.05[b]	921	0.00
					(38,14,6)	5.3	0.04[b]	2083	0.00
8. S1									
(-34,-28,60)	10.2	0.02[a]	2708	0.00	No difference	-	-	-	-
9. PFC									
(-48,28,14)	4.2	0.08[b]	156	ns	(-46,34,34)	8.6	0.01[b]	495	0.04
(42,58,4)	7.5	0.01[b]	192	ns	(32,60,12)	6.9	0.04[b]	2083	0.00
10. IPC									
(38,-56,42)	4.7	0.03[b]	330	ns	(-28,-50,44)	7.7	0.06[a]	774	0.00
					(30,-50,44)	9.0	0.03[a]	1845	0.00

Table 5.3: Shows the regions with significantly greater BOLD response during HI compared with the Imagined condition (HI>Imagined) and during PI compared with the Imagined condition (PI>Imagined). The areas are tabulated in terms of brain regions as illustrated in figure 5.3. P.Insula = posterior insula. Other details and abbreviations are as for table 5.1.

To directly assess the dependence of brain activation upon pain rating, the subjects with the highest and the lowest pain ratings during HI pain were analyzed separately and the result shown in figure 5.5. A subject with an average pain rating during actual stimulation that matched the highest HI pain was also analyzed separately for comparison. As might be predicted from previous work (Coghill et al, 2003; Derbyshire et al, 1997) higher subjective ratings are associated with greater cerebral activity. Critically this effect is comparable whether the pain source is noxious heat or hypnotic suggestion.

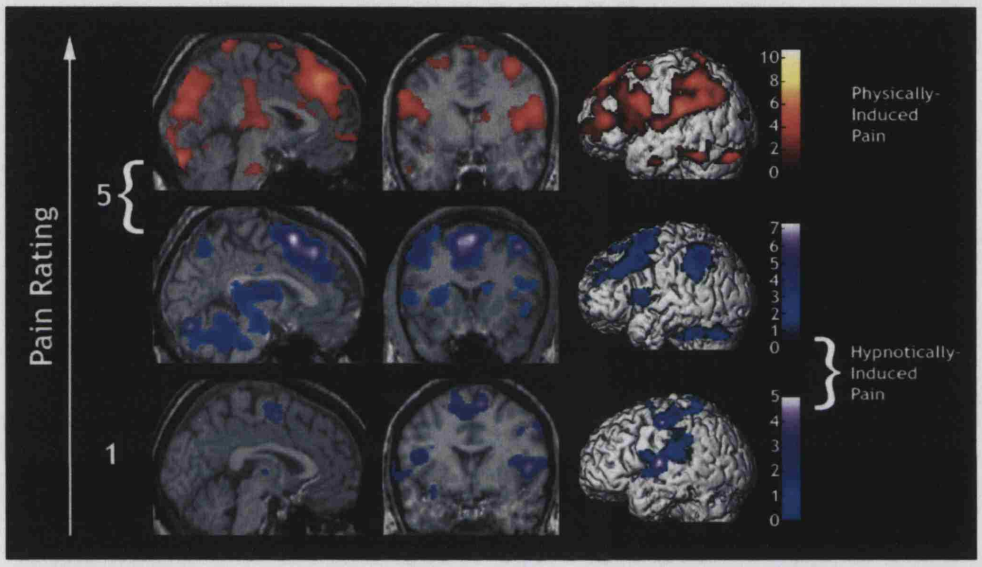


Figure 5.5: Shows the results from three individual participants. At the bottom are the activations during HI pain for the subject with the lowest average pain rating (average rating of six HI = 1); in the middle are results for the subject with the highest average rating (=5) for HI; at the top are results from a single subject with a PI rating matching the highest HI rating (=5). The SPM results are shown superimposed on a left, contralateral, sagital slice, a coronal slice and projected onto the left surface of each subject's own brain.

5.3 Discussion

fMRI data were obtained during conditions of physically-induced and hypnotically-induced experiences of heat pain interleaved with periods of rest, revealing common activation of the thalamus, ACC, mid-anterior insula and parietal and prefrontal cortices (see table 5.1 and figure 5.3). These findings indicate the efficacy of suggestion following hypnotic induction in producing altered sensory experience, as has been claimed elsewhere, with specificity of the response to the stimulus under investigation (Rainville et al, 1997; Szechtman et al, 1998; Kosslyn et al, 2000). Compared to the rest condition, pain from a nociceptive source and hypnotically induced pain both activated regions of the brain that have been variously described as belonging to a pain

network or neuromatrix (Treede et al, 1999; Casey, 1999; Peyron et al, 2000; Price, 2000; Derbyshire, 2000). In contrast, merely imagining the presence of a noxious heat stimulus resulted in only minimal activation of the pain network, extensively reduced compared with both physically and hypnotically induced pain experience. These results are comparable to those demonstrated using auditory sensation where physically presented and hypnotically induced sounds resulted in activation of the right ACC but imagining the same sound in hypnosis did not. These results from the IM condition, an incomplete activation of the pain matrix, compare well with the results observed in response to 'felt' pain (e.g. Willoch et al, 2000) and imagined pain (e.g. Rosen et al, 2001). Results concerning imagination in other modalities also appear to support this much-reduced pattern of activity underlying imagined relative to actual percepts.

	S-I	S-II	ACC	Thalamus	Insula	PFC	PAG	SMA	Basal Ganglia	Cerebellum	Striatum	IPC (BA39/40)	OFC	Brainstem	Frontal Cortex	Lentiform Nucleus
Porro (2003) Review of activations in response to acute pain	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑						
Peyron et al (2000) Review of activations in response to acute pain	↑	↑	↑	↑	↑		↑	↑		↑	↑					
Derbyshire (1999) Review of activations in response to acute pain	↑	↑	↑	↑	↑	↑					↑	↑				↑
HI	↑	↑	↑	↑	↑	↑				↑		↑				
PI		↑	↑	↑	↑	↑				↑		↑				
IM		↑			↑											

Table 5.4: Activations observed in this study shown in comparison with those commonly found functional imaging studies of acute pain.

Though hypnosis was used here as a tool to produce the intended subjective effect, it is possible to interpret the pain experienced during the HI condition in terms of phenomena other than hypnosis per se, such as a form of conditioned response to the double tap. However, the results described in chapter 3 would argue against this; only highly hypnotisable individuals are able to consistently report hallucinated experience in the absence of a stimulus, and only high hypnotisables were selected for the current study. The precise role of hypnosis can not be ascertained until further

studies investigating non-hypnotic suggestion are conducted. Research indicates that the hypnotic induction may be neither necessary nor sufficient to produce response to suggestion (Braffman and Kirsch, 1999). And, as reviewed in chapter 1, Schweiger and Parducci (1981) demonstrated the non-hypnotic production of functional headaches in normal participants. None of this materially alters the interpretation of the present findings. Activation observed during the hypnotically induced pain experience can be interpreted without the usual caveats concerning incidental sensory or motor processing that might be associated with an actual stimulus regardless of the precise influence of hypnosis in the study.

Higher levels of activation when comparing physically with hypnotically induced pain were demonstrated in contralateral thalamus, ACC and orbitofrontal cortex and in the ipsilateral parietal cortex. These larger responses could be due to the more intense pain experience during PI but may also reflect the presence of peripheral sensory information (Coghill et al., 2003; Derbyshire et al., 1997). Greater activation in the HI relative to PI condition incorporated bilateral S1 (overlapping with adjacent primary motor cortex (M1)) partly as a consequence of decreased response in the PI condition (decreases not shown). Variable S1 responses to noxious stimuli have been reported with a mix of both increases and decreases (Peyron et al., 2000; Derbyshire et al., 1997; Derbyshire, 2000). In general, S1 activation occurs in about 50% of pain studies and is usually within the appropriate somatotopical region (Derbyshire et al., 1997). Regions of S1 not currently engaged by the stimulus (such as the foot area when stimulating the hand) have been demonstrated as reducing blood flow possibly to enhance the spatial localization of the stimulus (Apkarian et al., 1992; Drevets et al., 1995). These spatial localization mechanisms may be more apparent when delivering an actual stimulus relative to the hypnotically induced pain experience. Significant activation in the PI condition relative to HI also incorporates the perigenual ACC (pACC, A24 approaching A25). This effect follows decreased response in the HI condition. Decreased pACC activation has been previously reported during the anticipatory phase prior to delivery of stimulation that may be similar to the anticipation or internal monitoring of sensory information during HI pain (Porro et al., 2002). Although the activations observed have been taken to reflect pain processing, it is also possible that they subsume some other non-pain-specific effects such as anticipation of pain, and the control systems which are generating and monitoring the experience. Additionally, since participants were given a suggestion to ignore the background noise, activity underlying this process could be present. Some of these caveats are common to 'baseline' and 'pain' conditions and may be cancelled out in the analysis, and additional correlational analysis whereby subjective pain scores are correlated with BOLD response presents an opportunity to study more closely the factors of interest. However, since there is significant overlap in activations common to pain and hypnosis (in areas such as the ACC and PFC) it is difficult to completely

separate the two. Future studies focussed more specifically on these issues will clarify expected activation patterns (e.g. anticipation of pain: Ploghaus et al, 1999).

Overall, however, figure 5.3 illustrates a considerable overlap in the processing of both hypnotically and physically induced pain. Figure 5.5 further demonstrates predictable levels of activation based on the perceptual report of pain experience independent of actual nociceptive input. These findings extend beyond the general suggestion of a neural network for pain by providing direct evidence that regional activation is specifically and actively involved in the generation of pain in the absence of stimulation. This is the first demonstration of a functional pain experience measured with brain imaging in neurologically intact normal controls. By demonstrating a material basis for pain experience in the absence of injury or other physical stimulus these findings raise the possibility of direct cortical involvement in the generation of functional pain. One key point to come from this investigation is confirmation that hypnotic suggestion is a useful cognitive tool and that with appropriate modification of technique its use can be successfully extended to the fMRI environment for group studies. This ability of hypnotic suggestion to produce reversible changes in subjective experience promises to be a useful manipulation in future psychological investigation (Raz & Shapiro, 2002).

Chapter 6 - Hypnotic pain modulation with chronic pain patients

6.0 Introduction

The results detailed in the previous chapter indicate that it is possible to generate an experience of functional pain in healthy volunteers, and that this experience is underscored by specific neural activation similar to that observed with physically-induced pain. The success of using hypnosis in fMRI in that study led to the opportunity to conduct a functional imaging investigation on patients with chronic pain. As detailed in section 4.4, most current neuroimaging studies of functional pain have resorted to 'stressing the system', observing differences between control and patient populations in response to a physiological stressor. By using hypnotic suggestion as a cognitive tool, however, it is possible to overcome the 'baseline' problem found with chronic pain and to modulate patients' experience of their own pain. This allows for statistical analysis which can reveal neural activity associated with those changes.

The aims of this pilot study were twofold: for MW to gain experience of using hypnosis for pain relief with patients suffering from functional pain; and to test the practicality of a set of suggestions and imagery for pain relief which would be acceptable to these patients and translate well into fMRI (chapter 8 reports the results of the subsequent imaging study). A consultant psychiatrist at the Eastman Dental Hospital gave MW access to patients in her clinic under the expectation that patients with temporomandibular joint dysfunction (TMJD) and fibromyalgia would be relatively easily available.

Temporomandibular disorders (TMDs) are characterised by pain and discomfort in the jaw joint and its muscles. Patients sometimes also experience 'clicking' and 'popping' feelings in the joint and other symptoms such as spasm in the jaw muscle which extends into the head and down into the neck. It is acknowledged that the term TMD is a 'catch-all' encompassing a wide range of clinical symptoms and that scientifically-based guidelines for the diagnosis and management of patients with TMD have not yet been formulated (Temporomandibular Joint Disorders Interagency Working Group, 2000). Fibromyalgia is characterised by widespread musculoskeletal pain, fatigue, poor sleep and tenderness at multiple sites (Gran, 2003; Wolfe et al, 1990). Citing significant diagnostic overlap with disorders such as IBS and CFS Wessely et al(1999) and Aaron & Buchwald (2001) group fibromyalgia and TMD with the other functional disorders. At present no organic basis plausibly exists to account for the severity of symptoms of TMD or fibromyalgia and psychological factors are acknowledged to play a part in its

maintenance. As such these patient populations were considered adequate as a group for preliminary testing of hypnotic analgesia on functional pain patients.

The use of hypnosis with chronic functional pain patients has, until recently, not received strong support from the experimental literature. Current evidence from controlled trials with a credible placebo condition has focussed mainly on the treatment of chronic headache although other conditions such as cancer pain and fibromyalgia have been studied. In their review of all available controlled studies investigating hypnotic treatment for chronic pain Patterson & Jensen (2003) conclude that hypnosis provides greater pain relief than no-treatment, standard care or structured attention conditions but that it does not necessarily give better results than autogenic or relaxation training conditions. In a study comparing hypnosis with physical therapy specifically in fibromyalgia patients Haanen et al (1991) found greater improvements in the hypnosis group on measures of fatigue, muscle pain and sleep disturbance that were maintained at follow-up. Additionally, there is some evidence that temporomandibular joint disorders are responsive to hypnotic treatment (Somer, 1997).

The effectiveness of hypnosis in the long-term treatment of chronic pain conditions is, however, only of partial relevance here. The present aim is to acutely modulate patients pain in a controllable way, not to effect a long-term change. As such, the strong evidence regarding the efficacy of hypnotically-induced analgesia across different pain types, including clinical and experimental pains (Montgomery et al, 2000; Hilgard, 1994), indicates that such pain manipulation should be possible. Limitations of time and clinical opportunity restricted these pilot observations to two dental clinic patients; one with chronic temporomandibular joint pain, the other with a diagnosis of fibromyalgia. For convenience of presentation further background information on both these patients is given as part of the clinical observations in the Results section.

6.1 Method

Both of the participants in this pilot study were patients recruited from a clinic at the Eastman Dental Hospital, a specialist postgraduate dental hospital and were invited to take part in a brief study, that day, investigating the use of hypnosis in pain control. Qualitative and quantitative data from these patients are reported here. These sessions were conducted by MW in the presence of a chartered clinical psychologist who was familiar with the pain control techniques being used.

Participants were taken into a quiet room in the Eastman Dental Hospital. The role of hypnosis in pain control was discussed and any misconceptions about hypnosis allayed. Expectations of outcome were positively reinforced by a quick briefing regarding the utility of hypnotic suggestion in the amelioration of pain, specifically mentioning that up to 75% of people who try it find it helpful (Montgomery et al, 2000). Early and

current models of pain were also reviewed, and the variable link between pain and injury was stressed.

Participants were asked to describe their pain symptoms, including indexes of location, current intensity and average intensity. The outline of the session was then explained followed by the opportunity to ask questions. Participants were told at this point about the imagery which would be used in the session. In particular, the idea of a dial to represent their pain was introduced and they were asked to rate their pain at that moment (see figure 6.1). The rating on the dial was 'tied' to wherever they experienced the most pain. When asked for a rating on the dial participants were instructed to give a rating for the area which they had identified as the most painful. It was also acknowledged, however, that pain in other parts of the body may well be affected by the hypnotic suggestions. Participants were then led step-by-step through the procedures that would be used and again given the opportunity to ask questions.

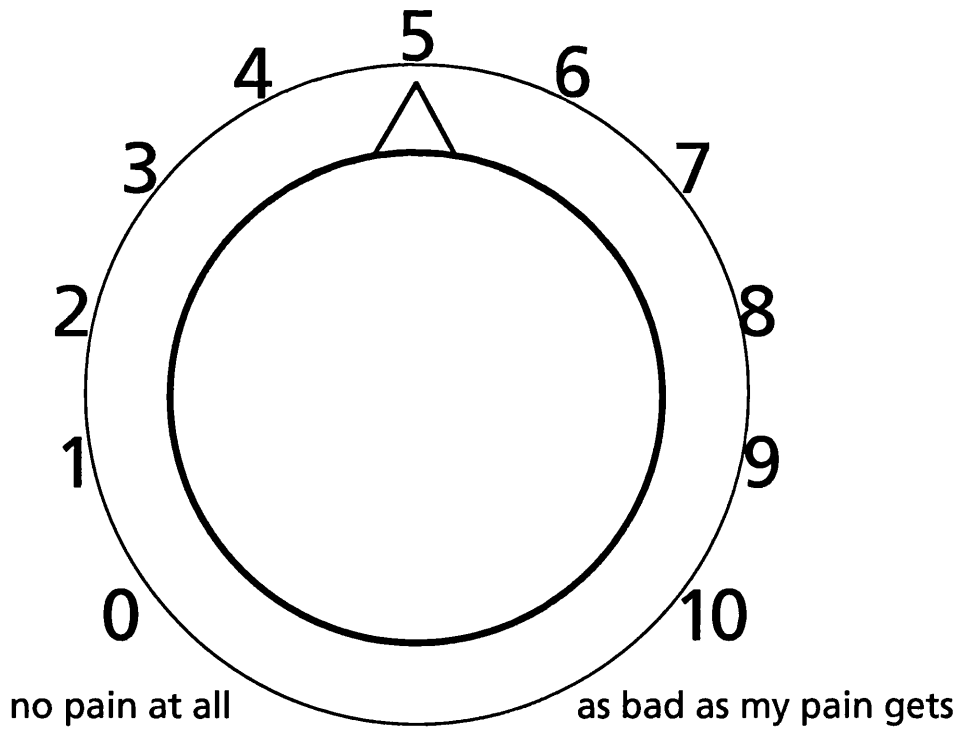


Figure 6.1: Diagram of the dial shown to participants to facilitate imagery in hypnosis and enable pain reports to be easily taken.

A standard hypnotic induction was given, with instructions for calm breathing, muscle relaxation, a descent into deeper feelings of relaxation, and a special place procedure. Participants were then asked to nod their head if it was alright to move on, and when a positive signal was given they were asked to picture very clearly in their mind a dial representing the pain they felt at that time. After the initial rating had been obtained

suggestions were given to *"allow the dial to move up"*, the pain becoming more intense as it did so. This is similar to the "paradoxical injunction" technique used in clinical settings to engender a feeling of control in the patient regarding their pain (Heap & Aravind, 2002). A further pain rating was obtained at this point. Permissive instructions were then given asking the patient to allow the dial to be turned down. Examples of the suggestions given include: *"and on the dial now which goes from 0-10 can you just give me a number which represents that feeling just at the moment [rating] just focus on that number X feeling, and see if you can allow it to go up/down"*; *"just noticing it becoming more and more [less and less] as time goes by"*; *"letting it go down, and noticing that feeling less and less"*. Each participant's pain experience was modulated up and down a number of times with ratings taken after each modulation.

Anticipating that these hypnotically unselected participants might not all respond well to the same suggestions alternative formulations were also prepared. These included asking patients to visualise a colour or shape representing their pain and giving suggestions to alter the colour/shape. Both participants responded to the dial imagery, however, and these alternatives were not utilised. Once control of the pain had been satisfactorily demonstrated the dial was left at as low a position as possible, the patient was then taken back to their special place and the hypnosis was terminated. Participants were then debriefed.

6.2 Results

Statistical analysis of the present data is not appropriate considering the small number of participants and observations. Instead, clinical observations for each participant are presented.

6.2.1 Participant 1

'Barbara' was a 60 year old female presenting with chronic temporomandibular joint pain (TMJ) that spread from her jaw to her eyes. She had previously had an unsuccessful operation to attempt to relieve the pain which she now regularly rated at 5/10. She described the pain as a kind of numbness and dull ache. Prior to the induction of hypnosis Barbara gave a description of a cool sandy beach as her special place. She described being alone on the beach, under the shade of a palm tree, lying on a lounger with a book and a drink. Asked to describe her feelings there while in hypnosis she said she could see the waves and yachts on the water. She could hear the sound of the water and the waves, apart from which there was silence. She was not feeling too hot or sticky and there were trees and rocks. Her description of her feelings in the special place were "not a care in the world" and "lovely, peace and quiet". After moving on from the special

place the imagery of the dial was elicited. Asked after hypnosis to describe what the dial looked like she responded that it looked like an egg timer.

Suggestion	Rating	Description
Before session	2/10	
First dial rating	9/10	"bad, instantly thought it was bad"
Turn dial down	2/10	"warm"
Turn dial down more	2/10	"numbness was warm"
Turn dial up	5/10	"a numb feeling, unpleasant"
Turn dial up more	7/10	"more intense, eye ache"
Turn dial down	0/10	"I was away, thin sort of numbness"
After session	0/10	"not so good as when I woke up"

Table 6.1: Ratings and pain descriptions given by patient one over the course of the experiment.

Barbara's pain ratings, taken after each suggestion for dial movement, and descriptions of each pain, taken after the termination of hypnosis, are given in table 6.1. In response to hypnotic suggestions of dial movement she reported large changes in ratings on the dial which were described after hypnosis as ranging from a numbness to an intense pain in her eye. Asked after the termination of the hypnosis how long it felt like the session (under hypnosis) has had lasted the patient said that it felt like 10 minutes. The actual time was 24 minutes. Time distortion is a common accompaniment of hypnotic procedures (Naish, 2003).

6.2.2 Participant 2

'Theresa' was an 18 year old female patient diagnosed with fibromyalgia. She had pain in her neck, shoulder, knees and jaw. The worst pain was described as being in her shoulder and jaw. At the time of the session, before hypnosis, she rated the pain in her shoulder as 3/10 and described it as "sharp and stabbing". She rated the pain in her jaw at 3 or 4 out of ten and described it as "constant cramped spasms" and "hot and tight". She admitted to being more anxious about the jaw pain. Prior to hypnosis she reported that she can become absorbed in films and books. Her pre-hypnosis description of her special place was of 100 Acre Wood (Winnie the Pooh). She described standing in the wood, on a warm sunny day with lots of space around her. On questioning in hypnosis she said she was on her own but that the characters were around her. She could see mounds of earth around and "other fun things" such as a lake, sandboxes and birds. Her words in the special place were that she was "wandering around, can see waterslide, tree house, balloons (red, green). Smell grape. It's fun. Can hear birds". After moving on from the special place Theresa was asked to visualise the dial representing her pain. Questioning after hypnosis determined that it looked like the dial she had been shown (figure 6.1).

Suggestion	Rating	Description
Before session	3/10	
First dial rating	1/10	"felt relaxed"
Turn dial up	4/10	"clenched up... pain in jaw... burney"
Turn dial up more	5/10	
Turn dial up more	7.5/10	"knew it wasn't real" Unp? "in a way"
Turn dial down	3/10	
Turn dial down more	2/10	
Turn dial down more	1/10	
Turn dial down more	0/10	
After session	1.5/10	

Table 6.2: Ratings and pain descriptions given by patient two over the course of the experiment.

Theresa's pain ratings and descriptions are given in table 6.2. In response to hypnotic suggestion she demonstrated substantial control over the dial and subsequently reported changes in pain intensity. Asked after the termination of the hypnosis how long it felt like the session (under hypnosis) has had lasted the patient said that it felt like 10 minutes. The actual time was 23 minutes. Asked about the location of the pain when the dial went up she responded that she felt the pain in her shoulder, which matched her earlier pain description.

6.3 Discussion

This pilot investigation demonstrated the efficacy of using hypnotic suggestion in the short-term control of pain associated with chronic pain conditions. Significant subjective control of pain was demonstrated with both TMJD and fibromyalgia. Both participants reported the experience of both increases and decreases relative to their presenting level of pain despite being unselected in terms of hypnotic ability. The clear time distortions and engagement with the imagery shown by both participants, however, is indicative of their absorption in the procedures as is typically seen in hypnotised subjects (Naish, 2003).

In the light of these observations it was concluded that the imagery and methodology used here was suitable for transfer into a functional imaging environment. Whilst it is not possible to comment on its potential long-term effectiveness, as an acute technique it demonstrated excellent control. Both patients understood the concept easily and responded positively to the suggestions. An important issue raised by these observations is whether the pain manipulation affected the clinically reported pain experience, as intended, or introduced a new pain experience. In both sets of observations the reported pain change related to a prominent component of the clinically presented

picture – eye pain in the case of Participant 1 (TMJD) and shoulder pain in Participant 2 (fibromyalgia). On this evidence it is tentatively concluded that it is the participant's clinical pain experience that is affected by the dial imagery manipulation in hypnosis.

It seems clear that the procedure was effective in producing altered pain ratings, but the demand characteristics of this experiment are strong and obvious. On the strength of these pilot observations it was decided to conduct a neuroimaging investigation of pain in patients with functional disorders (chapter 8) to provide more objective evidence regarding the hypnotic modulation of functional pain. Additionally, the success of acutely modulating pain supports the idea that hypnotic suggestion as part of a package of psychological therapies might be effective for the treatment of chronic functional pain.

Chapter 7 – Investigating the hypnotic susceptibility of fibromyalgia patients

7.0 Introduction

Oakley (1999b) proposes that pain disorder, conversion disorder and somatization disorder, which are categorised in DSM-IV (APA, 1994) under the Somatoform Disorders, fall within the scope of his description of 'auto suggestive disorder' for which hypnotic susceptibility is implicated as a risk factor. Wessely et al (1999) identify somatoform disorders as part of the 'functional somatic syndromes', drawing parallels between superficially diverse diagnoses as fibromyalgia, irritable bowel syndrome and chronic fatigue syndrome. If functional pains belong in the category of 'auto-suggestive disorder' as proposed by Oakley (1999b) then those who suffer from them are predicted to score higher than average on scales of hypnotic susceptibility.

Currently there exists some evidence for this hypothesis. Roelofs et al (2002), for example, measured the hypnotic susceptibility of a sample of 50 patients with conversion disorder and a sample of matched control patients with an affective disorder. It was found that conversion patients scored significantly higher on the Stanford Hypnotic Susceptibility Scale: Form C (Weitzenhoffer & Hilgard, 1962) than did the control group of affective patients, and that this difference was not due to possible repression of hypnotic susceptibility associated with depressed psychopathology in the affective disorders control group. Additionally, conversion patients scored significantly higher than a sample of non-psychiatric adults and demonstrated a strong link between hypnotic susceptibility and conversion symptom severity. One doubtful aspect of the study though, is the absolute mean score of the Stanford scale observed in the patient population. Conversion patients responded positively to 5.6 out of twelve items, placing them within the 'medium' range of scores on the Stanford rather than in the expected 'high' group. Other investigators have measured the hypnotic susceptibility of patients with functional symptoms. A study by Kuyk, Spinhoven and van Dyck (1999) demonstrated increased hypnotic susceptibility in a group of patients with pseudo-epileptic seizures compared with a group suffering from epileptic seizures. Bliss (1984) also found increased hypnotic susceptibility in a group of conversion patients, but Roelofs et al (2002) criticise previous work assessing this research question on methodological grounds, citing the common failure to include a control group. The results with regard to hypnotic susceptibility and conversion symptoms are not unambiguous though; a number of studies have failed to find a relationship between them. Moene, Spinhoven, Hoogduin, Sandyck and Roelofs (2001) failed to find higher

hypnotic suscpetibility in conversion patients and Goldstein, Drew, Mellers, Mitchell-O'Malley and Oakley (2001) failed to find higher hypnotic susceptibility in a group of pseudoseizure patients.

With even greater relevance to the specific symptomatology of functional pain, Crawford, Knebel, Kaplan and Vendemia (1998) tested the hypnotic susceptibility of a sample of chronic low back pain patients, often considered to have a functional component, and found them to score significantly above average on a modified Stanford Hypnotic Susceptibility Scale (mean of 7.87 [on an 11 point scale], compared to a norm value of 5.19 [on a 12 point scale]). However, the sample size of 17 makes it difficult to classify this as anything other than a tentative result, especially with no control group concurrently tested. Additionally, the authors acknowledge that the *"extraordinary magnitude"* of the pain-control demonstrated in the study was unusual when compared to typical hypnotic control of experimental pain in the laboratory and questioned whether the make up of the group was biased by self-selection. Stam, McGrath, Brooke and Cosier (1986) investigated the hypnotic susceptibility of 61 patients diagnosed as suffering from temporomandibular pain and dysfunction syndrome (TMPDS). Using the Carleton University Responsiveness to Suggestion Scale (CURSS) as a measure of hypnotic susceptibility it was found that facial pain patients scored significantly higher on both the objective and subjective scales than the norms reported from a population of college students (Spanos et al, 1983). However, the authors acknowledge that the differences in score could be due to differences in administration of the tests: college students had been tested in groups with the script played from a tape recorder, the patients had been tested individually with a live reading.

Wickramasekera's high risk model of threat perception (HRMTP: Wickramasekera, 1979, 1988, 1998a, 1993, 1995) hypothesises that risk factors including high or low hypnotic susceptibility and high social desirability, when they interact with negative affect, are predicted to amplify somatic symptoms or transduce threat into somatic symptoms. Specifically he states that *"high hypnotizables who block threatening secrets from consciousness will develop both psychological and somatic symptoms, whereas low hypnotizables and people with high Marlowe Crown [social desirability] scores will develop mainly somatic symptoms"* (Wickramasekera, 1998). If the model is correct then we might expect the hypnotic susceptibility scores of chronic pain patients to display a bi-modal distribution, as lows and highs should be more strongly represented in the clinical population. Kermit, Devine and Tatman (2000) tested this relationship in a sample of chronic pain patients, using the Tellegen absorption scale as a proxy measure of hypnotisability (although doubt has been expressed concerning the strength of the relationship between absorption and hypnotisability: Milling, Kirsch, Burgess, 2001). They concluded that their data supported the predictions of the HRMTP that patients with persistent pain will demonstrate psychometric risk factors hypothesised to drive

somatization disorders. Specifically their patient population (108 chronic pain patients who had not responded to standard medical management) scored significantly lower than a normative sample on the measure of absorption and significantly higher on a measure of social desirability. Wickramasekera, Pope and Kolm (1996) confirm a relationship predicted by the HRMTP that hypnotic susceptibility in chronic pain patients should correlate with physiological responses to stress or threat. Despite these and other indications of support for the HRMTP (e.g. Jorgensen & Zachariae, 2002; McGrady, Lynch, Nagel, Wahl, 2003) no investigations have specifically addressed the distribution of hypnotic susceptibility scores in a group of functional pain patients with relation to the HRMTP.

The aim of this study was to assess the hypnotic susceptibility of a group of fibromyalgia patients and to compare it with the results of a concurrently tested control group. Consistent with Oakley's (1999b) description of auto-suggestive disorder it was predicted that fibromyalgia patients would score higher than control participants on measures of hypnotic susceptibility.

7.1 Method

Participants for this study were recruited as part of a functional imaging investigation into the neural correlates of fibromyalgia (reported in chapter 8). Letters were sent to patients on the University of Pittsburgh Rheumatology Center database who met Fibromyalgia diagnostic criteria as specified by the 1990 American College of Rheumatology tender point protocol for FM (Wolfe et al, 1990). The letter invited patients to take part in an experiment investigating the effects of hypnotic suggestion upon the experience of fibromyalgia in fMRI. Patients who contacted the investigators were invited to take part in group hypnotic susceptibility screening sessions. Control participants were recruited through advertising placed around the campus of the University of Pittsburgh. Inclusion criteria for both groups were right handedness and an age of between 18 and 65. Participants were excluded if they reported being claustrophobic or had any metal implants.

Participants who contacted the investigators and satisfied the inclusion criteria were invited to take part in a group hypnotic susceptibility screening session. Sessions were run on groups of between two and twelve participants, consisting of a mix of patients and control participants. Participants were invited to read and sign the consent form for the full experiment and also completed the Hospital Anxiety and Depression scale (HAD: Zigmond & Snaith, 1983). A briefing regarding hypnosis was given as per the instructions in the manual for the Harvard Group Scale of Hypnotic Susceptibility: Form A (HGSHS:A: Shor & Orne, 1962). Specifically, participants were told that hypnosis is characterised by focussed attention and absorption, much like being

involved in a book or a play; they were assured that nothing would be done to embarrass them and that no personal information would be obtained during the test. Participants were given the opportunity to ask questions before the induction of hypnosis. The scale was delivered according to the instructions in the manual with the script being read to the participants by MW. The procedure lasted approximately 42 minutes. Participants then completed the standard response booklet, yielding an objective score (on a scale of 0-12), and an additional page to record the subjective strength of each suggestion (yielding a subjective score of 0-48).

7.2 Results

Forty-six fibromyalgia patients took part in this stage of the study (4 male). The average age was 52.35 (SD=11.82, range 21-74). Forty-three control participants took part (17 male). Their average age was 24.70 (SD=9.26, range 18-65). Age differed significantly by group $t(87)=12.227, p<0.0001$, 95% CI [26.99, 28.31], as did the ratio of males to females $t(87)=-3.933, p<0.0001$.

	N	Gender ratio M/F	Harvard Objective	Harvard Subjective	HAD Score
Patients	46	4/42	7.3 (2.77)	29.7 (10.25)	16.2 (7.82)
Controls	43	17/26	8.2 (2.38)	32.2 (8.45)	6.8 (4.30)

Table 7.1: Objective and subjective Harvard and H.A.D scores (Standard Deviation in brackets) for patients and controls.

T-tests were used to assess the difference in scores between the patient and control groups given in table 7.1. An independent samples t-test revealed no significant difference between the scores of the two groups on the objective measures of the Harvard scale ($t(87)=1.641, p=0.104$). Similarly, no difference between patients and controls scores was found for the subjective scale of the Harvard ($t(81)=1.208, p=0.230$). Analysis of the participants scores on the Hospital Anxiety and Depression Scale revealed that patients were significantly more depressed than controls $t(86)=7.065$, $p<0.0001$, 95% CI [4.58. 14.22]. Scores for patients and controls on all scales are given in figure 7.1. The potential relationship between depression and hypnotic susceptibility was examined for all participants revealing a non-significant correlation of r=-0.047, $p=0.660$. In light of the significant age difference between the control and patient groups the relationship between age and hypnotic susceptibility was assessed. For both patients and controls no significant relationships were observed (patients $r=0.075, p=0.618$; controls $r=-0.197, p=0.205$; combined $r=-0.155, p=0.146$).

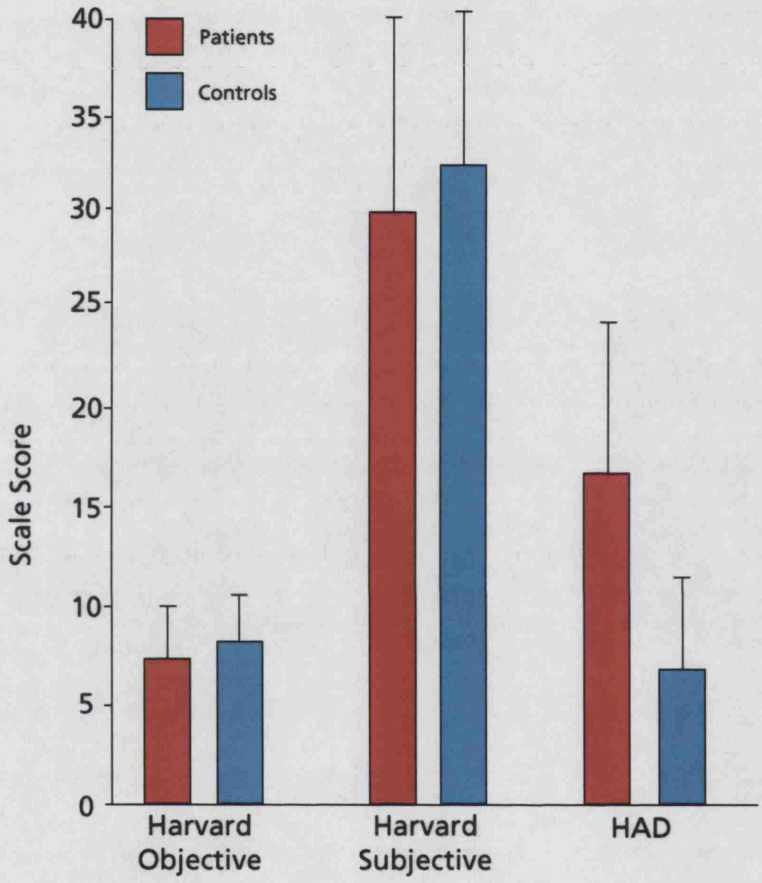


Figure 7.1: Scale scores for patients and controls.

A one-sample t-test was conducted to examine whether the mean of the Harvard objective scale for the patient population differed significantly from the norms reported by Shor & Orne (1963). The norm value taken from Shor & Orne (1963) was 7.39. The

This investigation was carried out collaboratively with Dr Stuart Derbyshire at the University of Pittsburgh Magnetic Resonance Research Centre. All contact with participants was by MW. The design of the study was constrained by the need to incorporate hypnosis procedures in the fMRI environment and the chosen methodology reflects the balance of competing interests such as time in scanner and pain to participants decided by MW to enable maximal acquisition of meaningful data. MW conducted all steps of the data analysis.

result was non-significant $t(45)=0.262$, $p=0.794$. However, the Harvard objective score of the present control group was significantly higher than that reported by Shor & Orne $t(42)=2.190$, $p=0.034$. The scores for patient and control groups were also tested against the most recent 'meta-norm' for the Harvard scale (Benham, Smith and Nash, 2002) which is given as 6.73. Patients did not score significantly differently from this norm $t(45)=1.349$, $p=0.184$, control participants scored significantly higher $t(42)=4.007$, $p<0.001$.

The distributions of hypnotic susceptibility for patient and control groups are presented in figure 7.2. The control group demonstrates a slight positive skew and the patient group more closely approximate a normal distribution.

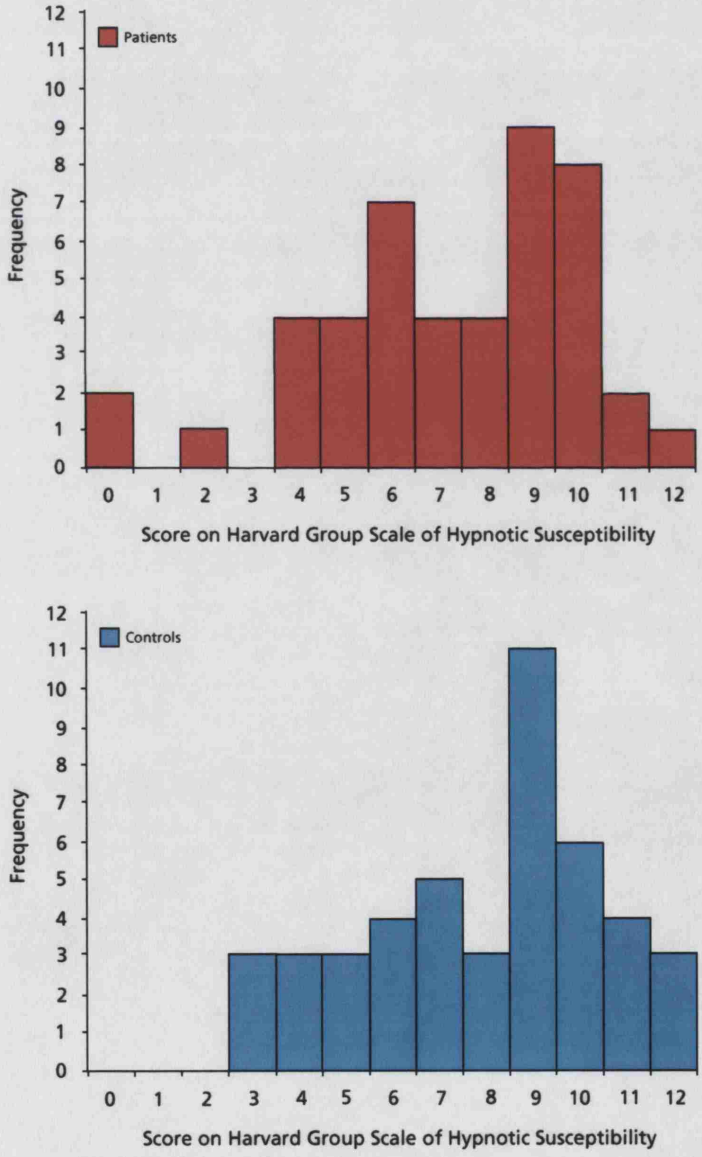


Figure 7.2: Distributions of hypnotic susceptibility for patients and controls.

7.3 Discussion

The results presented here do not demonstrate a significant difference in hypnotic susceptibility score between patients and control participants: in fact there was a trend for control participants to score higher on both the objective and subjective scales. The use of the Harvard Group Scale of Hypnotic Susceptibility instead of the individually-administered Stanford Scale would be considered by some investigators to be less reliable as a means of measurement. The Stanford Hypnotic Susceptibility Scale is typically considered to be the gold-standard of hypnotic susceptibility assessment (Heap & Aravind, 2002), often used to confirm scores obtained on a previously obtained Harvard. However, patients and controls were treated identically in this investigation and the choice of measurement tool cannot reasonably be considered to have systematically biased the result. A key criticism of the design of this experiment is that participant groups were not matched. Compared to the patient group the control participants were significantly younger, less depressed and consisted of a higher proportion of men. A more ideal comparison group might also have consisted of patients with similar levels of pain, of more obviously organic source, such as rheumatoid arthritis. The incomplete matching of controls to patients in the present study was the result of a number of factors. The primary purpose of the hypnotisability assessment was to provide highly hypnotisable patients for the functional imaging experiment described in chapter 8 and it was necessary to recruit these participants first in order to expedite the study. A more appropriate control group for the fibromyalgia patients might have been represented by an age-matched population of predominantly female patients with a known organic pain condition, such as rheumatoid arthritis. However, such a patient population was not easily accessible in the three months available to conduct and analyse the functional imaging study, and the compromise reached was to test a control group recruited from Pittsburgh University's undergraduate population.

A significant difference in age between the patient and control groups was observed and since age is a factor known to correlate negatively (albeit weakly, after peaking between the ages of 8 and 12) with hypnotic susceptibility (Morgan & Hilgard, 1973) the relationship between the two was investigated for present data. No significant correlations were observed and as a consequence the age differential between the groups is not believed to influence the hypnotic susceptibility scores obtained. Similarly, female participants are known to score slightly higher than males on tests of hypnotic susceptibility (Rudski, Marra, Graham, 2004) and the patient group in this study had a strong female bias. However, the observed result demonstrates a trend towards lower hypnotic susceptibility in the mainly female patient group and this factor is not believed to have influenced the result.

Although a non-significant correlation was observed between hypnotic susceptibility and depression the differential on HAD scores between patients and controls is noted

as a factor with potential to influence hypnotisability. There is very little literature available which directly examines the relationship between hypnotic susceptibility and how depressed individuals are. Spiegel, Hunt and Dondershine (1988) report the results of a study which compared the hypnotic susceptibility (assessed by the Hypnotic Induction Profile: Spiegel & Spiegel, 1987) of patients suffering from post traumatic stress disorder (PTSD) with patients suffering from affective disorders and also with a control group. The authors do not specifically report whether the depressed patients scored significantly lower than control subjects but a close examination of the statistics reported makes this a likely conclusion. Gruzelier, Champion, Fox, et al (2002) also report a significant negative relationship between hypnotic susceptibility and depression (as assessed by the HAD scale), although the small number of patients involved (N=21) makes it difficult to draw firm conclusions regarding this intriguing possibility.

One line of further investigation rests on the fact that Roelofs et al (2002) did not find that conversion patients scored significantly above the norm on measures of hypnotic susceptibility, although they did score higher than a matched affective disorders control group (half of whom were depressed). Their key finding was that hypnotic susceptibility correlated significantly with the number of pseudoneurological symptoms reported by the conversion patients. Despite the lack of increased hypnotic susceptibility observed in the present study an obvious extension to the design would be to investigate the relationship between hypnotisability and the number of somatic complaints. Since many patients are given multiple diagnoses (e.g. fibromyalgia patients often also have IBS), and if the auto-suggestion hypothesis is correct, then we could expect to see higher levels of hypnotic suggestibility in patients with multiple functional somatic syndromes.

The predictions of the high risk model of threat perception (Wickramasekera, 1979, 1988, 1988a, 1193, 1995), that patients with a functional illness (*"somatoform and psychophysiological disorders"*: Wickramasekera, 1996) should demonstrate abnormally high or low hypnotisability scores, are not borne out by the results presented here (see figure 7.2). The data presented here do not tally with other studies investigating hypnotisability and chronic pain (e.g. Stam et al, 1986) which are cited in support of the model and as a result cast some doubt on to the empirical base of the HRMTP.

The present finding that fibromyalgia patients are not more highly hypnotisable than controls, does not support the hypothesis that functional pain should be considered an auto-suggestive disorder. There remains the possibility, however, that depressed mood in the fibromyalgia patients could be masking differences in hypnotic susceptibility, and investigation of the number of symptoms associated with functional somatic syndromes is worthwhile as another potential covariate of hypnotic susceptibility. The clear conclusion indicated by these results is that patients suffering from fibromyalgia do not as a group exhibit altered hypnotic susceptibility.

Chapter 8 – The functional neuroanatomy of fibromyalgia

8.0 Introduction

The aim of this investigation was to use fMRI to investigate the neural correlates of fibromyalgia. A major difficulty in the functional imaging of chronic pain conditions is the 'baseline problem'. As outlined in chapter 4, the traditional method of conducting functional imaging studies is to use subtraction methodology: brain activity due to task X is subtracted from brain activity due to task Y, thereby removing the components which are common to both and leaving activity related to the condition of interest (Frackowiak, Frith, Dolan, Mazziotta, 1997). Acute pain studies are well suited to this technique as the pain can be switched on and off, with the power of the study increased by multiple repetitions and longer acquisition times. With chronic pain though, subtraction methodology is not such a useful tool. Chronic pains, almost by definition, are not easily switched on and off. Techniques that are traditionally used to ameliorate chronic pain, such as drug treatments, unbalance the subtraction equation invalidating the contrast: brain activity might represent a drug effect as well as change in the experience of pain per se, and the two are not easily separable. In an attempt to overcome this problem researchers have resorted to alternative techniques.

As discussed in chapter 4 a number of teams have attempted to 'stress the system'. By comparing the responses of patients and controls to painful and non-painful stimuli it is possible to portion out the activity underlying augmented pain processing in functional pain syndromes such as fibromyalgia or IBS. Experiments by Gracely et al (2002) and Cook et al (2004) have demonstrated increased pain-related activation in patients compared to controls in response to a stimulus of the same intensity. Gracely et al argue that their result defies a 'psychological re-labelling' interpretation of how patients are reporting their pain experience, citing research by Coghill et al (1999) demonstrating a strong relationship between the subjective intensity of a pain experience and the strength of activations in the pain matrix. Cook et al go further, claiming that their results support a physiological explanation of FM pain. Functional imaging results will of course tend to be interpretable in terms of physiology, but psychological factors can also play an explanatory role in understanding changes in rCBF: for example, what is undoubtedly a psychological effect in Kosslyn et al's (2000) hypnotic modulation of colour perception is accompanied by significant blood flow changes to areas of the cortex involved in colour perception. Stressing the system has so far provided us with

clues to help us to understand some aspects of functional pain but has not tackled the mechanisms underlying the pain itself.

8.0.1 Wik, Fischer, Bragée, Finer, Fredrikson (1999)

In 1999 Wik and colleagues published an experiment aiming to investigate the mechanisms of hypnotic analgesia. They chose fibromyalgia patients on which to use hypnosis, recruiting eight highly hypnotisable (9+ on the Harvard Scale) women fulfilling the American College of Rheumatology criteria for fibromyalgia (Wolfe et al, 1990). Participants were scanned in two conditions using PET: resting wakefulness and hypnotic analgesia. One clear deficiency in this study design, as discussed in chapter 4, is that the investigators are not comparing like with like. A more suitable design would be to have the participants hypnotised in both conditions, but with suggestions for analgesia in only one of the conditions. As it stands the design by Wik does not allow possible neural activations due to the hypnosis (neutral hypnosis) to be partialled out from the effects from suggestions of analgesia. Therefore, any differences observed in rCBF could be due to any hypnotic analgesia obtained, or due to the induction of hypnosis. As a control for 'the visual aspect of resting differences' the participants were told, in both scanning conditions, to watch videos with scenes of individuals walking in a park; the authors do not explain why participants could not simply close their eyes in both conditions. During 'resting wakefulness' scans participants simply watched the videos. For the hypnotic analgesia scans participants were hypnotised by *"gently talking to the[m], instructing them to be relaxed and go into a deep trance, to watch the videotapes and not to feel any pain whatsoever"*. Pain ratings were taken on a VAS (0= no pain, 10=unbearable pain) directly after each scan.

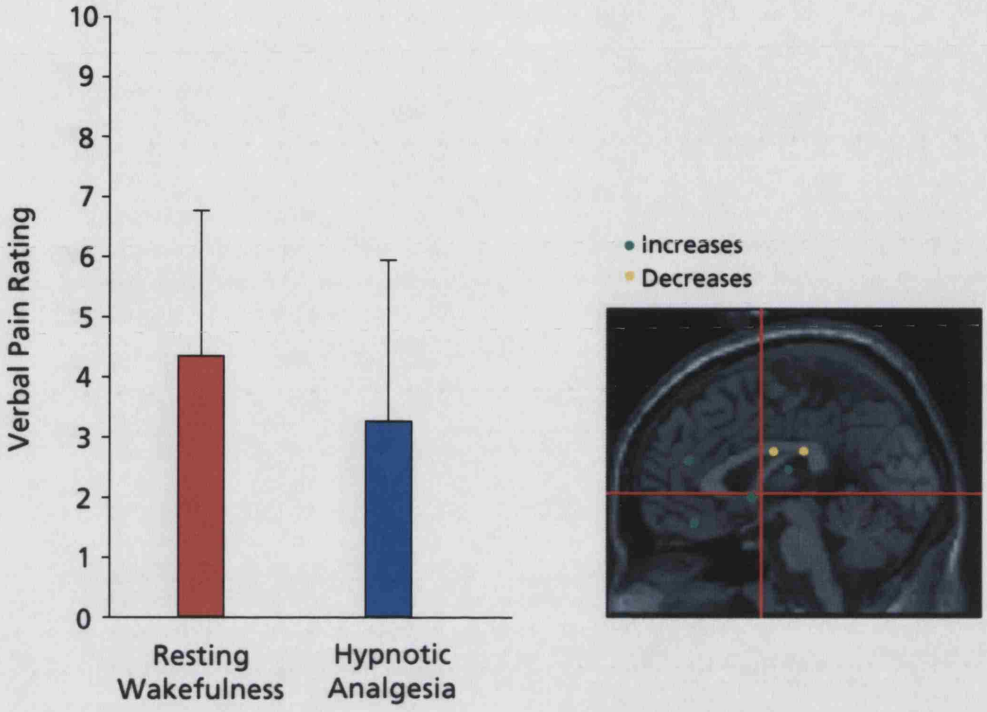


Figure 8.1: Graph displaying pain ratings obtained from fibromyalgia patients in conditions of resting wakefulness and hypnotic analgesia. Standardised brain volume displaying increases (green) and decreases (yellow) obtained when comparing conditions of resting wakefulness and hypnotic analgesia. Activations displayed on a standard brain normalised to MNI space. Saggital slice shown is at a 4mm X offset. Red grid intersects at 0, 0, 0 (x, y, z). Positions shown are approximate after translation from Talairach space (Data reconstructed from Wik et al, 1999).

A reconstruction of the data obtained by Wik et al (1999) is displayed in figure 8.1. Pain ratings were not significantly lower in the hypnotic analgesia condition compared to resting wakefulness. Subtracting the analgesia condition from rest (fibromyalgia pain as normal) led to increases in rCBF being observed in the subcallosal cingulate gyrus, left inferior parietal cortex, right thalamus, and orbitofrontal cortex. Decreases in rCBF were observed in anterior and posterior cingulate. Changes in rCBF in the thalamus, anterior cingulate and inferior parietal cortex could reflect changes in subjective pain experience, but overall interpretation of this data is difficult because of the methodological limitations. In a sense, drawing conclusions from the functional imaging data concerning the effects of hypnotic analgesia is not justified because it is not clear from their study that hypnotic analgesia was appropriately induced: only weak (non-significant) changes in subjective pain experience were observed. This is critical as it is uncertain what an increased thalamic activation means in the context of reducing pain.

Whilst it is difficult to draw firm conclusions from this investigation, a number of points should be noted. One key issue is that participants should not only be tested

on a hypnotic susceptibility scale but also on a test specific to the phenomenon being investigated in order to assure more chance of success in the scanner. The investigation described in this chapter advances the findings of Wik by using relatively standard hypnotic analgesia techniques (the pilot investigation of which was presented in chapter 6) that allow for repeated changes in pain experience, more suitable for an fMRI investigation. Participants in the present study also received suggestions for analgesia both in and outside hypnosis in a balanced design.

8.0.2 Choice of clinical group for study

Fibromyalgia patients were chosen as the focus of this investigation because they comprise a key component group representing functional somatic syndromes and represent a large and growing clinical population that imposes heavy costs on health care systems (Wessely et al, 1999). Alongside widespread tenderness the primary complaint of fibromyalgia patients is body-wide pain. Thus, in the context of investigating functional pain, fibromyalgia patients are a preferable group for study compared to patients presenting primarily with IBS or CFS where chronic pain is often present but the primary symptoms are gut discomfort or fatigue. On a practical level, the Pittsburgh Rheumatology Centre was able to provide a database of fibromyalgia patients available for hypnotic susceptibility testing, enough to generate a large cohort of high-hypnotisables most suitable for testing in fMRI.

8.1 Method

8.1.1 Selection information

Fibromyalgia patients were recruited into the study by means of information letters sent from the Rheumatology Centre at the University of Pittsburgh Medical Center. Letters were sent to 397 registered FM patients inviting them to take part in the study. 85 patients responded to the invitation and 46 were screened (as described in chapter 7).

8.1.2 First stage: hypnotic suggestibility screening

In the first stage of screening participants were given information about the study and gave their informed consent to take part. Hypnotic suggestibility was assessed using the Harvard Group Scale of Hypnotic Susceptibility, Form A (HGSHS:A: Shor & Orne, 1962). Participants scoring >8/12 on the objective scale were invited to take part in a second-stage screening. Forty-six patients attended this hypnotic susceptibility assessment, details of which are given in chapter 7.

8.1.3 Second stage: pain control screening

For the second stage of screening participants were assessed individually. They were informed that they had been invited back based on their hypnotic suggestibility score. They were reminded that the aim of the study was to use hypnotic suggestions for pain control and were given positive information to boost their expectations regarding the efficacy of hypnotic interventions especially in highly-hypnotisable subjects. Participants were informed about the range of pain conditions hypnosis is used to treat (Hilgard & Hilgard, 1994) and were briefed about some of the changes in brain activity observed in response to hypnosis and pain (Derbyshire, Whalley, Stenger, Oakley, 2004).

As with the pilot study (chapter 6) the specific imagery to be used was discussed with participants before the induction of hypnosis. A diagram of a dial was shown (figure 8.2), numbered from 0 (no pain at all) to 10 (as bad as my pain gets). Participants were told that the dial would represent how much fibromyalgia pain they were feeling at any particular moment and that hypnotic suggestions would be given to allow the dial to move up and down. They were informed that at various points throughout the session they would be asked for 'a number on the dial' and at this point they were to give a number from zero to ten representing their current level of fibromyalgia pain. Before hypnosis commenced participants were asked to give a brief description of their pain, naming the areas with the most severe pain. They were told that the dial should relate to their area of most severe pain, and that they were to give pain ratings for this area.

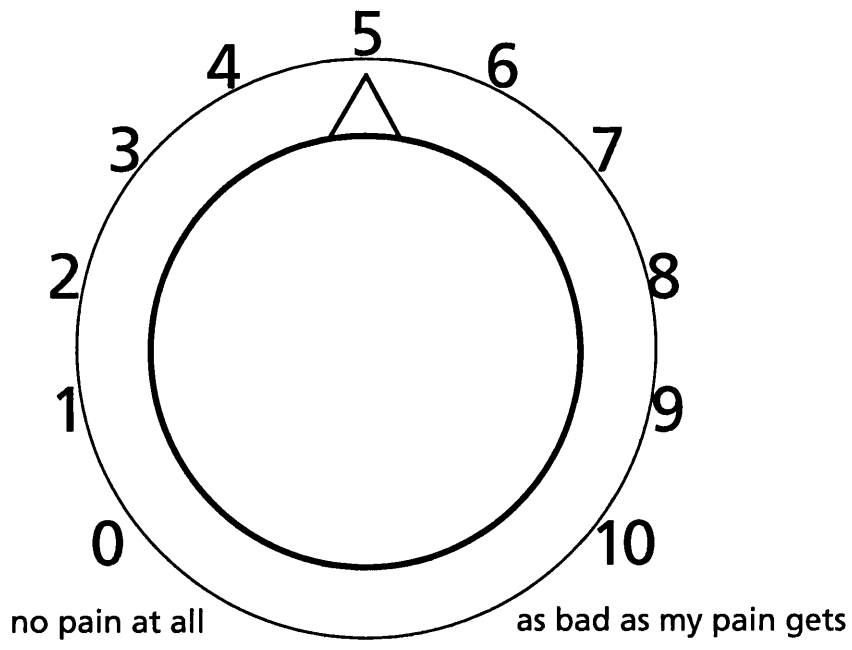


Figure 8.2: Diagram shown to patients to illustrate the suggested dial imagery.

Hypnosis was induced using a standardised induction procedure described elsewhere (Whalley & Oakley, 2003; see also chapter 2). Following the induction participants were asked to *"Bring that dial to mind, just picture it very clearly And to tell me where that dial is just at the moment"*. Participants were then asked to focus on the dial and to *"just allow that dial to turn up, and feel that experience changing, becoming stronger and stronger as time goes by"*. This technique of initially turning pain up is similar to the 'paradoxical injunction' in clinical settings (Heap & Aravind, 2002), and is used to engender an experience of control in the individual regarding their ability to modulate their pain. Participants were then asked to *"allow the dial to be turned down, noticing the feeling changing, becoming less and less as time goes by"*. Ratings on the dial were taken after each attempted dial movement. Short breaks from the dial were taken half-way through the session to deepen the hypnosis (typically instructions were given to *"relax deeper and deeper as I count to ten"*) and a suggestion was given that *"this time when I ask you to move the dial up and down I would like you to allow the dial to move as quickly as it can and as far as it can in whichever direction I ask"*. The dial was then brought to mind and its position manipulated once again.

A number of criteria were used to select participants for scanning. Only patients able to change their pain score by at least 6 points from highest to lowest were considered. In addition to absolute scores the reported method of pain control was taken into account. All participants reported being able to increase their pain by visualising the dial. However, despite instructions to focus on the dial some participants reported spontaneously using distractive/dissociative pain control techniques (e.g. finding themselves on a pleasant beach and unaware of the pain). Participants who reported using anything other than the prescribed pain control imagery were excluded from further participation in order to maintain consistency.

8.1.4 Third stage: scan

From the second-stage screening thirteen patients were selected to take part in the scanning phase of the study. Average age of this group was 51.4 (range 21-63), all were female. Mean Harvard objective score was 9.7 (SD 0.92; range 0-12). Mean Harvard subjective score was 37.0 (SD 3.55; range 3-45) out of a possible 48. Seven of the thirteen participants also reported suffering from irritable bowel syndrome. Of these thirteen participants, 5 were identified as being medication free (no current usage of centrally acting medication including opioids, anti-depressants and tranquilisers for at least one week prior to the scan), 5 were identified as using medication (current use of both anti-depressant and opioid medication), and 3 were only using antidepressants. Participant drug information, including their usage at the time of the scan is presented in table 8.1.

Patient #	Drugs Taken	Stopped for scan?	IBS diagnosis?
9575	Zoloft, Desipramine, Valium	Stopped Zoloft 2 weeks prior	Yes
9656	Clonazepam, Alprazolam, Nortryptyline, Fentanyl patch	Off patch for 5 days prior	Yes
9734	Effexor		Yes
9602	Lorazepam	Taken on as-need basis	No
9558	Paxil		No
9570	Effexor	Off for 24 hours	No
9613	Paxil, Trazadone	Off for 1 week	Yes
9596	Zoloft, Trazadone	Off for 1 week	No
9652	Lorazepam, Flexeril, Neurontin		No
9659	Trazadone, Effexor		No
9622	Trazadone		Yes
9579	Nothing		Yes
9650	Nothing		Yes

Table 8.1: Drug information for patients selected for scanning.

Before the scan participants were fully briefed about the procedure and were given an information sheet detailing exactly what would happen (Appendix 8.1). Key points of the pre-scan briefing were that due to the noise of the scanner verbal suggestions for the dial to be moved up and down would be impossible and that the experimenter (MW) would signal the position of the required dial setting by tapping on the participants' foot with pre-arranged signals. A single tap indicated that the dial was to be moved as low as possible and then held there. Two taps indicated that the dial was to go to a 'medium' position and held there. Three taps indicated that the dial was to be turned up as high as it could go and then to be held there. A diagram was given the participants to aid memorisation of these instructions (figure 8.3).

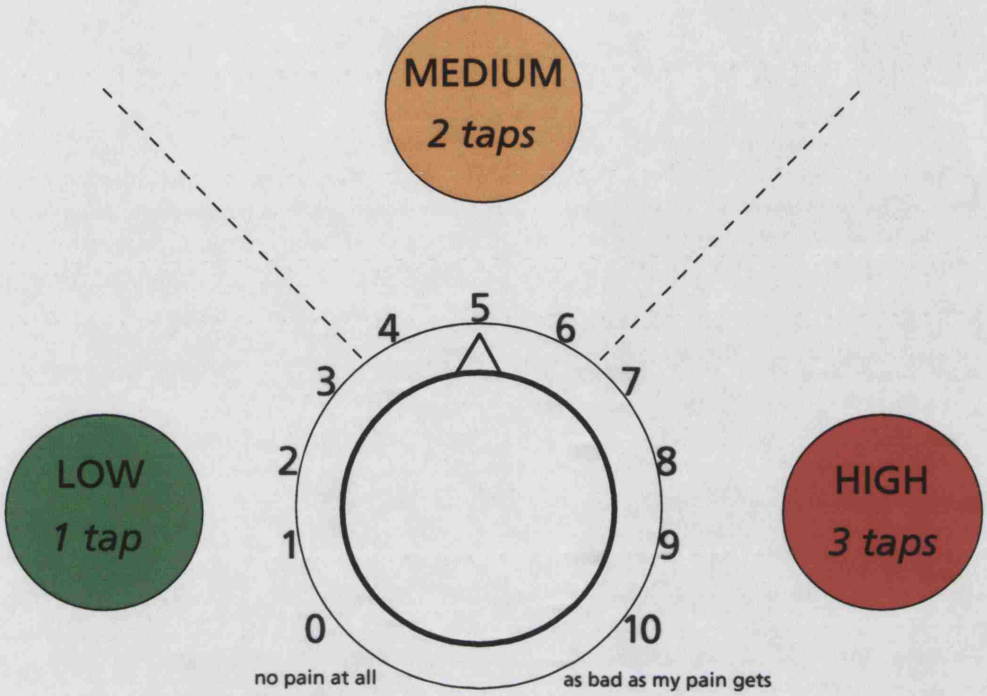


Figure 8.3: Dial diagram shown to participants to aid memorisation of the experiment schedule.

At this stage, just prior to the scan, participants were reminded that during the second stage screening session suggestion and imagery had been used in hypnosis to alter their perception of pain. They were informed that it is also possible to use the same imagery and suggestion before the induction of hypnosis in order to modulate pain and that this would be another factor in the experiment. They were informed that for half of the scan they would be hypnotised and that for the other half they would be wide awake and unhypnotised, but that the same imagery and suggestion (the dial) would be used to alter pain perception in both hypnotised and unhypnotised sections of the experiment. It was made clear to participants that in the unhypnotised block they were to close their eyes and picture the dial very clearly in their mind, but that they were stay 'wide awake and alert' and not to become hypnotised. Depending upon how their individual experimental protocol had been randomised participants were either given a hypnotic induction at the beginning of the scan and taken through a standard hypnosis termination procedure halfway through, or they completed the first half unhypnotised and were then given a hypnotic induction. The induction routine in the scanner was the same as described for the screening session.

8.1.5 Protocol

This investigation was a 2x3 design, with patients given suggestions either before or after a hypnotic induction and three levels of pain. These factors were randomised across participants. Functional imaging was conducted in four minute blocks. Each participant underwent four blocks – two hypnotised and two unhypnotised. Each block was split into 30 second segments. Before each block participants were given suggestions that they would not find the noise of the scanner bothersome. They were then asked to focus on the image of the dial and were reminded of the tapping schedule. Confirmation that they understood the instructions was obtained with a foot movement and scanning began. The participant's foot was tapped 1, 2 or 3 times every 30s, according to how their schedule had been randomised as illustrated in figure 8.4.

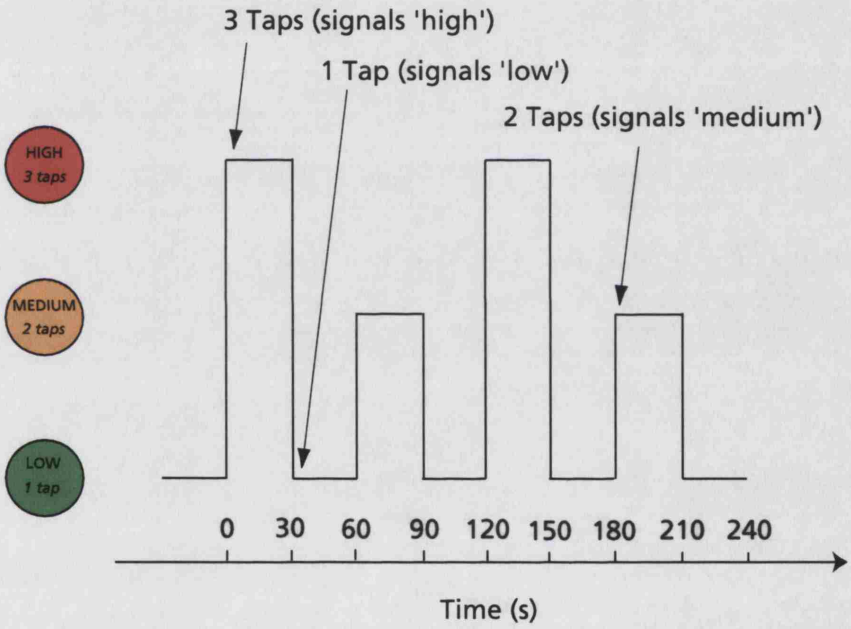


Figure 8.4: Diagram illustrating the design of a functional imaging block. The participants foot was tapped 1, 2, or 3 times every 30s to suggest that the position of the dial should be moved.

After each block participants were asked to verbally report on a scale of 0-10 the dial/pain levels that were reached in response to the low, medium and high instructions during the preceding block. Depth of hypnosis was assessed by a rating on a 0-10 scale (0 = not at all hypnotised, 10 = as deeply hypnotised as I have ever been). Each of the pain ratings was necessarily an average of a number of pain experiences but this was considered a preferable alternative to asking participants to remember, in sequence, up to eight separate pain ratings. In the experiment described in chapter 5 participants had been asked to remember a sequence of six pain experiences and one of these (healthy control) participants had found it difficult. Miller's (1956) classic work would indicate that increasing the length of the sequence would increase the likelihood of errors.

In the break between the two hypnosis blocks participants were asked to find themselves back in their special place for the duration of a deepening 0-10 count and to relax while the feeling of being there became stronger and stronger. In the break between the two unhypnotised blocks the participant was asked to open their eyes in order to stave off any drowsiness induced by lying still in the confines of the scanner with closed eyes. The hypnotist engaged them in conversation to check that the participant was wide awake.

After the functional imaging component was completed participants were debriefed. Retrospective pain scores (low, medium and high) and hypnotic depth ratings were taken. Participants were also asked how much control they felt they had over the movement of the dial in each block.

8.1.6 Apparatus and scanning parameters

Scanning took place in a General Electric 3.0 Tesla MRI scanner. Brain activation was inferred based on measurement of the blood oxygen level dependent (BOLD) contrast (Ogawa et al, 1990). These measurements were acquired at 3 Tesla using a reverse spiral technique (TE=25ms, TR=1.5s, flip angle=60°, 64x64 matrix) described in detail elsewhere (Noll et al, 1995; Stenger et al, 2000).

8.1.7 Statistical analysis

Data analysis was performed using SPM2 (Wellcome Trust Centre for the Study of Cognitive Neurology), described in detail elsewhere (Friston et al., 1995). In summary, head movement between scans was corrected by aligning all subsequent scans with the first. Each re-aligned set of scans from every participant was coregistered with her own hi-res structural MRI image and reoriented into the standardized anatomical space of the average brain provided by the Montreal Neurological Institute (MNI). To increase the signal to noise ratio and accommodate variability in functional anatomy, each image was smoothed in X, Y and Z dimensions with a Gaussian filter of 10mm (FWHM). A box-car model with a haemodynamic delay function, weighted according to the pain ratings derived for each condition using parametric modulation, was fitted to each voxel to contrast the pain conditions generating a statistical parametric map. Baseline drifts were removed by applying a high-pass filter. Brain regions with a large statistic correspond to structures whose BOLD response shares a substantial amount of variance with the patients own experience of pain. Images were thresholded using a FWE $p<0.05$ and the results are displayed in figure 8.7.

8.2 Results

8.2.1 Pain reports during screening

Prior to the induction of hypnosis participants rated their current pain at 4.69 (SD 2.21: Range 2.5-9.5). An ANOVA was performed on the verbal pain reports taken during the screening session in conditions of pain-at-start, dial-turned-up, and dial-turned-down. Table 8.2 gives the mean pain reports for each of these conditions.

	Pain Report
Screening Pain Start	2.6 (2.25)
Screening Pain High	8.2 (1.01)
Screening Pain Low	0.6 (1.04)

Table 8.2: Mean (and standard deviation) of pain reports for all participants during the three conditions of the screening session.

Repeated measures ANOVA revealed significant differences in pain report scores between the start of the screening and the high and low pain conditions $F(2, 24)=93.434, p<0.001$. Planned comparisons revealed significant differences between pain levels at the start of the screening and when the dial was at 'high position' ($t(12)=7.789, p<0.001$, 95% CI [4.91, 6.29]), between pain levels at the start of the screening and when the dial was at 'low' position ($t(12)=3.464, p<0.005$, 95% CI [1.3, 2.7]), and between pain levels when the dial was at 'high' vs. 'low' positions ($t(12)=19.800, p<0.001$, 95% CI [7.05, 8.15]). During the screening session participants were asked to describe where they felt their pain worst. As shown in figure 8.5 all but one participant named the upper or lower back as the worst location.

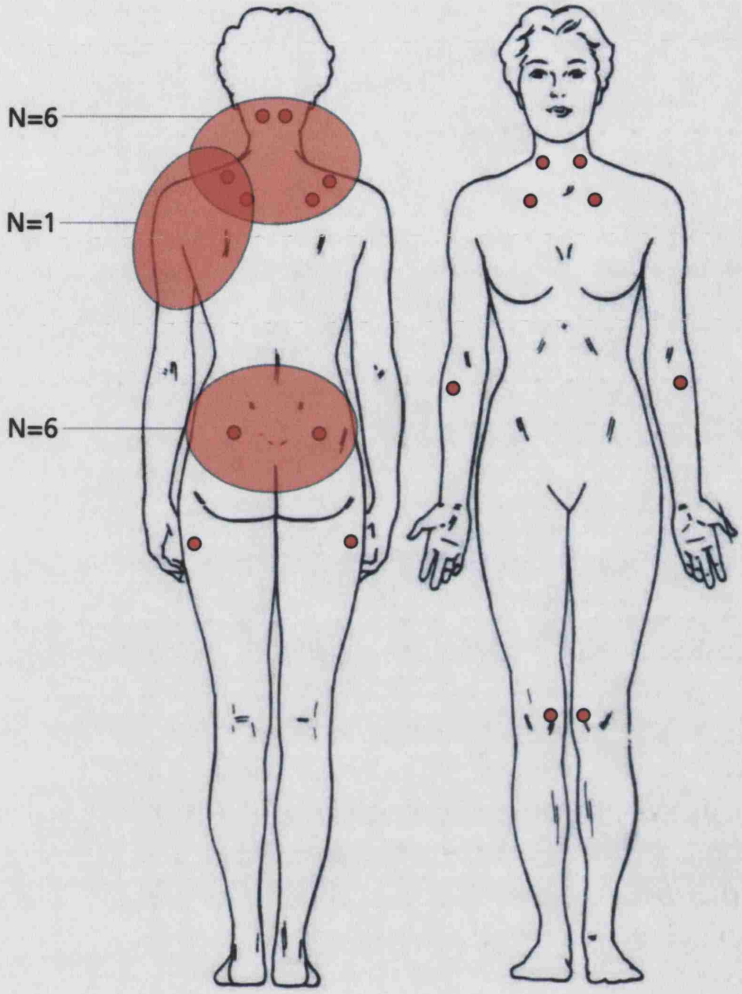


Figure 8.5: The American College of Rheumatology (Wolfe et al, 1990) diagnostic criteria for fibromyalgia include a history of widespread pain and tenderness on palpation at least 11 of the 18 tender points marked on the diagram above. The faded ellipses demonstrate the regions named as most painful by the participants in the present study.

8.2.2 Pain reports during scanning

The means and standard deviations of verbal pain reports given by participants after each block of functional imaging are given in Table 8.3 and Figure 8.6. A two-factor repeated measures ANOVA showed that the main effect of hypnotic state was not significant. The main effect for the level of the pain dial was significant $F(2,24)=196.42$, $p<0.001$. The interaction between hypnotic state and level of the pain dial was significant $F(2,24)=7.691$, $p=0.003$.

	Hypnotised	Unhypnotised
Low	1.3 (0.83)	2.3 (1.80)
Medium	5.3 (0.64)	5.7 (0.99)
High	8.9 (1.09)	8.5 (1.65)

Table 8.3: Mean (and standard deviation) of verbal pain reports given by all participants during hypnotised and unhypnotised blocks of functional imaging.

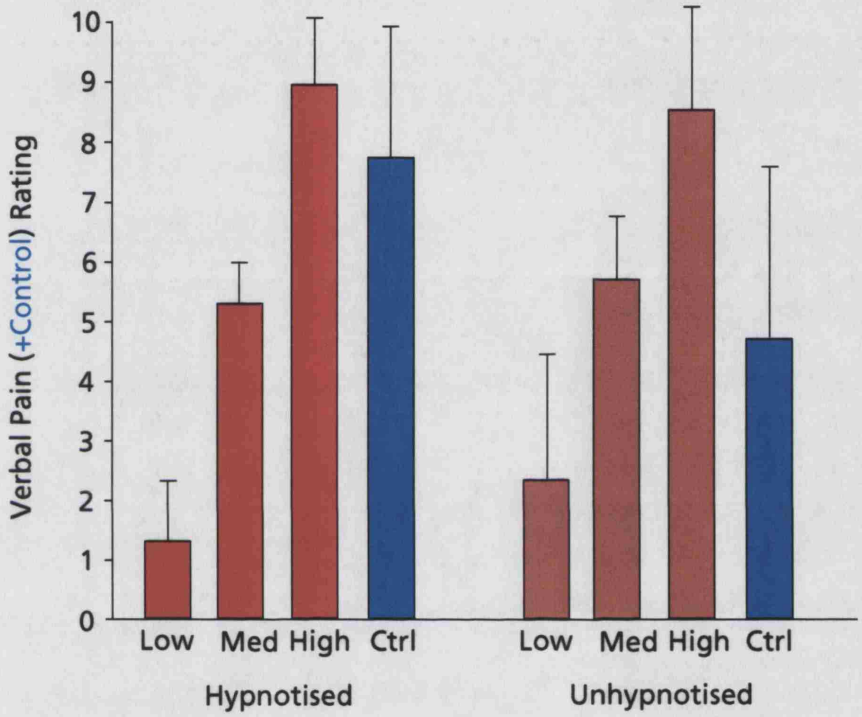


Figure 8.6: Pain reports and 'sense of control' data from all participants in hypnotised and unhypnotised blocks. Ctrl = control.

Paired samples t-tests were used to assess the differences in pain scores by condition (pain dial: low, medium, high; state: hypnotised, unhypnotised). Bonferroni correction was made for multiple comparisons. In the hypnotised blocks participants gave significantly different pain reports between the low and medium, low and high, and medium and high pain conditions ($t(12)=16.297$, $p<0.001$, 95% CI [3.54, 4.46]; $t(12)=20.069$, $p<0.001$, [7.07, 8.13]; $t(12)=14.039$, $p<0.001$, [3.1, 4.11]). In the unhypnotised blocks participants also gave significantly different pain reports between the low and medium, low and high, and medium and high pain conditions ($t(12)=10.566$, $p<0.001$, [2.75, 4.05]; $t(12)=9.595$, $p<0.001$, [5.49, 6.91]; $t(12)=7.525$, $p<0.001$, [2.18, 3.42]). Paired samples t-tests were used to assess the pain associated with each dial position across hypnotised and unhypnotised conditions. Only the comparison

(hypnotised vs. unhypnotised) of pain reports with the dial at the 'low' position reached significance at the 0.05 level, uncorrected for multiple comparisons: Low $t(12)=2.235$, $p=0.023$; Medium $t(12)=1.357$, $p=0.100$; High $t(12)=1.397$, $p=0.094$).

8.2.3 Pain reports taken during debriefing

The means and standard deviations of verbal pain reports given by patients during the debriefing session are given in Table 8.4. A two-factor repeated measures ANOVA showed that the main effect of hypnotic state was not significant. The main effect for the level of the pain dial was significant $F(2,24)=156.70$, $p < 0.001$. The interaction between hypnotic state and level of the pain dial was significant $F(2,24)=5.551$, $p=0.001$.

	Hypnotised	Unhypnotised
Low	1.2 (0.66)	2.7 (2.14)
Medium	4.8 (0.93)	5.3 (1.33)
High	8.6 (1.13)	8.2 (1.84)

Table 8.4: Mean (and standard deviation) of pain reports given by participants during the debriefing session.

Paired samples t-tests were used to assess the differences in pain scores by condition (pain dial: low, medium, high; state: hypnotised, unhypnotised). Bonferroni correction was made for multiple comparisons. For the hypnotised blocks participants gave significantly different debriefing pain reports between the low and medium, low and high, and medium and high pain conditions ($t(12)=18.318$, $p<0.001$, 95% CI [3.12, 4.68]; $t(12)=21.399$, $p<0.001$, [6.89, 7.91]; $t(12)=11.658$, $p<0.001$, [3.25, 4.35]). For the unhypnotised blocks participants also gave significantly different debriefing pain reports between the low and medium, low and high, and medium and high pain conditions ($t(12)=6.728$, $p<0.001$, [1.88, 3.32]; $t(12)=7.923$, $p<0.001$, [4.73, 6.27] ; $t(12)=7.388$, $p<0.001$, [2.22, 3.58]). Paired samples t-tests were used to assess the pain associated with each dial position across hypnotised and unhypnotised conditions. Only the comparison (hypnotised vs. unhypnotised) of pain reports with the dial at the 'low' position reached significance at the 0.05 level, uncorrected for multiple comparisons: Low $t(12)=2.926$, $p<0.01$, 95% CI [0.86, 2.14]; Medium $t(12)=1.180$, $p=0.130$; High $t(12)=0.950$, $p=0.180$).

8.2.4 Comparing ratings taken in the scanner with those from the debriefing

Pain ratings taken between the scanning blocks were compared with verbal ratings of the intensity of the low, medium and high intensity pain elicited during the debriefing.

Means and standard deviations are given in Table 8.5. Data from hypnotised and unhypnotised conditions were assessed separately using two-factor repeated measures ANOVA.

	Hypnotised		Unhypnotised	
	Scanner	Debrief	Scanner	Debrief
Low	1.3 (0.83)	1.3 (0.83)	2.3 (1.80)	2.7 (2.14)
Medium	5.3 (0.64)	5.3 (0.64)	5.7 (0.99)	5.3 (1.33)
High	8.9 (1.56)	8.9 (1.56)	8.5 (1.65)	8.2 (1.84)

Table 8.5: Comparison of mean (and standard deviation) of pain ratings given by fibromyalgia patients during scanning [blocks] and debriefing.

For hypnotised data the two-factor repeated measures ANOVA showed that the main effect of whether ratings were taken in the scanner or at debriefing, and the interaction between this factor and levels of the pain dial, were not significant.

For the unhypnotised data the two-factor repeated measures ANOVA showed that the main effect of whether ratings were taken in the scanner or at debriefing (rating time factor) was not significant. The interaction between the rating time factor and levels of the pain dial was significant $F(2,24)=5.858$, $p=0.008$. Post-hoc paired samples t-tests revealed that in the scanner in the unhypnotised condition the patients rated the level of the 'low' pain as lower than when they rated the same pain at debriefing ($t(12)=2.456$, $p=0.03$, 95% CI [-0.36, 1.16]). Comparisons for 'medium' and 'high' levels were non-significant.

8.2.5 Hypnotic depth in scanner

Hypnotic depth was assessed by asking participants to rate how deeply hypnotised they felt on a scale from 0 (not at all hypnotised) to 10 (as deeply hypnotised as I have ever been), ratings are given in table 8.6.

	In Scanner		Debrief	
	Hypnotised	Unhypnotised	Hypnotised	Unhypnotised
Depth	6.1 (2.49)	0.5 (1.26)	6.8 (2.37)	0.7 (1.55)

Table 8.6: Means (and standard deviations of hypnotic depth rated by the participants in the scanner and during the debriefing session.

Paired samples t-tests were conducted on the hypnotic depth data collected while participants were in the scanner. They self-rated their hypnotic level as significantly deeper during the blocks which followed the hypnotic induction (In scanner: $t(12)=7.94$, $p<0.001$; At debrief: $t(12)=9.73$, $p<0.001$, 95% CI [5.34, 6.86]).

8.2.6 'Sense of control' over the pain

Sense of control data, assessed during the debriefing and presented in table 8.7, was compared by condition (hypnotised vs. unhypnotised) and revealed that patients felt significantly more control over their pain when hypnotised $t(12)=3.400$, $p=0.005$, 95% CI [2.49, 3.71].

	Hypnotised	Unhypnotised
Sense of control	7.8 (2.20)	4.7 (2.82)

Table 8.7: Means (and standard deviations) of patients sense of control over their pain during the hypnotised and unhypnotised conditions.

8.2.7 Clarity of dial

The clarity with which the patients 'saw' the dial during the hypnotised and unhypnotised conditions was assessed during the debriefing and showed significantly greater assessment of clarity in the hypnotised condition $t(12)=2.886$, $p=0.014$, 95% CI [0.55, 2.25].

	Hypnotised	Unhypnotised
Clarity	8.9 (1.98)	7.5 (2.96)

Table 8.8: Means (and standard deviations) of the clarity with which participants 'saw' the dial during the hypnotised and unhypnotised conditions

8.2.8 'Ownership' of the pain

During the debriefing participants were asked whether the increases and decreases in the pain that they felt corresponded to changes in their fibromyalgia pain or changes in any other kind of pain. All participants reported that it had been their fibromyalgia pain which had been modulated.

8.2.9 Functional imaging data

The profile of brain activation covariant with changes in pain report is illustrated in figure 8.7 and tabulated in tables 8.9 and 8.10.

	Hypnotised			Unhypnotised	
Figure Label	Brain Area (x, y, z coordinates)(region)	Side	T-Score	Brain Area (x, y, z coordinates)(region)	T-Score
1	Thalamus				
	(-2,-22,8)	L	8.7	(-24,-28,14)	8.4
	(16,-8,2)	R	10.6	-	-
	(2,-24,10)	R	9.9	(12,-28,14)	5.4
2	MCC				
	(-18,20,44)(A24')	L	8.6	-	-
	(14,18,40)(A24')	R	12.2	(12,20,38)(A32')	6.4
3	Medial frontal cortex				
	(-6,22,68)(BA 6/8)	L	12.4	-	-
	(2,16,64)(BA 6/8)	R	12.6	(10,16,64)(BA 6/8)	6.9
4	Infragenual ACC				
	(-8,18,-16)(BA 25)	L	18.8	(-2,14,-16)(A 25	8.5
	(12,22,-12)(A 32/25)	R	20.7	(16,22,-10)(A 32/25)	9.7
5	Cerebellum				
	(-8,-60,-10)	L	14.0	(-8,-60,-12)	9.1
	(12,-64,-12)	R	11.9	(2,-64,-12)	8.6
6	Midbrain				
	(-10,-18,-20)	L	11.3	(-10,-24,-10)	6.1
	-	R	-	(8,-8,-10)	4.7
7	Caudate				
	-	L	-	-	-
	(12,10,8)	R	16.6	(12,12,8)	7.8
8	Insula				
	(-42,8,-8)	L	15.0	(-50,4,0)	7.1
	(44,30,-8)	R	14.3	-	-
9	Prefrontal cortex				
	(-30,48,38)(BA 9)	L	11.7	-	-
	(38,48,24)(BA 9/46)	R	11.5	(52,42,14)(BA 10/46)	8.4
10	Orbitofrontal cortex				
	(-28,28,-18)(BA 47/11)	L	20.4	(-20,54,-14)(BA 10/11)	6.9
	(26,32,-16)(BA 47/11)	R	14.4	(50,38,-10)(BA 47)	6.7
11	S1				
	(-40,-26,62)	L	8.9	(-58,-34,36)	10.3
	(-14,-22,74)	L	9.6	(-28,-37,74)	7.9
	(18,-20,74)	R	11.7	(66,-32,26)	11.3
12	Inferior parietal cortex				
	(-62,-34,36)(BA 40)	L	18.9	(-58,-38,36)(BA 40)	10.1
	(66,-30,24)(BA 40)	R	16.7	(64,-42,30)(BA 40)	9.9
13	S2				
	(-64,-34,14)	L	13.4	-	-
	-	R	-	(66,-28,24)	11.3
14	Occipital cortex				
	(-18,-92,0)(BA 18)	L	14.3	(-24,-92,4)(BA 18)	6.2
	(20,-92,4)(BA 18)	R	17.0	-	-
15	Lateral frontal cortex				
	-	L	-	(-43,16,50)(BA 8/6)	5.4
	-	R	-	-	-

Table

8.9: Shows the regions with increasing BOLD response dependent upon hypnotically induced increases in pain experience. The areas are tabulated in terms of the brain region, as illustrated in figure 8.7, and their approximate cytoarchitecture. The *x, y, z* coordinates plot each peak (defined as the voxel with the highest T-score within each region) according to the MNI coordinate system (negative is left, posterior and inferior). MCC = mid anterior cingulate cortex; pACC = perigenual anterior cingulate cortex; ACC = anterior cingulate cortex; S2 = secondary somatosensory cortex; S1 = primary somatosensory cortex.

	Hypnotised			Unhypnotised	
Figure Label	Brain Area (x, y, z coordinates)(region)	Side	T-Score	Brain Area (x, y, z coordinates)(region)	T-Score
16	Amygdala/Hippocampus				
	-	L	-	(-24,-16,-12)	-6.1
	(22,-6,-18)	R	-6.8	(28,-8,-16)	-6.4
17	PCC				
	(-10,-26,32)(BA 23/32)	L	-6.7	(-2,-38,34)(BA 31)	-6.1
	(8,-60,40)(BA 31)	R	-6.6	(10,-60,14)(BA 31)	-6.8
18	pACC				
	(-10,34,-4)(A 24/32)	L	-17.7	(-12,30,-8)(A 24/32)	-5.8
	(12,48,-16)(A 24/32)	R	-12.7	(6,38,-2)(A 24/32)	-6.5
19	Temporal cortex				
	(-60,-36,-10)(BA 21)	L	-19.9	(-60,-38,-10)(BA 21)	-8.3
	(42,-30,4)(BA 21/22)	R	-17.2	(66,-26,-6)(BA 21)	-9.8
20	Parietal cortex				
	-	L	-	(-26,-74,40)(BA 7)	-5.2
	(22,-70,44)(BA 7)	R	-9.2	(22,-78,52)(BA 7)	-10.8
6	Midbrain				
	-	L	-	-	-
	(22,-12,-12)	R	-11.3	-	-
7	Caudate				
	-	L	-	(-18,22,-6)	-11.3
	-	R	-	-	-
9	Prefrontal cortex				
	-	L	-	(-30,36,42)(BA 9)	-7.8
	-	R	-	(38,24,30)(BA 9)	-7.1
10	Orbitofrontal cortex				
	-	L	-	(-42,34,-4)(BA 11/47)	-6.6
	-	R	-	(36,52,-6)(BA 11/10)	-11.7
14	Occipital cortex				
	-	L	-	-	-
	(46,-76,-2)(BA 18/19)	R	-16.1	(42,-74,-2)(BA 18/19)	-9.9
15	Lateral frontal cortex				
	-	L	-	-	-
	(34,22,52)(BA 8)	R	-12.4	-	-

Table 8.10: Shows the regions with *decreasing* BOLD response dependent upon hypnotically induced increases in pain experience. The areas are tabulated in terms of the brain region, as illustrated in figure 8.7, and their approximate cytoarchitecture. The *x, y, z* coordinates plot each peak (defined as the voxel with the highest T-score within each region) according to the MNI coordinate system (negative is left, posterior and inferior). MCC = mid anterior cingulate cortex; pACC = perigenual anterior cingulate cortex; ACC = anterior cingulate cortex; S2 = secondary somatosensory cortex; S1 = primary somatosensory cortex.

The increase in pain experience dependent upon hypnotic suggestion resulted in widespread significant activation (increases in BOLD response) as well as some more focal deactivations (decreases in BOLD response). Activations centred upon the thalamus, mid-anterior cingulate (including both posterior and anterior extents) extending superiorly into medial frontal cortex, infragenual ACC, cerebellum extending anteriorly into the midbrain region of the PAG, caudate, anterior insula, prefrontal and orbitofrontal cortices, inferior parietal cortex and primary and secondary somatosensory cortices. Except for the caudate, which was only activated on the right side, these responses were all bilateral and often extended into adjacent cortical or subcortical regions. Deactivation centred upon bilateral posterior cingulate cortex, bilateral pACC extending into the caudate on the left side, right midbrain, bilateral temporal cortex, right occipital cortex and right lateral frontal cortex.

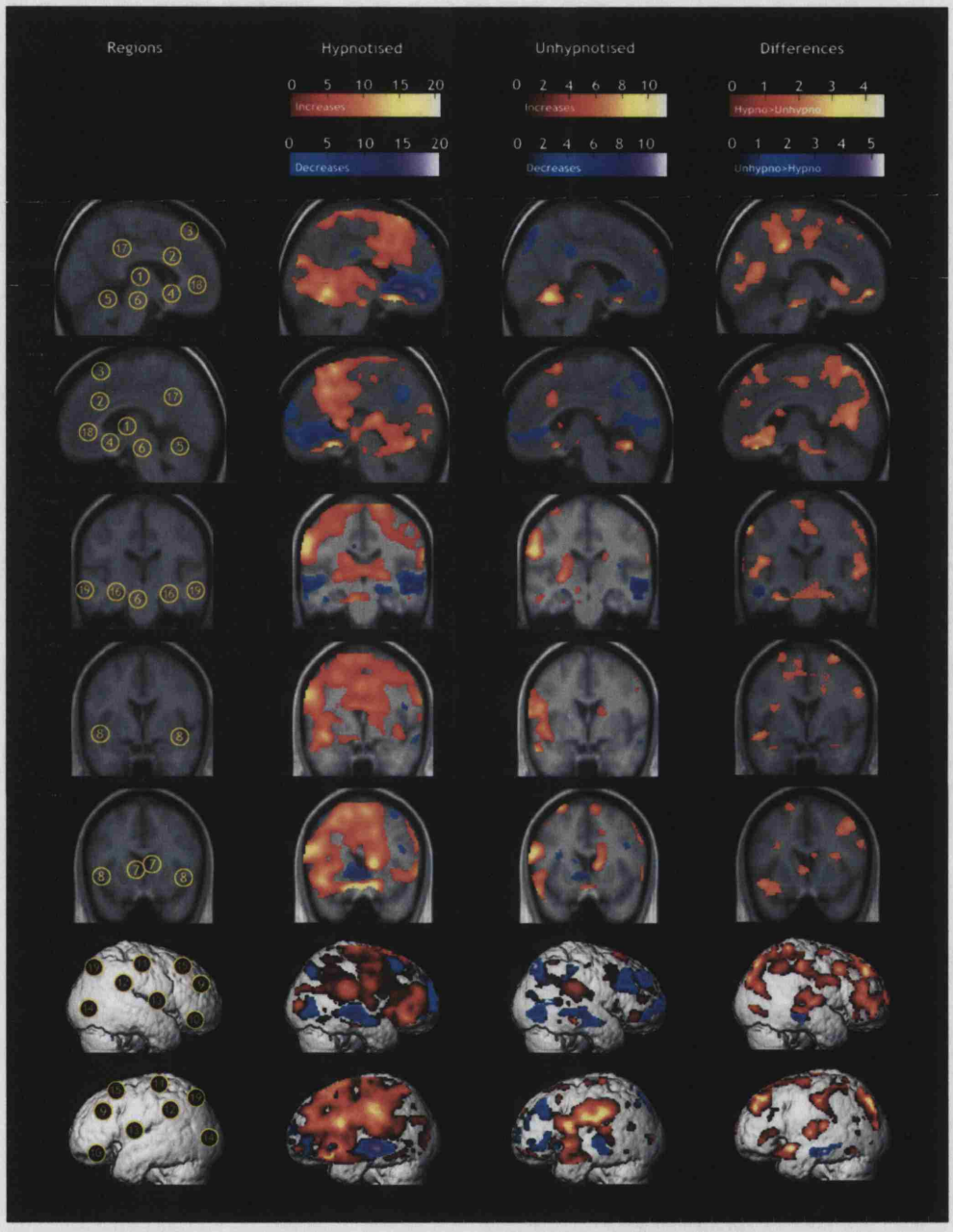


Figure 8.7: Shows increased (red/orange scale) and decreased (blue/purple scale) activity covariant with subjective pain report in response to suggestion delivered in hypnosis (left-middle column) and outside hypnosis (right-middle column). Differences are shown in the right column, with regions displaying greater activity in the hypnotised condition shown on the red/orange scale and regions displaying greater activity in the unhypnotised condition shown on the blue/purple scale. Numbered areas in the left hand column relate to numbered regions reported in the tables. The effects are shown as SPMs superimposed on an averaged structural MRI derived from the participant's own structural scans. At the top are saggital slices 6mm and 2mm lateral to the midline. Below are coronal slices 20mm posterior (negative), on (0mm), and 12mm anterior (positive) to the anterior commisure. At the bottom are surface projections.

8.3 Discussion

The fMRI data presented here reveals for the first time the specific pattern of neural activation associated with changes in fibromyalgia patients' *own* pain, adding to what we already know about functional pain patients' augmented responses to stressors (e.g. Gracely et al, 2002; Cook et al, 2004). Changes in reported experiences of pain in the hypnotised condition in the present study were highly significant with participants producing marked differences in pain ratings between dial positions. These significant changes compared to the results of Wik et al (1999) indicate that specific suggestions within hypnosis for fibromyalgia pain control are more effective than simple hypnotic relaxation in producing changes in experienced pain.

Activations were found in predicted areas of the pain matrix which is consistent with the view that the hypnotic suggestions were instrumental in modulating the pain experienced by the participants. This reveals, for the first time, the neural signature associated with fibromyalgia pain. Specifically, activity covarying with subjective pain reports was observed in S-I, S-II, ACC, insula, thalamus, PAG, caudate, pre-frontal and orbitofrontal cortices, cerebellum and inferior parietal cortex. The results presented here are similar to those obtained by Gracely and colleagues (2002) when they contrasted patient and control participants' neural responses to a low pressure mechanical stimulus; a stimulus which only the patients perceived as painful. Gracely observed activations in S-I, S-II, ACC, insula, cerebellum and IPC. Importantly though, in addition to the activations observed by Gracely increases were also observed in the present study in thalamic blood flow, a central component of the pain matrix, in response to direct modulation of fibromyalgia pain. These data from participants in the hypnotised condition again indicate the efficacy of suggestion following hypnotic induction in producing altered sensory experience, with specificity of response to the stimulus under investigation (Kosslyn et al, 2000; Szechtman et al, 1998, Derbyshire et al, 2004).

A different pattern of results was obtained when participants received suggestion without a prior induction procedure. The absence of a hypnotic state in this condition was confirmed by the significant differences in hypnotic depth ratings before and after the delivery of an hypnotic induction and through dialogue the experimenter had with participants in both phases. As in the hypnotised condition patients reported significant changes in subjective pain experience in response to suggestions to move the position of the dial. The activations observed in the unhypnotised condition, although in identical regions to activations in hypnosis (including thalamus, ACC, infragenual cingulate, cerebellum, S-I, S-II), were much smaller in intensity and in extent. This finding raises interesting questions since very similar changes in subjective pain experience were reported by patients in both conditions, resulting in different activation patterns. The problem posed concerns the veracity of subjective reports in the unhypnotised condition and whether doubt should be extended to the hypnotised condition. Since

subjective intensity is known to be correlated with activity in the pain matrix (Coghill et al, 1999) it is difficult to explain the diminished strength of activations in the unhypnotised condition in the presence of strong changes in reported pain intensity.

A number of possible explanations are available to us. In the debriefing patients were asked to give a rating for each four-minute block of scanning for how clearly they could 'see' the dial and how much control they felt they had over its movement. Patients reported being able to see the dial significantly more clearly in the hypnotised blocks than in the unhypnotised blocks. This factor differentiates between the hypnotised and unhypnotised conditions and it is possible that it accounts for at least some of the differential in activation patterns. One other mechanism seems possible: patients felt significantly less control over the movement of the dial in the unhypnotised condition and it may have taken them longer to change its position, and with it the pain experience, which would reduce data acquisition time affecting final signal strength.

In some senses this was not a perfectly 'fair' hypnotic/non-hypnotic investigation. Best practice is to perform tests of non-hypnotic suggestibility *then* to perform the same tests in hypnosis, only telling participants about the second half of the experiment after completion of the first half, so as to avoid possible hold-back effects (Zamansky, Scharf & Brightbill, 1964; Braffman & Kirsch, 1999). It was not possible to accommodate such a design within the constraints of this functional imaging investigation where a major concern was choosing participants capable of performing the chosen primary task reliably (hypnotic pain modulation). Order of blocks (hypnotised/unhypnotised) was randomised across participants. Participants who had unhypnotised blocks first rated 'low' pain in the unhypnotised condition as significantly lower than participants who had hypnotised blocks first (analysis of order effects presented in Appendix 8.2). This relationship, although statistically significant, is not in the direction that would be predicted by a classic hold-back effect, and no other differences between groups were observed.

Intensity and extent of activations aside though, this investigation has demonstrated similarities in both behavioural and blood flow (measured by BOLD activity) responses to a suggestion delivered before and after an hypnotic induction. The only other neuroimaging investigation to attempt to directly compare response to suggestion in and outside hypnosis was conducted by Kosslyn et al (2000) and found different patterns of activation in response to suggestions for a visual hallucination. However, Kosslyn's team delivered differently worded suggestions across conditions and the differential activations can most parsimoniously be attributed to different cognitive processes. The present result indicates that non-hypnotic suggestion can affect subjective pain experience but leaves unresolved the question of why similar magnitudes of pain change-scores in the hypnotic and non-hypnotic conditions did not result in similarly closely matched neural activity.

To see how the present results tally with what is already known about neural responses to modulation of fibromyalgia pain it is worth attempting to compare the results obtained by different teams where possible. Acute pain modulation has been best attempted by two other groups working with fibromyalgia patients (Wik et al, 1999; Gracely et al, 2002) and the resulting activations are presented in table 8.11. As can be seen, the spread of activation observed in the present investigation encompasses almost all areas of the pain matrix, significantly more than previous investigations which assessed fibromyalgia patients pain less directly.

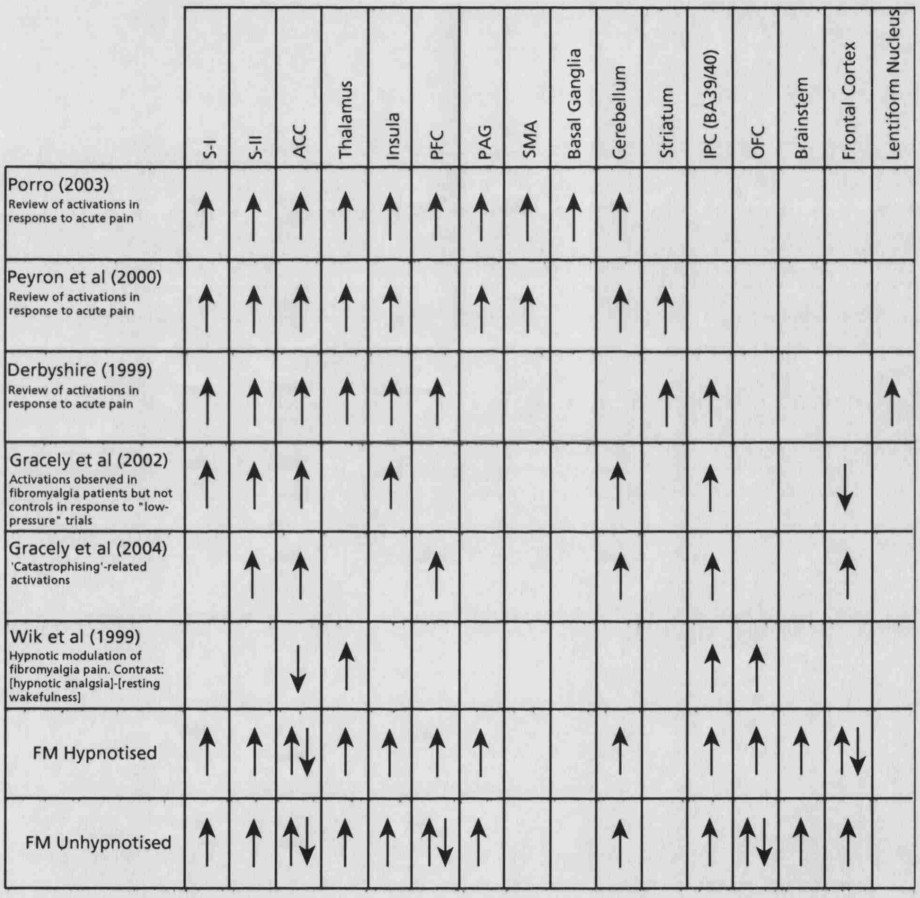


Table 8.11: Comparison of activations observed in the present investigation with three acute pain review studies and three investigations of fibromyalgia. ↑ = increases in rCBF, ↓ = decreases in rCBF, ↑↓ = increases and decreases in rCBF.

8.3.1 Specific activations.

Thalamic activity in this investigation covaried with patients subjective pain report. As a major gateway for noxious information the activation of thalamus in combination with reports of greater pain strongly implies that the reported changes in pain reflected actual noxious perception rather than the demand characteristics of the experiment.

Prior studies of FM have demonstrated hypoactivity of the thalamus at rest (Mountz, Bradley, Modell, et al, 1995; Kwiatek, Barnden, Tedman, et al, 2000) and this reduced activity has been suggested to cause pain through a loss of inhibitory input to the cortex. In our study we have demonstrated activation in the thalamus to increase linearly with pain experience, which could be viewed as inconsistent with hypoactivation causing pain. If reduced thalamic activation were a cause of pain we might expect to see further reduced thalamic activation as pain increases. These findings, however, are not necessarily in conflict. It could be that reduced thalamic responses cause pain in the basal state via an absent inhibitory mechanism but that further pain enhances ascending system activation causing pain via an increase in excitation. These inhibitory and excitatory pathways are likely to be anatomically distinct but below the resolution of our current imaging techniques. Future comparisons of FM patients with control subjects using similar techniques can be used to test the hypothesis that basal pain is associated with thalamic hypoactivation while further induced pain is associated with normal thalamic activation. The results of Gracely et al (2002) support this interpretation by demonstrating increased activation to pressure pain in thalamus but from a lower baseline. Furthermore, Gracely et al (2002) state that determination of rCBF in the resting state should have little predictive value for evoked responses and that these two types of investigation should be mutually informative. Further studies will be needed to define the precise role played by this component of the pain matrix in fibromyalgia pain.

The widespread occipital cortex activation observed in the present study seems likely to reflect the use of the dial imagery by patients to modulate their pain. Whilst this may be the case here recent findings indicate that such a focussed use of imagery is not necessary for hypnotic reduction of pain: Röder and colleagues (2004) demonstrate preliminary results indicating that hypnotic depersonalization, a different analgesic technique, reduces activity in the pain matrix (not including thalamus and ACC) compared to rest. It will be interesting to compare the specific effects of different suggestions for pain relief as more neuroimaging studies of cognitive pain modulation become available. Additionally, it is interesting to note that occipital activations were observed only unilaterally in the unhypnotised condition, and at much decreased intensity: possibly a reflection of the decreased clarity with which patients reported seeing the dial in this condition.

Orbitofrontal and frontal activations are not commonly reported in response to acute pain. Their presence in the hypnotised and unhypnotised conditions may reflect cognitive processing relating to attentional control: Bantick and colleagues (2002), for example, observed activation in the OFC when subjects were distracted during painful stimulation. Additionally, orbitofrontal activity has been linked to cognitive processing underlying hypnotic analgesia (Crawford et al, 1993; Wik et al, 1999). Activity in the pre-frontal cortex and the inferior parietal cortex is commonly observed in association

with painful stimuli. Mesulam (2000) also discusses these regions with reference to top-down modulation of attentional responses. Further experimentation is required to illuminate further their role in the hypnotic modulation of pain and pain modulation via alternative techniques.

8.3.2 Implications

Methodological compromises made to allow fMRI experimentation make conclusions regarding the relative effectiveness of hypnotic and non-hypnotic suggestion tentative: participants were aware at the beginning of the scan that the investigation would include blocks of hypnotic and non-hypnotic pain modulation, therefore it remains possible that the lesser activation in the non-hypnotic condition reflects a 'hold back' effect (Zamansky, Scharf & Brightbill, 1964; Braffman & Kirsch, 1999). Greater activation in PFC, OFC and frontal cortex in the hypnotised condition may reflect utilisation of differential pain control mechanisms across the conditions; although sophisticated designs using alternative hypnotic pain control strategies (e.g. dissociative strategies used in Röder et al, 2004) may serve to clarify this issue in future. Since the activations observed are the product of a correlational analysis between participants' subjective pain report and BOLD response it is likely that they primarily relate to pain experienced rather than to control systems generating and monitoring the experiences. However, activity of control systems and the strength of pain experienced may not be orthogonal and there is likely to be some overlap which places some limits on the interpretation of these results.

Within the group of fibromyalgics it was originally intended to scan patients showing exclusively fibromyalgia symptoms, but such a high proportion of the original sample group had also been diagnosed with IBS that a selection of this nature was not possible. Similarly, the aim of asking all patients to discontinue their fibromyalgia-related medication for the two weeks prior to the scan had to be abandoned, especially in the case of SSRI antidepressants: these require a slow weaning-off which was not possible in the time-scale available. More positively, a sample of patients with a concurrent diagnosis of IBS and on antidepressant medication is more representative of the patient population as a whole; and a recent review of pharmacological therapies for fibromyalgia reported only equivocal results from trials of SSRIs used to treat fibromyalgia symptoms (Rao & Bennett 2003).

The present investigation demonstrates the effectiveness of using suggestion as a cognitive tool, in and outside hypnosis, to modulate the pain experienced by fibromyalgia sufferers. Effectiveness is evinced by significant changes in BOLD response covarying with subjective reports of pain. Importantly, patients felt increases and decreases in their pain in the absence of any additional peripheral input. The cognitive

modulation was generating and ameliorating the experience of the patients' own pain. This investigation therefore links regional activation specifically to the modulation of fibromyalgia pain.

Chapter 9 - Conclusions

"Empirical attempts to distinguish psychological pain from physical pain have not been successful. Certainly... psychological states can aggravate feedback cycles and increase frustration and depression if not diagnosed or treated effectively. But whatever distinctions we make with respect to pain, the psychological/organic one should not be it... In short, we have found precious little evidence that pains differ from one another in a fundamental or significant way. In all likelihood, all pains are physical in origin."

(Hardcastle, 1999)

"The phenomenon of phantom limbs has allowed me to examine some fundamental assumptions in psychology. One assumption is that sensations are produced only by stimuli and that perceptions in the absence of stimuli are psychologically abnormal. Yet phantom limbs, as well as phantom seeing, indicate that this notion is wrong. The brain does more than detect and analyse inputs; it generates perceptual experience even when no external inputs occur"

(Melzack, 1999)

The results of the induced pain studies have been discussed and set in context with the evolving body of work in the Discussion sections as the end of each chapter. This final chapter briefly draws together some overall conclusions, relating the results to other theoretical positions and looks at possible future development of the research that has been started here.

9.1 The scope of this thesis

The experiments presented here derived from the view that functional pains should fall under the rubric of 'auto-suggestive disorder'. In chapter 1 evidence was reviewed that disorders such as fibromyalgia and irritable bowel syndrome are usefully grouped as *functional somatic syndromes* (or sometimes *chronic multisymptom illnesses*) and that they have core similarities as well as differences (Wessely et al, 1999; Barsky & Borus, 1999; Aaron & Buchwald, 2001; Gardner et al, 2003; Fukuda et al, 1999; Nisenbaum et al, 2000). The symptom of pain is common to many of these functional syndromes and was singled out for special attention in the context of the research carried out here. Hypnosis was chosen as an experimental tool as it is well established as a procedure that is effective

in modulating pain experience, and in the light of some preliminary evidence that it may be possible to use hypnotic suggestion to induce pain in the absence of a physical stimulus.

Oakley (1999b) drew together 'traditional' conversion symptoms, such as functional paralysis and blindness, and the more strongly debated symptom of functional pain, in his conception of auto-suggestive disorder. Testable predictions of this model include the idea that it should be possible to model naturally-occurring functional symptoms using hypnotic suggestion and that brain activity underlying the two should be similar. These predictions have previously been explored in the case of functional paralysis (Marshall et al, 1997; Halligan et al, 2000) but had remained untested in the case of functional pain. Additionally, since the conceptualisation of auto-suggestive disorder is that symptoms are self-generated it is hypothesised that the hypnotic suggestibility of sufferers of functional disorders will be higher than usual. In the case of conversion disorder this hypothesis has already gained some empirical support (Roelofs et al, 2002). A final implication of the theory is that functional symptoms should be malleable to manipulation by hypnotic suggestion (although Patterson & Jensen [2003] clearly state that no-one would expect a single session of hypnosis to cure chronic pain). The series of experiments presented here aimed to test these predictions in order to investigate the extent to which psychological factors, particularly hypnotic suggestibility, could play a role in functional pain disorders.

9.2 Key findings

The results of the experiments investigating hypnotically-induced pain in this thesis oppose traditional arguments for a peripheral physiological basis to every pain. Highly hypnotisable and hypnotised participants were able to experience a sensation of pain as a result of direct suggestion (chapter 2) and via manipulation of expectation (chapter 5). Further investigation into the subjectively experienced differences between imagining a pain and experiencing a hypnotically-induced pain proved inconclusive on measures of perceived externality, clarity, intensity and unpleasantness (chapter 3). However, differences in distribution relating to the hypnotic susceptibility of participants able to imagine and hypnotically-experience pain suggests that hypnotisability may play a key role in the ability to experience these suggested effects as 'real' (chapter 3). The opportunity remains for further work examining the capacity for the imagination of pain in unhypnotised participants.

Functional neuroimaging investigation of imagined pain compared with physically-induced (PI) and hypnotically-induced (HI) pain yielded significantly different patterns of activation between imagined pain and HI or PI pains (chapter 5). Activation for the former was minimal whereas the latter two produced patterns of activation consistent

with previous reported studies of acute pain. This indicates that hypnotised participants in these investigations are not simply imagining their experiences in the hypnotically-induced pain condition, instead the evidence suggests they are feeling the changes in experience as if they are actually happening. This result compares well with other investigations of hypnotically-induced hallucination (e.g. Szechtman et al, 1998; Kosslyn et al, 2000), including pain (Willoch et al, 2000), but extends the focus to hallucinated pain in healthy controls. One shortcoming of the present investigation that should be addressed in future studies concerns the lack of additional subjective measures of the pain experience taken on-line in the scanner. Measures of the externality and clarity of the pain experiences, similar to those taken by Szechtman et al (1998), would have allowed for more in depth analysis of the relationship between the subjective experience of the pains and rCBF measures of neural response. Importantly though, these results demonstrate, for the first time, the activation of the pain system in healthy controls in the absence of peripheral noxious stimulation. This evidence of a truly functional pain experience supports the view that functional pain symptoms can be psychologically determined and has fundamental implications for theories of pain as well as for our understanding of the aetiology and treatment of functional pain conditions.

The hypnotic susceptibility of fibromyalgia patients was assessed and compared with a concurrently tested group of control participants (chapter 7). No significant differences in scores were found although there was a trend, opposing our hypothesis, for control participants to score higher on the objective scale of the HGSHS:A. The fibromyalgia patients scored significantly than controls higher on an index of depression but there is little empirical evidence indicating that this may have attenuated hypnotic susceptibility scores. This result does not provide support for the notion of functional pain as an auto-suggestive disorder if high levels of hypnotic susceptibility are construed as a risk factor.

The results presented here concerning the neural signature of fibromyalgia were obtained by using hypnosis as a cognitive tool to modulate patients experience of their own pain (chapter 8). This technique is a significant advancement upon previous investigative techniques concerning fibromyalgia pain. It demonstrates activations underlying patients experience of their own pain rather than reactions to external stimuli (augmented processing), and provides useful preliminary evidence indicating that hypnotic suggestion could be an effective component of treatment for fibromyalgia (the only other controlled evidence comes from a small study by Haanen, Hoenderdos, van Rommunde, et al, 1991). The pattern of neural activation observed is considered salient to the generation of fibromyalgia pain and extends previous findings with this patient population, but the type of experiment conducted (modulation of pain which was already there) arguably precludes direct observation of hypothetical sites of fibromyalgia pain generation. Activations located outside the commonly cited areas of the pain matrix are perhaps most parsimoniously explained in terms of the modulation

of the pain. In particular, frontal cortex and orbito-frontal activity demonstrated here may in this view relate more to the cognitive effort involved in producing the changes in the experience of pain rather than being intrinsic to the pain itself. It is important to note here that the modulation of fibromyalgia pain by hypnotic suggestion does not of itself address the issue of whether the fibromyalgia pain is wholly or in part truly functional. Hypnotic suggestion is well established as a means of modulating the experience of pain which has a demonstrable physical origin.

The activation patterns obtained from the two neuroimaging investigations reported in this thesis are presented in table 9.1 and clearly demonstrate pain-related activity in response to suggestions for pain hallucinations and suggestions for functional pain modulation. Similar activations are observed in response to a variety of physically-induced pains in other studies. These observation are consistent with the idea that HI, PI and fibromyalgia pains are all mediated by the same central mechanisms as predicted by the Oakley (1999b) model.

	S-I	S-II	ACC	Thalamus	Insula	PFC	PAG	SMA	Basal Ganglia	Cerebellum	Striatum	IPC (BA39/40)	OFC	Brainstem	Frontal Cortex	Lentiform Nucleus
Porro (2003) Review of activations in response to acute pain	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑						
Peyron et al (2000) Review of activations in response to acute pain	↑	↑	↑	↑	↑		↑	↑		↑	↑					
Derbyshire (1999) Review of activations in response to acute pain	↑	↑	↑	↑	↑	↑					↑	↑				↑
Physically-Induced Chapter 5		↑	↑	↑	↑	↑				↑		↑				
Hypnotically-Induced Chapter 5	↑	↑	↑	↑	↑	↑				↑		↑				
Imagined Chapter 5		↑			↑											
FM Hypnotised Chapter 8	↑	↑	↑↓	↑	↑	↑	↑			↑		↑	↑	↑	↑↓	
FM Unhypnotised Chapter 8	↑	↑	↑↓	↑	↑	↑↓	↑			↑		↑	↑↓	↑	↑	

Table 9.1: An overview of the neural activations observed during studies of functional pain reported in this thesis and in reviews of acute pain by Derbyshire (1999), Peyron et al (2000) and Porro (2003).

9.3 Putting these findings into context

The idea that pain can be felt in the absence of a physical stimulus remains controversial. Patient support-groups for fibromyalgia, chronic fatigue syndrome and temporomandibular joint disorder commonly oppose explanations with a psychological emphasis and much time and money is spent on the search for a physiological basis to these disorders (Temporomandibular Joint Disorder Interagency Working Group, 2000). From a psychological perspective, however, examination of two theoretical models can help to place the results presented here into context. Vogeley (1999) usefully considers the ontological status of imagined, real and hallucinated percepts, and Melzack and Loeser's (1978) proposition of a central pattern generator for pain can account well for the findings observed here.

9.3.1 Hallucination, imagination and perception

Vogeley (1999) observes that *"The relevant functional brain systems involved, e.g., the visual system or the auditory system, are involved in normal perception and imagery as well as in hallucinatory experience. There is probably a common neuroanatomic basis constituting a "conservation principle"."* In light of this he postulates a 'perceptual continuum' which encompasses perception, imagination, hallucination and pseudo-hallucination (an as-yet poorly investigated state where an individual knows that a hallucinated percept is unreal). The properties of the percepts in Vogeley's continuum are illustrated in table 9.2, and account for the experimental evidence presented in chapter 5. Physically-induced pain, hypnotically-induced pain and imagined pain are represented by perception, hallucination and imagination respectively and Vogeley describes the perceived properties of each. Interestingly, the properties described for hallucinations and pseudo-hallucinations in Vogeley's model could be thought to tally with the differences between hypnotically-hallucinated (e.g. Derbyshire et al, 2004) and hypnotically-suggested pain (e.g. Whalley & Oakley, 2003; chapter 2): with the possibility that participants knew at some level that the hypnotically-suggested effect was not 'real'. This view is supported by classic reports of hypnotic hallucination: visual hallucinations, for example, are often experienced as not being completely opaque which lends credence to their possible categorisation as pseudo-hallucinations (Orne, 1959; Spanos, Bridgeman, Stam, et al, 1983; Spanos, 1986). Since Vogeley's description of hallucination pertains mainly to auditory hallucination in schizophrenia, with research hampered by obvious attendant methodological difficulties, it would certainly be interesting to use hypnosis to further investigate the difference between hallucinations and pseudo-hallucinations. It would be possible in hypnosis for example to manipulate and measure the strength of a hallucination, and to assess the degree to which it was perceived as real. Such a manipulation would lend itself to further exploration using functional imaging.

Perceptual Capacity	Sensory Richness	Subjective Location	Source Monitoring	Reality Status	Monitoring Certainty	Reality Judgement	Representation Status
Perception	Rich	Externally	Externally	Real	Certain	Real	Correct
Imagination	Poor	Internally	Internally	Virtual	Certain	Virtual	Correct
Pseudo-Hallucination	?	Externally	Internally	Virtual	Uncertain	Virtual	Incomplete
Hallucination	?	Externally	Externally	Virtual	Certain	Real	False

Table 9.2: The perceptual continuum and its properties (Taken from Vogeley, 1999).

Vogeley's 'conservation principle' is supported by the evidence presented here concerning the neural underpinnings of a hallucinatory pain experience. Hallucinated pain involved activation of the traditional pain matrix at an intensity consistent with the subjective experience of the pain (see figure 5.5). Imagined pain activated some of the key areas of the pain matrix (S-II, insula), but at a much reduced intensity, commensurate with absence of reports of 'feeling' pain in this condition. These findings complement earlier functional neuroimaging investigations of hypnotic hallucinations and imagination (Kosslyn et al, 2000; Szechtman et al, 1998) but extend beyond the auditory and visual capacities to focus on pain. From experimental and review evidence Levy et al (1999a) concluded that imagined odour and imagined motor movement (Roth et al, 1996) activated the same circuits as actual perception/action but at an intensity of approximately 30% of the 'true' activation. Levy's proposed relationship is not easily verifiable from the imagined pain data in the present study, especially since intensity ratings were not taken in the imagined condition, but a similar relationship is predicted for imagined vs. real pain. The current work is nevertheless useful in that it allows us to recognise some pains as hallucinated percepts which can then be studied within an established framework. Further work using covariate analysis of the strength of a percept (real, imagined or hallucinated) and rCBF would allow us to determine more clearly the nature and neural representations of hallucinated and physically-induced pain within such a perceptual continuum, and more importantly give us a framework to help us to understand the underpinnings of functional pain

9.3.2 A pattern generator for pain?

"In 1978, Loeser and I [Melzack & Loeser, 1978] described severe pains in the phantom body of paraplegics with verified total sections of the spinal cord, and proposed a central "pattern generating mechanism" above the level of the section... These observations, as well as the fact that most chronic pain syndromes do not have a discernable sensory "cause" or are characterised by intense pain that is disproportionate to input, reveal that the brain

itself can generate every quality of experience, including pain, which is normally triggered by sensory input" (Melzack, 1999).

Melzack and Loeser (1978) were trying to contextualise their observations of phantom body and limb patients when they proposed the idea of a central pattern generator for pain. Observations of patients with pain in parts of their body that were below the level of total transection of the spinal cord convinced them that pattern generating mechanisms must also lie above the level of the spinal cord. Their model, reproduced in figure 9.1, asserts that many more factors than just nerve firing from the periphery can generate the experience of pain. The acknowledgement of top-down pain modulation is made in the gate control theory (Melzack & Wall, 1965; see section 1.1.2.2) but this 1978 model specifically includes the concept of central generation.

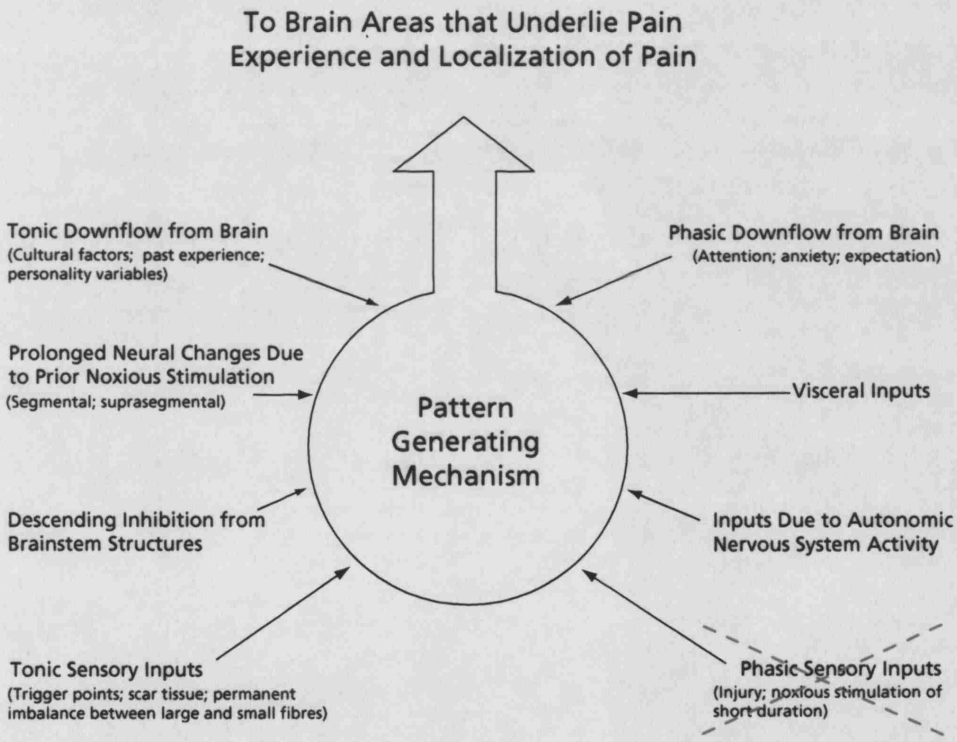


Figure 9.1: Concept of a pattern generating mechanism controlled by multiple inputs (Modified from Melzack & Loeser, 1978).

The results presented in chapter 5 support this model, providing evidence for the activity of such a mechanism in healthy control participants. A hallucinatory experience of pain, which can be considered truly functional, was generated through manipulation of expectation in hypnosis: what Melzack and Loeser refer to as 'phasic downflow from brain'. Supporting this modified conception of pain is Lang's (1978) theory of emotional imagery, with the idea that individuals have the capacity to self-generate the feelings associated with emotional situations. As Melzack argues above, results such

as those reported in this thesis disconfirm the notion that all sensations are produced by external stimuli and powerfully make the case for psychological generation of some strong sensations. Although the results presented here are confined to a population of highly-hypnotisable participants the production of suggested headaches in two thirds of Schweiger and Parducci's (1981) hypnotically unselected sample indicates that this ability might not be limited to such a restricted group. Specifically in relation to Melzack & Loeser's (1978) model, the results of chapter 5 confirm the possibility of pain generation in the absence of noxious sensory input, this finding is represented by the dashed cross in figure 9.1.

Modulation of fibromyalgia pain using suggestion confirms further that perceptual experience of the strength of experienced pain is related to the strength of activations in areas of the pain matrix (Derbyshire et al, 1997; Coghill et al, 2003). In a strict sense the results of the study presented in chapter 8 cannot address the issue of pattern generation since patients' pain was not absent before manipulation. A more accurate description of the effects of the suggestions is that they *modulated* patients pain. The base level of each patient's pain assumes less importance as it is the range of modulation effected by the suggestion that concerns us. The present results do not lead to a claim for a specific site of fibromyalgia pain generation outside the traditional pain matrix. The frontal cortex activation that was observed seems best explained in terms of cognitive effort needed to affect the subjective intensity of the pain (Crawford et al, 1993). Despite this lack of clear evidence for a specific site of generation, an interpretation of a central origin for fibromyalgia pain is, however, consistent with the pattern generating mechanism proposed by Melzack & Loeser: "*...once the abnormal central pattern generating processes are underway, the peripheral contributions may assume less importance. They are, to be sure, avenues for modulating the activities in the pattern generating mechanisms, but their removal may not stop pain once it is established*" (Melzack & Loeser, 1978). This interplay of peripheral and central factors accounts well for the symptoms observed in fibromyalgia patients: the central sensitisation leading to pain being experienced from a non-noxious peripheral input, the pattern of 'flare-ups' being affected by psychological factors, and the absence of any observable peripheral pathology.

9.3.3 Functional pain as an auto-suggestive disorder

The results of the hypnotically-induced pain investigations demonstrate that it is possible for highly-hypnotisable individuals to experience pain in the absence of peripheral noxious stimulation. Hypnotic suggestion, and to a lesser extent non-hypnotic suggestion, were shown to be tools capable of modulating fibromyalgia pain allowing direct fMRI investigation into its neural correlates. Activations underlying a pain known to be functional (HI pain) encompass the same network of regions as fibromyalgia pain but, as noted earlier, it is not possible from these data to draw

conclusions regarding the functional or organic nature of the latter. A prediction of the theory placing functional pain within the category of auto-suggestive disorders is that patients with such pain will exhibit enhanced hypnotic suggestibility. No such relationship was found in the sample of 46 fibromyalgia patients reported in chapter 7, indicating that high hypnotic susceptibility is not a contributory factor in fibromyalgia pain.

9.4 Future directions

One key outcome of this thesis has been to demonstrate the usefulness of hypnosis as a cognitive tool. It has allowed for repetitive manipulation of subjective experiences of pain suitable for study in fMRI: this has allowed the capture of objective measures of participants' experiences, tackling the problem of demand characteristics common to much hypnosis research. Using hypnosis to demonstrate functional pain experiences in healthy control participants affects the way we conceptualise pain. It provides support for the theory of a pattern generator for pain. Melzack & Loeser's (1978) conceptualisation of such a generator was driven by observations of phantom limb and paraplegic patients, but the results presented here indicate that its scope should be extended to encompass functional pain. In addition to the pain-related results a finding of interest to hypnosis researchers is the evidence presented in chapter 8 concerning the effects of non-hypnotic suggestion for pain modulation. This represents the first controlled examination of hypnotic vs. non-hypnotic suggestions in the functional imaging environment.

On a practical level, key concepts regarding the conduct of functional imaging investigations involving hypnosis have been observed (the trance/suggestion distinction: Oakley & Halligan, 2002; Heap & Aravind, 2002). Additionally, the (mainly) non-verbal administration of suggestions proved successful for obtaining repetitive pain modulation during an fMRI 'run' whilst attaining maximum acquisition time. Conceptually it has been demonstrated that suggestion is a useful tool with which to model and manipulate functional pain, but the question of whether such pains should fall within the category of auto-suggestive disorders is challenged by the hypnotic susceptibility scores demonstrated in chapter 7. A number of research questions remain to be addressed:

1. Whether the hypnotic susceptibility score of functional disorder patients correlates with the number of somatic complaints each patient has.

2. How imagined pain compares to physically-induced pain in hypnotised and unhypnotised participants (for all levels of hypnotisability, not just highs)

3. Examination of whether suggestion can be used to model other functional symptoms such as fatigue in CFS or bowel discomfort in IBS.

To address the first question, hypnotic suggestibility testing will need to be carried out individually with functional disorder patients (and with a matched affective control group) and the scores correlated with each patient's number of somatic symptoms including the commonly cited fatigue, tenderness and bowel discomfort. A well controlled investigation would also test a patient population with similar levels of pain but no functional symptoms.

To address the second question a fuller investigation needs to be conducted to assess the ability of unhypnotised participants (of varying levels of hypnotic susceptibility) to imagine pain. The 'unhypnotised' results of the experiment described in chapter 8 indicate that suggestion in the absence of hypnosis is effective in producing changes in brain function, but the results described in chapter 5 indicate that instructions to imagine pain did not result in significant changes in brain activity – as such, the line between 'instructions to imagine pain' and 'suggestions to experience pain' needs to be investigated in more detail. In line with Lang's (1978) theory of emotional imagery and Vogeley's (1999) perceptual continuum it is expected that the strength of a percept will correlate with brain activity in the appropriate brain regions.

Hypnotic suggestion has demonstrated itself to be a useful tool in the modelling of functional pain and it seems obvious to extend the list of symptoms which could be modelled with hypnosis. Suggestions to produce tenderness (allodynia) could allow control subjects to be compared with functional pain patients in a design similar to Gracely et al's (2002) examination of augmented pain processing in fibromyalgia: further helping us to understand the mechanisms underlying central sensitisation. It may also prove possible to manipulate the level of fatigue felt by CFS patients or to model the symptom in control participants, allowing examination of the neural basis of fatigue in this population. Finally, in the case of irritable bowel syndrome where gut-directed hypnotherapy has already demonstrated long-term efficacy (Gonsalkorale et al, 2003) it is starting to become possible to use functional imaging techniques to obtain another metric of effectiveness of treatment. Measuring response to a physiological stressor (e.g. rectal or colonic distention for IBS, pressure-pain for fibromyalgia) before and after treatment allows for objective verification of the effect of its effectiveness.

Evidence has been presented here linking the psychological intervention of hypnotic suggestion with specific activity in the human pain system in healthy controls and functional pain patients. This confirmation of the existence of psychogenic pain supports the continued psychological investigation of functional pain conditions. Future investigations must consider the role of psychological factors in the initiation and maintenance of these conditions.

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Appendix 2.1 - Hypnotic induction

Now close your eyes, and take a deep breath in ... hold it for a moment ... and out, and just allow your body to float down into the chair, letting all your muscles relax.

Breathing

In order to relax, some people find it helpful to visualise breathing out all the tension in their body. So pick a colour representing tension, and imagine ... and begin to feel ... yourself breathing out breath tinged with that colour of tension ... and as you do so just allow yourself to feel the tension draining out of your body. Breathing out that tense coloured breath and allowing it to float away and disperse, so it can't bother you.

See yourself breathing out the tense, coloured breath ... and notice all of the muscles in your body relaxing more and more with each breath. Breathing out all of the tension in your body, and being left with relaxed, easy feelings of comfort and ease. Just keep breathing out that tense coloured breath for as long as you need, becoming more and more relaxed with each breath. Your breathing becoming slower, deeper and calmer every time you breathe out that tension. And you might find that as you successfully breathe out the tension, that the colour becomes paler and paler, as all of the tension leaves your body ... breath, by breath.

And as you breathe away the tension, you might like to imagine replacing the tension with calm, relaxed feelings. So imagine a colour representing calm, easy feelings of relaxation and visualise breathing in air tinged with this calming, soothing colour. And as you do so, you might feel waves of calm spreading through your body with every breath you take. Becoming calmer and more relaxed with every breath you take. Just allowing this calm to spread through your body ... relaxing all of your muscles ... with every breath you take. Every breath making you feel calmer, and more relaxed than before.

Muscles

Now as you continue to breathe calmly and steadily, I would like you to pay attention to the muscles in your legs. And I would like you to pay attention to the contact between the backs of your legs and the chair. Feel the warmth of that contact ... and allow those feelings of warmth to spread into the muscles of your legs ... relaxing them ... easing them. That feelings of warmth easing away any tension in the muscles of your legs. Allowing those muscles to become loose, and limp, and completely relaxed. Those feelings of warmth spreading and radiating through your legs, easing and relaxing the muscles as those feelings spread down your legs, past your knees, and down your calves. Feelings of ease and relaxation spreading through the muscles of your thighs and calves, and spreading down to your feet. Allowing any tension to flow down your legs and down to the tips of your toes. All the muscles in your legs completely relaxed ... completely at ease ... the muscles loose and limp.

And as you enjoy those feelings of warmth and relaxation in your legs I would

like you to pay attention the contact between your back and the chair. And as you pay attention to that contact you can feel the warmth created ... that feeling of warmth spreading over your back ... soothing all of the muscles in your back ... allowing them to unwind and relax completely. All of the tension draining away from the muscles of your back as the feeling of warmth penetrates in to the muscles of your back ... easing them ... soothing them ... allowing the muscles of your back to relax completely.

And allowing those feelings of warmth and relaxation to spread to the muscles of your stomach ... and your chest ... those muscles loose ... and limp ... and very relaxed. Completely at ease ... just allowing any tension to drain away from your stomach and chest. Your breathing slow and regular, allowing the tension to drain away with each breath. The muscles of your stomach and chest relaxed and completely at ease.

And that warmth spreading up to your shoulders ... relaxing the muscles of your shoulders ... easing the joints ... soothing away any tension ... just allowing your shoulders to relax completely ... to become limp and heavy, completely relaxed.

And that relaxation spreading down your arms ... easing the muscles ... allowing any tension in your arms to just drift away as your arms relax. Those relaxing feelings travelling down your arms ... right down to the tips of your fingers ... soothing away any remaining tension in the arms as they become limp and heavy ... completely relaxed.

And now allow those feelings of relaxation to spread to your neck ... easing the muscles in your neck, allowing tension to drain away, as you become more and more relaxed. The waves of relaxation spreading up your neck, to your head ... to the muscles around your eyes, easing them ... relaxing them ... to the muscles of your jaw and cheeks ... relaxing all the muscles of your head.

Your whole body feeling very limp and relaxed ... your muscles loose and limp ... your breathing slow and regular ... relaxing more and more with each breath.

Garden

I'd like you now to imagine, and then find yourself in a very pleasant, very relaxing garden on a warm sunny day. It can be a real or imaginary garden, but find yourself there in the garden ... feeling pleasantly relaxed and calm. Look around and see the sights of the garden ... maybe some trees or flowers ... maybe a fountain.

Listen for any sounds there in the garden ... ... maybe birds singing ... the sound of a gentle breeze ... just enjoy being there in that pleasant relaxing garden.

Smell any smells there in the garden ... maybe the smell of freshly cut grass ... maybe flowers.

All these sights, sounds and smells add to the feeling of relaxation. There may be a warm breeze which blows over your face ... soothing, warm and comfortable.

Just being there ... a pleasant relaxing feeling of being in this beautiful garden. And as you look around the garden you see some steps which lead down into another even more pleasant and relaxing part of the garden which you perhaps had not noticed before. Just moving towards the steps now, and pausing at the top, contemplating descending down into the other part of the garden ...

In a moment or two ... when I say ... I would like you to begin to travel down the steps towards the other part of the garden. That very special relaxing place. So I'm now going to count from one to ten, and as I count you can descend the steps, finding yourself at the bottom when I reach ten, and finding that you relax deeper and deeper with each count.

...

One ... two ... down, down, deeper and deeper into this special place ... three ... four ... all the sights, sounds and smells even more pleasant and relaxing than before ... five ... ... six ... deeper and deeper, relaxing more and more ... seven ... eight ... your whole body relaxing as you descend deeper than ever before into hypnosis and relaxation ... nine ... and ten. Very deeply relaxed and hypnotised. Completely relaxed ... completely comfortable.

Special Place

And I'd like you now to find yourself in your special place. A place where you can be alone with you own thoughts and feelings. A relaxing, pleasant place to be.

Begin to imagine, and then to see, hear, smell and feel all of the sensations which are associated with that place.

Any sounds which don't belong to the special place can slip to the back of your mind where they can't bother you.

You're feeling good and confident ... pleasantly relaxed ... deeper and deeper. Feeling happy ... and comfortable ... enjoying the sensations of being there.

And I'm just going to count to ten, to give you some time to enjoy being there in your special place.

And as I count feel yourself becoming more and more relaxed. More and more comfortable.

One ... deeper and deeper ... two ... three ... relaxing more and more ... four ... five ... deeper and deeper ... six ... seven ... deeper still ... more and more relaxed ... eight ... nine ... and ten. Deeper and deeper, deeper than ever before.

Appendix 2.2 - Suggestions

I'd like you now to place your left/right hand on the table in front of you, and I would like you to pay careful attention to the feelings and sensations in that hand.

When the sensations in your hand become painful, but not before, I would like you to move your hand back to your lap and the sensations in it will become normal. Remember that you should only move your hand back to your lap when the sensations become painful, or when I tell you to move it.

0s I would like you to imagine … and begin to feel …
3s that a powerful light bulb has been switched on
7s and that the beam of light is focussed on your left/right hand.
10s The energy from the light bulb shining directly down onto your hand.
16s The heat from the lamp warming the skin on the back of your hand.
21s The heat penetrating into the skin
24s … and the feeling of warmth in your hand becoming stronger and stronger.
30s Pay attention to the feelings in your hand as the light shines down onto it,
37s heating the skin … raising the temperature … hotter and hotter.
45s Uncomfortably hot.
50s Feel the temperature of your hand increasing.
53s The feelings of heat getting stronger and stronger …
57s more and more intense as time goes by.
61s The heat building and building … until it begins to hurt …
67s becoming a painful sensation.
70s The temperature in your hand continuing to rise
75s as the heat-lamp shines down onto the back of your hand
79s … the penetrating heat getting hotter and hotter
84s … stronger and stronger… more and more painful.
90s Just allow those feelings of heat to become stronger … and stronger
98s … hotter … and hotter …
101s those painful feelings becoming more intense as time goes by
104s … becoming stronger … and stronger … more and more painful
110s as the heat from the lamp is radiated onto the back of your hand.
115s Your hand hurting now.
118s That heat becoming more and more intense … so intense.
123s So intense, so painful. More and more painful, the pain becoming intolerable.
130s Feel the heat spreading through your hand,
134s the intense feelings of heat, as the lamp shines down onto your hand.
139s Heating it hotter and hotter. So hot … so intense…so painful.
147s The sensation of pain becoming stronger and stronger.
152s The pain increasing as your hand becomes hotter and hotter.

157s More and more pain, hurting more and more
162s

Removal

That's fine, your hand no longer exposed to the heat of the lamp. No longer being heated. Your hand cooling down now … the sensations returning to normal. Completely normal … just like your other hand. And feel free to move your hand and wiggle your fingers just to check that it is completely back to normal. Just resting your hand back in your lap, feeling completely back to normal.

Appendix 2.3 - Post experimental questionnaire

Hypnotic Pain

Did you feel heat when you were asked to imagine a light shining on your hand?
(y / n)

Did you feel pain when you were asked to imagine a light shining on your hand?
(y / n)

If you felt pain, what did you feel to be the cause of it?
(i.e. was it the increasing heat or something else?)

Please give any other information you think might be helpful about the sensations in your hand when asked to imagine a light shining on it:

Physical Pain

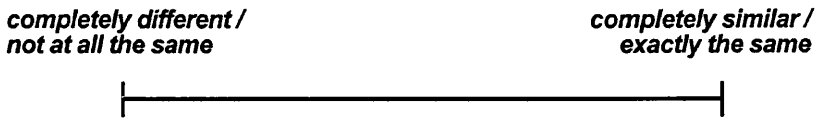
Did you feel heat when the lamp was shone on your hand?
(y / n)

Did you feel pain when the lamp was shone on your hand?
(y / n)

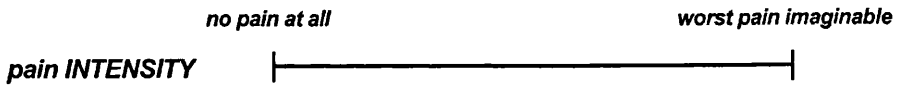
If you felt pain, what did you feel to be the cause of it?
(i.e. was it the increasing heat or something else?)

Please give any other information you think might be helpful about the sensations in your hand when the lamp was shone on it:

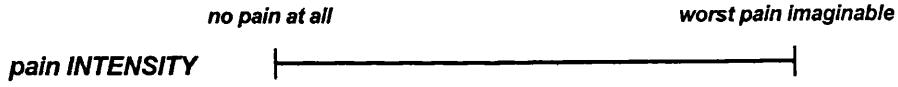
How similar was the heat-lamp pain to the hypnotically-induced pain?



Heat-lamp pain:



Hypnotically-induced pain:



Appendix 2.4 - McGill Pain Questionnaire

McGill-Melzack Pain Questionnaire

Name: _____ Age: _____ Date: _____

This questionnaire only relates to the HEAT-LAMP pain

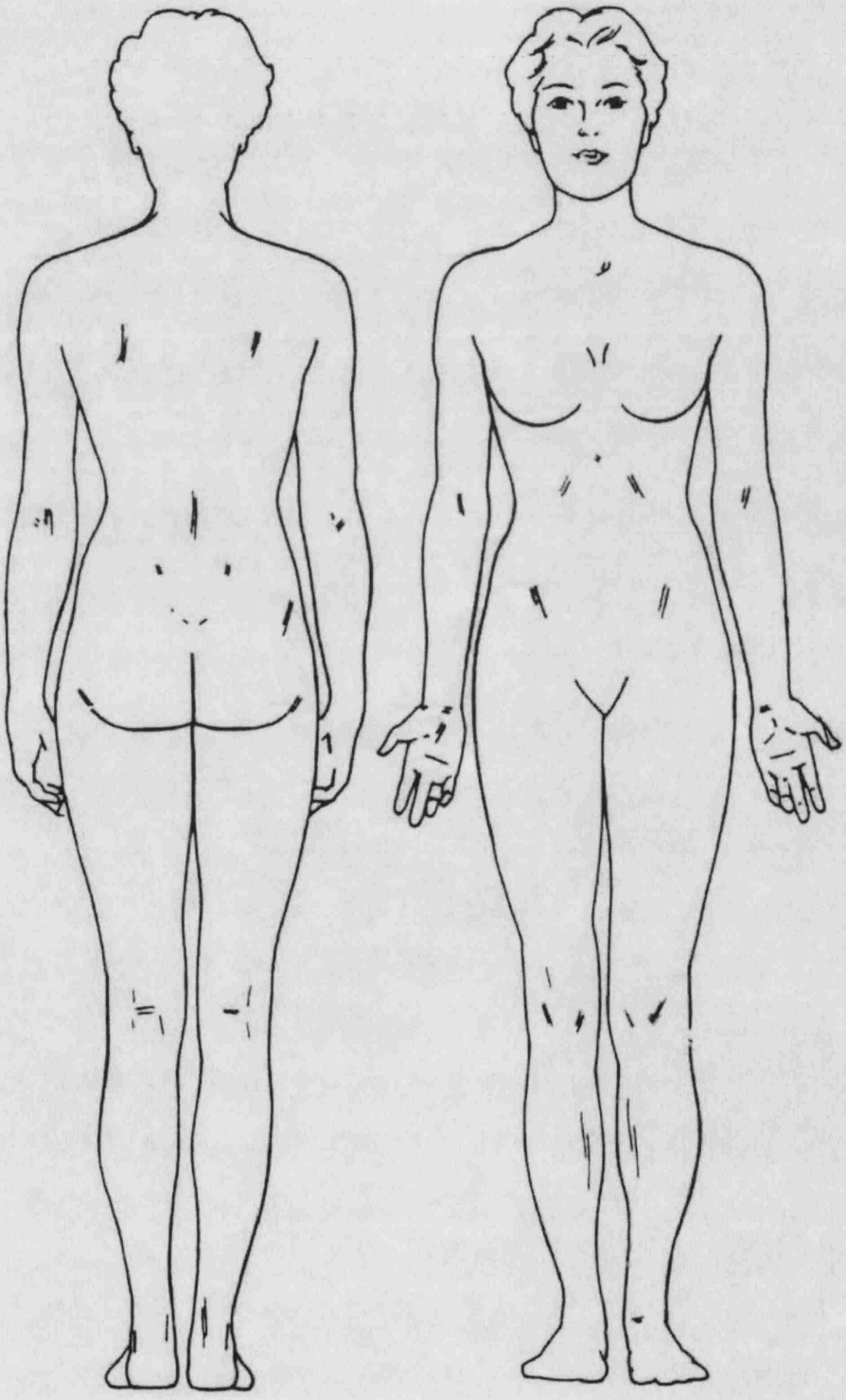
This questionnaire has been designed to tell us more about the HEAT-LAMP pain you just experienced. Four major questions we ask are:

1. Where is your pain?
2. What does it feel like?
3. How does it change with time?
4. How strong is it?

It is important that you tell us how the HEAT-LAMP pain you just experienced felt. Please follow the instructions at the beginning of each part.

Part 1 *Where is your pain?*

Please mark, on the drawings below, the area where you just felt pain. Put E if external, or I if internal, near the areas which you mark. Put EI if both external and internal.



Part 2 *What does your pain feel like?*

Some of the words below describe the HEAT-LAMP pain you just experienced. Circle ONLY those words that best describe it. Leave out any category that is not suitable. Use only a single word in each appropriate category – the one that applies best.

1	2	3	4
Flickering	Jumping	Pricking	Sharp
Quivering	Flashing	Boring	
Cutting			
Pulsing	Shooting	Drilling	Lacerating
Throbbing		Stabbing	
Beating		Lancinating	
Pounding			

5	6	7	8
Pinching	Tugging	Hot	Tingling
Pressing	Pulling	Burning	Itchy
Gnawing	Wrenching	Scalding	Smarting
Cramping		Searing	Stinging
Crushing			

9	10	11	12
Dull	Tender	Tiring	Sickening
Sore	Taut	Exhausting	Suffocating
Hurting	Rasping		
Aching	Splitting		
Heavy			

13	14	15	16
Fearful	Punishing	Wretched	Annoying
Frightful	Gruelling	Blinding	Troublesome
Terrifying	Cruel		Miserable
	Vicious		Intense
	Killing		
Unbearable			

17	18	19	20
Spreading	Tight	Cool	Nagging
Radiating	Numb	Cold	Nauseating
Penetrating	Drawing	Freezing	Agonising
Piercing	Squeezing		Dreadful
	Tearing		Torturing

Part 3 *How did the pain change with time?*

1. Which word or words would you use to describe the pattern of the HEAT-LAMP pain?

1	2	3
Continuous	Rhythmic	Brief
Steady	Periodic	Momentary
Constant	Intermittent	Transient

2. What kind of things relieved the HEAT-LAMP pain?

3. What kind of things increased the HEAT-LAMP pain?

Part 4 *How strong was the pain?*

People agree that the following 5 words represent pain of increasing intensity. They are:

1	2	3	4	5
Mild	Discomforting	Distressing	Horrible	Excruciating

To answer each question below, write the number of the most appropriate word in the space beside the question.

1. Which word describes your pain right now? ____
2. Which word describes it at its worst? ____
3. Which word describes it when it is least? ____
4. Which word describes the worst toothache you ever had? ____
5. Which word describes the worst headache you ever had? ____
6. Which word describes the worst stomach-ache you ever had? ____

Appendix 2.5 - Pain Beliefs Questionnaire

For each item please indicate your opinion by underlining one of the following words in each sentence:

always / almost always / often / sometimes / rarely / never

There are no right or wrong answers: it is important that you respond according to your actual beliefs, not according to how you feel you should believe or how you think we want you to believe.

Please make sure you answer ALL the questions.

1) Pain is (always/almost always/often/sometimes/rarely/never) the result of damage to the tissues of the body.
2) Physical exercise (always/almost always/often/sometimes/rarely/never) makes pain worse.
3) It is (always/almost always/often/sometimes/rarely/never) impossible to do much for oneself to relieve pain.
4) Being anxious (always/almost always/often/sometimes/rarely/never) makes pain seem worse.
5) Experiencing pain is (always/almost always/often/sometimes/rarely/never) a sign that something is wrong with the body.
6) Being in pain (always/almost always/often/sometimes/rarely/never) prevents you from enjoying hobbies and social activities.
7) When relaxed pain is (always/almost always/often/sometimes/rarely/never) easier to cope with.
8) The amount of pain is (always/almost always/often/sometimes/rarely/never) related to the amount of damage.
9) Thinking about pain (always/almost always/often/sometimes/rarely/never) makes it worse.
10) It is (always/almost always/often/sometimes/rarely/never) impossible to control pain on your own.
11) Pain is (always/almost always/often/sometimes/rarely/never) a sign of illness.
12) Feeling depressed (always/almost always/often/sometimes/rarely/never) makes pain seem worse.

Appendix 3.1 - Intoductory briefing

Instructions for Experimenter – Read Verbatim

This study will involve hypnosis.
You've all been hypnotised at least once on the group test in a first year lab class.
Today's experience will probably feel quite similar, you'll be given some relaxation instructions and we'll ask you to imagine and feel some things.

Here's a run-through of what we'll be doing:
You'll close your eyes.
Then there will be some instructions to concentrate on your breathing.
Then some instructions about relaxing all of the muscles of your body.
Then there's what we call a 'descent image', it just helps you to descend deeper into hypnosis. You'll be asked to find yourself in a garden, it can be real or imaginary, and will be asked to find yourself at the top of a set of steps. Then the voice will count from one to ten, and as it does you can descend the steps, deeper into hypnosis. The important thing to remember is that there don't have to be ten steps, that's just to pace the experience, and you can descend at any pace you want – as long as you find yourself at the bottom of the steps at around 10.
Next we'll have a part we call the 'special place'. Basically this is a place, real or imaginary, where you can be on your own with your own thoughts and feelings. Somewhere where you can be happy and comfortable. People often choose a beach or a garden, but it can be anywhere you'll be happy and comfortable.
After that we'll have the experimental suggestions, which involve you paying attention to your dominant or writing hand, then we'll end the hypnosis and there will be a few questionnaires.

The important thing to remember about hypnosis is to not try too hard, and try not to think about what's happening. Just let happen whatever you find is happening, don't question it, just go along with it and enjoy the experience. Ignore any distracting sounds and just concentrate on your own experience. We're not going to make any of you do anything embarrassing, should be an interesting experience.

Any questions about hypnosis?

Before we start we need to make sure that everybody is very clear on some terminology:
It's important that you understand the difference between **experiencing something** and **imagining something.**
Now close your eyes and we're just going to play a piece of music
#Music# (20s)

Now open your eyes.
Now close your eyes again and just **imagine** that same piece of music playing
#Silence/Imagining# (20s)
Now open your eyes
Now you've all had a chance to *experience* and *imagine* sounds.

Last minute instructions:
MAKE SURE MOBILE PHONES ARE TURNED OFF, NOT JUST ON VIBRATE – WE DON'T WANT ANY DISTRACTIONS
Anybody with contact lenses – comfortable with having your eyes closed for about 20 minutes?

Appendix 3.2 - Hypnotic Scripts

Script: Instructions to Experience and Imagine Pain

Now close your eyes, and take a deep breath in ... hold it for a moment ... and out, and just allow your body to float down into the chair, letting all your muscles relax.

Breathing

In order to relax, some people find it helpful to visualise breathing out all the tension in their body. So pick a colour representing tension, and imagine ... and begin to feel ... yourself breathing out breath tinged with that colour of tension ... and as you do so just allow yourself to feel the tension draining out of your body. Breathing out that tense coloured breath and allowing it to float away and disperse, so it can't bother you.

See yourself breathing out the tense, coloured breath ... and notice all of the muscles in your body relaxing more and more with each breath. Breathing out all of the tension in your body, and being left with relaxed, easy feelings of comfort and well-being. Just keep breathing out that tense coloured breath for as long as you need, becoming more and more relaxed with each breath. Your breathing becoming slower, deeper and calmer every time you breathe out that tension.

And you might find that as you successfully breathe out the tension, that the colour becomes paler and paler, as all of the tension leaves your body ... breath, by breath.

And as you breathe away the tension, you might like to imagine replacing the tension with calm, relaxed feelings. So bring to mind a colour representing calm, easy feelings of relaxation and visualise breathing in air tinged with this calming, soothing colour. And as you do so, you might feel waves of calm spreading through your body with every breath you take. Becoming calmer and more relaxed with every breath you take. Just allowing this calm to spread through your body ... relaxing all of your muscles ... with every breath you take. Every breath making you feel calmer, and more relaxed than before.

Muscles

Now as you continue to breathe calmly and steadily, I would like you to pay attention to the muscles in your legs. And I would like you to pay attention to the contact between the backs of your legs and the chair. Feel the warmth of that contact ... and allow those feelings of warmth to spread into the muscles of your legs ... relaxing them ... easing them. That feelings of warmth easing away any tension in the muscles of your legs. Allowing those muscles to become loose, and limp, and completely relaxed. Those feelings of warmth spreading and radiating through your legs, easing and relaxing the muscles as those feelings spread down your legs, past your knees, and down your calves. Feelings of ease and relaxation spreading through the muscles of the upper parts of your legs and the lower parts of your legs, and spreading down to your feet. Allowing

any tension to flow down your legs and down to the tips of your toes. All the muscles in your legs completely relaxed ... completely at ease ... the muscles loose and limp.
And as you enjoy those feelings of warmth and relaxation in your legs I would like you to pay attention the contact between your back and the chair. And as you pay attention to that contact you can feel the warmth created ... that feeling of warmth spreading over your back ... soothing all of the muscles in your back ... allowing them to unwind and relax completely. All of the tension draining away from the muscles of your back as the feeling of warmth penetrates in to the muscles of your back ... easing them ... soothing them ... allowing the muscles of your back to relax completely.
And allowing those feelings of warmth and relaxation to spread to the muscles of your stomach ... and your chest ... those muscles loose ... and limp ... and very relaxed. Completely at ease ... just allowing any tension to drain away from your stomach and chest. Your breathing slow and regular, allowing the tension to drain away with each breath. The muscles of your stomach and chest relaxed and completely at ease.
And that warmth spreading up to your shoulders ... relaxing the muscles of your shoulders ... easing the joints ... soothing away any tension ... just allowing your shoulders to relax completely ... to become limp and heavy, completely relaxed.
And that relaxation spreading down your arms ... easing the muscles ... allowing any tension in your arms to just drift away as your arms relax. Those relaxing feelings travelling down your arms ... right down to the tips of your fingers ... soothing away any remaining tension in the arms as they become limp and heavy ... completely relaxed.
And now allow those feelings of relaxation to spread to your neck ... easing the muscles in your neck, allowing tension to drain away, as you become more and more relaxed. The waves of relaxation spreading up your neck, to your head ... to the muscles around your eyes, easing them ... relaxing them ... to the muscles of your jaw and cheeks ... relaxing all the muscles of your head.
Your whole body feeling very limp and relaxed ... your muscles loose and limp ... your breathing slow and regular ... relaxing more and more with each breath.

Garden

I'd like you now to imagine, and then find yourself in a very pleasant, very relaxing garden on a warm sunny day. It can be a real or imaginary garden, but find yourself **there** in the garden ... feeling pleasantly relaxed and calm. Look around and see the sights of the garden ... maybe some trees or flowers ... maybe a fountain.
Listen for any sounds there in the garden ... ... maybe birds singing ... the sound of a gentle breeze ... just enjoy being there in that pleasant relaxing garden.
Smell any smells there in the garden ... maybe the smell of freshly cut grass ... maybe flowers.
All these sights, sounds and smells add to the feeling of relaxation. There may be a warm breeze which blows over your face ... soothing, warm and comfortable.
Just being there ... a pleasant relaxing feeling of being in this beautiful garden.
And as you look around the garden you see some steps which lead down into

another even more pleasant and relaxing part of the garden which you perhaps had not noticed before. Just moving towards the steps now, and pausing at the top, contemplating descending down into the other part of the garden
...
In a moment or two ... when I say ... I would like you to begin to travel down the steps towards the other part of the garden. That very special relaxing place. So I'm now going to count from one to ten, and as I count you can descend the steps, finding yourself at the bottom when I reach ten, and finding that you relax deeper and deeper with each count.
...
One ... two ... down, down, deeper and deeper into this special place ... three ... four ... all the sights, sounds and smells even more pleasant and relaxing than before ... five ... ... six ... deeper and deeper, relaxing more and more ... seven ... eight ... your whole body relaxing as you descend deeper than ever before into hypnosis and relaxation ... nine ... and ten. Very deeply relaxed and hypnotised. Completely relaxed ... completely comfortable.

Special Place

And I'd like you now to find yourself in your special place. A place where you can be alone with you own thoughts and feelings. A relaxing, pleasant place to be.
Begin to imagine, and then to see, hear, smell and feel all of the sensations which are associated with that place.
Any sounds which don't belong to the special place can slip to the back of your mind where they can't bother you.
You're feeling good and confident ... pleasantly relaxed ... deeper and deeper. Feeling happy ... and comfortable ... enjoying the sensations of being there.
And I'm just going to count to ten, to give you some time to enjoy being there in your special place.
And as I count feel yourself becoming more and more relaxed. More and more comfortable.
One ... deeper and deeper ... two ... three ... relaxing more and more ... four ... five ... deeper and deeper ... six ... seven ... deeper still ... more and more relaxed ... eight ... nine ... and ten. Deeper and deeper, deeper than ever before.

HI Pain

This time I would like you to begin to have the experience of lying in the shade on a hot sunny day, with only your writing hand exposed to the sun.
Feel energy from the sun shining directly down onto your hand.
The heat from the sun warming the skin on the back of your hand. The heat penetrating into the skin ... and the feeling of warmth in your hand becoming stronger and stronger.
Pay attention to the feelings in your hand as the light shines down onto it, heating the skin ... raising the temperature ... hotter and hotter. Feel the temperature of your hand increasing. The feelings of heat getting stronger and stronger ... more and more intense as time goes by.
The temperature in your hand is continuing to rise as the sun shines down onto the back of your hand ... the penetrating heat getting hotter and hotter ... stronger and stronger. Just allow those feelings of heat to become stronger ... and stronger ... hotter ... and hotter ... those feelings becoming more intense as

time goes by ... becoming stronger ... and stronger ... as the heat from the sun radiates down onto the back of your hand.
That heat becoming more and more intense ... so intense.
Feel it becoming hotter and hotter and hotter, until it is painfully hot
Feel the heat spreading through your hand, the intense feelings of heat, as the sun shines down onto your hand. Heating it hotter and hotter. So hot ... so intense...so painfully hot.
Those feelings of heat so strong, so intense, so intolerable, that your hand is becoming painful. The sensation of pain becoming stronger and stronger. And feel the pain increasing as your hand becomes hotter and hotter. That painful sensation stronger and stronger, more and more uncomfortable as time goes by. (**Timed at about 2min**)

And now you can move your hand into the shade with the rest of your body. Your hand no longer exposed to the heat of the sun. And your hand cooling down ... back to normal temperature. No longer painful or hot ... completely back to normal. And feel free to move your hand and wiggle your fingers just to check that it's ok. And when it's fine and feeling normal again just rest your hand back in your lap.

Back to Special Place

Now I would like you for a few moments just to go back to your special place. Just find yourself there ... and enjoy the sensations of being there ... completely relaxed .. completely calm ... feeling very peaceful ... very contented. Just allowing yourself to enjoy the feelings associated with this place ... pleasant, relaxing feelings.
And I'm just going to count from one to ten, to give you some time to enjoy being there in your special place ... just allowing yourself to relax deeper and deeper with every count.
1 ... 2 ... pleasant feelings of relaxation and calm ... 3 ... 4 ... 5 ... very calm, very contented ... 6 ... 7 ... 8 ... relaxing more and more ... 9 .... and 10.

Imagined Pain

This time I would like you to imagine that you're lying in the shade on a hot sunny day, with only your writing hand exposed to the sun.
Just imagine the energy from the sun shining directly down onto your hand. Visualise the heat from the sun warming the skin on the back of your hand. Just imagine the heat penetrating into the skin ... and imagine the feeling of warmth in your hand becoming stronger and stronger.
Picture in your minds eye the feelings in your hand as you think about the light shining down onto it, heating the skin ... raising the temperature ... hotter and hotter. Imagine the temperature of your hand increasing. Imagine the feelings of heat getting stronger and stronger ... more and more intense as time goes by. Think about the temperature in your hand continuing to rise, think about the sun shining down onto the back of your hand ... imagining the penetrating heat getting hotter and hotter ... stronger and stronger. Visualise those feelings of heat becoming stronger ... and stronger ... hotter ... and hotter ... imagining those feelings becoming more intense as time goes by ... becoming stronger ... and stronger ... as you imagine the heat from the sun radiating down onto the back of your hand.

Just think about that heat becoming more and more intense ... so intense. Imagine it becoming hotter and hotter and hotter, up to the point where it becomes painfully hot.
Imagine the heat spreading through your hand, the intense feelings of heat, as you imagine the sun shining down onto your hand. Imagining it getting hotter and hotter. So hot ... so intense.
Imagining a heat so strong, so intense, so intolerable, that you can imagine your hand becoming painful. You can visualise that pain becoming stronger and stronger and imagine the pain increasing as your hand becomes hotter and hotter.
(**Timed at about 2min**)
And you can stop imagining that painful sensation now, and just allow your hand to feel completely normal. Completely back to normal, just normal sensation and feeling in that hand. And feel free to move your hand and wiggle your fingers, just to check that it feels fine.

Ending

Remember that you cannot slip into a state of deep relaxation or hypnosis accidentally. And that you cannot be hypnotised if you don't want to be.

Though if you wish to be hypnotised again ... and agree to go through these or similar procedures ... you will find that you reach the deepest level of relaxation and hypnosis that you have experienced today very much more readily and quickly. And you will be able to find much greater depths of relaxation and hypnosis next time.

There are no unpleasant after-effects of being in a state of deep relaxation, only a feeling of well-being and confidence. You will remember everything that has happened in this session when you return to your normal alert waking state in a few moments.

In a moment I will count slowly from three to one and on "one" I want you to open your eyes ... feeling good ... completely normal ... still pleasantly relaxed. Able to remember everything and happy to talk about your experience
Three. Getting lighter and lighter
Two. Lighter still. Feeling good. Feeling relaxed, and
One. Wide awake.

Appendix 3.3 - Response booklet

Name:_____ Date:_____

Are you left or right handed? _____ Age: _____

You are now going to be given some questionnaires about the experiences you have just had.
Be sure to read the questions carefully, and note the difference between when you were asked to ***imagine*** *a pain in your hand and when you were asked to* ***experience*** *a pain in your hand.*

Name:_____ Date:_____

*While hypnotised you were asked to **experience** a painfully hot sensation in your dominant hand. The following questions all relate to that sensation.*

1. Did you experience the sensation of pain in your dominant hand?
   Yes [ ] No [ ]
2. Did you experience the sensation of heat in your dominant hand?
   Yes [ ] No [ ]

   If yes to both of these, did the heat sensation you experienced seem to be the cause of the pain? Yes [ ] No [ ]

If you answered Yes to questions 1 and 2, please complete the rest of this booklet.

If you just answered Yes to question 1 only, then please answer the questions on page 2 of this booklet.

If you just answered Yes to question 2 only, then please answer the questions on page 3 of this booklet.

If you answered No to both questions please leave the rest of the booklet blank.

Page 1

*The questions on this page are all about the sensation of **pain** you just **experienced**. Please place a mark at the appropriate place on the line.*

***Intensity** - how intense was that pain?*

***Unpleasantness** - how unpleasant was that pain?*

***Externality** - did it feel like you were generating the painful sensation?*

***Clarity** - how clear was the sensation of pain?*

Page 2

*The questions on this page are all about the sensation of **heat** you just **experienced**. Please place a mark at the appropriate place on the line.*

***Intensity** - how intense was that heat?*

***Unpleasantness** - how unpleasant was that heat?*

***Externality** - did it feel like you were generating the sensation of heat?*

***Clarity** - how clear was the sensation of heat?*

Page 3

Name:_____ Date:_____

*While hypnotised you were asked to **imagine** a painfully hot sensation in your dominant hand. The following questions all relate to that sensation.*

1. Did you imagine the sensation of pain in your dominant hand?
   Yes [ ] No [ ]
2. Did you imagine the sensation of heat in your dominant hand?
   Yes [ ] No [ ]

   If yes to both of these, did the heat sensation you imagined seem to be the cause of the pain? Yes [ ] No [ ]

If you answered Yes to questions 1 and 2, please complete the rest of this booklet.

If you just answered Yes to question 1 only, then please answer the questions on page 2 of this booklet.

If you just answered Yes to question 2 only, then please answer the questions on page 3 of this booklet.

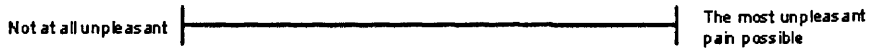
If you answered No to both questions please leave the rest of the booklet blank.

Page 1

*The questions on this page are all about the sensation of **pain** you just **imagined**.*
Please place a mark at the appropriate place on the line.

***Intensity** - how intense was that pain?*

***Unpleasantness** - how unpleasant was that pain?*



***Externality** - did it feel like you were generating the painful sensation?*

***Clarity** - how clear was the sensation of pain?*

Page 2

*The questions on this page are all about the sensation of **heat** you just **imagined**.*
Please place a mark at the appropriate place on the line.

***Intensity** - how intense was that heat?*

***Unpleasantness** - how unpleasant was that heat?*

***Externality** - did it feel like you were generating the sensation of heat?*

***Clarity** - how clear was the sensation of heat?*

Page 3

Name:_____ Date:_____

*The questions on this page are about the relationship between the **imagined** and the **experienced** pain.*
*You only need to answer these questions if you **experienced** pain when it was suggested that you would feel a pain in your hand.*

***Similarity** - how similar was the imagined pain to the experienced pain?*

Not at all the same ——————————— Exactly the same

Please use the space below to make any comments about the similarities/differences between the experienced and the imagined pains:

Appendix 8.1 - Pre scan briefing

1. Keep your head still at all times in the scanner – any movement makes our pictures blurry. During the actual scanning (when we're moving the dial up and down) keep your body as still as possible too – any body movement causes activations in the part of the brain controlling movement.
2. Speak loudly and clearly, people often speak softly in hypnosis but speaking loudly and clearly won't disturb or distract you. If I can't hear you I'll ask you to speak up.
3. I'm going to ask you at various points throughout the scan how hypnotized or deep you feel. I want you to give me a rating from 0 to 10.
0 = not at all hypnotized, 10 = as deep as I've ever been.
4. We'll be turning the dial up and down in the scanner, and changing the pain correspondingly. When we do this in the scanner I'm going to need you to allow the dial to turn as far as it can and as quickly as it can – in whichever direction I tell you to move it. Once the dial has turned as far as it can I'll need you to hold it there until you get the next signal from me – just paying attention to the dial. Always paying attention to the dial.
5. When we're actually doing the scans – taking pictures of what is happening in your brain – the scanner is very noisy and I can't talk to you over the noise. So I can't verbally tell you to turn the dial up and down. So I'm going to signal instructions to you by tapping you on the foot. I'll give you the necessary instructions before each scan, but here are the signals:
1 tap = low – turn dial as low as it will go
2 taps = medium – turn the dial to somewhere in between high and low
3 taps = high – turn dial as high as it will go
*Diagram (Figure 8.3)
6. The way we run the experiment is in blocks – we scan for a few minutes at a time, then take a break. Before each block I'll give you the instructions you need for that block. Basically I'll recap the tapping instructions and will ask you to twitch a foot if you understand.
7. Instructions IN and OUT of hypnosis (read verbatim):
We've been using hypnosis and imagery (the dial) to help you to turn your pain up and down. But we're also going to use the same imagery (the dial) OUT of hypnosis. I'll unhypnotise you, and check you're awake. I'll then ask you to close your eyes and imagine the dial in your mind and we'll use the same tapping signals as before. You'll have your eyes closed, but I don't want you to become hypnotized. Keep your eyes closed for all scanning blocks.

8. Whatever happens just do your best and keep following my instructions. If you can't hear me then say so or wiggle your hand. If you don't understand my instructions say so or wiggle your hand.
9. When we're doing the actual scanning I want you to pay attention to the dial, try to stay focused on it. We'll go to the special place in the gaps between blocks, I'll tell you when. I'll always give you the appropriate instructions.
10. Any questions you have for me?

Appendix 8.2 - Order effects

Examination of potential order effect: Pain scores in hypnosis

Group 1 = Patients who had hypnotised blocks before unhypnotised blocks
Group 2 = Patients who had unhypnotised blocks before hypnotised blocks

	Hyp Low	Hyp Med	Hyp High
Group 1	1.50 (0.78)	5.16 (0.64)	8.75 (1.08)
Group 2	0.87 (1.35)	5.56 (0.82)	9.37 (1.18)

Table A8.1: Pain scores for each level (low, medium high) in hypnotised patients. Group 1 had hypnotised blocks before unhypnotised blocks, group 2 vice versa.

A 2x3 mixed ANOVA was conducted to assess differences in pain scores for each pain level between thee two groups. The main effect of pain level was significant $F(2,22)=323.38, p<0.001$, but the interaction between pain level and group, and the main effect of group, were not significant.

Examination of potential order effect: Pain scores outside hypnosis

Group 1 = Patients who had hypnotised blocks before unhypnotised blocks
Group 2 = Patients who had unhypnotised blocks before hypnotised blocks

	UnHyp Low	UnHyp Med	UnHyp High
Group 1	2.89 (2.26)	5.89 (1.29)	8.34 (1.80)
Group 2	1.06 (1.14)	5.25 (0.46)	8.93 (1.47)

Table A8.2: Pain scores for each level (low, medium high) in unhypnotised patients. Group 1 had hypnotised blocks before unhypnotised blocks, group 2 vice versa.

A 2x3 mixed ANOVA was conducted to assess the differences in pain scores for each pain level between the two groups. The main effect of pain was significant $F(2,22)=103.16$, $p<0.001$. The main effect of group was not significant. The interaction between pain level and group approached significance $F(2,22)=3.382, p=0.052$.
Independent samples t-tests were performed to examine for differences in pain scores for each pain level between the two groups.
Low $t(24) = 2.144$ $p = 0.042$
Medium $t(24) = 1.350$ $p = 0.190$
High $t(24) = -0.811$ $p = 0.425$