DEVELOPMENT AND EVALUATION OF AN ONLINE HYPNOSIS PROGRAMME FOR THE TREATMENT OF MIGRAINE

Thesis submitted for the Degree of Doctor of Philosophy

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Abstract

This study examined the development and evaluation of an online hypnosis programme for the treatment of migraine. 43 participants who suffered with two or more migraines a month and who satisfied other study criteria enrolled. A mixed methods design was employed. 7 surveys were delivered online over 6 weeks. Pain Catastrophizing (PCS), Headache Disability (HDI), number of migraines, hours of migraine, frequency and severity of migraine, and mg of medication were measured. Each week, from week two to week six the intervention group had access to a different hypnosis mp3s specifically developed for the study. Significant improvements were found from Time 14 (pre-intervention) to Time 84 (6-week follow up). There was a 48% reduction in mean HDI score in the treatment group. The control group experienced a 2% reduction in HDI. The percentage change in the mean PCS score corresponded to a 60% reduction in the treatment group. The control group experienced an average increase of 7% in PCS score. There was no evidence of a significant difference between the change in number of migraines between groups. The median change in total hours of migraine was significant. The treatment group and control group at 6-week follow up vs Time 14 showed a decrease of 8 hours and 0 hours respectively per week. There was evidence of a significant difference in the proportion of participants experiencing a decrease in severity of migraine in the Treatment vs the Control group at Time 42 but not at Time 84. Attrition rates were 9.3% at Time 42 and 21% at Time 84 (6-week follow up). In conclusion, data from the studies presented in this thesis provides evidence that hypnosis is an effective tool for assisting migraine sufferers to reduce headache disability and pain catastrophizing associated with the condition.

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List of Acronyms

AI: Anterior Insula
ACC: Anterior Cingulate Cortex
CAHS: Computer Assisted Hypnosis Scale
CBT: Cognitive Behavioural Treatment
CM: Chronic Migraineurs
COMT: Cathechol-O-methyltransferase
EEG: Electroencephalogram
EM: Episodic Migraineurs
EMG: Electromyography
HH: Highly Hypnotizable
HDI: Headache Disability Index
HIP: Hypnotic Induction Profile
LH: Low Hypnotizable
MIDAS: Migraine Disability Assessment Questionnaire
MIS: Medication Index Score
MRC: Medical Research Council
MWA: Migraine With Aura
MWOA: Migraine Without Aura
PAG: Periaqueductal Gray Matter
PEMF: Pulsed Electromagnetic Field
PCS: Pain Catastrophizing Scale
PFO: Patent Foramen Ovale
SHSS:C: Stanford Hypnotisability Scale C
SMT: Spinal Manipulation Therapy

Note: The words 'Higher Hypnotizable' and the letters 'HH' are used interchangeably in the literature to denote a higher level of suggestibility or hypnotizability. Both terms are also used in the present study.

Chapter 1: Clinical, Theoretical and Conceptual Issues in Chronic Pain, including Migraine

1.1 Theories and Conceptual Models of Pain

Pain is a complex phenomenon and several authorities have proposed theories to help explain how pain is experienced. Many of these theories of pain were initially based on biomedical conceptualisations of pain and later evolved to include psychological and social factors. Given the range of factors affecting chronic pain patients, and migraine patients in particular, an understanding of how pain is experienced, will influence treatment choice and protocol.

Moayedi and Davis (2012) identified several of the influential biomedical models in the literature, such as Specificity Theory, Intensity Theory and Pattern Theory. In their paper, Moayedi and Davis (2012) described each of the theories, working from the current definition of pain outlined by the International Association for the Study of Pain (IASP) which describes pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of tissue damage, or both." The authors cautioned that while each of the theoretical frameworks contributes to the understanding of the physiological basis of pain, none yet accounts for a full explanation of pain perception.

1.1.2 Biomedical Models of Pain

The Specificity Theory suggests there is a specific pathway in the nervous system to communicate messages about pain and that these pathways carry signals via specific pain receptors in the periphery and spinal cord to the sensory region of the brain (Basbaum, 2011). However, several researchers have pointed out that this model assumes a direct link between tissue damage and pain experience,

yet the experience of pain does not provide a reliable indication of the presence of tissue damage. Phantom limb pain is an example of this – pain can be perceived as being within the missing limb, yet the limb is no longer present. Indeed, it is not uncommon for people reporting pain not to have evidence of there being damage to that part of the body. Similarly, the presence of tissue damage is not always associated with the presence of pain.

Another biomedical theory described by Moayedi and Davis (2012) is the Intensity Theory of Pain based on experiments. This theory evolved from experiments which involved tactile stimulation, below the threshold for tactile perception, being repeated between 60 and 600 times in patients who quickly reported the pain as being unbearable. These findings led a conclusion that some type of summation of stimuli must be occurring for subthreshold stimuli to become very painful and that pain was an emotion which occurred when a stimulus was stronger than normal, as opposed to pain being a unique sensory experience (Moayedi & Davis, 2012). The Intensity Theory as it is understood today, developed from these earlier theories that weak stimuli produce non-painful sensations while strong stimuli trigger a greater activation of nerve fibres resulting in pain. No differentiation of variations in response to different stimuli was made by the proponents of this theory, thus, all stimuli were considered to have the same effect on neural activity. This theory considered stimulus intensity and central summation to be the critical determinants of pain (Perl, 2007). The Intensity model, like the specificity model was concerned with acute pain and did not address persistent pain or chronification of pain, which may as Moayedi and Davis (2013) explained, be due to the belief at this time that the nervous system was 'hard wired'. Furthermore, when different patterns of neural activity were identified in response to different stimulus modalities, for example, mechanical, chemical and thermal (Chen, 2011) the Intensity Theory lost support. At the very beginning of the 20th century it was determined that there

were two classes of somatic sensory pathways subserving discriminating sensations such as touch and pressure and crude sensations such as pain (Chen, 2011) and the Pattern Theory emerged.

The Pattern Theory was based on the belief that signals travelling along large diameter nerve fibres may inhibit signals being carried by thinner pain fibres and thereby were able to modify pain intensity. However, the theory assumed the presence of tissue damage and as Chen (2011) pointed out, the Pattern Theory has been found to be 'a great simplification for the central nervous system or even plainly wrong for the organization of the peripheral input to the spinal cord'(p.347). Other aspects of the theory such as the dorsal horn organisation of presynaptic links between A and C fibres have also been shown to be incorrect (Chen, 2011).

These early biomedical theories of pain suggested that pain arose specifically from a physiological anomaly or pathology. However, modern conceptualisations of pain recognise that pain experience is more complex and is influenced by psychological (affective, cognitive, behavioural) and social factors, leading to the adoption of biopsychosocial models of pain.

1.1.3 The Biopsychosocial Model of Pain

The current IASP definition of pain can be considered to reflect a biopsychosocial model. This conceptualisation of pain has implications for how pain is treated, meaning that due consideration in treatment be given to addressing the psychological and social factors in addition to addressing the physiological factors.

The earliest biopsychosocial theory of pain was the Gate Control Theory by Melzack and Wall (1965). The GCT proposed that there is a 'gate' in the dorsal horn of the spinal cord which closes and opens in response to different factors. When the gate is 'open' pain messages are permitted to travel to the brain while when the gate is 'closed' pain messages are inhibited from reaching the brain. The concept includes the notion that there is a flow of information both

to and from the brain so that the brain also has the ability to 'open' and 'close' the gating mechanism. Three types of sensory nerves have been identified as being involved in transmission of noxious stimuli, namely a-Beta fibres, a-Delta fibres and C fibres. Of interest from a psychological perspective, the Gate Control Theory suggested that mood and thoughts had an impact on whether the 'gate' remained open or closed. It incorporated the notion of sensory-discriminative, motivational-affective and cognitive-evaluative factors (Melzack & Wall, 1965).

While the GCT is one of the more comprehensive models of pain perception, it has been shown to have limitations, for example, no actual 'gating mechanism' has yet been identified (Hardcastle, 1999). The GCT reflects the current IASP conceptualisation of pain by as having an emotional component and referring to both 'actual' and 'potential' tissue damage.

Moseley (2007) argued that clinical approaches to the treatment of pain require consideration of somatic, psychological and social factors. Moseley pointed out that (1) the presence of pain does not provide an assessment of the state of the tissues (2) that biological, somatic, psychological, and social factors modulate pain (3) that when pain is persistent, the relationship between the perception of pain and the condition of the tissues becomes less clear and (4) that pain can partially be interpreted as being dependent on the degree to which there is a perception of threat to the body tissues. Moseley explained that attention, anxiety and expectation of pain seem to be underpinned by a shared context, that is, the meaning of pain. This, he stated, has been demonstrated by studies investigating pain catastrophizing (a particular way of thinking about pain). He noted that higher catastrophic interpretations of pain were associated with higher pain ratings. Biopsychosocial models emphasise the important contribution of psychological processes in the physical experience of pain. Arising from a greater understanding of how

psychological processes influence pain perception, theoretical models have emerged that aim to explain how pain-related disability develops and indicating potential targets for psychological intervention. One such model that has received a good deal of attention is the Fear-Avoidance Model (Vlaeyen, Kole-Snijder, Boere & van Eek, 1995) .

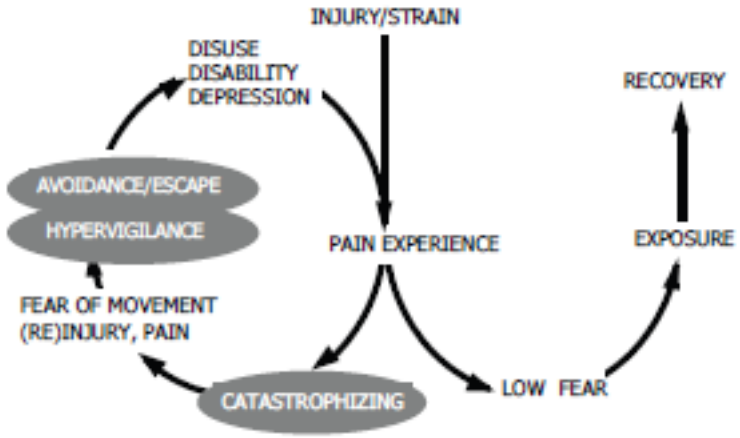


Figure 1.1: The fear-avoidance model of chronic pain (Vlaeyen et al. 1995)

Fear Avoidance (FA) Model of Pain

The FA model of pain (Fig 1.1)is a cognitive behavioural account of how patients develop chronic musculoskeletal pain as a consequence of avoiding activity (Lethem, Slade, Troup & Bentley, 1983). The FA model explains how avoidant behaviour is useful when a patient's injury is still healing but becomes counter productive in the context of a chronic pain condition because reduced physical activity leads to physical deconditioning and this in turn leads to more pain when activity is undertaken. Increased pain leads to hypervigilance and increased fear of movement and activity, leading to worsening disability (Fig.1) . The FA model has been used to explain the transition of acute pain to chronic pain.

A meta-analysis conducted by Zale, Lange, Fields and Ditre (2013) synthesised the findings of 41 studies and found a positive relation

between pain-related fear and disability which was moderate to large in magnitude. The authors suggested the findings indicate that pain-related fear may be considered an important risk factor for pain-related disability with related implications for the treatments designed to treat pain.

While the fear avoidance model literature has focused on musculoskeletal pain, the key constructs of catastrophizing and pain-related fear which underlie the contemporary fear avoidance model (Turk & Wilson, 2010) have also been investigated in the migraine literature. One study by Black, Fulwiler and Smitherman (2015), which examined fear of pain (FOP) in headache patients looked at how FOP differed between headache sufferers and those who do not suffer with headaches. They defined FOP as the fear of physical movement because of it's assumed threat of pain. Like FA, FOP, they affirmed, has the ability to restrict physical ability and can lead to over-prediction of pain. Black et al. (2015) examined FOP differences across headache categories, the degree to which FOP could predict headache severity, frequency and disability and also whether FOP had an effect on the relationship between pain severity and headache disability. They found that FOP was higher in migraineurs than in individuals with tension type headache (TTH) and that FOP partially mediated the relationship between pain severity and disability. They concluded by stating that knowledge of FOP and its various associations could have a therapeutic benefit in decreasing disability and improving functioning.

1.2 Migraine: Classification, Prevalence, Pathophysiology

1.2.1 Headache Classification

There are several categories and sub-categories of headache according to the International Headache Society (IHS). Published by the International Classification System of Headache Disorders (Headache Classification Committee of

the International Headache Society, 2018), the classification system is divided into three parts; The Primary Headaches, Secondary Headaches and the third part which includes Cranial Neuralgia, Facial Pain and Other Headaches. The classification system is an hierarchical system with Part I, which is primarily relevant to the current research, being divided in to 1. Migraine 2. Tension-type headache 3. Cluster headache and other Trigeminal Autonomic Cephalagias and 4. Other primary headaches. The IHS website (www.ihs-classification.org) recommends firstly assigning a patient into one of these primary categories before obtaining information which will permit a more detailed diagnosis. In general practice, the diagnosis is generally confined to this primary diagnosis and the IHS guidelines suggest that more specialised headache practices will make a third or fourth digit diagnosis. An example of a secondary digit diagnosis would be 1.2 Migraine with aura. The third digit diagnosis would be 1.2.1 Typical aura with migraine headache. The IHS (2013) noted that the frequency of primary headache disorders can vary from attacks every one to two years to attacks which are daily.

The most common type of headache is a tension-type headache and this diagnosis can be subdivided into infrequent episodic tension-type headache, frequent episodic tension-type headache, chronic tension-type headache and probable tension-type headache. Tension-type headaches are described by the IHS as the most common type of primary headache with a prevalence among the general population varying from between 30% and 78% in different studies. The tension-type headaches are further categorised in to 2.1 Infrequent episodic tension–type headache, 2.2 Frequent episodic tension-type headache, 2.3 Chronic tension type headache and 2.4 Probable tension-type headache. The third primary category, Cluster Headaches and Trigeminal Autonomic Cephalalgias (TACs)

is subdivided into cluster type headaches, paroxysmal hemicrania, short-lasting unilateral neuralgiform headache attacks, hemicrania continua and probable trigeminal autonomic cephalalgia. The TAC's are characterised by clinical headache features such as lateralization and cranial parasympathetic autonomic features (IHS, 2013). Each of these subcategories has it's own diagnostic criteria, for example, cluster headaches are described as being 'attacks of severe, strictly unilateral pain which is orbital, supraorbital, temporal or in any combination of these sites, lasting 15-180 minutes and occurring once every other day to eight times a day' (p. 665). There are ten types of headache in the fourth and final primary category. These include for example primary cough headache, external pressure headache and primary exercise headache.

Migraine Diagnostic Criteria

The IHS divide migraine into two major subtypes; migraine without aura and migraine with aura (IHS, 2013). Migraine without aura (1.1 in the IHS classification system) is defined as 'a clinical syndrome characterized by headache with specific features and associated symptoms' (p.33). Migraine with aura (1.2 in the IHS classification system) is listed as having characteristic transient focal neurological symptoms that will often precede or occasionally accompany the headache. The various phases of migraine listed in the classification system include the premonitory phase which occurs prior to the headache and a headache resolution phase which occurs after the headache.

The diagnostic criteria for migraine as specified by the International Headache Society (2011) includes having at least five attacks without aura or two attacks with aura and which fulfill the following criteria:

Lasting between 4 and 72 hours

Has two of the following characteristics:

- Characteristic of pulsating quality
- Intensity is moderate to severe
- Aggravated by physical activity

During the headache at least one of the following is present:

- Nausea
- Photophobia or phonophobia

Migraine without aura (MWOA) is generally unilateral and may or may not be accompanied by nausea. Migraine with aura (MWA) is accompanied by neurological features such as auditory, visual and sensory hallucinations or alterations, such as paresthesias and speech disturbance (Benoit, 2009).

Stages of Migraine

Four stages of a migraine episode have been identified by IHS.

Stage 1 Prodrome Stage

Up to 60% of migraine sufferers have a prodrome. Blau (1980), differentiated between prodrome and aura which, in the past, were regarded as synonyms. He defined migraine prodromes as 'symptoms with an insidious onset, which last several hours and affect mood, behaviour, wakefulness, gut motility or fluid balance' (p.659). Aura was defined as 'beginning suddenly, lasts minutes and commonly affects vision and, less often, somatic sensation, motor, speech or brain stem function' (p.659). Prodromes are a frequently neglected stage when an enquiry is made into migraine history (Rozen, 2004). There may be changes in mood and the patient may experience very high or very low energy levels. Food cravings can be quite intense.

Stage 2 Aura Stage

The aura can take the form of auditory, sensory, tactile or visual phenomena as outlined previously. It is common to see flashing lights or zigzag lines if visual hallucinations are present. This stage usually occurs about 20 to 60 minutes prior to the migraine.

Stage 3 Migraine

The migraine headache can last anywhere between 4 and 72 hours. There is throbbing pain and most people will seek a quiet and dark room away from sunlight while experiencing the migraine.

Stage 4 Postdrome Stage

Once the migraine has gone, the recovery begins. Fatigue, difficulty concentrating and gastrointestinal symptoms are typical of this stage.

Migraine Triggers

A variety of trigger factors are commonly reported by migraineurs. They are subsequently a necessary consideration in any migraine preventative plan. Stress, hormones, nutrition, sleep and environment are among the triggers most frequently investigated. Each will be discussed in turn. One study by Yadav, Kalita and Misra (2010) conducted in India, involved interviewing 182 migraine patients to gain an insight into the factors which trigger migraines. Their findings revealed that 160 of the 182 people they spoke with were aware of specific triggers for their migraines, and more than two triggers were present in 34.4% of the patients. Emotional stress was the most pervasive factor with 70% of respondents blaming it for their migraines. Mollaoglu (2013) reported a similar, albeit slightly higher, percentage (79%) of individuals attributing emotional stress as a trigger for their migraines in a study of 126 Turkish migraine patients. Hormones are also known to influence the incidence and management of migraines. In one study exploring the prevention of migraine in women, it was noted that menstruation, pregnancy, oral contraception, menopause and hormone therapy should be considered when devising a migraine management strategy (Tozer, Boatwright, David, Verma, Blair, Mayer & Files, 2006). The researchers pointed out that 60% of women who had migraines related those migraines to their menstrual cycle and were more likely to report such migraines as migraine without aura. When

oestrogen declines during the menstrual cycle, this can act as a trigger for migraine (MacGregor, 2004). The research also quoted a review by the International Headache Society Task Force on Combined Oral Contraceptives and Hormone Replacement Therapy which indicated that female migraineurs who experience aura or who present with other risk factors for stroke and who smoked and used combined oral contraceptives should be assessed very carefully. The combination of combined oral contraceptives, cigarette smoking and migraine increased the risk of stroke 34-fold. The study reported the curious fact that despite the high incidence of migraine amongst women and the debilitating effect it had on day-to-day living, only 3-5% of women receive preventive therapy.

Migraine is more common than diabetes, osteoarthritis or asthma. Given that women are approximately three times more likely than men to suffer with migraine and that approximately 20% to 60% of female migraineurs have migraine attacks associated with their menstrual cycle (MacGregor, 2010), particularly when oestrogen levels drop in the days prior to menstruation, hormones clearly have a role to play in causing migraines. Some dietary triggers have been attributed to causing the onset of migraine. While studies disagree on the actual percentage of people affected by dietary triggers - anywhere between 12 and 60 % of patients (Finocchi & Giorgia, 2012) – there is a considerable volume of information written on the topic with an emphasis on substances such as Tyramine, Phenylethylamine, Histamines and supplements. Fasting is also cited frequently in the literature as a trigger for migraine (for example, Latsko, Silberstein & Rosen, 2011; Yadav, Kalita & Misra, 2010). Tyramine is released in food when the amino acid tyrosine is naturally broken down. It is often attributed with migraine provoking properties. The levels of Tyramine increase in food that is aged, fermented or stored for a long time. Fermented soya products such as Miso soup, alcohol and aged cheeses like cheddar cheese often contain high levels of Tyramine. A study

published in The Lancet (Littlewood, Glover, Davies, Gibb, Sandler & Clifford, 1988) looked into the matter further, by giving their patients a cold drink in a dark bottle. Some of the patients were given red wine and some were given vodka with a dilutent mixture of equivalent alcohol content to the wine. Both drinks thus contained the same volume of alcohol. The researchers found that even though the red wine had a negligible amount of Tyramine, 9 of the 11 participants suffered a migraine attack while none of the 8 who consumed the vodka had an attack. The researchers concluded that something other than the alcohol and the Tyramine content of the red wine was responsible for provoking migraine. The small amount of Tyramine present in red wine may not be responsible for triggering migraine but other studies suggest that Tyramine is still implicated as playing a role in the pathophysiology of migraine. D'andrea et al. (2012) in their review of neurotransmitters and neuromodultators as contributory factors in the aetiology of migraine noted that current research as well as older studies provide support for the notion that Tyramine may behave as either a neurotransmitter or a neuromodulator via a variety of receptors. They proposed that anomalies in these, and other biochemical pathways act in determining migraine.

Compounds such as phenylethylamine, histamine, nitrates and sulphites have also been singled out (Millichap & Yee, 2003) for their contribution to food intolerance headache. The theory behind this is that dietary triggers influence the various stages of the migraine process either by influencing the release of serotonin and norepinephrine, thereby causing vasoconstriction or vasodilation or by direct stimulation of the brainstem and other pathways. One problem with studying food or alcohol as triggers is measuring the quantity of particular foods ingested and their relation, if any, to other triggers such as weather or travel and/or stress. Silberstein (2004) suggested that the food intolerance which patients complained of was nothing more than a psychological response to a

particular food itself. Even though the author of this research dismissed elimination diets, they concluded their article by advising migraine patients to consume alcohol with caution, to avoid large amounts of monosodium glutamate, aspartame and perhaps cured meat. Although the search for particular agents within foods and drinks that are implicated in triggering migraines is ongoing and the debate as to whether the dietary triggers are "all in one's head" or have a valid physiological basis persists.

A low fat diet has also been shown to be beneficial for managing migraines. One study (Bic, Blix, Hopp, Leslie & Schell, 1999) involved 54 migraine patients aged between 24 and 71 years who were asked to follow a low fat diet. After reducing the fat content of their diet the results were very positive. In addition to having fewer migraines, the migraines they did have were less intense. They also lost weight and lowered their body fat percentages. The authors pointed out that because the diet change was dramatic, there was an accompanying change in the nutrients which the participants were consuming. They also noted that lower circulating free fatty acids and other blood lipid levels will affect serotonin levels so they cannot categorically say that the outcome was solely due to a low fat diet. The overall fat grams in the study dropped from an average of 65.9g per day to 27.8g per day. For some, the use of magnesium has been recommended (Gerber, 1997) to reduce migraine frequency and severity. 28 million people in the USA suffer with migraine and of these it is estimated that 7 million experience hunger as a migraine trigger. Latsko et al. (2011) pointed out that the pathophysiology of fasting-induced headache is still not fully understood but may be due to an effect on fatty acid metabolism. They also noted there is some evidence to suggest that lack of water for a lengthy period can also act as a trigger for migraine. Other migraine triggers which have some representation in the literature include sleep and the environment. The relationship between

migraines and sleep is a hazy one. Despite advances in science, our understanding of sleep itself is limited. Research by Vassalli and Dijk (2009) pointed out that it was difficult to decipher the optimal level of sleep and to decide on how units of sleep should be measured. The same study also asked if we should rely on the sleep deprivation paradigm to enlighten us about sleep itself and whether sleep should be measured in units of time or in terms of Rapid Eye Movement (REM) and Non-REM cycles. REM is a normal stage of the sleep cycle characterised by fast and random movements of the eyes. Non-REM sleep refers to the first three sleep stages which are typified by distinct electroencephalographic markers. There are many unanswered questions about sleep. Nevertheless, in the context of migraines what we do know is that sleep is important. While we do not fully understand *why* it is important, research has indicated that migraine is positively associated with many sleep-complaints such as restless-leg syndrome. Furthermore, questions have been raised about the association between migraines and insomnia, snoring and sleep apnea (Cevoli, Giannini, Favoni, Pierangeli & Cortelli, 2012). The cause and effect relationship is not clear. Research studies to date have been unable to decipher whether migraine leads to problems where one finds it difficult to fall asleep or stay asleep (insomnia) and problems where there is an excessive sleepiness and extended sleep time (hypersomnia) or whether these issues play a causative role in the development of migraines.

One study by Calhoun, Ford, Finkel, Kahn and Mann (2006), looked at the subjective impact of sleep deprivation on its participants and asked patients to report whether they awoke 'feeling refreshed' or 'tired'. Of the 147 women who took part in the study none of them reported awakening 'refreshed' and 83.7% said that they woke up feeling tired. There was no control group in the study. The researchers concluded that sleep complaints were commonplace and assorted. Another study, conducted a few years

earlier, uncovered similar findings (Kelman & Rains, 2005). This study evaluated 1,283 migraineurs and assessed variables such as sleep and demographics. Over half of the participants, all of whom suffered with migraines, found it difficult either getting to sleep or staying asleep (Kelman & Rains, 2005). The irony of the findings of Kelman and Rains was that sleep was seen as a palliative agent for their headache, with 75% of the migraineurs saying that they had no choice but to sleep or rest because of the pain. The people who suffered with chronic migraine, that is, migraine on 15 or more days each month, were classified as 'short sleepers'. This refers to the fact that they routinely slept an average of six hours in twenty four. Those who slept more were more likely to be episodic migraineurs i.e. they had fewer migraines. A study published in The Lancet by Hsu, Kalucy, Crisp, Koval, Chen, Carruthers and Zilkha (1977) measured a number of physiological markers such as tryptophan, glucose and free fatty acids in a group of 19 migraine sufferers who awoke regularly from sleep with a migraine. They also made polygraph sleep recordings and found that when the migraineurs woke from sleep it was predominantly during REM sleep. Studies have examined the relationship between migraine and environmental factors such as the weather, bright lights, odours, noise and air travel, among other elements. Some migraineurs complained that odours such as cigarette smoke trigger their migraine. Others cited humidity and flickering lights as instigating their pain. Some of the studies which have explored environment were reviewed in an article by Friedman and De Ver Dye (2009). The article described a list of studies which illustrate the link between weather and barometric pressure changes, and the onset of migraine. However, it pointed out that when the migraine diaries on which some of the data was based was compared with weather reports, the effect of the weather may have been over-estimated. The article suggested that other environmental factors such as pollution, exposure to chemicals and air quality may be partially responsible. In the same review, when the researchers looked at studies

investigating the area of odours and migraine, they unearthed quite a few studies which found that odours were identified as a trigger in over 40% of migraineurs. They also noted that osmophobia, which is an aversion to odours, was present in the same percentage of migraineurs. The review concluded that migraineurs were often more sensitive to specific stimuli in the environment and that this possibly led to a deviation from normal activation in the cerebral cortex and brain stem.

Goadsby (2006) identified two ways in which the International Headache Society distinguishes migraine from tension-type headache. The first difference was that migraine has associated features such as throbbing pain or the presence of photophobia and phonophobia while tension-type headache does not. The second pertained to what they refer to as the biological signature of migraine in that it was classified as a headache with a tendency to result from specific environmental triggers such as heightened sensitivity to bright lights. Goadsby pointed out that diagnosis was complicated by the fact that there was no known biological marker on which to make a decision that what the patient is presenting with is a migraine as opposed to a tension-type headache, but that it is helpful for diagnosis to note if there is a familial history of migraine because of the lack of biological markers available. This genetic information has its limitations nonetheless. When Ulrich, Gervil, Kyvik, Olesen and Russell (1999) studied the genetic influence on cause of migraine with aura they found that the pairwise concordance rates were significantly higher in Monozygotic twins (34%) than in Dizigotic twin pairs (12%), emphasizing the importance of genetic factors in migraine with aura. When the same researchers in a separate study examined migraine without aura (Gervil, Ulrich, Kaprio, Olesen & Russell, 1999) they concluded however that environmental factors are equally as important as genetics in the aetiology of migraine without aura. They acknowledged that while their data demonstrated a significant

genetic contribution in migraine without aura, the size of this contribution was modest and the demonstration of susceptibility genes was likely to be laborious and difficult. In keeping with the biopsychosocial model of pain, external factors also need to be considered in the treatment of migraine.

1.2.2 Prevalence and Demographic Differences in Migraine

Migraine was listed as the seventh highest cause of disability in the world in The Global Burden of Disease (GBD) Survey 2010 published by the World Health Organisation (WHO) (Martelletti, Birbeck, Katsarava, Jensen, Stovner & Steiner, 2013) and the third most prevalent disease in the world to affect both males and females (Steiner, Stovner & Birbeck, 2013). Steiner et al. (2013) suggested that at any given time at least 10% of adults are disabled by headache disorders which are treatable and therefore should not be as disabling as they are. Severe migraine attacks are categorised by the WHO as comparable to dementia and quadriplegia in terms of disability and yet receive the least amount of funding among neurological disorders respective to impact on the economy (Shapiro & Goadsby, 2007). The International Association for the Study of Pain (2011) stated that approximately 13-18 % of women and 5-10% of men are affected by migraine and approximately 20-30% of these individuals will experience aura and neurological symptoms such as visual disturbances. The prevalence of migraine among children and adolescents is reported to be 7.7% (IASP, 2011).

Racial and ethnic differences in migraine prevalence were noted by Stewart, Lipton and Liberman (1996) who found lower migraine prevalence in African and Asian populations than in European and

North American populations. They attributed the differences to probable race-related genetic differences after considering the possible effects of diet, socioeconomic status and symptom reporting on differences in prevalence. The financial burden of migraine to society is considerable, estimated by the IASP (2011) to amount to €25 billion per year in Europe and in the U.S. direct medical costs alone in 1999 were calculated to have reached $1 billion. Other costs arise from absenteeism and lost productivity.

1.2.3 Aetiology and Pathophysiology of Migraine

There are several potential explanations for the pathogenesis of migraine (Benoit, 2009). These include a vascular theory (Willis 1664; Wolff, 1937), a neurovascular theory (Blau, 1984), a neurotransmitter theory and a brain stem theory. A brief overview of each will be examined in this section. There are other explanations for the pathogenesis of migraine but essentially no definitive explanation has yet been established (Welch, 1987; Maizels, Aurora, Heniricher, 2012) and no one theory accounts for all the symptoms which occur in a single attack (Goltman, 1936). Edmeads (1991) suggested that researchers need to step outside the polemic as to whether migraine is primarily a vascular or neurological dysfunction and consider the role of neurotransmitters as being a link between neural and vascular systems and the impact which neurotransmitters have on both of these systems as well as the gastrointestinal tract.

Vascular Theory of Migraine

Historically, it was believed that migraine was primarily vascular in nature (Wolff, 1937). This vascular theory persisted up to the mid to late twentieth century. The theory was based on three factors : 1. pain is registered in large cranial vessels, proximal cerebral vessel, large veins, venous sinuses and dural arteries; 2. Observations that

during a migraine attack the carotid artery becomes engorged and 3. Egotamine, a vasoconstrictor, was the most effective antimigraine drug (Goadsby, 2001). Since the late-twentieth century other explanations for the pathogenesis of migraine have emerged.

Neurovascular Theory of Migraine

Goadsby (2006) acknowledged that migraine during the 1960's and 70's was still considered a vascular phenomenon based on the observation by Wolff that migraine aura was the result of vasoconstriction and the ensuing headache a result of reactive vasodilation. The experiments by Graham and Wolff which instigated the vascular theory (as cited in Hines, 1938), involved giving ergotamine (a vasoconstrictor) to migraineurs and when this had the effect of alleviating the migraines, they administered histamine (a vasodilator) and subsequently reproduced the headache.

Goadsby wrote that this vascular theory was later rejected for many reasons. These included the fact that not everyone who had migraine had aura, and furthermore, non-vascular acute medications had been shown to be effective in tackling migraine. He discussed the brain stem hypothesis for migraine which developed as a result of an observation that brainstem aminergic neurones e.g. noradrenergic neurones of the locus coeruleus, could be causing the unusual features typical of the aura phase in migraine, such as sensitivity to light and sound and unilateral head pain. This notion, Goadsby outlined, was supported by PET studies which demonstrated that activations in the rostral brainstem lingered after a migraine attack but were not present in the period between migraines i.e. interictally (Weiller, May, Limmroth, Juptner, Kaube, Schayck, Coenen & Diener, 1995). These findings, Weiller et al. (1995) proposed, supported the concept that the pathogenesis of migraine is related to an imbalance in activity between brain stem nuclei regulating anti-nociception and vascular control. Goadsby concluded by saying that

clinicians could feel confident telling patients the disorder was localised in the brain and is a brain function disorder and not a disorder of blood vessels, as was previously speculated. Blau (1984) was not as anxious to discount the vascular element of migraine and instead defined migraine as a 'primary neurological disturbance with secondary vasomotor changes' (p.437). He considered migraine theories to be incomplete and used the analogy of a house where theories are based on the roof and both the main building (the symptoms of migraine e.g. irritability, mood changes, tiredness) and also the foundations (prodromes and aura for example) have been neglected.

Blau (1984) listed eight points which support a neurological pathogenesis for migraine and proposed that the vasomotor features were secondary to neural stimulation. This, Blau explained was consistent with two theories supported by Living and Gowers (1888). The first of these was based on changes in the blood vessels which were visible in the colour of the patient's skin which was attributed to flushing of the skin due to dilation of the blood vessles and pallor of the skin due to contraction of the arteries. The alternate explanation of migraine was described as a primary disorder of the nerve cells of the brain leading to peculiar vaso-motor disturbances occuring from time to time. The eight points described by Blau (1984) to support this latter theory are as follows:

- Migraine attacks can be precipitated internally by stimuli from the nervous system (stress or sleep disturbance) or externally from the environment (light) which leads to excitation of neural pathways.
- The hypothalamus is implicated in the instance of neurological prodromes such as tiredness or food cravings.
- The classic sensory aura cannot be explained by vascular functioning.
- Neurological symptoms such as lack of focus and tiredness continue after the prodrome and into the headache phase of a migraine.

- Neurological symptoms have been found to persist after the headache phase of migraine.
- Sleep is a solution for many migraine attacks.
- Changes in cerebral blood flow during a migraine with aura cannot be explained in vascular terms.
- Electroencephalogram (EEG) changes have been found before during and after the headache stage of migraine.

Blau (1984) concluded by saying that both vascular and neurological hypotheses needed to be considered and the implication of altered neural transmission in migraine merited further investigation.

Neurotransmitter Theory of Migraine:

Serotonin-based medication is currently prescribed for migraineurs, with evidence indicating that this neurotransmitter is the one most commonly implicated in migraine pathophysiology (Hamel, 2007). Interest in serotonin-based treatment stems from observations that drugs which reduce serotonin seem to increase the number of migraine attacks and intravenous serotonin has been shown to abort migraines (Benoit, 2009). Low serotonergic disposition has been observed among migraineurs, leading researchers to suggest that migraine is a consequence of a neurochemical imbalance (Hamel, 2007). Yaknitsa, Pilyavskii, Limansky and Bulgakoa (1996) observed that serotonin is moderated by neuronal calcium channels and advised that dysfunction in the calcium channels could compromise the release of serotonin and subsequently predispose individuals to a migraine.

A review by D'Andrea, D'Arrigo, Carbonare and Leon, (2013) examined biochemical studies. They found evidence for an occurrence of metabolic abnormalities in the synthesis of neurotransmitters and neuromodulators and attributed the

abnormalities to impaired mitochoncrial function and high levels of glutamate in the CNS of migraineurs. This led them to hypothesise that migraine attacks are triggered by a process which starts in the frontal lobe and which progresses to abnormal activation of nuclei in the pain matrix. The idea that there is a 'pain matrix', that is, that pain emerges from multiple areas of the brain rather than there being the existence of one specific locus of pain, is widely accepted in the pain literature (Maizels, Aurora & Heniricher, 2012). Based on neuroimaging studies which showed altered functional connectivity between brainstem pain-modulating circuits and limbic centres in the brains of migraineurs, Maizels et al. (2012) also proposed the existence of a 'limbic' influence in the aetiology of migraines. They suggested that there was a bidirectional interaction between pain and mood and that neurolimbic dysfunction can increase when migraine becomes chronic.

Brain Stem Theory of Migraine

Benoit (2009) suggested that abnormal brainstem activity may be a part of the pathophysiological jigsaw that causes migraine. Welch, Nagesh, Aurora and Gelman (2001) proposed that the Periaqueductal Gray (PAG) region of the brain stem may be one possible 'generator' of migraine attacks. This hypothesis was supported by previous observations made by Raskin, Hosobuchi and Lamb (1987). Raskin et al. (1987) reported that fifteen patients with no prior history of headaches who underwent the placement of an electrode in the PAG region subsequently reported headaches with migraine type features in the few days post implantation. They concluded that disturbance in this region of the brain could initiate migraine.

A more recent study by Mathew (2011) compared the brains of chronic migraineurs with episodic migraineurs. He found more advanced change in specific structural areas of the brain. One of these changes was iron accumulation in the periaqueductal gray

matter of patients with chronic migraine. Mathew (2011) observed that this iron accumulation was different from episodic migraine sufferers and these changes correlated with the duration of the migraine disorder. Other physiological differences between the brains of episodic migraineurs (EM) and chronic migraineurs (CM) included greater cortical excitability in CM and a greater incidence of cutaneous allodynia. Mathew (2011) explained that cutaneous allodynia, which correlates with migraine frequency and duration of illness, is a marker of central pain sensitization which generates free radicals and damages the PAG. Reisman and Fuller (2009) noted that repeated attacks of headache or aura cause iron accumulation in the PAG which in turn impairs the antinociceptive system which controls the trigeminovascular system, the part of the brain associated with migraine pain (Pietrobon & Striessnigh, 2003). Further support for the brain stem hypothesis comes from the findings that regional Cerebral Blood Flow (rCBF) increases in many areas of the dorsal rostral brainstem during a migraine attack which may indicate defective activity (Pietrobon & Striessnigh, 2003). This defective activity would, the researchers suggested, either 'trigger a migraine (brainstem generator of migraine) or contribute to central hyperexcitability of trigeminal pathways' (p.387). Pietrobon and Striessnigh (2003) explained this was important because two of the issues which remain misunderstood about migraine are the primary cause of migraine which leads to activation of the trigeminovascular system and the process of pain generation after the trigeminovascular system (TGVS) is activated.

Other Theories of Migraine Aetiology

Some research which has been conducted and which may be relevant in the future understanding of migraine pathophysiology include studies investigating the role of the Patent Foramen Ovale and the role of genetics in migraine. Harder (2005) described the unusual findings of a Swiss neurologist who treated a stroke patient by shutting the Patent Foramen Ovale (PFO), a residual tunnel in the

heart. The patient, a lady in her thirties, wrote to the surgeon to thank him for subsequent decrease in her migraines. In his article Harder (2005), described how the PFO can act as a valve and occasionally blood clots which pass through the PFO will go to the brain and instigate a stroke. He cited further examples of cases where cardiologist, Peter Wilmshurst found several scuba divers whose PFOs were surgically closed, as a means to prevent decompression sickness, also reported having fewer migraines after the operation. As the research in this area was related to individuals who had other problems, the author reflected that further investigation was needed in order for the procedure to be considered as a treatment option for migraine. Reisman and Fuller (2009) commented on the only randomized controlled trial (RCT) examining PFO closure in migraine patients and compared the results with retrospective single centre studies. The RCT did not confirm the results from the retrospective studies and Reisman and Fuller (2009) stated that this may have been due to slow enrolment in the RCT and the narrow inclusion criteria which excluded many migraineurs. Nonetheless the researchers cautioned that the impressive results from single-centre non-randomized trials should not be ignored and that PFO closure has potential to reduce the functional disability of migraine.

Some research has been conducted in the area of genetics and migraine but migraine genes have been, and continue to be, difficult to identify (Ducros, 2013). The susceptibility to migraine is set by one's genes but twin studies have shown that the phenotype influences manifestation of migraine (Kors, Vanmolkot, Haan, Frants, Van Den Maagdengerg & Ferrari, 2004). In a recent review of the literature, D'Andrea, D'Arrigo, Carbonare and Leon, (2012) noted that although specific mutations of genes involved in the pathogenesis of migraine are yet to be determined, those polymorphisms and mutations which regulate neurotransmitter

metabolisms and ion channels in the central nervous system are considered to be the main biological factors influencing migraine.

1.2.4 Psychological Aspects of Headache, Including Migraine

Nicholson, Houle, Rhudy and Norton (2007) recommended that clinicians should consider the various factors which have an influence on headache development, course and severity and the subsequent disability with a view to minimizing the frequency of attacks, reducing severity and limiting the effect of headaches on functioning. The researchers considered the cognitive and affective processes which influence headache and reviewed the influence of cognitions and negative affect on the perception of headache and the development of headache. Two types of cognitions were identified as being specifically influential in relation to headaches, namely locus of control and self-efficacy. The researchers also proposed that negative affect in headache patients' results from a combination of anxiety, depression and anger.

A co-occurrence of depression and anxiety in migraineurs has frequently been reported, for example, Merikangas, Angst and Isler (1990) and Breslau, Davis and Andreski, (1991). Notably, Brown, Newman, Noad and Weatherby (2012) suggested that there is a complex bidirectional association between mood disorders and migraine, as experiencing a migraine can in and of itself be a cause of psychological stress. They stated that pain management strategies can assist people to manage their pain more effectively and recommended that rather than adopting one approach on its own, a combination of medical and psychological approaches can be employed to treat migraine. Hamelsky and Lipton (2006) suggested that the co-morbid relationship between migraine, depression and anxiety disorders can have clinical significance and that treatment of one condition could help prevent progression to one or both of the other two conditions. With respect to the treatment of patients who suffer with both depression and migraine, the authors suggested that

treatment options which address both of these conditions should be considered.

A prospective cohort study with a follow up time of eight years involving 9,288 participants conducted by Swanson, Zeng, Weeks and Colman (2013) found that the association between migraine and depression may be explained by stress. Swanson et al. (2013) initially defined several types of stressors including childhood trauma, chronic stress, work stress, change in social support, financial strain, recent marital problems and recent unemployment. They were interested in finding out which particular stressors might confound the migraine-depression association. Their results showed chronic stress was strongly predictive of the onset of migraine and depression while recent changes in marital relationship status and recent employment changes were not strongly predictive of either depression or migraine. They pointed out that these results are relevant for developing intervention strategies and recommended that effective stress-management strategies for migraineurs and individuals suffering with depression could have significant implications for prevention and may have a positive impact on helping to alleviate the economic burden which these disorders have on society. Hernyk-Gutt and Linford Rees (1973) and Mollague (2012) also found that emotional stress can act as a precipitating factor in migraine. To test the hypothesis that psychological factors contribute to the aetiology of migraine, Henryk-Gutt and Linford Rees (1973) matched a random sample of 50 male and 50 female migraineurs with similar groups who suffered non-migraine headaches and groups which did not experience headaches. Their findings indicated that over 50% of attacks documented during a two month observation period were related in time to a stressful event and 50% of the random sample experienced migraine for the first time ever during a period of emotional stress. Henryk-Gutt and Linford Rees (1973) also found evidence to suggest an increase in the activity of the autonomic nervous system in migraine subjects

and noted the importance of this factor in the development of migraine attacks.

Brown, Newman, Noad and Weatherby (2012) said that while it was important to recognise that migraine 'is a biological and not a psychological entity' (p.78) it was also important to acknowledge the role which psychological factors have in the treatment of migraine. Brown et al. (2012) listed psychological factors which could influence migraine in four ways: 1. Migraines can be triggered by psychological stressors, 2. Migraine can itself lead to significant psychological stress and subsequently can exacerbate the problem, 3. Pain management strategies can assist migraineurs in coping with their pain more effectively and 4. the existence of a bidirectional association between mood disorders and migraine. The researchers suggested that functional imaging studies could provide a physiological explanation for the processes by which psychological interventions in pain management function as studies have shown that changes in cognition and affect alter the way in which the brain processes pain. There is evidence in the literature to support this. Bantick, Wade, Ploghaus, Clare, Smith and Tracy (2002), building on the copious support in the literature that pain perception is reduced when distraction techniques are utilised, used fMRI to examine the neural systems and mechanisms involved when participants were distracted while being subjected to painful stimuli. Bantick et al. (2002) found that when tasks were cognitively demanding (an analogue version of the Stroop test was used) there was an increasing activation in the affective division of the anterior cingulate cortex and orbitofrontal areas and reduced activation in areas of the pain matrix such as the thalamus and insula. They also found that while the areas of the brain involved in sensory components of pain remained stable across time, activation in areas of the brain pertaining to cognitive-emotional components of pain increased across time. Their findings supported the behavioural results of a reduction in pain perception and they surmised from

their research that a patient's thoughts, emotions and pain experiences alter how the brain interprets pain. Phan, Wager, Taylor and Liberzon (2002) conducted a meta-analysis of emotion activation studies in PET and fMRI and concluded that many of the regions of the brain which are associated with pain processing are involved with emotions and other psychological processes such as attention. Thus, as Nicholson et al. (2007) and Brown et al. (2012) suggested, modulating pain by psychological factors may occur in these shared circuits and consequently alter the pain signal within the brain. Pain intensity can also be influenced by psychological interventions. Garland (2012) noted that activation of part of the brain implicated in emotion, the ventrolateral cortex, is positively associated with the extent to which pain is perceived to be controllable and negatively correlated with subjective pain intensity.

Garland (2012) examined the notion that pain involves a process of cognitive appraisal where an individual is evaluating the significance or meaning of sensory signals from their body and assessing whether or not there is harm. He determined that this appraisal is subjective in nature and is possibly determined by a neurobiological dissociation between sensory and affective aspects of the pain experience. He gives an example of changes in pain intensity altering activation of the somatosensory cortex and changes in pain unpleasantness resulting in altered activation of the ACC. Garland (2012) surmised that whether an individual interprets a sensation as threatening or not is somewhat dependent on whether the person believes that they have the capability to deal with the sensation or not. If, during this complex cognitive process of appraisal, available coping resources are deemed sufficient to deal with the sensation, then pain can be perceived as controllable. The corollary is that when pain is cognitively perceived to be controllable, pain intensity is reduced. This, Garland (2012) found, is irrespective of whether the person acts to control the pain. When a pain is interpreted as a harmless sensation, for example, warmth,

there is an increased likelihood they will feel as though they have control over the pain. Psychological interventions, Garland explained, can reduce pain severity by altering the interpretation of pain sensations such that they are interpreted as innocuous sensory information. Conversely, he explained, when pain is perceived as overwhelming and uncontrollable (pain catastrophizing) there is an association with increased pain intensity regardless of the physical trauma. Pain catastrophizing can therefore be considered an important factor in the treatment of migraine.

Personality traits have also been implicated in migraineurs. Hines (1938) described research conducted by Wolff (1937) as a 'thorough study of the personality features and reactions of patients who had migraine' (p.989). He listed the features of these patients as 'hardworking, hard drivers, and have the ability to accomplish much in a short space of time' (p.989) and suggested that the features led to resentment when things did not go according to plan. This resentment, he posited, caused emotional upset which was then likely to precipitate a migraine. As Maizels et al. (2012) suggested there appears to be a bidirectional relationship between migraine and mood and the stress of chronic headache can cause changes in mood, for example, anxiety. A current review of personality traits, personality disorders and migraine (Davis, Smitherman & Baskin, 2013) found that individuals who suffer with migraine frequently endorse higher levels of neuroticism compared to individuals without migraine. This was consistent with the findings from a review by Silbersetin, Lipton and Breslau (1995). No other personality traits were found to be associated as much with migraineurs.

Given the cyclical relationship between stress and migraine and the notion that stress can be both a cause and effect of the social and medical disabilities brought about by migraine (Malone,Bhowmick & Wachholtz, 2015), there is a strong argument for interventions

such as hypnotherapy where the focus of treatment is to reduce stress by targeting components of pain such as unhelpful cognitions (e.g. catastrophizing) and behaviour (e.g. activity avoidance). Neurological and clinical research literature strongly suggest that hypnosis can alter the manner in which emotion is experienced by patients and subsequently impacts on sensation, behaviour and cognition (Nash & Barnie, 2012).

Pain Catastrophizing

Haythornthwaite (2009) described catastrophizing as the cognitive and emotional responses to pain, negative in nature and typified by rumination, magnification of pain and helplessness. She draws attention to the fact that there is a strong correlation between catastrophizing and disability which is independent of pain severity. Sullivan, Bishop, and Pivik (1995) developed a Pain Catastrophizing Scale (PCS) and found that, as an instrument for measuring catastrophizing in pain patients, the PCS is a valuable, reliable and valid tool. They also noted the ability of the PCS to significantly predict the intensity of both emotional and physical distress of individuals participating in a cold pressor task and in electro diagnostic evaluation. The fact that catastrophizing remains stable over time unless an intervention is undertaken to address it, was also noted.

Catastrophizing in migraine patients has been associated with impaired functioning and quality of life, independent of migraine characteristics and other psychological variables (Holroyd, Drew, Cottrell, Romanek & Heh, 2007). However, Chiros and O'Brien (2011) studied 74 individuals with migraine headaches and found that pain-related acceptance reduced the impact of catastrophizing and led to an increase in daily activities. A pilot study by Jensen, Ehde, Gertz, Stoelb, Dillworth, Hirsh, et al. (2011), tested whether cognitive restructuring would have a stronger impact on catastrophizing than an hypnotic intervention, and found both

treatments had a significant effect on lowering the levels of catastrophizing in 15 patients with Multiple Sclerosis.

Thorn, Pence, Ward, Kilgo, Clements, Cross, Davis and Tsui (2007) cited several studies which illustrated that migraineurs as well as individuals suffering with tension-type headache endorsed more catastrophic thoughts when coping with painful events than individuals who did not suffer with either condition. Thorn et al. (2007), evaluated the efficacy of CBT with 40 participants who had been diagnosed either with tension type headache or migraine and, among other measures, monitored changes in pain catastrophizing. Thirty one participants completed their randomized controlled trial and in this instance treatment was not found to influence pain catastrophizing. The researchers suggested that this may be due to the fact that the mean PCS score for their patients was lower than the average reported by O'Sullivan et al. for patients enrolled in a multi-disciplinary treatment programme. Thorn et al. (2007) explained that none of their participants scored in the 80th percentile which, according to Sullivan et al. is indicative of patients who show poor progress in pain rehabilitation programmes.

Keefe et al. (2004), described pain catastrophizing as the 'tendency to focus on pain and negatively evaluate one's ability to deal with pain' (p.196). These researchers summarised the research on catastrophizing, finding that patients who catastrophize have longer hospitalizations, higher rates of health care usage, higher levels of psychological distress, and higher levels of pain-related disability. They also quoted Sullivan et al's theory that pain catastrophizing is a coping response which has the aim of eliciting support from others.

High scores on the PCS are linked with high levels of disability (Keefe et al., 2004) but changes in catastrophizing are associated with improvements in disability. For example, Scott et al. (2013)

treated 166 occupationally disabled individuals who had subacute pain in a seven week multidisciplinary rehabilitation programme with a view to promoting functional recovery. They measured PCS scores before and after intervention and found that PCS reductions of 38% to 44% post intervention were best associated with return to work and low pain intensity ratings.

1.3 Treatment of Migraine

1.3.1 Pharmacological Treatments

Traditionally, medication has been prescribed for the treatment of migraine. More recently, exercise and psychological interventions have also been considered.

Medication is typically prescribed for migraines and is often effective. There are both advantages and disadvantages with taking medication. Irrespective of whether the medication is prophylactic (preventive) or abortive (stopping or interrupting a migraine attack), it can be expensive, and overuse of medication can lead to further problems. The excessive consumption of analgesic (pain relieving) medications for example can lead to further headaches, referred to as medication overuse headache, and this can make it more difficult to diagnose and manage chronic migraine (Vargas & Dodick, 2009).

Prophylactic Medication

Preventive, prophylactic medications approved in the U.S. by the Food and Drug Administration (FDA) are on a sliding scale of medications which have established efficacy right down to those which are probably ineffective.

The drugs in the Level A category which satisfy FDA criteria for having established efficacy in 2 or more class 1 trials include:

- Antiepileptic Drugs such as Topiramate
- Beta blockers such as Timolol and Propanolol
- Triptans such as Frovatriptan

One step down from these, there is a category of drugs which are deemed to be 'probably effective', that is they have established efficacy from one Class 1 trial or two Class 2 trials. These include:

- Antidepressants/SSRI/SSNRI/TCA such as Amitriptyline
- Triptans such as Zolmitriptan

The drugs which are considered to have a possible but unconfirmed role to play in preventing migraines include:

- Antihistamines such as Cyproheptadine
- ACE inhibitors such as Lisinopril

(Silberstein, Holland, Freitag, Dodick, Argoff & Ashman, 2012)

In 2000 the American Academy of Neurology (AAN) published guidelines for migraine prevention and examined NSAIDs and complementary therapies in their guidelines. Holland, Silberstein, Freitag, Dodick, Argoff and Ashman (2012) addressed the efficacy and safety of histamines/antihistamines; NSAIDs and analgesics in addition to herbal, vitamin and mineral preparations. They concluded that regular use of specific NSAIDs for the treatment of frequent migraine may lead to development of medication overuse headache but that NSAIDs are probably effective and were categorised as Level B, C or U depending on the type of NSAIDs considered.

Botox and migraine

In October 2010, the FDA gave approval for the use of Botox (Botulinum Toxin A) as treatment for chronic migraine. This approval was granted on the basis of results from two clinical trials. A recent review of the literature (Jackson, Kuriyama & Hayashino,

2012) examined the efficacy of Botox in reducing the frequency and severity of migraine. They examined 27 randomised controlled trials on migraine which compared the use of Botox with a placebo and 4 studies which compared the use of Botox with other medications. These medications included Topiramate, Valproate, Prednisone and Amitriptline. The review found that Botox is modestly effective in the treating chronic migraine (≥15 headache days per month) but ineffective in treating episodic migraine (<15 headache days per month). Those with chronic migraine had approximately two fewer headaches each month when using Botox. In real terms the number of days patients suffered with migraines when given Botox decreased from 19 days to 17 days. In their study the researchers also note that there was a greater frequency of paresthesias (numbness or tingling), neck pain and muscle weakness among those using Botox compared with using placebo.

Abortive medications

For some people, migraine attacks are not frequent enough to warrant prophylactic medication. In such instances abortive medication might be prescribed. Some research (Gilmore & Michael, 2011) advised that when using abortive medications, they should be used as soon as possible once the migraine symptoms manifest. Triptans are considered first-line abortive treatment for moderate to severe migraine but, as has been pointed out by Gilmore and Michael (2011) complete pain relief is not always possible and abortive medications are not advisable for anyone who has vascular problems. For milder migraines, the authors of the study quoted the U.S. Headache Consortium guidelines which suggest the use of non-steroidal anti-inflammatory drugs (NSAIDs) or caffeine containing combination analgesics. While these are the recommendations for acute treatment of migraine, in a study (Bigal, Borucho, Serrano & Lipton, 2009) examining 14,540 responses from individuals with episodic and chronic migraine, a pattern emerged to show that a considerable proportion were using

medications which were not first-line according to the US Headache Consortium Guidelines. Of those with chronic migraine, only 22% were using migraine-specific medications and more than 34% were using opiates or barbiturates. Of those with episodic migraine, 19.2% of subjects used migraine specific treatment, 11% used opiates and 6% used compounds with barbiturates.

The complex pathophysiology of migraine means that no single medication is expected to treat all patients and large unmet migraine treatment needs still exist (Bigal & Ho, 2009). Bigal and Ho (2009) also pointed out that patients define efficacy of treatment in ways that vary considerably from patient to patient. The authors listed some of the variables of interest such as speed of efficacy, duration of efficacy, tolerability, ease of use and associated symptoms. The various side effects of prophylactic medications were described by Jackson, Cogbill, Santana-Davila, Eldredge, Collier, Gradall, Sehgal and Kuester (2015). The most common side effect was drowsiness and was most likely to be reported among patients taking gabapentin, pizotifen, topiramate, TCA and valproate. The authors reported dry mouth and weight gain as side effects from Tricyclic antidepressants while depression, dizziness and insomnia were associated with beta blockers. Weight gain was also a side effect with Pizotifen. Side effects of nausea and paresthesia were associated with Topiramate. Medication overuse headache is common and has significant morbidity (Bajwa, Smith, Swanson, Dashe, 2015). Bajwa et al., (2015) suggested that all acute sympotmatic medications used to treat headaches have potential for causing medication overuse headache and recommended that acute medications be limited to less than 10 days per month or less than 15 days per month where aspirin, acetaminopen and NSAIDS are used. Given the potential unpleasant side effects of medical intervention and the recommendations to limit use of acute medications psychological intervention for migraines has been explored.

1.3.2 Psychological Treatments

Cognitive Behavioural Therapy (CBT), Behavioural Therapy and Acceptance and Commitment Therapy (ACT) are three of the more prominent psychological treatments currently used for pain management. Morley, Eccleston and Williams (1999) identified 25 trials using CBT with chronic pain for meta-analysis. They compared alternative active treatments with CBT and found that CBT produced significantly greater changes in measures of pain experience and there was reduced expression of behavioral pain. No significant difference was found for changes in social functioning, mood or in negative cognitive appraisal such as catastrophizing. The authors of the paper pointed out that psychological intervention for chronic pain patients is complex, takes a long time and the outcomes are variable. Regardless of these shortcomings the authors concluded that psychological treatments based on CBT are effective. This review did not include headache patients and hypnotherapy was not one of the treatments compared with CBT in this meta-analysis.

A Cochrane Review on the effect of CBT on neck pain by Monticone, Cedraschi, Ambrosini, Rocca, Fiorentini, Restelli, Gianola, Ferrante, Zanoli and Moja (2015) concluded that while CBT was statistically significantly better at improving pain, disability and quality of life when compared with no treatment, the effects could not be considered clinically meaningful. When CBT was compared with other interventions such as medication, education, physiotherapy and manual therapy no differences were found with respect to changes in pain and disability. Thirty five trials were included in another Cochrane Review which examined CBT and behavioural therapy for the treatment of chronic pain. The review, conducted by Williams, Eccleston and Morley (2012) found no evidence for behaviour therapy apart from a minor improvement in mood directly following treatment and when compared with an

active control. Immediately after treatment CBT, when compared with other active treatment controls, was found to exert a small positive effect on disability and catastrophizing but not mood and these improvements were not sustained at follow up. When compared with waitlist or treatment as usual, CBT had small to moderate effects on pain, disability, mood and catstrophizing immediately after treatment but, with the exception of a small effect on mood, the changes had disappeared at follow up.

The efficacy of Acceptance and Commitment Therapy was examined in a paper by Dionne, Blais and Montestes (2013). The researchers suggested that so far, clinical studies show ACT to be a relevant and empirically supported treatment for chronic pain. They concluded by saying that ACT can currently be considered as effective as traditional cognitive and behavioural therapy for chronic pain but more research is required into the processes involved in the treatment. Ost (2014) in a review and meta-analysis of sixty randomized controlled trials (RCTs) concluded that a small effect size of 0.16 was obtained when ACT was compared with various CBT or behavioural treatments but the size of the effect was not significant. Various conditions including somatic disorders, stress at work and psychiatric disorders were included in the analysis. The author suggested that ACT is probably efficacious for chronic pain.

A review of psychological treatments, which included hypnosis, by Eccleston, Palermo, Williams, Holley, Morley, Fisher and Law (2014) in a population of children and adolescents (<18 yrs of age) found that face to face psychological treatments were effective in reducing disability and pain intensity for headache sufferers (including migraine). They found that the gains were maintained but noted that only two studies were included in the follow up and that the findings should be treated with caution. The authors of the paper also concluded that psychological therapies were beneficial at reducing anxiety in headache patients post treatment. In another review, specifically focused on hypnotherapy Hammond (2012) found that hypnosis is an effective and specific treatment and is

statistically superior or equal to other treatments including medication and bio feedback.

Nicholson (2010) noted the absence of recommendations for inclusion of psychological strategies for all headache patients in the U.S. headache Consortium's publication for evidence-based guidelines for nonpharmacological treatment for headache explaining that their beliefs were clearly that psychological interventions would only be useful with selective cases. This lack of awareness or support for psychological interventions was echoed in a study by Serrano, Buse, Adams, Reed and Lipton (2015) which documented the results of the American Migraine Prevalence and Prevention (AMPP) Study. The AMPP study used structural equation modelling to compare and contrast episodic migraineurs and chronic migraineurs on their response to a migraine treatment optimization questionnaire (mTOQ), a questionnaire designed to look at responses to acute treatment and, in turn, ways to optimize treatment. One of the aims of their study was to identify headache and treatment features which were associated with treatment optimization. Their findings were that both CM and EM had poor treatment opmtimization and that there were greater deficits in treatment optimization among the CM population. In both groups the return to functioning, rapid pain relief, sustained pain relief, tolerability, perceived ability to plan things and internal locus of control all fared poorly. Their suggestions for treatment optimization confined non-phamacological intervention to non pain-relief areas such as perceived control. This may be limiting the potential for improvement among migraineurs given the fact that psychological treatments such as hypnotherapy have been shown to be effective in reducing pain severity as well as other psychological issues. Thus while this American Migraine Prevalence and Prevention (AMPP) Study provided useful insights into the response of migraineurs to pharmacological treatment it has, perhaps unintentionally, limited its recommendations for migraine solutions

largely to pharmaceutical solutions. Several pharmaceutical companies provided grant support for the study by Serrano et al. (2015) which could explain to some degree why the focus on recommendations for the treatment of migraine was largely confined to pharmacological treatment.

It is now accepted that psychological factors play an important role in the experience of persistent pain (Keefe, Rumble, Scipio, Giorddano & Perri, 2004). Eccleston, Palmero, Williams, Lewandowski, Morley, Fisher and Law (2013) reviewed thirty-seven studies using a range of psychological treatments for the management of chronic pain in children and in adolescents. Twenty one of these studies involved treatments for headache and migraine. The psychological treatments included relaxation, coping skills training, hypnosis, biofeedback and CBT. For this age population the researchers concluded that relaxation and CBT were effective in reducing the severity and frequency of chronic pain and in improving mood. Disability and mood were improved immediately after treatment for some pain conditions but not for chronic headache. The findings were inconclusive regarding lasting effects of such treatments on pain and disability in children and young people. When Chakravarty, Mukherjee and Roy (2008) compared 800 adult migraineurs with 200 children who suffered with migraine they found significant differences in migraine pain location. Unilateral pain was only reported in 10.5% of children compared with 40.5% of adults.

Wells and Loder (2012) also reviewed non-pharmacological treatments for patients, most specifically headache patients. The intention of their review was to define behavioural and mind/body treatments, evaluate the evidence for both treatment categories and finally describe their role in the treatment of headaches. They defined CBT, Biofeedback and Relaxation Training as falling into the behavioural category and meditation, guided imagery,

biofeedback, hypnosis, progressive muscular relaxation, yoga and Tai Chi as belonging to the mind/body category. Quoting The National Institute of Health's National Center for Complementary and Alternative Medicine, Wells and Loder (2012) stated that mind/body practices are those which 'focus on the interactions among the brain, mind, body and behaviour with the intent to use the mind to affect physical functioning and promote health'(p.71). The article acknowledges however that there is a substantial overlap between behavioural and mind/body treatments and that this may be due to the fact that relaxation is often the same outcome for all treatments. The authors concluded that both mind/body and behavioural treatments have the potential for meaningful improvements in a headache population and cited a 35%-50% reduction in migraines and tension type headaches with these treatments. This they say is similar to results seen in medication trials, a fact supported by Linde (2006) who found that the reduction in score on the headache severity index is virtually identical for patients using prophylactic drugs and patients using behavioural treatments such as cognitive behavioural treatment and relaxation techniques.

The Linde (2006) review article stated that non-pharmacological treatment offered an opportunity for participants to be more influential in their recovery process by offering patients an opportunity to feel 'empowered' because they are actively participating in the process. Linde (2006) noted too that non-pharmacological treatment is believed to activate endogenous, positive mechanisms. The review cited the most common behavioural therapies for migraine as falling into the categories of relaxation, cognitive-behavioural therapy and biofeedback.

Given the inclusion of psychological components in the current pain paradigm proposed by the IASP there is a strong argument for employing psychological treatments with migraine patients.

1.3.3 Other Treatments for Chronic Pain and Headache

Complementary and alternative medicine (CAM) represents a group of diverse medical and healthcare therapies, systems and products which are not part of conventional medicine (Tan, Craine, Blair, Garcia, Giordana, Jensen, McDonald, Patterson, Sherman, Williams & Tsao, 2007). In a review of the efficacy of specific CAM as interventions for chronic pain, Tan et al., (2007) found that some CAM were effective and others required additional research. The review divided CAM into four areas; (a) biologically based medicine, (b) energy medicine, (c) manipulative body-based medicine and (d) mind-body medicine. Acupuncture and homeopathy were considered separately. Biologically based medicine encompassed dietary supplements for chronic pain. 63% of clinical trials reviewed in this area showed a statistically significant effect on pain when compared with placebo. Studies examining energy medicine included the use of electro-magnetic fields and biofield therapies to treat pain. In this category, Pulsed Electromagnetic Field (PEMF) was limited in terms of number of studies and the small number of participants. Nonetheless, the researchers concluded that pulsed electromagnetic field generators could be highly effective for patients with migraine but not for patients with tension-type headache. Cranial electrotherapy which also came under the energy medicine category was also found to be effective in reducing chronic pain. Little evidence was found for Reiki as a means of reducing chronic pain although Qi Therapy was considered possibly efficacious.

Spinal manipulation therapy (SMT), massage therapy and cranio sacral therapy were examined in the Manipulative and Body-based Medicine category. The researchers stated that SMT might reduce pain severity and disability in a variety of chronic pain conditions but to date it has been shown to be more effective than bed rest and traction for lower back pain only. Massage therapy was also useful

for chronic low back pain and also several other chronic pain conditions. Meditation, yoga, biofeedback and hypnosis were reviewed under the mind-body medicine category. There was insufficient evidence to support the use of meditation or yoga for the treatment of chronic pain. Studies examined in the review provided support for biofeedback in helping patients both directly and indirectly to deal with chronic pain and the researchers concluded that hypnosis was also an efficacious treatment for chronic pain. In addition, they suggested that hypnosis and hypnotic analgesia had been underutilised as treatments for clinical conditions.

Other research supports this review and examines the use of hypnosis compared with other complementary therapies. Berman and Swyers (1999), for example, looked at studies which used a variety of complementary treatments for fibromyalgia syndrome. These treatments were divided into three categories: mind-body interventions, acupuncture and manipulative techniques. They found that the strongest support was for the mind-body interventions which included hypnosis. A later review by Elkins, Jensen and Patterson (2010) examined thirteen studies which used hypnosis as a treatment for chronic pain conditions such as cancer, low back pain, arthritis and sickle-cell disease. This review found support to indicate that hypnosis produced significant decreases in pain. The authors pointed out the short-comings of past studies on chronic pain and hypnosis, most notably the lack of credible controls for placebo or expectation. Jensen and Patterson (2006), in a separate review of the literature, found a significant body of studies demonstrating the superior nature of hypnosis to medication management, physical therapy and education for the treatment of chronic pain and stated that it could be argued that each of the alternative treatments presumably also enlisted patient expectancy.

Hypnotic analgesia consistently results in greater decreases in a variety of pain outcomes when compared with standard care and/or no treatment. A review of randomized controlled trials of hypnotic

analgesia for the treatment of chronic and acute pain in adults found hypnosis to be more effective for neuropathic pain or vascular pain than in musculoskeletal pain (Stoelb, Molton, Jensen & Patterson, 2009). Ezra, Gotkine, Goldman, Adahan and Ben-Hur (2012) for example, acknowledging the efficacy of both pharmacological and behaviour interventions for headache patients, conducted a study to assess patient intervention preference, long-term compliance and feasibility of behavioural intervention in a typical neurological outpatient clinic setting. Their study offered patients a choice between taking the prophylactic medication amitriptyline or engaging in hypnotic relaxation provided by their neurologist. Self-hypnosis training formed part of the hypnotic relaxation intervention. Ezra et al., (2012) concluded that hypnotic relaxation was the preferred treatment for headache patients and those who participated in the hypnotic relaxation treatment had greater relief of symptoms than those choosing amitriptyline. Their recommendation was that patients should be given the choice of hypnosis therapy as an alternative to pharmacological treatment. Although this study by Erza et al., (2012) was confined to patients with tension-type headache another study by Olness, MacDonald and Uden (1987) selected to teach juvenile patients who had a diagnosis of migraine with aura (classic migraine) self-hypnosis strategies. Initially, twenty-eight patients were randomized into two groups. For three months one group took the prophylactic drug propranolol and the other group were given a placebo. They then crossed over for three months. After this six month time frame each child was taught self-hypnosis and used it for three months. The researchers found that there was a significant association between self-hypnosis training and a decrease in headache frequency. The mean number of headaches per child during the self-hypnosis period was 5.8 compared with 14.9 during the propranolol period and 13.3 during the placebo period. None of the treatments was found to have an effect on headache severity. Olness et al., (1987) pointed out that their findings of self-hypnosis as an effective non-pharmacological

treatment in reducing headache frequency was consistent with other studies in both adult and child populations utilising both biofeedback or self-hypnosis. Jensen and Patterson (2006), in a review of non-pharmacological treatments for chronic pain found that self-hypnosis training worked equally well as relaxation strategies for the treatment of chronic pain and they suggested that this may be due to the fact that relaxation techniques may incorporate elements of hypnosis.

The label given to interventions for chronic pain may have an influence on the outcome obtained from hypnotic intervention. Hylands-White and Derbyshire (2007) found that describing the same intervention as hypnosis rather than relaxation had a significant effect on study participants. The label of hypnosis led to a greater decrease in the participants' perception of pain experience and they also reported increased feelings of being hypnotized. They also proposed that hypnotizability does not, as such, have an effect on reducing pain experience but the label of 'hypnosis' does reduce the pain experience. The authors suggest that it is more important for the participant to believe they are hypnotizable rather than for them to fall into the category of 'highly hypnotizable'. Thus, patient expectation is an important factor in treatment outcomes.

The efficacy of face to face hypnosis in the treatment of migraines is well documented. Hammond (2010) reviewed eleven studies which used hypnosis for tension-type headaches and migraines. He described hypnosis as a cost-effective, non-addictive, rapid and safe alternative to medication. In the review, four of the studies employed hypnotic interventions specifically for migraines. All demonstrated significant benefit of an hypnotic intervention for migraine sufferers. For example, a study by Anderson, Basker and Dalton (1975) compared an hypnotic intervention (n=23) with medication treatment (n=24) and conducted a one year follow up of

a six session treatment intervention. The researchers found that the number of patients in the hypnosis group who experienced complete remission of migraines during the previous 3 months was 43.5% (10 patients) compared with 3 of the patients (12.5%) from the medication group. Another study reviewed by Hammond was a study by Olness, MacDonald and Uden (1987), which assessed the impact of a self-hypnosis intervention on a population of children aged between 6 and 12 years over a 12 week treatment period. The children were asked to use self-hypnosis for ten minutes twice a day. At the end of one year, the mean number of migraines per child in the placebo group was 13.3. In the medication treatment group the mean number of migraines was 14.9 and in the hypnosis group the mean number of migraines per child was 5.8. A third study which Hammond cites used a combination of group hypnosis and vascular manipulation. The focus of the study was to investigate whether hypnosis could reduce medication usage, migraine duration, frequency and severity using a twelve week treatment programme with 32 patients. All variables were significantly reduced - medication usage was reduced by 50%, and migraine frequency, severity and duration were also significantly reduced. Hammond cites a study by Andreychuk and Skriver (1975), which found that self-hypnosis training, biofeedback and autogenic training and a third treatment intervention of biofeedback with an intervention to enhance alpha brain waves were all effective in reducing the number of migraines. One more study in the review confined solely to a migraine population as opposed to chronic headache was conducted by Emmerson and Trexler (1999). This study also found a significant reduction in the number of migraines and also reported a significant reduction in the duration and severity of migraines as well as a 50% reduction in medication usage. With the exception of one study by Spanos, Liddy, Scott, Garrard, Sine, Tirabasso, Tirabasso and Hayward (1993) where 15% of the participants suffered with migraine, the remainder of the studies were based on a chronic headache population. In summary,

Hammond's review noted improvements for participants in terms of decreases in headache frequency, headache severity, reduced disability, reduction in pain medication and reduced psychological distress.

Eight of the nineteen studies on hypnotic analgesia and chronic pain included in a review by Jensen and Patterson (2006) involved a headache population. The remaining eleven studies examined a variety of other chronic pain conditions such as cancer, sickle-cell disease and temporomandibular pain disorder. Jensen and Patterson (2006) found evidence to suggest that hypnotic analgesia was more effective than medication management, physical therapy and education/advice. In this review, comparable to the findings in a previous review (Patterson & Jensen, 2003) the authors found similar treatment effects for self-hypnosis training compared with autogenic and relaxation training. Jensen and Patterson (2006) suggested that this may stem from the fact that both of these interventions frequently include hypnotic suggestions.

1.3.4 NICE Guidelines for Treatment of Migraine

The National Institute for Health and Care Excellence (NICE) was established in 2005 when the National Institute for Clinical Excellence merged with the Health Development Agency. The aim of NICE is to create a uniform standard of care in the availability and quality of treatments and care on the National Health Service in the United Kingdom and to offer public health guidance with a view to preventing ill health and promoting healthier lifestyles.

For the treatment of migraine, the NICE guidelines recommend a combination of triptan and non-steriodal anti-inflammatory drugs which was shown in trials to be more effective than taking one drug (www.migrainetrust.org). Topiramate was recommended by NICE as the most clinically effective and cost effective treatment but as The Migraine Trust cautioned, this drug can cause congenital

abnormalities and can stop hormonal contraceptives from being effective. They pointed out that NICE recommended propranolol and gabapentin as an alternative and advised that medication should be reviewed after six months as few migrainuers require ongoing medication. Nutritional supplemenation of riboflavin (vitamin B2) was also recommended for migraine patients.

Specific recommendations for women of child bearing age were also included in the NICE guidelines (www.migrainetrust.org). These included avoiding combined hormonal contraception with patients who are diagnosed as having migraine with aura because of the increased risk of stroke. When the migraine is categorised as severe and is related to the menstrual cycle, NICE recommended that frovatriptan or zoimitriptan is taken in anticipation of the migraine. NICE also stated that during pregnancy medication should be minimized and medical advice should be sought as early as possible in to the pregnancy. Sharpe, Williams, Martin, Nicholas, Welgampola, McPhee, Baillie, Dudeney and McGuire (2016) noted that NICE guidelines (2012) stated that psychological therapies have been found to be effective for chronic pain in general and thus have the potential to be a useful adjunct to the medical management of headache, including migraine. The researchers emphasised the need for psychological treatments which have the potential to reduce the personal and economic cost associated with migraine. Hypnosis is one such psychological treatment. Thus, an understanding of how hypnosis can assist in the treatment of pain is useful.

Chapter 2: Clinical, Theoretical and Conceptual Issues in Hypnosis

2.1 Theories and Models of Hypnosis

Hypnosis is a heightened state of awareness typified by specific objective indicators such as eyes fluttering and subjective indicators such as time distortion. The state of hypnosis typically involves an induction followed by suggestions. The ability of someone to experience a hypnotic state and the extent to which they can be hypnotized is described as hypnotizability or hypnotic susceptibility. While the uses of hypnosis are ubiquitous, and hypnosis can arguably be traced back to the sleep temples utilised by the Greeks and Egyptians over 4000 years ago, academic research in the area of hypnosis as an intervention for chronic pain is relatively recent. Higher hypnotizability (HH) has been associated with relatively greater response to hypnotic analgesic suggestions (Milling, Coursen, Shores & Waszkiewicz, 2010). Hypnosis has a long history of reducing emotional distress and pain (Flory, Salaza & Lang, 2007). Psychological factors are accepted as playing a role in the treatment of migraine with emotional distress being cited as the single, most frequent trigger (Pearce 1977). Bushnell, Čeko and Low (2013), commented on how emotions can affect behaviour, and stated that what makes pain "pain" is 'usually the affective component of the experience — that is, how unpleasant it is. It is the unpleasantness that motivates the individual to engage in a behaviour, whether it is to flee, fight or freeze. (p.503)'.

2.1.1 **Historical Background to Hypnosis**

The earliest reference to hypnosis relates to sleep temples in Egypt (3000-1000 BC) and Greece (2000-500BC) which provided refuge for patients whose healing experience involved hypnotic chanting. Some time later, Paracelsus, a German-Swiss physician, botanist, alchemist and astrologer who lived from 1493 to 1541 was documented as using hypnotic techniques. He had a preference for unorthodox methods of healing and is quoted as saying that 'Medicine is not only a science; it is also an art. It does not consist of compounding pills and plasters; it deals with the very processes of life, which must be understood before they may be guided. (www.egs.edu/library/paracelsus/biography).' He believed that the body could heal itself and that the mind and body are intertwined in the healing process. He is also attributed with being the first person to mention the word 'unconscious', a word used synonymously with 'subconscious' in hypnotic literature and teachings. Two centuries later, Father Maximilian Hell (1720-1792) an Austrian-Hungarian Jesuit developed an interest in magnetism. Among other applications, he used magnets to reduce pain and successfully alleviated his own rheumatic pain through the use of magnets. This attracted the attention of Franz Mesmer who developed his own theories about cosmic fluids in the body. With their unconventional approaches to healing, both men were attributed with introducing the concept of hypnosis to medicine (MacDonnell, 2013). Terms used in hypnosis such as 'somnambulism', and 'suggestibility' can be traced as far back as the 18th and 19th Centuries to Marquis de Puysegur (1751-1825) and Bernheim (1837-1919) respectively. James Esdaile, a Scottish surgeon (1808-1859) was widely regarded as being one of the most influential people in the world of medicine and hypnosis. Esdaile travelled to Calcutta from England and performed many major operations using hypnosis as the sole anaesthetic, at a time when pain relief was not available (Ernst, 2004). Amongst the operations documented is one which involved

the removal of a scrotal tumour weighing 103lbs, (Report of the committee.., 1846:26 as quoted in Ernst, 2004). Hypnosis was subsequently influenced by many well-known figures in psychology such as Freud who studied hypnosis and later replaced it with psycho-analysis, believing that patients could become 'addicted to hypnosis'. Freud also believed that hypnosis did not provide an insight into the processes which led to the formation of the problem (Bachner-Melman & Lichtenburg, 2001). However, as Bachner-Melman and Lichtenberg (2001) pointed out, Freud is often criticised for his inexperience in hypnosis. Milton Erickson (1901-1980) could therefore be regarded as the antithesis to Freud as he dedicated 50 years of his life to the study and practice of hypnosis. The term 'Ericksonian hypnosis' is used to describe an approach which tailors treatment to each patient and in which 'insight is not necessary for change' (Feldman 1985 p155). As Feldman (1985) explained, Erickson rejected psycho-analysis and was, at the time, probably viewed as an anarchist because he broke many of the established rules for the conduct of treatment.

2.1.2 Theories of Hypnosis

Hypnotizability is considered a stable trait. In a study by Piccione, Hilgard and Zimbardo (1989) hypnotic susceptibility over a 25 year period had a .75 test-re-test correlation. There are several theories about the concepts underlying hypnotizability (suggestibility). The most prominent theories are dissociation and absorption. More recently these have been divided into 'state theories' and 'non-state theories'.

State theorists refer to the stability of hypnotizability and the notion that altered states of consciousness explain the trance state. The Neo-dissociation theory and Dissociated Control theory fall into this category. The neo-dissociation theory posits that higher cognitive functions disengage from what is happening during hypnosis.

Ernest Hilgard (1904-2001) who proposed this theory believed that there was also a 'hidden observer' in the mind which was aware of what was being said (Coon & Mitterer 2008, p. 194). In terms of pain, Hilgard believed that while the patient may not experience pain, they were aware and could, at some level, report details about that pain. The dissociated control theory proposed by Woody and Bowers (1994) formerly suggested that there was a segregation of higher level brain systems in the highly hypnotizable (HH) person during hypnosis which left a dependency on lower level, automatic processes that were influenced by external cues. Typically, the highly hypnotizable individual will be characterised by his ability to 'get so absorbed in an activity that he tends to lose awareness of where he is' (Spiegel, 1977, p.139). More recent reflections (Jamieson & Woody, 2007) on studies investigating this theory have suggested that the hypnotic state is more complex.

Non-state theories propose that dynamic factors such as motivation, attitudes and expectancy are responsible for hypnotic phenomena. The sociocognitive theorists, who support this view of hypnosis, believe that suggestion will have the same effect as hypnosis on behavioural change. These theorists reject the idea that an altered state of consciousness is necessary for hypnotic experiences (Lynn & O'Hagan, 2009) and Dienes et al. (2009) noted that 'correlates of hypnotic suggestibility are notoriously difficult to find' (p.837.) The researchers looked at dissociation and cognitive inhibition, the two proposed correlates of hypnotizability on which two of the better known theories of hypnotic suggestibility – Neo Dissociation and Dissociated Control Theory – are founded. Their results, from a study population of 180 individuals, showed no correlation between hypnotic suggestibility and dissociation or cognitive inhibition. The advent of imaging techniques has allowed us to see physiological differences in the brains of those classified as 'highs' or 'HH's' and 'lows' or 'LH's'. For example, Horton, Crawford, Harrington and Downes (2004) used MRI with HHs and LHs and found that HHs

had a signficantly (P< 0.0003) larger (31.8%) rostrum, the part of the corpus callosum involved in the transfer of information between prefrontal cortices and involved in the allocation of attention, than the LHs. Higher Hypnotizability (HH) has been associated with relatively greater response to hypnotic analgesic suggestions (Milling, Coursen, Shores & Waszkiewicz, 2010) and HH's experience the most significant relief (Milling, 2008). Coupled with the growing interest in physiological correlates of hypnosis, non-state theories of hypnosis are now being challenged.

The Construct of Hypnotizability

Green, Barabasz, Barrett and Montgomery (2005) described hypnotizability as a cognitive, multidimensional trait related to the ability to accept hypnotic suggestions and stated that it can be measured by hypnotizability scales. A number of scales are employed in research settings to assess hypnotizability such as The Hypnotic Induction Profile (HIP) (Spiegel, 1977) or Stanford Hypnotic Susceptibility Scales (SHSS:C) (Spiegel & Spiegel 2004) and a computer generated system has been developed to test hypnotic ability (Grant & Nash, 1995).

While being highly hypnotizable (HH) is associated with excellent memory, a capacity for intense concentration and an easy acceptance of logical incongruities and those who fall in to this category have the ability to affiliate with new events and respond rapidly to treatment (Spiegel, 1974), being highly hypnotizable is not necessary for successful analgesia using hypnosis (Milling, 2008). The effects can also persist over time. Some studies have found no relationship between hypnotizabiltiy and performance, although these are in the minority. In a study examining the relationship between information processing and hypnosis, Friedman, Taub, Sturr and Monty (1987) looked at visual processing speed in hypnotized and in non-hypnotized subjects. Hypnotized subjects were found to be significantly faster than non-

hypnotized subjects in the speed of information processing during a backward masking task.

The Harvard Group Scale of Hypnotic Susceptibility (HGSHS:A) (Angelini, Kumar & Chandler, 1999) is the most widely used in hypnosis research because of its cost effectiveness and the ability to test several people at the same time (Angelini, Kumar & Chandler, 1999). However, as Angelini et al., (1999) pointed out, both group testing and individual testing of hypnotic responsiveness have their limitations. They highlighted the fact that social interaction in a group may skew findings by increasing or decreasing the desire to perform in front of others. Individual testing on the other hand may be influenced by the individual's desire to 'please' the researcher. The Stanford Scale of Hypnotic Susceptibility For C (Weitzenhoffer & Hilgard, 1962) is also used frequently in studies. It consists of twelve items and one mark is given to each item. It is time consuming, however; a shorter version of this scale has been developed (Morgan & Hilgard, 1978).

The Tellegan Absorption Scale (TAS) measures how absorbed a person becomes in an activity or an object. It only measures one proposed correlate of hypnotizability (absorption) although it has been used as a predictor of hypnotic suggestibility (Nadon, Hoyt, Register & Kihlstrom, 1991). A computer assisted hypnosis scale (CAHS) was devised by Grant and Nash (1995) as a means of assessing hypnotizability online. The scale was shown to be psychometrically sound (Grant & Nash 1995) for measuring hypnotic ability and it compared favourably with the SHSS:C on three dimensions, namely behavioural, subjective depth and relational involvement. However the software has not progressed from a DOS Windows programme and so is no longer in use and no longer available for research purposes (M.R. Nash personal communication 12th September 2011).

The eye roll test for hypnotizability was devised by Herbert Spiegel in 1972 following an observation that participants who were highly hypnotizable had the unusual capacity to roll their eyes upwards so that mainly just the white part of the eye is visible. In 75% of 2,000 consecutive clinical cases, a five second assessment using the Eye Roll sign accurately predicted the level of hypnotizability (Spiegel, 1972). In one out of four cases, positive eye roll was misleading. Spiegel later elaborated on the eye roll test, developing the Hypnotic Induction Profile (HIP) which takes approximately ten minutes to perform. As Spiegel (1977) pointed out, laboratory tests for hypnotizability can take 60 minutes or more per person, they can fatigue the client, some of the instructions are aesthetically inappropriate and potentially embarrassing. The high correlation between the eye roll test and hypnotizability prompted Spiegel to speculate that hypnotizability is physiologically determined and he suggested that this trait is either genetically pre-determined or is a skill learned early in life (Spiegel, 1972). One study by Orne (1979) found that the HIP did not correlate highly with other scales, which may explain why HIP assessment does not appear all that frequently as a test of hypnotizability in the literature. It must be noted, however, that the HIP was tested on 2,000 psychotherapy cases (Spiegel, 1972) as opposed to laboratory tests which have been standardized on non-patients i.e. college students (Spiegel, 1977). The physiological investigations with respect to assessing hypnotizability are relatively recent despite these earlier observations by Spiegel. Stoelb, Molton, Jensen and Patterson (2009) in a review of the literature on hypnotic analgesia for adults, noted that hypnotizability was associated with hypnosis treatment outcomes. Santarcangelo and Sebastiani (2004) were interested in looking at the changes in autonomic activity in response to stress and in relation to hypnotizability and hypnosis. Their research supported the state-theory of hypnosis; they found that in an awake situation, when asked to recall an unpleasant situation, there was no cardiac response from either group. When the exercise was repeated

following an hypnotic induction, individuals who are highly hypnotizable showed autonomic changes. The researchers attributed this to the greater capacity for imagery-attentional capabilities among HHs. They explored the concept further by measuring post-ischaemic flow-mediated vasodilation (FMD) as they were interested in seeing whether this key pathophysiological variable in triggering cardiovascular events would be influenced by suggestion. They found that highs have a natural protection against stress and that their natural tendency to engage in multiple spontaneous episodes of relaxation could have led to persistent vascular changes which were favourable to them, in terms of protection against stress at vascular level.

It is unclear whether hypnotizability and the benefits experienced by HHs are related to genetics. Interest in genetics and hypnotizability has come to the forefront only in the past fifteen years and is still in its infancy. One study (Lichtenberg, Bacher-Melman, Gritsenko & Ebstein, 2000) found that participants with the met/val COMT heterozygote geno-type scored highest on hypnotizability as assessed by the Stanford Hypnotic Susceptibility Form C (SHSS:C). Geno-type is the genetic constitution of the person which can determine the potentials limitations of that individual. Lichtenberg et al. (2000) pointed out that post-hoc testing revealed a significant difference between the val/met vs val/val genotype. Individuals tested who had the met/val COMT heterozygote gene type showed the highest mean values for hypnotizability. The researchers suggested that this may be related to dopamine activity. Those with the met allele, they explained, would be expected to have higher dopaminergic tone and low COMT activity would raise dopamine levels; higher dopamine levels would augment attentional processes. But the researchers pointed out that it is likely that other genes are involved in hypnotizability and their findings should be treated with caution. Spiegel and King (1992) also reported a correlation between hypnotizability and homovanllic acid (HVA), a dopamine

metabolite. More recent support of an association between higher hypnotizability and a genetic association with the COMT gene comes from a study of 127 Hungarian young adults conducted by Skekely, Kovacs-Nagy, Banyai, Gosi-Greguss, Varga, Halmai et al. (2010). On one level, their findings corroborate the findings of Lichtenburg et al. (2004) and Raz (2005). However, Szekely et al. (2010) found that hypnotizability scores were highest in the Val/Val homozygote group, scores in the Val/Met hetrozygote group were lower and Met/Met homozygotes demonstrated the lowest hypnotizability. The researchers suggested that the differences may be due to differences in hypnotizability measurement scales used or differences in population structure and ethnicity.

2.1.3 Biological Correlates of Hypnosis

The placebo effect is now universally recognised in the field of pain (Benedetti, 2007). A placebo is an inert substance used for psychological effect, and frequently employed in drug comparison trials. Examining the physiological correlates of placebo, Benedetti and Amanzio (1997) observed that a placebo response has the capacity to increase pain (hyperalgesia) and decrease pain (analgesia) depending on the instructions given to a patient when administering the tablet. If the patient was told that the pill was hyperalgesic, an increase in pain could occur. Conversely, if the instructions were directed towards a decrease in pain, a decrease in pain could occur. Exploring the neurobiology of this phenomenon, the researchers pointed to evidence showing that the opioid antagonist naloxone has the capability to reduce placebo analgesia. Poistron Emission Tomography scans have shown that the exact same pathways are activated in the brain by both placebo and an opiod drug, and furthermore when a substance designed to block a placebo analgesic response, e.g. Naloxone, is administered, it was successful in preventing the pain relief which would otherwise would have ensued as a result of the placebo. This does not occur with hypnosis. That is to say that when hypnotic analgesia (as

opposed to placebo analgesia) is utilised, naloxone is not effective in blocking the pain relief which occurs following analgesic suggestions given during hypnosis (Spiegel & Albert, 1983). It is therefore reasonable to assume that hypnosis works on a very different physiological basis to placebo.

Words and suggestions are clearly powerful tools both in the waking state and in the hypnotic state. Nusbaum (2011) described a suggestion as 'a colourful communication given to induce a specific, involuntary and often unconscious response by the subject (P.28)'. The extent of the power of words was demonstrated very clearly in an article by Benedetti (2007) who described an experiment where post operative oral surgery patients were divided into two groups. One group were openly given an injection of what they perceived to be morphine, which was actually a placebo and the other group were given 6 to 8 mg of morphine by way of a hidden infusion, so they did not know when the painkiller was being injected. Both had the same pain-relieving effect, leading the researchers to surmise that telling the patient that they are receiving six to eight miligrams of morphine (when it was actually a placebo) was as powerful as an actual 6 to 8 mg of morphine. The researchers only noticed an increased analgesic effect when the hidden morphine dose was increased to 12 mg.

Words and suggestions delivered in an hypnotic state are even more powerful. One research study by Nusbaum, Redouté, Le Bars, Volckmann, Simon, Hannoun, et al. (2011) examined the way in which analgesic suggestions given to low back pain patients might alter the physiological processes in the brain. They found that during hypnosis, both analgesic suggestions of the direct (e.g. "you can sense a numb feeling spreading in that area") and the indirect variety (e.g. "it may be that now.. or perhaps some time later… you start to notice you feel more comfortable..") were equally successful in decreasing pain intensity by 64%. In the group who were not

hypnotized, only the direct suggestions were effective and the decrease in pain intensity was 20%. Although direct analgesic suggestions were effective in both normal alertness and hypnotic conditions, the results confirmed increased efficacy of appropriate suggestions on pain modulation in the hypnotic state. A significant finding of this functional imaging study was that different networks in the brain were activated depending on whether the suggestions were given in the hypnotic state or in normal alertness. For those in the group who were not hypnotized, (normal alertness) the parts of the brain which deal with problem solving, attention, and decision making (cognitive network) and the parts of the brain which deal with intensity and location of pain (sensory network) were activated. In the hypnotic state, the same analgesic suggestions activated an emotional weighted network.

The recent advent of imaging techniques such as Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) has permitted a new dimension to research in this area. Horton, Crawford, Harrington and Downs (2004) examined the brains of highly hypnotizable individuals using MRI and found that the rostrum in the anterior corpus callosum was 31% greater in volume than the rostrum volume of low hypnotizable individuals. Although the sample size of the study was small (8 HH's) a considerable effect size was found and the results were statistically significant. Horton et al. (2004) concluded from this research that this physiological distinction would explain the more effective frontal attentional systems and gating of emotions, cognition and sensation that is attributed to HH's (Nash, 2005). Other techniques investigating brain activity during hypnosis, for example EEG, have also been examined in the hypnosis literature.

Burrows, Stanley and Bloom (2001) examined the literature comparing electroencephalogram (EEG) activity for low and highly hypnotizable individuals. They provided evidence of studies which show that as individuals enter hypnosis, irrespective of

hypnotizability, EEG theta power increased although, prior to hypnotic induction, in a normal waking state HHs are more likely to generate more theta than LHs. The authors suggested that 'theta power (3-7 Hz) hypothesized to be associated with focused attention (e.g. Schacter, 1977) is positively related to hypnotic susceptibility (e.g. Crawford, 1990)' and concluded that overall, research on brain wave activity using EEG support behavioural research which has found that HHs had superior focusing and attentional abilities as measured by the Tellegen Absorption Scale and the Differential Attentional Processes Inventory. Burrows et al. (2001), also reviewed studies which looked at hemispheric asymmetries among HHs and stated that at neurophysiological level in both hypnotic and non-hypnotic conditions Highly Hypnotizable (HHs) individuals appear to have greater EEG hemispheric specificity. The researchers speculated this may be connected with the fact that HHs are more adept at sustaining attention, becoming deeply involved in something and also seem to possess a greater ability to switch from one task to another. Trippe, Weiss and Miltner (2004) in an EEG experiment tracking changes in brain activity during hypnosis found a breakdown in functional connectivity of the gamma band between somatosensory and frontal cortices. They hypothesised that the state of hypnosis signified a comprehensive breakdown in the organisation of oscillations by the areas in the frontal cortices when a person enters a state of hypnosis. These oscillations refer to activity of the neurons which can be measured by EEG because of the electrochemical impulses which register at different frequencies.

Fingelkurts, Fingelkurts and Kahonen (2005) described functional connectivity as the mechanism for the co-ordination of activty between different neuron assemblies with the purpose of accomplishing a complex cognitive task or perceptual process. One HH subject, studied by Fingelkurts, Fingelkurts, Kallio and Renonsuo (2007) on two independent occasions which were a year apart found that hypnosis caused a reorganization in the

composition of the brain oscillations which did not immediately return to baseline when the individual emerged from hypnosis. They summarised their results in four points. 1. Hypnosis altered the complete amount of time (percentage of EEG segments) that particular types of brain oscillations were observed, as opposed to their amplitude or power; 2. Hypnosis induced significant changes in the organization of the brain oscillations in EEG; 3. The types of SPs during hypnosis were the same as those found in baseline but in the Fp1 and FP2 electrodes, seven of the seventeen SP types were only present during hypnosis and 4. They observed that the dominant SPs did not alter during hypnosis. Rather, the altered patterns represented non-dominant spectral patterns in the EEG. Additionally, these changes were specific with respect to their spectral composition and the brain area. They concluded from their case study that hypnosis may be accompanied by a changed pattern of neural activity in the brain. Their findings were not replicated by Jensen, Sherlin, Askew, Fregni, Witkop, Gianas, Howe and Hakimian (2013) who studied the effects of hypnosis and three other non-pharmacological pain therapies on brain states in 31 participants. Their objective was to look at brain oscillations occurring in response to these treatments and evaluate the associations, if any, with changes in pain intensity. Their findings were that changes in pain intensity were not associated with changes in brain oscillations. They concluded that brain activity as measured by EEG was not a useful method of measuring or explaining the benefits associated with these treatments. The different findings in the studies by Jensen et al., (2012) and Fingelkurts (2007) may possibly be explained by the fact that the participant in Fingelkurts study was highly hypnotizable and in the study by Jensen et al., (2012) hypnotizability was not an inclusion factor for the thirty-one individuals who completed the study.

The perception of pain is a complex process. De Benedittis (2003) described pain as a multidimensional experience which is essentially

sensory-discriminative, motivational-affective and cognitive and which is registered on a number of levels and sites of the central nervous system. The demarcation of different brain networks involved in hypnotic analgesia is well supported in the literature. Neuroimaging techniques have been used to determine brain structures linked to sensory and affective dimensions of pain (Feldman, 2004) and the changes in pain perception when in a state of hypnosis (Vanhaudenhuyse, Boly, Laureys & Faymonville, 2009). A thorough review of the literature by Patterson and Jensen (2000) found that highly hypnotizable subjects show different patterns of cortical responding than those who rate as low (LH) on suggestibility measures. They say however that based on a meta-analysis by Montgomery, DuHamel and Redd (2000) up to 75% of the population could gain significant benefit from using hypnotic analgesia and that hypnotic analgesia works equally well in the medical and in the laboratory setting.

The systematic review which follows, will appraise the evidence in relation to the quality and effectiveness of hypnosis as a treatment, specifically for the management of headaches.

Chapter 3: Systematic review of the effectiveness of hypnosis for the management of headache

Abstract

Headaches can be well controlled by medication. However, some patients are unable to tolerate the side effects accompanying medication, leading them to seek alternative treatment options. The aim of this systematic review of the literature is to determine the efficacy of hypnosis in the treatment of headache and summarise the findings of previous studies. A systematic review of four scientific databases was conducted using the primary search terms, headache, hypnosis and hypnotherapy. Eight studies were identified which either examined hypnotic techniques alone or in combination with other non-pharmaceutical techniques such as visual imagery, relaxation and pain displacement techniques. Quality assessment using a modified version of the PEDro scale showed the studies to be of fair quality. A significant reduction in headache frequency, duration and intensity were observed for patients in the treatment groups in comparison to non-treated controls. There was also an associated reduction in pain medication and increased quality of life (QoL) for individuals in the treatment groups in comparison to the control groups. This study demonstrates that hypnotherapy and relaxation techniques are effective in reducing short and long-term headache activity in headache sufferers.

Introduction

During the past century, interest in the use of hypnosis for chronic pain disorders has been growing and many studies, some of which date back to the 1950's (Barber, 1959), have been conducted to investigate the use of hypnosis for chronic pain. Hypnosis is a therapeutic technique during which individuals undergo mind focused relaxation procedures, following which, suggestions are made to help individuals change habits, such as losing weight and quitting smoking. Randomised controlled trials (RCTs) examining the efficacy of hypnotic interventions began to be published in the 1970's (Andrechuck & Skriver, 1975; Melzack & Perry, 1975). To date, many studies have been conducted into the use of hypnosis for chronic pain causing conditions including, fibromyalgia (Caste, Pérez, Sala, Padrol, & Rull, 2007; Hartman, 2010), multiple sclerosis (MS) (Hartman 2010), irritable bowel syndrome (Hammond 2004; Roberts, Wilson, Singh, Roalfe & Greenfield, 2006) sickle cell disease (Wallen, Middleton, Ames, Brooks, & Handel, 2014), spinal injuries (Hartman 2010), disability related pain (Wickramasekera, 2008), cnacer (Johannsen, Farver, Beck, & Zachariae, 2013) and headache (Zitman, van Dyck, Spinhoven, & LInssen, 1992).

In many individuals, tension type headaches can be well managed with medications such as paracetamol and ibuprofen. For other primary headache disorders such as migraine, Triptans and anti-emetics are sometimes prescribed. However, some individuals are unable to tolerate migraine medications due to allergies or side effects while others may have disease co-morbidities such as heart disease and asthma which

conraindicate their use (Chaibi, Tuchin, & Russell, 2011). Other individuals may choose to avoid medication due to personal preferences or beliefs and seek non-pharmacological alternatives such as massage, physiotherapy, osteopathic treatments and psychotherapies including hypnosis. The application and duration of non-pharmaceutical treatments vary between practitioners while pharmacological treatment regimens can be standardized and a specific dose administered. Hypnosis and other alternative or complementary treatments are not uniform in delivery.

The American Psychological Association (APA, 2015) acknowledged that while the use of hypnosis for medical purposes has been controversial, clinicians now agree that it can be an effective technique for many conditions, including anxiety, mood disorders and chronic pain. A National Institute of Health Technology Assessment Panel has determined that hypnotherapy met appropriate criteria to be defined as a 'well-established therapy' (Chambless & Hollon, 1998; Wickramasekera, 2007). While psychological interventions such as hypnosis are known to be beneficial in relieving chronic pain and offer benefits over medication, the National Institute of Clinical Excellence (NICE) has not approved hypnotic techniques for use as an alternative therapeutic strategy in the treatment of migraine (Sullivan & Cousins, 2016). Thus, currently, hypnosis is only available privately.

While several systematic reviews have been conducted investigating the efficacy of psychological interventions such as relaxation and cognitive behavioural therapy (CBT) for migraine, no reviews have specifically looked at the efficacy of hypnosis interventions in the treatment of headache. The aim of this research is to conduct a systematic review on the efficacy of hypnosis in the treatment of headache in adults.

Materials and Methods

Search strategy

A systematic search of four scientific databases 1) PUBMED, 2) EMBASE, 3) PsychInfo (OVID) and 4) ProQuest was conducted on March 13, 2018 using the search terms and phrase combinations detailed in table 3.1.

Search terms
#1 –Headache **#2 – Hypnotherapy** **#3 – Hypnosis** **#4 –#2 OR #3** **#5 – #1 AND #4**

Table 3.1: Search Terms and Phrases for Systematic Review

Inclusion Criteria

Studies were included if they were 1) written in English, 2) were a Randomized Controlled Trial (RCT), 3) included adults or children with any diagnosis of headache, 4) employed hypnosis or hypnotherapy techniques.

Primary Outcome

The primary outcome was 1) Headache Frequency, defined as the number of days with headache in a 4-week period based on a patient-reported headache diary.

Secondary Outcomes

Secondary outcomes were 1) Headache Intensity: based on self-reported verbal or numerical rating scale or visual analogue scale, 2) Headache duration, defined as the number of hours with headache per day, 3) Headache-related quality of life or disability based on self report questionnaire measures assessing the impact of headaches on quality of life or daily functioning. 4) mood, based on self-reported scales of

depression, anxiety and distress. 5) Headache-related medication usage, defined as (i) the number of headache days treated with acute/abortive (symptomatic) treatment (ii) the number of doses consumed.

Quality assessment

The methodological quality of the included RCT studies was assessed using a modified version of the PEDro scale (Verhagen, de Vet, de Bie, Kessels, Boers, Bouter, & Knipschield 1998), the details of which are summarized in Table 3.2. PEDro is a valid measure of the methodological quality of clinical trials (De Morton, 2009). An RCT is considered to be of high quality if a PEDro score of ≥6 is achieved out of a maximum of 10 (Moseley, Herbert, Sherrington, & Maher, 2002). A score of <3 is considered to be of poor quality. In the analysis, a modified 8-point version of the PEDro scale was used because 2 of the criteria are not possible for psychological treatment studies (numbers 4 and 5). Therefore criteria 4 and 5 were removed from the analysis as it is not possible to blind participants or therapists to treatment allocation. Based on the modified scale ≥5 is considered good quality, 3-4 fair quality, and <3 poor quality.

Extraction of data

Individual analysis of each study was conducted and information, including author, year of publication, participant characteristics, methods, intervention description, summary of outcomes and adverse events were recorded for each study.

Ethical considerations

As this study was carried out as a systematic review of peer-reviewed data, ethical approval was not required. However, each article included in this review was screened to ensure that the appropriate and correct ethical approval had been sought prior to undertaking the study

Table 3.2: Modified PEDro scale criteria

1.	Subjects were randomly allocated to groups.
2.	Allocation was concealed.
3.	The groups were similar at baseline regarding the most important prognostic indicators.
6.	There was blinding of all assessors who measured at least one key outcome.
7.	Measurements of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups.
8.	All subjects for whom outcome measurements were available received the treatment or control condition as allocated, or where this was not the case, data for at least one key outcome were analysed by “intention to treat”.
9.	The results of between-groups statistical comparisons are reported for at least one key outcome.
10.	The study provides both point measurements and measurements of variability for at least one key outcome measure.

Results

The literature search identified 702 RCTs which investigated the impact of hypnosis on migraine and chronic headache (Figure 3.1). Of these, eight met the inclusion criteria. The details of the studies included in this analysis are summarized in Table 3.3

Fig. 3.1 Systematic Review Study Selection Process

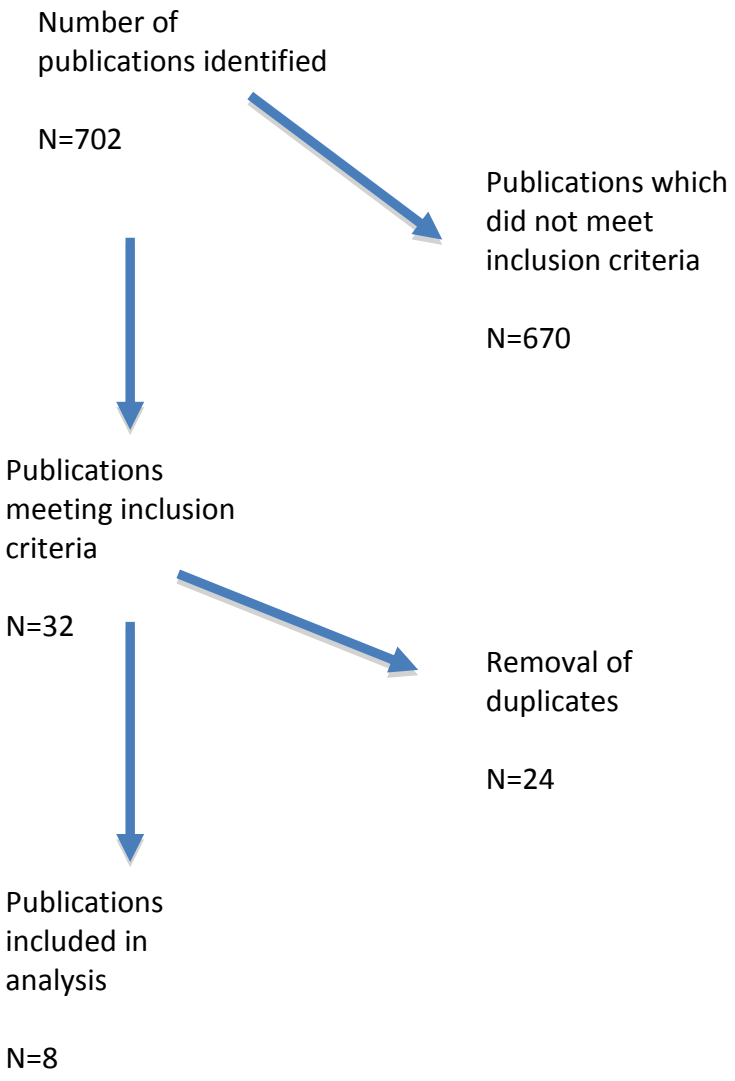


Table 3.3: Summary of Selected Publications

	Study	Title	Intervention	Intervention Groups	Publication	Year
1	De Fazzano	Effectiveness of hypnosis in the treatment of migraine – The role of hypnotizability	Self hypnosis & hand warming 8x 30-45 min session	Placebo group Waiting list Control Group	University of Vermont PhD thesis	1980
2	Freidman and Taub	Brief Psychological Training Procedures in Migraine Treatment	Hypnosis with thermal imagery. Hypnosis (4 groups: high/low susceptibility, high/low with thermal imagery) Self hypnosis (for HHS Simulated self hypnosis (for LHS)	Biofeedback, relaxation, Waiting List Control Group	American Journal of Clinical Hypnosis	1984
3	Levinthal	The effects of direct hypnosis, indirect hypnosis and relaxation on the primary and secondary symptoms of chronic headache	Direct or indirect hypnotic techniques	Relaxation Waiting List Control Group	University of Cincinnati, Doctor of Education Thesis	1987
4	Melis	Treatment of chronic tension type headache with hypnotherapy: a single blind time controlled study	Hypnosis with visual imagery Self hypnosis	Waiting List Control Group	Headache	1991
5	Spinhoven	Autogenic training and Self-Hypnosis in the control of tension headache	Hypnosis with visual imagery Self hypnosis	Autogenic training	Augogenic Training and Self Hypnosis	1992
6	Spanos	Hypnotic suggestion and placebo for the treatment of chronic headache in a University volunteer sample	Hypnosis with visual imagery	Placebo group Subliminal reconditioning	Cognitive Therapy and Research	1993
7	ter Kuile	Autogenic training and cognitive self-hypnosis for the treatment of recurrent headaches in three different subject groups.	Autogenic training Cognitive self-hypnosis	Waiting List Control Group	Pain	1994
8	Nolan	The efficacy of Hypnotic and NonHypnotic response -based imagery for self managing recurrent headache	Hypnosis with visual imagery Self Hypnosis	Non-hypnotic imagery Placebo group	Imagination, Cognition and Personality	1995

Methodological quality

The PEDro scale was applied to all studies selected for final analysis (Table 3.3). Of the eight studies identified, none were shown to be of high quality (≥5) (Table 3.4). This was primarily due to the required information for assessment of quality not being reported in the articles. A part of the problem assessing the quality of these trials is the difficulty in concealing treatment allocation from the participants as it is not possible to blind participants as to whether they are in treatment or no treatment control group. One reason for the low-quality score for trials in this review can be attributed to the age of the articles. Several of the studies included the addition of a placebo treatment group (e.g. Waiting list control group) to help overcome this bias which is now standard practice when conducting a clinical trial. All of the studies were published prior to the latest update (June 1999) to the PEDro scale. Therefore, required information which is now routinely reported in the publication of RCTs was not reported in the studies included in this review. Due to the problems associated with assessing the quality of the studies, none were excluded from analysis based on the PEDro score.

Publication year

The literature search revealed that research in this field was primarily conducted in the 1980's and 1990's with very little research having been conducted within the past 20 years. Of the eight studies identified, three were carried out in the 1980's (De Fazzano, 1980; Fried & Taub, 1984; Levinthal, 1987) and five were conducted in the 1990's (Melis, 1991; Nolan, 1995; Spanos, 1993; Spinhoven, 1992; ter Kuile, 1994).

Table 3.4: Quality Scores based on the modified PEDro scale

NR: Not reported

Study	Criteria 1	Criteria 2	Criteria 3	Criteria 6	Criteria 7	Criteria 8	Criteria 9	Criteria 10	Score
Spinhoven 1992	Yes	NR	NR	NR	No	Yes	Yes	No	3
Friedman and Taub 1984	Yes	NR	NR	NR	No	Yes	Yes	No	3
Melis 1991	Yes	NR	NR	NR	No	Yes	Yes	No	3
ter Kuile 1994	Yes	NR	NR	NR	No	Yes	Yes	No	3
Levinthal 1994	Yes	NR	NR	NR	No	Yes	Yes	No	3
Nolan 1995	Yes	NR	NR	NR	No	Yes	Yes	No	3
Spanos 1993	Yes	NR	NR	NR	No	Yes	Yes	No	3
De Fazzano 1980	NR	NR	NR	NR	No	Yes	Yes	No	2

Headache classification criteria

The criteria for headache classification varied between studies with three using published criteria such as the Blanchard headache criteria (Friedman & Taub, 1984), the International Headache Society (IHS) criteria for chronic tension type headaches (TTH) (Melis, 1991) and the International Association for the Study of Pain (IASP) criteria for chronic pain (Nolan, 1995). Four studies classified migraine based on diagnosis by a healthcare professional, headache frequency

and duration (De Fazzano, 1980; Levinthal, 1987; Spinhoven, 1992; ter Kuile, 1994). Time from diagnosis differed between studies with the minimum time being 6 months (Spinhoven, 1992; ter Kuile, 1994) to a maximum of 2 years (Levinthal, 1987). One study did not report the headache classification criteria used (Spanos, 1993).

Intervention delivery

A variety of hypnotic techniques were used to evaluate the efficacy in reducing symptoms of migraine, some of which have used hypnosis in isolation, while others used a combination of hypnosis and other techniques. Hypnosis was the most frequently used in conjunction with visual imagery (Melis, 1991; Nolan, 1995; Spanos, 1993; Spinhoven, 1992), while other studies used techniques such as thermal imagery (Friedman & Taub, 1984). Hypntoic techniqes also differed between studies, with the majority of studies using self-hypnosis techniques (de Fazzano, 1980; Melis, 1991; Nolan, 1995; Spinhoven, 1992; ter Kuile, 1994) while others used a combination of direct or indirect hypnotic techniques (Levinthal, 1987). Some of the interventions also evaluated the susceptibility of the participants to hypnosis (De Fazzano, 1980; Friedman & Taub, 1984).

Control and comparison groups

As the inclusion criteria for this review specified that only RCTs would be included in the final analysis, all of the studies had at least one control group as a means of comparison and several studies included non-hypnotic treatment groups as an additional means of comparison. Treatment comparison groups included biofeedback (Frieman & Taub, 1983), relaxation (Friedman & Taub, 1984; Levinthal, 1987), non-hypnotic imagery (Nolan, 1995), autogenic training

(Spinhoven, 1992; ter Kuile, 1994) and placebo groups (De Fazzano, 1980; Nolan, 1995; Spanos, 1993).

Headache activity assessment

All studies required participants to record headache activity in a pain diary throughout the duration of the study, however, different criteria were used between studies to assess pain activity. Several studies used a numerical scale to measure headache intensity (HI), with two studies using a scale of 0-5 (De Fazzano, 1980; Friedman & Taub, 1984), one study using a 0-6 point scale (Spanos, 1993(and one using a 0-10 point scale (Melis, 1991). Other studies used pain questionnaires such as the Migraine Index (MI) (ter Kuile, 1994), the McGill Pain Questionnaire (MPQ) and the Headache Symptoms Quesitonnaire (HSQ) (Levinthal, 1987).

Treatment outcomes

This study assessed the primary outcome of headache frequency, however, several studies selected for the analysis utilized the Headache Index (HI) which combines headache frequency, intensity and duration. Therefore the primary and secondary outcomes (Table 3.5) assessed in this analysis will be discussed together in the section which follows.

Headache frequency, intensity and duration

Of the 8 studies included in the analysis, 3 reported headache frequency as an outcome. Friedman and Taub (1984) showed a significant decrease in headache frequency for patients in the hypnosis groups ($p<0.05$). The study of Melis et al (1991) reported a significant reduction in the number of headache days experienced by patients in the hypnosis group compared to those in the control group ($p<0.05$) while Spanos et al (1993) reported a significant reduction in the number of

headache-free days for patients in the control group but not for patients in the treatment group (see Table 3.5).

Three studies reported a significant decrease in headache intensity for patients in the treatment groups compared to non-treated controls (Friedman & Taub, 1984; Melis, 1991; Nolan, 1995). Melis (1991) reported a significant difference in the number of headache hours ($p \leq 0.05$) and headache intensity ($p<0.05$) in comparison to the control group. ter Kuile (1994) showed a significant reduction in the Headache Index scores for subjects in the treatment group compared to controls ($p<0.05$). Spinhoven (1992) found that patients had significantly reduced headache activity in contrast to a control group during the intervention ($p<0.05$) and both short-term and long-term pain reduction was accompanied by an increase in perceived pain control ($p<0.003$). They also found that patients who attributed pain reduction as being due to their own efforts reported longer periods of pain reduction ($p<0.003$). Only one study by Nolan (1995) found no difference between the treatment groups and non-treated controls, and subsequently, the authors combined data from the hypnotic imaging groups for data analysis. Thus, it is not possible to tell whether hypnosis influenced the findings of this study.

Table 3.5: Primary and Secondary Outcomes NR: Not Reported

	Headache Frequency	Headache Intensity	Headache Duration	Patient reported outcomes: Quality of Life, Mood, depression, anxiety and distress	Medication Use
De Fazzano 1980	No significant difference between groups	No significant difference between groups	No significant difference between groups	NR	No significant difference between groups
Freidman and Taub 1984	Significant decrease in headache frequency for all hypnosis groups ($p<0.05$).	Significant decrease in headache intensity (HHI-0.9 $p<0.05$) compared with control group (HHI +0.5)	NR	NR	RMU -1.0 $p<0.01$). WL Control +0.05
Levinthal 1994	No significant reduction	No significant reduction	No significant reduction	Significant improvement in treated vs un-treated controls	NR
Melis 1991	Significant reduction in the number of headache days in treatment group vs control group ($p<0.05$).	Significant reduction for treatment versus control group ($p<0.05$).	Significant difference in headache hours per day for treatment vs control group ($p<0.05$).	Significant reduction in anxiety scores from baseline in the treatment group ($p<0.05$). No change in depression scores for patients in the treatment group.	NR
Spinhoven 1992	NR	Headache Index. No significant difference.	Non significant difference in the treatment group.	NR	NR
Spanos 1993	Significant reduction in the number of headache-free days for patients in the control group but not for patients in the treatment group	NR	NR	NR	Reduction in medication usage for treatment group
ter Kuile 1994	NR	NR	NR	NR	No significant difference ($p=0.128$)
Nolan 1995	NR	Significantly lower across treatment intervals in comparison to control group ($p<0.05$).	NR	NR	No significant difference

Several studies revealed no significant difference in headache activity between treatment and placebo groups (Friedman & Taub, 1984; Nolan, 1995; Spanos, 1993; ter Kuile, 1994). In the study of Spanos (1993) which investigated the number of treatment sessions (treatment dosage) on pain activity, no difference in headache activity was observed between participants receiving one or four sessions of treatment, revealing that the number of sessions did not impact on pain activity. While this study showed no improvements in headache activity between treatment and control groups, the analysis of baseline data reveals improvements in headache activity from baseline to post treatment for participants in all treatment groups. This demonstrates that the provision of therapies had a significant impact on pain activity from baseline.

Patient reported outcomes

A variety of criteria were used to assess the impact of the interventions on particpants' mood and QoL. A number of measurement scales were used such as the Profile of Moods States: Bi-Polar Form (POMS-BI) (Spinhoven, 1992), Zung Anxiety Scale and Zung Depression Scale (Melis, 1991) and Symptom Checklist-90 (SCL-90) (ter Kuile, 1994). Other studies assessed factors such as sleep, change in daily activities, absences from work and doctors visits (Levinthal, 1987).

Of the studies that assessed the impact of hypnotic interventions, a positive effect was seen on participants' mood and missed activities such as work, while Melis (1991) showed a significant reduction in anxiety scores of the experimental group ($p<0.05$). Several studies reported no effect on certain aspects of participant QoL. For example, ter Kuile (1994) found that at post-treatment and follow-up

almost no significant differences were observed in respect to psychological distress (SCL-90) scores and Melis (1991) found no change in the depression scores of the experimental group.

Headache related medication usage

Many studies in this review did not report the impact of the interventions on the use of medication but three studies reported a reduction in medication usage between participants in the treatment and control groups (Friedman & Taub, 1984; Spanos, 1993; ter Kuile, 1994).

Adverse events

None of the studies included in this analysis reported adverse effects in any way related to hypnosis or any of the comparison treatment groups. Participant drop out was attributed to time commitments (Spanos, 1993), personal or family problems (Melis, 1991), geographical location, illness unrelated to migraine, lack of transportation, lack of interest or inability to schedule follow-up appointments (Friedman & Taub, 1984).

Discussion

In this analysis a narrative review was performed as opposed to a meta-analysis. This was due to the manuscripts included reporting different outcomes which were assessed by different methods, therefore it was not possible to pool the data for a meta-analysis.

While several studies in this analysis showed an improvement in headache activity in treated participants compared to controls, this improvement often did not reach significance (Spinhoven, 1992, Levinthal, 1994). However, there was a significant improvement in pain activity and medication usage

from baseline to post-treatment for treated patients, including that hypnosis has significant benefits on pain activity.

The findings from this study have several implications for current clinical practice. While the literature demonstrates that hypnotic techniques have been well investigated for the treatment of pain disorders (Castel, Pérez, Sala, Padrol & Rull, 2007; Hartman 2010; Wallen, Middleton, Ames, Brooks & Handel, 2014), there is still some scepticism about the efficacy of such interventions among health care professionals and hypnotic techniques are currently only available privately. This review has demonstrated that hypnosis has a significant impact on the pain activity of individuals suffering from migraine and supports the findings of several double-blinded placebo controlled studies which have demonstrated hypnosis to be statistically superior or equivalent to commonly used treatments (Stoelb, Molton, Jensen & Patterson, 2009).

Clinical Implications for Future Psychological Interventions for Migraine

While significant differences were not observed between hypnosis and other treatment strategies there was a significant improvement in pain activity from baseline and in comparison to non-treated controls. This finding may be due to the comparison treatment groups used in these studies also providing therapies which evoke relaxation in the study participants. As relaxation techniques have been shown to improve pain activity in migraine sufferers it is plausible that no difference was observed between treatment groups as they all provided equal improvements in pain activity. This is supported by the finding that pain activity improved from baseline and in comparison to the non-treated controls in all treatment groups. This study supports the work of Stoelb et al (2009) who found that when hypnosis interventions are compared to therapies

with no hypnotic components (such as physiotherapy and medication management), hypnosis proved to be superior in reducing pain activity (Jensen & Patterson, 2006).

This study also provides limited evidence to suggest that hypnosis reduces the usage of medication in individuals suffering a migraine attack. This supports the findings from a large meta-analysis performed by Montgomery, Du Hamel, and Redd, (2000) which demonstrated that hypnosis meets the American Psychological Association Clinical Psychology Division's criteria for being an effective treatment for pain control, showing superiority to pharmacological treatments. Reducing medication usage not only has financial implications but also has health benefits for the patients from reduced dependency on analgesic medications and avoidance of side effects. This study also provides evidence that hypnosis can help reduce migraine attacks which would further reduce the need for medication and provided additional benefits to the patient, such as having less impact on daily activities, work and reducing doctors' visits.

Factors affecting response to hypnosis

There has been much interest in the susceptibility of patients to hypnotic techniques on the efficacy of hypnotic interventions and pain outcomes. This review has shown that subjects deemed to be highly susceptible to hypnotic techniques achieved a greater reduction in headache pain post-treatment and at follow-up in comparison to patients with low susceptibility to hypnosis (ter Kuile, 1994). This supports the findings of Jensen and Patterson (2006) which demonstrated that high hypnotic susceptibility and the ability to experience vivid images are significantly associated with improved treatment outcomes. This finding has also been observed for other therapies which incorporate hypnotic components such as autogenic training and progressive muscle relaxation. (Gauthier, Côté, & French, 1994; Patterson, 2004; Valente, 2006). However,

many patients who experienced significant reductions in pain control with relaxation or autogenic training alone also showed high susceptibility to hypnotic techniques, demonstrating that highly suggestible patients are likely to show improvement regardless of the treatment condition (Patterson & Jensen, 2003).

While multiple hypnotic techniques were analysed in this review, none of the trials included in the final analysis investigated aspects of intervention delivery, variables such as time spent with a therapist in comparison to self-hypnosis were not investigated. Additionally, patients' motivations for participating in the research were not investigated and could have influenced the findings of the studies as motivation and participants' beliefs have been shown to play a role in treatment outcomes (Patterson & Ptacek, 1997).

Future Recommendations

While hypnosis has been shown to be effective in helping control chronic pain, a number of questions remain unanswered and there is still much scope for research into the efficacy of hypnosis in the treatment of migraine.

Future research in this area should assess the impact of therapist-delivered therapy, self-hypnosis and duration of treatment on the efficacy of hypnosis as a treatment for migraine. It is also important to consider the effects of hypnosis on medication use.

A limiting factor of this study has been the age of the studies included in the analysis and future research in this area should ensure that methodologies used are current and robust.

Many studies have also compared hypnosis to other treatments which have been shown to reduce migraine and headache symptoms and this may account for the lack of difference between treatment groups. Future research in this area should ensure hypnotic techniques are first compared to non-treated controls to limit

variability and contamination of results from other sources. Treatment comparison studies would follow if hypnosis is confirmed to be more effective than placebo.

Study Limitations

Several limitations to this study have been identified;

1. Firstly the studies included in this analysis were conducted over 20 years ago and no new RCTs assessing hypnosis in the treatment of migraine have been conducted within the last 20 years.
2. Due to the age of the studies it was not possible to obtain all the articles identified in the literature search and it is possible that there may be additional studies that could have been eligible for inclusion in the review but which could not be obtained.
3. Another issue arising due to the age of the studies was that the interventions and methodology were often not well defined, therefore the quality of the studies was not consistent with modern RCTs.
4. There was also a high degree of heterogeneity between studies due to the diverse nature of the interventions, making it difficult for meaningful data comparisons to be made.
5. The studies also included participants who suffered other types of headache in addition to migraine, therefore it is not possible to determine that treatment effects were due to the treatment strategies and not influenced by the different types of headache such as tension headaches being more responsive to certain treatments.

Conclusion

This review has demonstrated that hypnosis in combination with relaxation and visual imagery techniques are effective in

reducing pain from migraine and chronic headache. Not only has hypnosis been shown to lead to a significant reduction in pain activity in comparison to untreated controls, it is also a relatively simple and cost effective technique. An additional benefit of hypnosis is the low risk of side effects and adverse reactions which have led to some individuals moving away from the standard medication regimens. With some evidence to support the use of hypnosis in treating chronic pain conditions, there is scope for higher quality studies to be conducted to determine if hypnosis should be accepted as an effective and alternative treatment.

As an alternative treatment which could potentially lend itself well to an online, E-Health platform, the chapter which follows examines the evidence and quality of E-health pain management programmes as well as ethical and clinical considerations.

Chapter 4: Online Psychological Therapies

E-health Programmes for Chronic Pain

Psychological interventions may be helpful for managing pain but access to such treatments can be limited, particularly for patients in poverty or those living in remote areas (Sturgeon, 2014). Some of these barriers can be addressed with E-health technology. DeMonte, DeMonte and Thorn (2015) investigated the potential of E-health technologies in rural settings. They pinpointed two major concerns as the lack of technological resources and the lack of appropriate materials for patients who have literacy problems but iterated that solutions can be found for these barriers and that E-health technologies are a valuable means of disseminating interventions.

The Evidence for E-health Pain Management

Nevedal, Wang, Oberleitner, Schwartz and Williams (2013) recruited 645 chronic pain patients for an online pain management programme. The programme involved cognitive behavioural intervention, motivational enhancement and promotion of health behaviour. Their participants recorded a significant decrease in pain intensity and pain unpleasantness from baseline to 1-month and 6 month. They recommended that further investigation of their programme was required in a randomized controlled trial to determine the significance and magnitude of the intervention's effects. Elbert, van Os-Medendorp, van Renselaar, Ekeland, Hakkaart-van Roijen, Raat Nijsten and Pasmans (2014) suggested that an alternate focus may be warranted. The researchers conducted a systematic review of systematic reviews and meta-analyses on the

effectiveness and cost effectiveness of eHealth interventions in somatic diseases and observed that most studies demonstrate the efficacy and the cost effectiveness of eHealth programmes. They recommended that future studies should focus on development and evaluation of strategies instead of conducting larger, well designed controlled studies with a view to strengthening evidence. A number of positive effects from e-Health interventions emerged from qualitative analysis of individual studies in the systematic review by Elbert et al. (2014). These included improved quality of life, increase of disease-related knowledge and self-management and a reduction in the number of visits to outpatient clinics. Macea, Gajos, Calil and Fregni (2010) focused specifically on cognitive behavioural interventions in their systematic review and meta-analysis of internet based programs for patients with chronic pain. These authors found reductions in pain for the intervention groups were small, but significant, compared with waiting list controls in the eleven studies which they examined. They recommended that future investigations examine which type of web-based interventions work best for each group of pain sufferers.

The efficacy of internet based treatment for headaches, in particular, for both children and adolescents (Trautman & Kroner-Herwig, 2010) and adults (Devinini & Blanchard, 2005) is supported in the literature. Devinini and Blanchard (2005) conducted a study where a significantly greater decrease in headache activity was found for the internet programme compared to a waitlist control group. During a follow up assessment, after two months, 47% of participants maintained improvement and there was a 35% within-group reduction of medication usage. Compared with clinic treatment the web-delivered programme was also more time efficient. Strom, Pettersson and Andersson (2000) conducted an internet trial using applied relaxation for a headache population. They considered cost-effectiveness as an important aspect of health care and that ‘psychological treatment for headache with reduced therapist

contact has been well studied (p.722)'. The researchers cited several studies which provide evidence that 'when treatments are based on relaxation and biofeedback, they produce equal or better results than equivalent clinical treatments and the most common pharmacotherapies (p.722)'.

The potential benefits of an internet based intervention for migraine patients are numerous. They include the possibility of reduced waiting lists, decreased travelling time, provision of access to treatment programmes by individuals who cannot access other modes of treatment and a reduction in therapist time (Cuijpers, Van Straten & Anderson, 2008). It can also offer assistance to patients and clinicians by reducing treatment costs and side effects (Macea et al., 2010). In spite of the initial and promising support for internet based programmes for chronic pain, the need for improvements in the efficacy and quality of studies has been raised (Trautman & Kroner-Herwig, 2010). Other studies (Macea et al., 2010) indicated the need to determine the type of people who respond best to internet based study interventions; the present study will specifically address one of these groups, namely migraineurs.

Ethical and Clinical Considerations in E-Health Management

The e-health code of ethics (Rippen & Risk, 2000) was developed following the e-health ethics summit held in Washington in 2000. The aim of the e-health code of ethics as surmised in their vision statement is to ensure that individuals worldwide can be informed about the known risks of using the internet to manage their health while at the same time appreciating the potential of the internet as a medium to deliver health care programmes. The eight guiding principles outlined in the code of ethics report are honesty, candour, quality, informed consent, privacy, professionalism in online health care, responsible partnering and accountability.

Honesty refers to the truthfulness in disclosure of all information pertaining to the efficacy, performance and benefits of the service or

product being provided. In relation to candour the recommendations state that the site should disclose all information which could influence a consumers' interpretation of the service or product. The provision of health information in a way which is timely, accurate and easy to understand is outlined under the heading of quality. A choice by the service or product user about how their personal data might be collected, utilised or shared is delineated under the heading informed consent. The main points in this section state that sites need to fully disclose any potential risks to users' privacy on the site, to clearly state what data is being collected when users visit the site, the consequences if a user does not wish to share personal information and how the site will use the data. The privacy principle refers to the obligations of the service or product provider to protect users' privacy e.g. by providing passwords. Professionalism in online health care states that all advice provided should abide by the code of ethics which govern the profession for the service, advice or care being provided. It also refers to the obligation to educate patients about the limitations of online health care. This includes being transparent about the provider's professional qualifications and describing the processes involved in the online interaction. Responsible partnering is concerned with making sure that any individuals or organisations which the service or product provider is partnering with is reputable and trustworthy. Finally, the accountability principle includes recommendations that e-health sites should provide a means for the user of the site to contact the provider if they have any problems and should indicate clearly who the party or parties involved are in managing the site or the service.

The British Psychological Society (BPS) document on ethics guidelines for Internet-Mediated Research (IMR) was published in 2013. It considered the four guiding principles outlined in the Code of Human Research Ethics (2011) document in an IMR context. These are listed as 1. Respect for the autonomy and dignity of

persons; 2. Scientific value; 3. Social responsibility and 4. Maximising benefits and minimising harm.

In relation to the first principle, 'Respect for the autonomy and dignity of persons', the issue of privacy is highlighted as being particularly problematic and it is noted that a key principle in IMR is to ensure that ethics procedures and safeguards are implemented which are proportional to the level of potential harm and risk to individuals who participate in the research. The importance of legislative principles is explored, in particular the issue of copyright. Acknowledging a common perception that personal web pages may appear to be public documents, the guidelines clarify that copyright remains with the author or the webhosting company and that 'for a document or online trace to be in the public domain it must not be protected by copyright law' (p.8). The difficulty of verifying a record of valid consent is flagged as being a challenge in an IMR context. The guidelines recommend that researchers need to inform participants about how the data they provide is stored and transported and that they should be clear about the extent, if any, that the collection and reporting of data over the internet may expose participants to harm of any sort. All reasonable precautions to minimise risk and safeguard the confidentiality of the data need to be taken by the researcher. The importance of a participants right to withdraw from participation is emphasised and the two factors which make this a challenge in IMR are stated as being 'a) the lack of face-to-face presence between researcher and participants and b) the automated collection of data during the research process' (p.11).

For these reasons the challenges need to be anticipated and withdrawal procedures, the document recommends, need to be made as clear as possible to participants. The second principle, 'Scientific Value' notes the importance of ensuring that a research project has 'quality, integrity and contribution' (p.14). Examples of the levels of control which can be an important consideration in IMR research

are listed. These include variations in the research procedure due to varying hardware and software configurations and the environmental conditions such as the location in which the participants are responding. The third principle 'Social Responsibility' addresses points in relation to maintaining respect for social structures and giving due consideration to the consequences and outcomes of research being undertaken. The scientific value of the research can, in high scientific value research, determine whether a researcher discloses their involvement in spaces considered as private by the participants. The example given in the document is when the researcher does not have consent to observe an online group but the value of research is considered high then the conflict between valid consent and individual research context needs to be considered carefully. The fourth principle 'Maximising benefits and minimising harm' summarises the main points from the previous principles and states that steps must be taken to ensure that participants are protected from any possible adverse effects associated with the research. These are listed as ensuring anonymity and confidentiality, obtaining valid consent, and asserting appropriate levels of control over the research process.

Summary

Elbert et al. (2014) has recommended that future studies focus on development and evaluation of strategies instead of conducting larger studies. Given the support in the literature for the efficacy of internet based treatments for headaches (Devinini & Blanchard, 2005; Trautman & Kroner-Herwig, 2010), and the potential benefits of internet based interventions (Cuijpers, Van Straten & Anderson, 2008), this internet based study focused on a specific category of headache pain, migraine. Study rationale, including aims and objectives, is explored in the section which follows.

Chapter 5: Rationale for Study

Study Rationale

The clinical effectiveness and cost effectiveness of face to face intervention in the form of hypnosis for the treatment of migraine and chronic pain is well documented (Hammond, 2007; Jensen & Patterson, 2006). The efficacy of hypnosis for migraine delivered in an online platform however is novel. Migraine is ranked number seven among all diseases causing disability and, as noted previously, there is a strong correlation between pain catastrophizing and headache disability (Haythornthwaite 2009). The current study was designed to assess the acceptability and potential efficacy of an online hypnosis intervention for migraine with a view to decreasing the disability caused by migraine, reducing the frequency of migraine and reducing the level of pain catastrophizing in migraine sufferers.

Given the complex nature of chronic pain and the multiplicity of factors affecting migraine, hypnosis may provide a means of addressing some of the emotional, cognitive, sensory and behavioural components of pain which affect migraineurs. Hypnotic suggestions have the capacity to influence disability and pain catastrophizing in multiple ways. These include modulating pain generation, secondary neurons sensitisation and endocrine immune responses (Carli 2009), altering pain perception (Vanhaudenhuyse et al., 2009) and modifying emotional responses (Nusbaum et al., 2011).

Dillworth, Mendoza and Jensen (2011) outlined several other reasons for using hypnosis for the treatment of chronic pain. Their rationale included the fact that while opioid analgesics are used

most frequently for treatment of moderate to severe pain, prolonged use of opioids can lead to hyperalgesia (increased sensitivity to pain) as well as dependency and medication withdrawal headache. Prior to the present research, no studies of online hypnosis interventions for migraine were found in the literature. This is the first study to evaluate the effectiveness of any online intervention for migraine and also the first to examine online hypnosis-based treatment in this population.

Study Aims and Objectives

The aim of this study was to design and evaluate an online hypnosis intervention for migraineurs.

Specific objectives were (1) to evaluate the statistical and clinical significance of the intervention on functional (disability index), psychological (pain catastrophizing) and physiological (pain intensity) indices in a controlled clinical trial (2) to evaluate the feasibility and satisfaction with the intervention using qualitative data (3) to determine if any treatment effects are maintained at a six week follow-up.

Primary Objective:

Hypothesis 1: Hypnosis delivered in an online programme will be more effective than usual care in decreasing disability due to migraine, as measured by the Headache Disability Index (HDI).

Secondary Objectives:

Hypothesis 2: Hypnosis delivered in an online programme will be more effective than usual care in decreasing pain catastrophizing scores for migraine sufferers.

Hypothesis 3: Hypnosis delivered in an online programme will be more effective than usual care in decreasing headache medication usage for migraine sufferers.

Hypothesis 4: Hypnosis delivered in an online programme will be more effective than usual care in decreasing (a) the severity of migraine (b) the frequency of migraine (c) the duration of pain for migraine sufferers measured in hours.

A mixed methods design was employed in order to achieve a more comprehensive view of the findings. Thus, the quantitative analysis was accompanied by a qualitative analysis. The aim of the qualitative research undertaken in this study is to position the quantitative data in the context of the participants' lives and deliver greater insight into the environment and thought processes underpinning the data.

Summary

The literature in the area of face to face hypnosis interventions for chronic pain suggests that hypnotic suggestions of analgesia may have the capacity to effectively moderate the sensory, cognitive and affective dimensions of pain perception and can alter physiological processes. Hypnosis has been shown to be more effective for neuropathic pain or vascular pain than for musculoskeletal pain (Stoelb, Molton, Jensen & Patterson, 2009). Much of the research to date has concentrated on establishing the efficacy of hypnosis in reducing pain and more recently, investigated how specific hypnotic suggestions affected the individual at a neurophysiological level. It is now time to consider the potential of hypnosis in reducing the disability created as a consequence of chronic migraine. The direct and indirect costs of migraine to society are high. For individuals, migraine can be painful, disruptive and expensive. Face to face interventions using hypnosis have been shown to be effective for pain management in some studies but are also limited in terms of accessibility, availability and scheduling. This research study is the first to develop and investigate the delivery of hypnosis for migraine

via the internet. It is also the first study to assess the impact of hypnosis on pain catastrophizing for migraineurs.

The thesis describes several steps undertaken to evaluate the intervention:

(a) The development of the novel intervention was described

(b) A pilot effectiveness study was carried out comparing the online hypnotherapy intervention with usual care

(c) A qualitative evaluation was undertaken to gather more detailed feedback from service users.

Chapter 6: Method

6.1 Methodology

A mixed methods, randomized, single-blind study design was employed to examine the efficacy of hypnosis in an online intervention for patients with migraine. Ethical approval was sought and received from both the National University of Ireland, Galway and The Galway Clinic (Appendix 7), indicating that the study did meet with recognised ethical standards for research involving human participants. Participants were recruited via the media, neurologists and pain specialists. Based on discussions with neurologist, Dr. Andreas Jahnke, The Galway Clinic, inclusion criteria were established. These included requirements that participants have a formal diagnosis of migraine from their physician as defined by the International Headache Society (IHS) International Classification of Headache Disorders III, guidelines 1.1 and 1.2 (HIS, 2011), and that they have had migraine headaches for at least three months. Other inclusion criteria required that participants must be 18 years of age or older, have a willingness to complete all components of the study, as outlined in the participant information sheet (Appendix 3) and have access to the internet on a daily basis. Exclusion criteria for this study included: any serious psychiatric illness or cognitive impairment at time of enrolment; problems of substance addiction; participation in other clinical trials; migraine specifically related to menstrual cycle; abuse of acute medication for migraine; and any other severe psychological disorders which would compromise adherence to the study.

6.1.1 Overview of Study Development Process

The study was developed according to guidelines from the Medical Research Council (MRC) Framework for Evaluation of Complex Interventions (Craig et al., 2008). The purpose of the framework

was to provide guidelines for best practice for developing and evaluating randomized controlled trials for complex interventions (Anderson, 2008). Craig, Dieppe, Macintyre, Michie, Nazareth and Petticrew (2008) summarised the key points of the guidelines. These included the observation that multiple phases involved in developing and evaluating a complex intervention may not follow a linear sequence, that experimental designs are preferable over observational designs and that the understanding of processes is valuable but evaluation of outcome must be considered. Other observations included the idea that interventions may work better if adapted to local circumstances and that study reports should include sufficient details so that the study can be replicated and implemented on a broader level. The present study has created a new, novel way to effectively work with migraineurs to reduce disability and pain catastrophizing with the delivery of hypnosis via an online platform. Transcripts are included in the appendices to comply with the MRC guidelines regarding replication and implementation at a broader level.

A literature search was conducted to establish an evidence base for the use of hypnosis in chronic pain, more specifically with migraine. The databases included in the search were EBSCO (Psychological and Social Science Collection), PubMed, Science Direct, Web of Science and Scopus (Elsevier). Search terms included, but were not restricted to, migraine, hypnosis, hypnotherapy, e-health including online therapy, chronic pain, disability and migraine and pain catastrophizing. A proposal was developed giving due consideration to the substantial evidence for one to one interventions using hypnosis for chronic pain (Adachi, Fujino, Nakae, Mashimo & Sasaki, 2013; Montgomery, DuHamel & Redd, 2000) and the limitations noted within e-health research. These include the lack of well-designed studies which have diverse patient groups (Bender et al., 2011) and high drop-out rates (Macea et al., 2010). This proposal was submitted to the research committee and, based on

their recommendation, was subsequently amended to replace a mindfulness control group with a wait list group. Hypnosis scripts to be used in the online mp3s were drafted by the researcher and given to two other experienced hypnotherapists for review. They positively assessed the inductions, deepeners and the suggestions which were specific enough to address the pain accompanying migraine and broad enough to apply to a large population. Development of hypnosis scripts is discussed in greater detail in a later section. In accordance with MRC guidelines (Craig et al., 2008) high quality reviews (e.g. Bender, Radhakrishnan, Diorio, Englesakis & Jadad, 2011; Macea, Gajos, Calil & Fregni, 2010; Vargus & Dodick 2009; Hammond, 2007), relevant to the research, were identified in the development phase of the study.

Piloting and Feasibility

A focus group of fifteen participants (1 male and 14 females) who had suffered with migraine was organised in a pre-pilot study to provide insight in to the main issues which migraineurs wished to address in a treatment process. The participants were recruited through email, distributed by a business colleague, to a large database of his clients. The email outlined the inclusion and exclusion criteria previously outlined in Appendix 1. Each person was given an opportunity to introduce themselves, describe the type of migraine they had, how long they had suffered with migraine, what treatments had worked for them in the past and what had not worked for them. They discussed migraine triggers which affected them and the information was then incorporated in to the development of the MP3s. All participants in the focus group reported stress as a migraine trigger and 5 of the 12 participants reported specific foods such as citrus fruits and ice-cream being a trigger. The researcher incorporated this information on the evening in to a live hypnosis session which was recorded and was later emailed to each individual in the group. This mp3 was later re-recorded and included as the analgesic mp3 in the study. A follow

up meeting was arranged one month later. Participants were asked to listen to the mp3 at least three times a week for a month. During this informal process ten out of the twelve people reported that the severity and number of their migraines reduced and mentioned that they would have preferred access to more mp3s because after one month they knew the words of the mp3 off by heart. Their feedback was used to modify the intervention during the main study. Other recommendations from the group included: changing the background music and targeting different areas which affected them personally e.g. specific food triggers. A pilot study followed this informal focus group and was run to estimate likely rate of recruitment and retention of participants. Five people were recruited for the pilot study. Recruitment took a considerable amount of time but retention was 100%. All five individuals completed seven surveys over six weeks. Several issues were highlighted by the pilot study including one major error which involved a link to the first survey which was not overwritten by a new survey link each subsequent week. This ultimately meant that the data collected could not be identified as being from the wait list group or the intervention group. This did not negate the value of the pilot as it raised awareness about the construction of templates which were carefully amended for use in the main study. A retention rate of 100% is unusual in internet studies. In the review of RCTs managing pain via the internet, dropout rates have been reported to be in the region of 27.4% (Bender, Radakrishnan, Diorio, Englesakis & Jadad, 2011).

Sample size calculation:

The primary outcomes of interest were PCS and HDI. Sample size calculations were based on the PCS score since the % change to be detected (and thus identify a clinically significant treatment effect) in PCS, a psychological variable, was expected to be impacted more

with this intervention, than HDI, a physiological variable. A clinically significant reduction in PCS is a 38% reduction from baseline (Scott, Wideman & Sullivan, 2013). The mean PCS level at baseline for the 5 participants in the pilot study was 23 with standard deviation of 11. A 38% reduction in PCS equates to requiring a sample size large enough to detect a difference of approximately 8.5 points. Using the approach of Diggle et al. (2002) which calculates N (the sample size in each group) for a longitudinal study

$$N = \frac{2(z_{\alpha} + z_{\beta})^2 (1 + (n-1)\rho)}{n[(\mu 1 - \mu 2)/\sigma]^2}$$

where

n = number of time-points in the study

ρ = the assumed correlation of the repeated measurements over time

$\mu^1 - \mu^2$ = the difference in means of the two groups

σ^2 = the common variance in the two groups

In this study:

n = 5 time-points

$\mu^1 - \mu^2 = 8.5$

$z_{\alpha} = 1.96$ (2-tailed test, significance level $\sigma = 0.05$

$z_{\beta} = 0.842$ (power =0.8)

ρ is assumed to be 0.6 allowing for moderate correlation between the repeated measurements over time.

This implied a sample size of N = 18 required in each group to achieve the desired power. Attrition rates in the pilot study were 0%, however we allowed for 20% attrition, leading to a final sample size of approximately N = 22 in each group.

Time Point Labels

The Tables and Figures are represented with various time points. Online surveys were administered at eight time points over a twelve week period in order to investigate the process of change in key outcome measures. HDI and PCS were administered at 5 time points; T1, T14, T28, T42, T84. Mg of medication, frequency, duration and severity of migraine were assessed at all eight time points.

Time 1 (T1) is Day 1. Pre intervention
Time 7 (T7) is Day 7. Pre intervention
Time 14 (T14) is Day 14. Day on which intervention commences.
Time 21 (T21) is Day 21. One week of intervention complete.
Time 28 (T28) is Day 28. Two weeks of intervention complete.
Time 35 (T35) is Day 35. Three weeks of intervention complete.
Time 42 (T42) is Day 42. Fourth and final week of surveys and intervention complete.
Time 84 (T84) is Day 84. A six week follow up survey is administered.

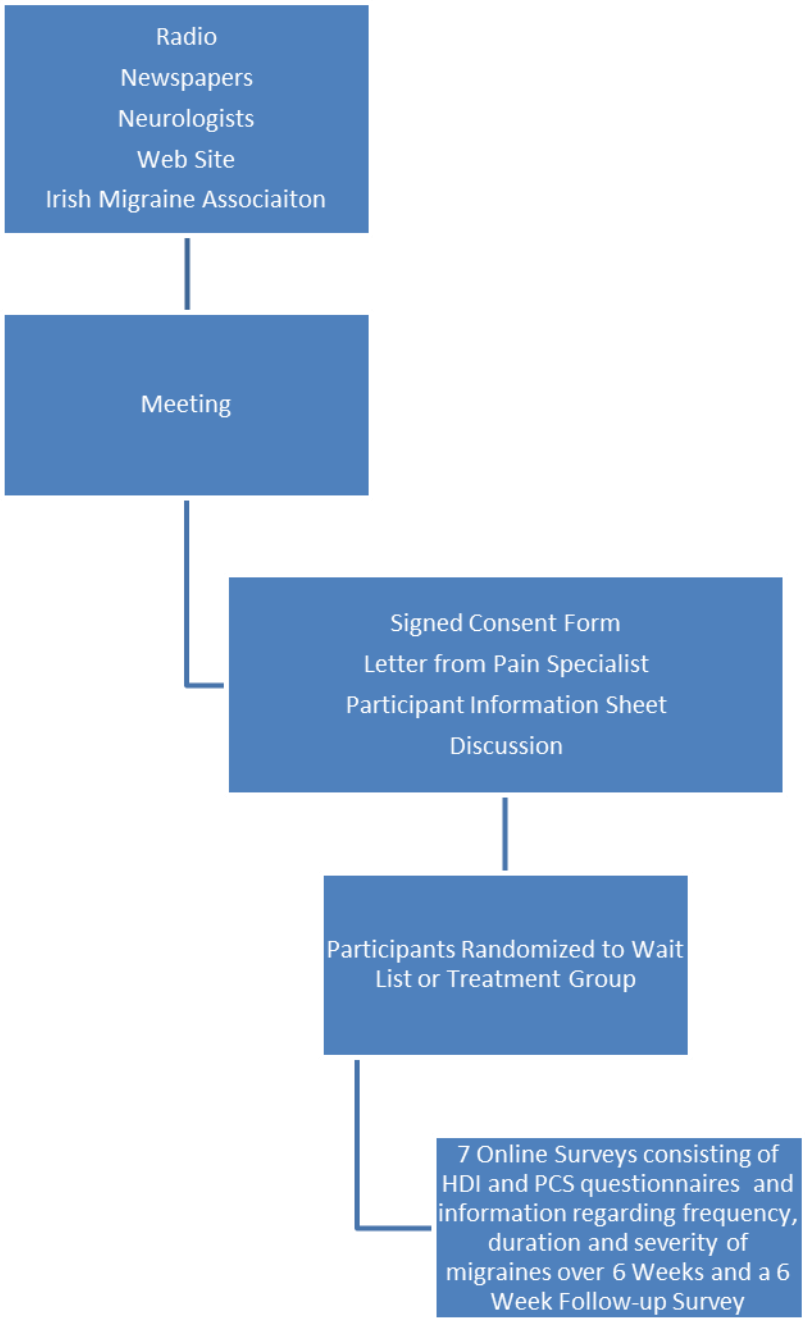
Recruitment

Initial enrolment in the online study was 43 participants who satisfied the study criteria, five of whom were male and 38 of whom were female.

A meeting was arranged with two neurologists regarding the study and two websites; www.promigraine.com and www.migraineintervention.com were created. The former was designed to distribute information about the study and assist in the recruitment of participants. The second was designed to provide study links to the downloads. All information about the study, eligibility details and other migraine related information was posted on the websites. Media outlets were notified about the study and several press and radio interviews were arranged (Appendix 8). This process raised awareness of the study and drew a large number

(over 130) telephone calls and emails from individuals wanting to know more about the study. The Irish Migraine Association were notified of the study and they placed several notices on their website advertising for participants. When those making enquiries appeared to satisfy the eligibility criteria they were directed to the website with instructions regarding the recruitment process. All participants were required to obtain a letter from their GP or neurologist to establish that they did indeed meet study criteria. A template of this letter was available for download from the website www.promigraine.com. All of those who were eligible to participate and who subsequently participated in the study had seen information in the written media, either articles in The Irish Times (n=40), an article in The Connacht Tribune (n=1) or an article in The Clare Champion (n=1). One participant in the study resided in the United States and one was based in the UK. The remainder were from Ireland. Although a variety of recruitment processes were employed, none of those participating became aware of the study by any other recruitment source other than newspapers. An outline of the recruitment process is illustrated in Fig.2 which follows.

Fig.6.1 Online Recruitment Process



6.2 Quantitative Study Procedure

6.2.1 Introduction

An initial meeting was arranged with eligible participants. During the meeting, each participant received a participant information sheet (Appendix 3), a list of the dates when each survey would be sent out (Appendix 5), a medication diary sheet (Appendix 6) and their own unique study number which would be required to complete the surveys. At this meeting they were also asked to sign a consent form (Appendix 4). In instances where the meeting was by phone, all relevant documents were emailed to the participant. They were also asked to sign the consent form and return it, with the appropriate letter from their health care provider, via post or fax to the author's office at The Galway Clinic. Each online survey was sent out on a Sunday morning at 9am. The commitment on behalf of each participant was to complete a series of seven surveys over six consecutive weeks. The surveys consisted of the HDI and PCS questionnaires and information pertaining to the frequency, duration and severity of their migraines.

Web Survey

All surveys were completed online using the online survey tool, www.SurveyMonkey.com. All emails, including passwords and links to hypnosis mp3s, were sent via the online mailing platform, www.MailChimp.com. Participants had access to information about the study at all times via two websites, www.promigraine.com and www.migraineintervention.com

Randomisation

Participants were randomized to the intervention group or wait list group via their study numbers on day one. The randomization process was carried out by an independent third party using the website www.randomizer.org to generate the randomization

sequence. The two lists of participants and their emails were compiled and entered into mailchimp, the software used to distribute the surveys. The emails with the surveys were set up to be sent automatically on the relevant days ahead of time. Once all the surveys were completed each week the researcher had access only to results which were documented with initials and a study number given to each participant in both groups. Once the results of the eight surveys (including the six week follow up) were collected the names of the participants were available to the researcher.

Process

Participants were asked to keep a manual daily diary, tracking headache frequency and intensity and any medication they were taking for the six weeks. On day 1 they were assessed for baseline measures of Pain Catastrophizing, Headache Disability and Mindfulness. This process is outlined in a table on the participant information sheet (Appendix 3). On days 7, 14, 21, 28, 35 and 42 they were asked to record the frequency of their migraines, the duration of migraines and the Medication Index Score (MIS) i.e. the amount of medication in mg they took in the week preceding that survey. On days one, fourteen, twenty-eight and forty-two Headache Disability Inventory (HDI) and Pain Catastrophizing Scale (PCS) were also recorded. On day 15 all participants were informed of the group i.e. wait list or intervention, to which they had been randomized. Participants in the intervention group were given a password to access their online hypnosis mp3 track for that week. A new password and new hypnosis mp3 track was issued each week for the subsequent three weeks. Participants in the intervention group were given access to the first of their four hypnosis mp3s and requested to listen to that mp3 three times per week. Authentication Cookies which are small pieces of data sent by a website which shows whether someone logged in or not, were used to track the number of times an individual logged in to listen to their mp3. A courtesy email was sent three times a week to gently remind

participants to listen to their hypnosis mp3 three times each week. A CD (Appendix 17) with all four tracks was sent to each participant in the intervention group on completion of the seven surveys. PCS, HDI, Mindfulness, MIS, duration of migraine, severity and number of migraines for the previous week were recorded on day eighty-four, six weeks post the initial intervention. The CD with all four hypnosis tracks used in the study was sent to the wait list group two days following completion of the eighth and final survey at the six week follow up. The number of participants who dropped out or were lost to follow up were recorded on days 42 and 84 (six week follow up), giving attrition rates of 9.3% and 21% respectively.

Ethical considerations

Confidentiality, autonomy and patient care were given priority in both design and implementation of the research project. The reasons for choosing the particular psychological assessments which were utilised in the study follows under the heading 'Measures'. Participants were informed in person and in writing (Participation Information Sheet, Appendix 3) that they could contact the researcher or supervisor at any stage throughout the study if they had any questions.

Confidentiality

The websites had public and private access areas. The public access areas of each website had general information about the study. The private pages could only be accessed via a password. Participants in the intervention group were given this password each week so that they could access the mp3s. All scores were accessible only on completion of the study and each individual had access to their own reports but not to those belonging to any other participant. Cookies were used to ensure that each participant was accessing the correct information relevant to their treatment protocol, these were deleted on completion of the treatment programme.

6.2.2 Guidelines Utilised

Guidelines established by the Medical Research Council (MRC) and Online Clinical Intervention Guidelines were observed.

Online Clinical Intervention Recommendations

Bender et al., (2011), conducted a systematic review of randomized controlled trials conducted to manage pain through the internet. Their recommendations for e-health pain interventions included recommendations for more well-designed studies with diverse patient groups and better description of withdrawals in order to 'strengthen the evidence concerning the impact of internet based interventions on people in pain' (Bender et al., 2011 p.1740). More recently, Ventura, Ohlen and Koinberg (2013) conducted a review of 28 quantitative studies which used the internet to deliver information and support to oncology patients. Their observations include the need for researchers to identify a series of outcomes that truly reflect the efficacy of supportive e-health interventions. They also direct attention to the differential preferences which patients will have with respect to the information and care they seek. Other factors such as the phase of a disease and personality are mentioned as potential considerations for the development phase of any study.

6.2.3 Measures

The measures used in the study were as follows:

Headache Disability Index (HDI)

Pain Catastrophizing Scale (PCS)

Medication Index Score (MIS)

Severity of migraines (Diary)

Frequency of migraines (Diary)

Duration of migraines (Diary)

Mindfulness Attention Awareness Scale (MAAS)

Headache Disability Index

The Headache Disability Inventory (HDI) is a 25 item survey which assesses emotional and functional disability as a consequence of headache (Jacobson, Ramadan, Aggarwal & Newman, 1994). To attribute changes to treatment effects, a clinically significant improvement must be observed, defined as a 50% reduction in headache index scores (Blanchard & Schwarz, 1988). There are three response options on the HDI: yes (score of 4 points), sometimes (score of 2 points) and never (score of 0 points). The HDI has been demonstrated to have good internal consistency reliability, long-term test-retest stability and good construct validity (Jacobson, Ramadan, Norris & Newman, 1995). Even though Jacobson et al., (1994), divided HDI into emotional and functional items as well as total score, only the total score was assessed in this study because, as Holroyd, Malinoski, Davis and Lipchik (1999) pointed out, despite the rational manner in which the items are categorized into the two streams, they found that the items were loaded on a single factor. An example of one item on the HDI scale is 'Because of my headaches I feel restricted in performing my routine daily activities'.

Pain Catastrophizing Scale

The Pain Catastrophizing Scale (PCS) consists of thirteen items. When responding to each item on the scale, participants are advised to think about a painful experience and to score each item on the Likert scale which extends from '0' representing 'not at all' to '4' representing 'all the time'. In spite of the increasing volume of research involving pain catastrophizing, Scott, Wideman and Sullivan (2013) acknowledged that it is not clear how clinicians might best interpret scores on catastrophizing before and after treatment. Scott et al. (2013) asked 166 occupationally disabled individuals who had sub-acute pain to complete seven weeks of a multidisciplinary rehabilitation programme with a view to promoting functional recovery. They measured PCS scores before

and after intervention and found that PCS reductions of 38% to 44% post intervention were best associated with return to work and low pain intensity ratings. The authors recommend that these percentages serve as a preliminary guideline in assessing clinical significance for interventions assessing changes in pain catastrophizing for patients with subacute pain after musculoskeletal injury. To date there are no guidelines for assessing clinical significance in pain catastrophizing for migraineurs.

Frequency, Duration and Severity of Migraine

Participants were asked to keep a daily record in their medication diary (Appendix 6) of the number of migraines they had, the number of hours they suffered with migraine and the severity of their migraine. At the end of each week they were asked to record the total number of hours of migraine for that week, the number of migraines per week and the average severity of the headaches. The severity scale was rated in terms of I (Little or no pain), II (Mild), III (Moderate) and IV (Severe).

Medication Index Score

The medication index score (MIS) used in this study is based loosely on that employed by Devineni and Blanchard (2005) in their randomized controlled trial of an internet-based treatment for chronic headache. When contacted by email, Dr. Devineni explained that for their study it was, as it is in this current study, a secondary measure, and thus they looked crudely at daily counts of total tablets consumed. Following a conversation with a neurologist and given the broad spectrum of medication currently prescribed, the MIS measured in this research was mg per week as recorded by participants in their daily medication diary (Appendix 6).

Mindfulness Scale

The subjective experience of pain is shaped by our own unique past experiences, our current cognitive state and our future expectations

and, for centuries, it has been believed that meditation can influence these processes and the sensory experience of pain (Zeidan, Martucci, Kraft, Gordon, McHaffie & Coghill, 2011). The Mindful Attention Awareness Scale (MAAS) is one example of a survey which is used to measure mindfulness and which is accepted as a valid measure (MacKillop & Anderson, 2007). Although hypnosis and mindfulness are perceived to be on opposite ends of the same spectrum (Harrer, 2009) the question is asked by Harrer (2009) whether hypnosis could benefit from the concept of mindfulness. In hypnosis, Harrer explained, the focus of attention is narrowed and the participant is generally receptive to the suggestion of the therapist. In contrast, during mindfulness meditation awareness is broader and the aim is to 'perceive the world as it is'. Despite the differences in practice, the same article highlighted the fact that both hypnosis and mindfulness share some similar neurophysiological components as well as some distinct neural correlates. To this end, a survey such as MAAS which can be administered online, if related to statistically and clinically significant improvements as a result of an online hypnosis intervention, may be useful in predicting future patients who could potentially benefit from hypnotic intervention for pain.

Statistical Analysis

Full descriptive analysis was performed to describe participant characteristics (e.g. age, gender, etc.) in the two treatment groups. Suitable descriptive and graphical summaries e.g. boxplots, case profile plots, scatterplots are used to describe the profile of the primary outcome (HDI) and secondary outcomes (PCS and MIS) over time and across treatment groups. An intention-to-treat analysis has been performed to compare HDI, PCS and MIS levels at baseline versus day 42 while adjusting for participant characteristics such as age, gender, etc. The linear mixed model is used to perform both analyses, allowing for account to be taken of the correlation induced by taking repeated measurements over time on the same

individual while adjusting for other patient characteristics such as age, gender, etc.

Data Analytic Procedure

For normally distributed outcomes, t-tests for independent groups were performed to determine if there was evidence of a difference between the mean baseline across groups. For non-normally distributed outcomes, the Wilcoxon rank sum test was used performed to determine if there was a difference between the medians in both groups. For both t-tests and Wilcoxon tests, a p-value of <0.05 indicated that there was a significant difference between the mean/median in both groups. To determine if there were significant changes over time between the two groups, predictive modelling using the linear mixed effects regression model, was carried out.

6.3 Qualitative Method

6.3.1 What is Qualitative Research?

Qualitative research is concerned with analysis of codes, themes and patterns within data (Ploeg 1999). It is a process of inquiry which allows for exploration of a central concept by asking general questions of participants in a study and subsequently analysing and coding the data with the aim of developing an overview of the processes and outcomes under inquiry (Cresswell, 2002). Qualitative research 'builds its premises on inductive, rather than deductive reasoning' (Williams, 2007 p.67) and data collection can take the form of focus groups, interviews or participant observation utilising audio or video recordings, transcripts and field notes. The qualitative study design, in comparison with quantitative research, usually involves asking open-ended questions in order to describe the experiences of participants and to explicate deviations of experience among participants. Using qualitative research alongside

quantitative research allows for a better understanding of data and a greater insight in to the meaning of the quantitative results.
Several approaches may be utilised in qualitative data collection and analysis. These include Phenomenology, Narrative Research, Case Study, Ethnography and Grounded Theory (Morse & Field, 1995). The approach employed will be dependent on the participants and the research question under investigation, for example, Narrative Research will focus on the life of an individual and data will be collated through a series of interviews and/or via documentation. The data analysis will then take the form of stories and historical content and will be used to build a comprehensive document of the participant's life. A Case Study Approach may involve one or several cases where data collection takes the form of interviews, observations or documents. Yin (2003) divided case studies into three categories: exploratory, explanatory and descriptive and also differentiated between single, holistic and multiple case studies. An example of a multiple case study cited by Yin (2003) is one where the researcher explores differences within and between case studies and which subsequently allows for prediction of similar results across case studies or to predict contrasting results based on a theory (Yin, 2003). In Grounded Theory the researcher creates an abstract outline of a phenomenon which attempts to explain the underlying process (McCaslin & Scott, 2003), in other words, the research process attempts to devlop a theory that will explain the process or experience under investigation. The means by which this process develops is by collecting data via interviews or observation and then developing and integrating categories of information. McCaslin and Scott (2003) suggest that based on Wolcott's (1994) recommendations, students need to start in the future and work backwards, holding the objective they wish to achieve in mind for example in the present study the objective was to record and better understand the observed changes in day to day activity and changes in thought processes such as catastrophizing which participants'

experienced. Questions were then devised bearing this objective in mind.

6.3.2 Designing Qualitative Research Questions

Qualitative research is a reflective process, a means by which details of social and cultural elements of peoples' lives can be represented (Geertz, 1973). Agee (2009) stressed the importance for qualitative researchers of framing good questions. She explained that while good questions do not guarantee good research, poorly constructed questions will have an influence on subsequent stages of a study. She acknowledges that while it is not always possible to wait until one is collecting data before developing research questions, this is the approach adopted by many who write about grounded theory. She quoted Janesick (2000) who recommended asking oneself what it is one wants to know in the study. One challenge which researchers frequently encounter, she suggested, was framing the qualitative question. Broad questions, she explained, give focus to the study and they should be formulated in a way that is relevant to the field of investigation. Good qualitative questions should also invite a process of exploration and discovery (Creswell, 2007). Some of the problems which can arise with poorly constructed questions include a lack of ability to see outside a narrow focus of enquiry and subsequent constraint of the information gathered and analysed as a result. When initial questions are broad and 'discovery oriented' (Agee, 2009, p434), the researcher has a base from which a more rigorous and flexible line of enquiry is feasible. Sub questions, Agee (2009) explained, can be categorised as 'issue' and 'procedural' questions with some questions incorporating both categories. The aim, she suggested was to delve deeper into the specifics of the issue being researched. The focus of the questions should be directed towards the initial theory about the concept being investigated. Expanding on the ethical considerations involved in the process, she asserted that it is a key component in developing questions but one which is largely ignored. The notion that there is a

reflective aspect in how the questions will impact on participants' lives is emphasised. In essence the recommendation is that ethical consideration as to how the issue being researched will affect the lives of participants is of the utmost importance.

When writing the questions, Agee (2009) emphasised the concept of a question being a tool akin to a photographic lens being used to document a journey. Focus is highlighted as important and the questions should, the author stated, reference a specific context, the recommendations being to avoid overly general questions and to reflect the details of the study. She quoted Maxwell (2005, p67) who stated that 'the function of your research questions is to explain specifically what your study is about'.

It is often recommended that good qualitative questions begin with words such as 'what' or 'how'. A question designed to elicit a description of what the participants experienced can be useful. This can be achieved by asking 'how did you find the experience'. It is also useful to avoid certain words which could be leading, for example, 'influence', 'effect' or 'cause'. Participants' own words are encouraged as opposed to closed questions where 'yes' or 'no' answers are standard. Open ended questions afford participants an opportunity to respond in ways which the researcher may not have expected. It is a means by which influences or information which was not anticipated by the researcher may come to light. Questions often take the form of 'what is this?' or 'what is happening here' (Ploeg, 1999).

The development of a central question and sub-questions initially starts with a research topic and a research problem. The purpose of this study was to describe the subjective experience of the individuals who participated in the study and to understand the adherence to or ease of use of an online hypnosis programme. A general question 'Is there anything I have not asked about your

experience that you would like to comment on?' was included to elicit information about what the participants experienced allowing for a process of exploration and discovery as encouraged by Creswell (2007).

The questions were guided by Ploeg's (1999) suggestion of uncovering 'what is happening here'. Sub questions can divide the central question in to more specific areas. For headache disability the authors of the scale methodically organized items into emotional and functional subscales but factor analysis revealed all items loaded on a single factor. For the purpose of the qualitative investigation however the questions were designed to inquire as to the overall changes which participants' noticed in their lives as well as delving deeper into the specifics of the issues as recommended by Agee (2009), for example, catastrophic thinking and disability. A more detailed, specific understanding of the way in which participants lives reflected the changes noticed in the quantitative study was of interest.

6.3.3 Describing Subjective Experiences in Qualitative Research

Good qualitative research is defined as research which illuminates the interpretation, by participants, of subjective meanings, actions and social contexts of a particular experience (Fossey, Harvey, Mcdermott & Davidson, 2002). Bashir, Afzal and Azeem (2008). described the function of both quantitative and qualitative research as paradigms seeking to find the same result: the truth. The nature of qualitative research therefore is to describe the subjective experience and/or views of a group of individuals or a sample of those individuals.

Sample Selection in Qualitative Research

In qualitative research, a subset of a population of interest is initially selected. Sampling can be divided in to probability sampling and

nonprobability sampling (Doherty, 1994). In probability sampling all participants have an equal chance of being included in the research and the results are likely to be reflective of the entire population (Doherty, 1994). The probability of getting each sample selected is known so a sampling error for the results can be calculated. This is indicative of the amount of variation in the results as a consequence of the sampling alone. Non probability sampling is often more convenient but can be more challenging to extrapolate results to an entire population (Wretman, 2010). Not all individuals in a population have an equal opportunity of being selected in this type of sampling. Probability sampling methods include simple random, systematic, and stratified sampling. Simple random is the simplest method, for example, throwing a dice, drawing a name out of a hat or using a computer generated software programme to determine participants. Each participant has an equal probability of selection. With Stratified random sampling (Williams, 2015) the population can be divided into groups that differ in significant ways and these should be relevant and determined before sampling. A random sample is then selected from within each group. Systematic random sampling is where each element has an equal probability of selection but differing probabilities associated with different combinations of elements (Williams, 2015).

Non-probability sampling methods include purposive sampling, quota sampling and snowball sampling (Latham, 2007). Purposive sampling is often used when a particular selection of a population are of interest (Latham, 2007), for example, to explore the experience of use of a particular medicine by children under the age of 10. Children aged above 10 and those not taking the medication would not be selected as they are not of interest to the central research question. The main advantage of purposive sampling is the ability to gather significant amount of data using a wide range of sampling techniques such as expert sampling and homogenous sampling. However, there is significant room for bias with non

probability sampling as the results could differ with a different sample selection and Latham (2007) advised not to generalize results to the general population with non probability sampling for this reason.

Quota sampling is a non-probability method which involves the collation of relevant categories such as age and gender which are relevant to the research and the collection of a sample which satisfy these criteria. As a method it is easy to conduct but is not useful for research where accuracy is important.
Snowball sampling is the term used to describe the means by which participants recruit other participants (Wretman, 2010). It is also a non-probability sampling method. Names are not mandatory in snowball sampling thus the anonymity suits in collection of data where participants may not wish to acknowledge points of view or certain behaviours, for example, abuse of alcohol.

6.3.4 Qualitative Method Adopted in Current Study

Maykut and Morehouse (1994) defined qualitative data analysis as a means by which the researcher uncovers patterns in the words of the participants and gives an account of those patterns while at the same time remaining respectful to the original experience of the participants. The qualitative methodology applied in this research study was based on the 'constant comparative method' developed by Maykut and Morehouse (1994). The constant comparative method involves listing units of information from the data and then allocating these units to categories. The categories can be created because the researcher feels they are important for the area of investigation or they can be driven by the participants' language. The categories are subsequently refined with an end goal of refining emerging concepts (www.qdatraining.eu).

The qualitative aspect of this study had several objectives: Firstly, to examine the experience and process of participating in the treatment programme. Secondly, to understand and delineate the changes which the participants noticed on a behavioural and cognitive level in their day to day interactions. The qualitative research regarding the experience and changes arising from the programme was predominantly carried out retrospectively and was not hypothesis-driven since the goal of qualitative research is to understand subjective experience. A minor qualitative component was carried out prospectively in the form of a focus group established prior to running a pilot study for the quantitative research. During this focus group each participant was invited to describe their personal experiences of migraine, the conditions which exacerbated their migraines and the type and nature of treatment plans they had employed up to that point. The successes and failures of the various interventions (primarily medical) mentioned were discussed. There was a noted disillusionment with traditional medical interventions which were perceived to be costly and only somewhat useful. The group were invited to experience a live group hypnotherapy session based on the information they provided that day and they were then invited to a follow up meeting a week later. During the second meeting their opinions about the viability of an online hypnosis programme, any changes they had experienced over the week since participating in a hypnosis session and any recommendations they had regarding what suggestions should be included in the mp3s.

Data collection and data analysis was carried out using the constant comparative method. This first step of the constant comparative method is interviewing the participants in order to record their experiences. The next step requires a breaking down of the interviews into what Lincoln and Guba (1985) described as ‘units’. Some units were set out by the researcher for the purpose of uncovering more information with respect to specific aspects of the study. Other units arise as a consequence of natural discourse,

allowing the participants to voice those issues and experiences which were important to them. Thus, as Lincoln and Guba (1985) determined, 'both descriptive and explanatory categories' (p.334) emerge. Initial units are then refined in terms of their names and their relationships with other units until a clear and cohesive set of data emerges.

On completion of the six week intervention, a sample of the intervention group (n=14) undertook an individual semi-structured interview either in person (n=8) or on the phone (n=6). All individuals in the intervention group were contacted and those who were available to participate over a two week period at that time were recorded. There were ten questions in total addressing what it was like listening to the MP3s, how they might use an online platform differently and what might incentivise them to use the MP3s regularly. Concepts related to headache disability and pain catastrophizing were of interest and questions such as 'Has the intervention had any impact in how you relate to people around you?' and 'Have you noticed any changes in the discomfort of your migraines as a result of the intervention?' were asked. The mean time of the interviews was 7 minutes. Once recorded, the interviews were then transcribed verbatim, imported and then analysed using NVivo Version 10 software.

Kolb (2012) noted that Glaser and Strauss (1967) described constant comparative methodology (CCM) as consisting of four stages: '1. Comparing incidents applicable to each; 2. Integrating categories and their properties, 3. Delimiting the theory and 4. Writing the theory.' (p.105). However, while there is considerable research in this area Boeije (2002) suggested that the process by which CCM is carried out was vague. Software programmes such as NVivo which was initially launched in 1999 (www.qsrinternational.com) have evolved to provide unique tools which are specifically designed to

allow detailed analysis and qualitative modelling in a systematic manner.

The stages described by Glaser and Strauss (1967) facilitate reflection on the data in order to elicit findings and draw conclusions. Initially the coding was non-hierarchical and no one question asked was considered more important than another. Relevant categories were then identified and codes were subsequently assigned to different categories. Several themes emerged from the categories and the categories were given new names to reflect content more accurately. Sub-themes were identified and this facilitated greater insight into various qualitative factors such as attitudes, beliefs and unexpected outcomes to be analysed. The data was reduced further to serve as a starting point for discussion. A self-audit was carried out in order to test and validate the findings. This included cross referencing with demographic data, literature and observations. The final phase involved the collation of analytical scripts into a succinct report.

6.4 Development of Online Hypnosis Recordings

The development of the "hypnoscripts" for this study was based on (a) a review of the literature to ascertain the nature and content of hypnotic suggestions that have been identified as effective for pain management (b) a focus group with chronic pain patients in order to identify important therapeutic targets and preferred format and duration of recordings (c) review by an independent expert hypnotherapist. The steps are described in more detail below.

6.4.1 Suggestion Management

The Role of Direct Hypnotic Suggestions in Pain Management

In light of the evidence that hypnosis can alter the sensory, affective and behavioural components of pain and the current acceptance of the biopsychosocial model of pain, findings of the FA model and recommendations by Martin (2001), hypnosis can sit comfortably in a treatment plan for chronic pain. Wiech and Tracey (2009) reviewed the literature in the field of emotions and pain. Noting the fact that present theories of pain perception include the influence of psychological variables, they highlighted hypnosis as a means of accessing the multidimensional aspects of pain such as cognitive-affective and sensory components. Hypnotic suggestions which change the sensory features of pain but not the affective components lead to changes in the primary somatosensory cortex (Hofbauer et al., 2001). Changes in the affective components of pain without the sensory changes were associated with activity in the anterior cingulate cortex (Rainville et al., 1997). Given that emotional factors can alter unpleasantness of the pain experience without altering pain intensity (Villemure & Bushnell, 2002) it is logical, Wiech and Tracey (2009) explained, that pain-related fear is a better predictor of disability than pain intensity. They drew a parallel between benzodiazepines and hypnosis. Benzodiazepines are frequently prescribed for pain relief in spite of the fact that they are not analgesic medication and thus do not directly target pain intensity. However, as the authors pointed out, these medications partially mediated pain relief by reducing anxiety and thereby reducing pain. Suggestions targeted at reducing anxiety over and above the relaxation effect which an hypnotic induction can confer may therefore work in a similar manner to anxiety reducing medications.

Direct hypnotic suggestions are intended to indicate a specific direction or course of action or outcome to the client. Jensen and Patterson (2014) suggested that three aspects should be considered

when using hypnotic suggestion for the treatment of chronic pain. These were to (1) include direct suggestions for both short term and long term pain relief, (2) include direct suggestions for the external benefits outside of a reduction in pain and (3) enhance outcome expectancies by directly articulating to the patient the many benefits associated with hypnosis. They gave the example of the following text to demonstrate the type of suggestion which can be used to provide both immediate and long term relief, 'and when you practice self-hypnosis, your mind can easily enter this state of comfort, and the comfort will stay with you for minutes and hours.. the more you practice the easier and more automatic this will be… and the longer the beneficial effects will last.' The review cited a study by Smith and Haythornthwaite (2004) which found that between 50% and 88% of patients with chronic pain reported problems with sleep. The review noted that effective chronic pain treatments frequently involve increased activity. They proposed that suggestions in hypnosis should involve meaningful statements to increase confidence to participate in exercise and to draw on inner strength when required. They have subsequently proposed that suggestions include those designed to improve sleep patterns, specifically falling asleep and getting back to sleep and waking refreshed, suggestions related to adaptive pain-related cognitions, suggestions which encourage an increase in physical activity. The researchers also noted that suggestions should rarely, if ever, focus exclusively on pain reduction. The need to clarify how hypnosis can benefit patients over and above pain relief was noted in this review. These possible benefits are listed as improvement in sleep patterns, overall feelings of calmness and reduced stress.

The Role of Indirect Suggestions

Indirect suggestions are used in the hypnotic context as persuasive words to bypass resistance of the participant. Examples of indirect suggestions include the use of metaphors, complex equivalence and lost performative. A metaphor for change for example, could be the

metamorphosis of a caterpillar to a butterfly through various stages. Complex equivalence is the term used to describe the way in which two things not normally associated are equated, for example ‘now that you made the decision to do this activity, your pain can decrease’. Lost performative refers to when the hypnotist makes a suggestion but does not say who it is attributed to or if indeed it is true, but the expectation of the person being hypnotized is that they will accept the suggestions without question. For example, ‘now the powerful subconscious mind has the capacity to make all of these things happen’. Another technique which falls into the indirect suggestions category is ‘mind reading’. The implication is that the hypnotherapist has the capacity to read the client’s mind, for example ‘part of you wants to drift in to a deeper state of relaxation’. Nominalization, another technique used frequently, involves turning words which imply processes into nouns. An example of nominalization might be ‘you may find that your relaxation is so comforting that you drift further and deeper down in to trance’. Cause and Effect is also commonly used, that is, the implication that one thing leads to another or that because one thing happens that what follows is also true, for example, ‘making that choice to do something to reduce your discomfort brings you great happiness’. Presuppositions and Truisms also fall in to the category of ‘indirect suggestions’. Presuppositions are assumptions made by the hypnotherapist, for example, ‘you are now so relaxed’ and Truisms are a group of sentences used in succession with the first two being true and the implication being that if A and B are true then C is also true. For example, if A is ‘it is possible to notice how your body can become more relaxed when you imagine yourself sinking in to the chair’ and B is ‘some people find it relaxing to imagine themselves in a place where they won’t be disturbed’ and C is ‘everyone likes to feel as though they are in control of their lives just as you are taking control of the situations in your life now’. A Universal Qualifier is a phrase or sentence which contains generalisations, for example ‘so many people find that their legs feel

very heavy at this point in time..' or 'every one finds this..' Pacing is another strategy often categorised under the label of 'indirect suggestion'. It involves matching and mirroring a participant's pattern, for example, the therapist matches the breathing rate of the client.

Compliance with Suggestions– Hypnotizability, Motivation, Attention

Larkin (2014) emphasised the lack of agreement in the literature regarding suggestibility. She cited an article by Shulik (1979) which found statistically significant evidence to support the idea that third person indirect grammatical suggestions, for example 'she is stuck to the chair', significantly enhanced the acceptance of hypnotic suggestions in comparison with the more commonly utilised first person direct grammatical suggestions such as 'you are stuck to the chair'. Larkin's summation was that indirect suggestions positively affect the hypnotic state more than traditionally used direct suggestions. The third person stories used by Milton Erickson are an example of third-person indirect suggestions. Metaphors are another example. In spite of positive intentions by a participant in hypnosis, there is a chance that the hypnotic suggestions will be ineffectual. Gruzelier (2000) stated that psychophysiological recordings may provide the key as to why this occurs. Recordings have shown that at a neurophysiological level attentional processes were not engaged or that the resultant inhibition of frontal lobe processes was absent.

Kallio and Kovisto (2013) suggested that even highly automatic processes such as colour perception can be influenced by hypnosis. In one experiment they gave an hypnotic virtuoso post hypnotic amnesic suggestions and found that hallucinations of changes in colour experience could not be reversed without further hypnotic suggestions. It does not necessarily follow however, as Gruzelier (2000) proposed, that hypnotic suggestions will be accepted

unconditionally. Bryant and Hung (2013) challenged the commonly accepted notion that hypnotized people will not respond to hypnotic suggestions which are in conflict with their moral and ethical standards. While accepting that the literature supports this idea the authors looked at the concept of how social compliance issues independent of hypnosis could possibly influence people to respond to suggestions which are at odds with what they would normally comply with. The researchers acknowledged that the literature has shown that motivation influences acceptance of suggestions and adopted a double-blind placebo study where they administered oxytocin or placebo to twenty eight highly hypnotizable participants. They then asked the participants to respond to post hypnotic suggestions involving socially unorthodox behaviours such as swearing or dancing in response to a post hypnotic cue. They found that the participants who had been given oxytocin were significantly more likely to respond to the suggestions than those who received the placebo. They interpreted their findings as suggesting that oxytocin increases social compliance by increasing trust in the hypnotherapist, by reducing social anxiety or by increasing their sensitivity to the cues used. However, while the experiment demonstrated that oxytocin may facilitate social compliance in hypnotic participants, oxytocin is not likely to be administered to hypnotic subjects generally and other psychological factors such as motivation (Gfeller, Lynn & Pribble, 1987) are more likely to affect compliance with suggestions on a day to day basis.

6.4.2 Focus Group

A focus group was initially organised at a hotel in Galway city. Fifteen individuals who suffered with migraines and the mother of a migraineur also attended. The latter participant explained that her daughter was in hospital at that time because of complications with her pregnancy. The meeting was chaired by a business associate of the researcher and was recorded but this recording was subsequently

lost. Several questions were posed to the group. These included the types of migraine triggers the group were most familiar with, what treatments the group had used already to treat their migraines, the treatments they felt were successful and which were unsuccessful. Food triggers and stress were identified as a major trigger for most individuals in the group. A live hypnosis session based on their contributions was given as a gesture of thanks and a follow up meeting was arranged for a week later to discuss their opinions on the session and any suggestions they may have. Ten of the fifteen were able to attend the second meeting. Some had noticed an immediate improvement, for example, one lady found that while she ordinarily avoided driving in bright conditions she was able to do so with ease following the hypnosis session. The duration of the recordings was discussed and most felt that a recording of 15-20 minutes was optimal. A majority of the group noticed an increase in their ability to go about day to day activities. These considerations were taken into account when writing the mp3 scripts.

6.4.3 Hypnosis Scripts for the Present Study

Four hypnosis tracks were subsequently written and recorded by the researcher and then used in the intervention (Appendices 10,11,12 and 13). When writing the scripts the researcher had ten years experience of using hypnotherapy with a variety of clients. She also teaches an internationally recognized hypnotherapy training programme. The scripts were given to another experienced hypnotherapist to review in terms of the appropriateness of the content for treatment of migraine. They were happy with the scripts and did not suggest any amendments.

Pain-specific and non-pain related suggestions were included, because the pain-related outcome was greater in studies using both type of suggestions (Dilworth & Jensen, 2010). Wiechman, Askay and Patterson (2007) gave examples of affective and sensory suggestions. ‘You may notice that you are more comfortable now

than you were' is an example of an affect suggestion while 'you will find that you can move the intensity of your feelings on a dial from a 10 down to a 9, 8, 7…' is an example of a sensory suggestion. A variety of suggestions were incorporated in the mp3 tracks for a number of reasons. The suggestions used address affect (emotion), analgesia, sensory components of pain, cognition and behaviour. Rainville, Carrier, Hofbauer, Duncan and Bushnell (1999) stated in their observation of sensory and affective processes by hypnosis that when a suggestion is directed solely towards affect, hypnotic suggestibility is a requirement. When the suggestions are sensory related, there is a corresponding reduction in affect and hypnotic suggestibility is irrelevant. The first mp3 'Analgesia for migraine' contained suggestions targeted at reducing the physical discomfort of the migraines as the sensory component of pain has been shown to respond to hypnosis in previous studies. Montgomery, DuHamel and Redd (2000) for example, calculated the effect sizes from 18 studies which used hypnosis for pain relief in experimental and clinical populations and found that hypnosis provided pain relief for 75% of the population. The second mp3, 'Living life to the full' was written to include suggestions targeted at reducing headache disability and pain catastrophizing as these were the primary focus of the research. The third mp3 was written as a metaphor for restoring full health. This approach is relevant as the suggestions are broad enough to be relevant to anyone with migraines and have the capacity to be interpreted in a personal manner according to each individual's understanding of full health. The fourth mp3 based on eliminating foods and reducing stress was written for two reasons. Firstly, emotional stress was reported as the most common trigger for migraine (Yadav, Kalita & Misra, 2010) and secondly, the focus group indicated that they would be interested in an mp3 or CD which helped them to reduce their stress levels and help them to avoid food triggers. Further information about each of the four mp3s recorded and used is included below.

1. Analgesia for migraine

2. Living life to the full (addressing migraine disability and catastrophizing)
3. A metaphor for health: connecting mind and body
4. Reducing stress and eliminating foods which trigger migraine
Each of these is described in more detail in the text which follows. .

1. Analgesia for migraine

Metaphors based on an Ericksonian type of hypnosis were also included in this MP3. The function of the metaphor was to relate otherwise unassociated objects with pain-related concepts. In this script the metaphor of a vice-grip being loosened was used with the purpose of helping the listener to imagine the internal pressure within their head being released. Another metaphor of two glass jars with taps attached was also used with the similar purpose of allowing the listener to imagine their discomfort draining away. Given the utility of hypnosis to modulate both affective and sensory dimensions of pain perception (DeBenedittis, 2003) and the discovery that both direct and indirect suggestions are useful inclusions for pain management (Nusbaum, 2011), all of these concepts were included. An example of a direct suggestion is 'You are engaged in more activities and you feel in control' while 'you may be surprised at how comfortable you feel right now or sometime later' is an example of one of the indirect suggestions.

2. Living life to the full

As pointed out previously, Holroyd et al., (1999) stated that assessment of the impact of recurrent headache disorders in clinical trials should consider affective distress as well as pain and disability. Thus, the suggestions in this mp3 were based on reducing emotional stress and on increasing confidence in one's ability to engage in more activities of interest. As pain is now accepted to have cognitive, sensory and affective components, these suggestions were designed to alter cognitive processes by helping migraineurs

re-interpret the sensations of pain and increase the motivation to engage in more activities.

3. Connecting mind and body hypnosis:
A metaphor to restore health
Indirect suggestions embedded in the form of a metaphor were the main focus of this mp3. A generic metaphor based on restoration of health was created with a view to being broad enough to be relevant to each participant and at the same time useful in terms of inspiring hope that full health could be restored.

4. Reducing stress and eliminating foods which trigger migraine
Stress has been identified as a migraine trigger in 70% of migraineurs (Yadav et al., 2010). Finocchi and Sivori (2012) explored the role of food as a potential trigger and aggravating factor of migraine, and noted that the percentage of migraine patients reporting food as a trigger ranged from 12 to 60% across studies. Latsko, Silberstein and Rosen (2011), highlighted that many migraineurs were able to identify the source triggers for their migraines. In their headache clinic, approximately 25% of attendees experienced hunger-induced or fasting-induced migraine. Once identified, these factors were within the control of the migraineur to change. For these reasons, the focus of the script for this mp3 was to assist participants in reducing their stress levels and secondly to identify and avoid any known food triggers. Suggestions were also included to encourage participants to avoid going for long periods of time without eating.

Other (direct) suggestions were incorporated to make it easier for participants to justify less demanding schedules with a view to reducing stress levels e.g. 'You accept that, just as we need time to complete specific tasks each day and week, we also need time to relax, recover and recuperate'. Logic was introduced with a suggestion that taking time out on a regular basis could prevent a

greater amount of time being high jacked by migraines caused by stress. The line ‘you could choose to spend your time off each day or week or month enduring the pain of migraines or you could choose to accept that time off is essential for recovery and good health’ was included to illustrate this point.

Chapter 7: Results

Introduction

In keeping with the time line in which the research was conducted, the quantitative results are presented initially in this chapter and the qualitative results follow.

Method

The rationale and details of the methodology used were outlined previously and are summarized in this chapter.

Procedure

A total of 43 participants were eligible to take part in the study. Each participant was allocated a sequential study number as they enrolled. Subsequently these numbers were randomized to either the wait list group or the treatment group. Twenty one were randomized to the wait list condition and twenty two to the intervention group. Once enrolled, participants were required to complete 7 online surveys over 7 consecutive Sundays. Those in the intervention arm of the study received four mp3s over 4 weeks between week two and week six. An additional survey was sent out on Day 84, 6 weeks following completion of the study. On completion of the surveys a CD with all four hypnosis tracks was posted to each individual in the wait list group. Participants from the intervention group were invited to give feedback in semi-structured interviews. In total, 14 interviews were conducted (response rate of 63.6%). The recordings of the interviews were transcribed verbatim, analysed using NVIVO and form the qualitative section of this research.

Participants

The participants were predominantly based in the East of Ireland, one was living in the U.S. and one was living in the U.K. 43 participants commenced the study, 39 participants completed the initial seven surveys and 34 completed the final survey which was sent out six weeks after the intervention.

Participant retention and description of withdrawals

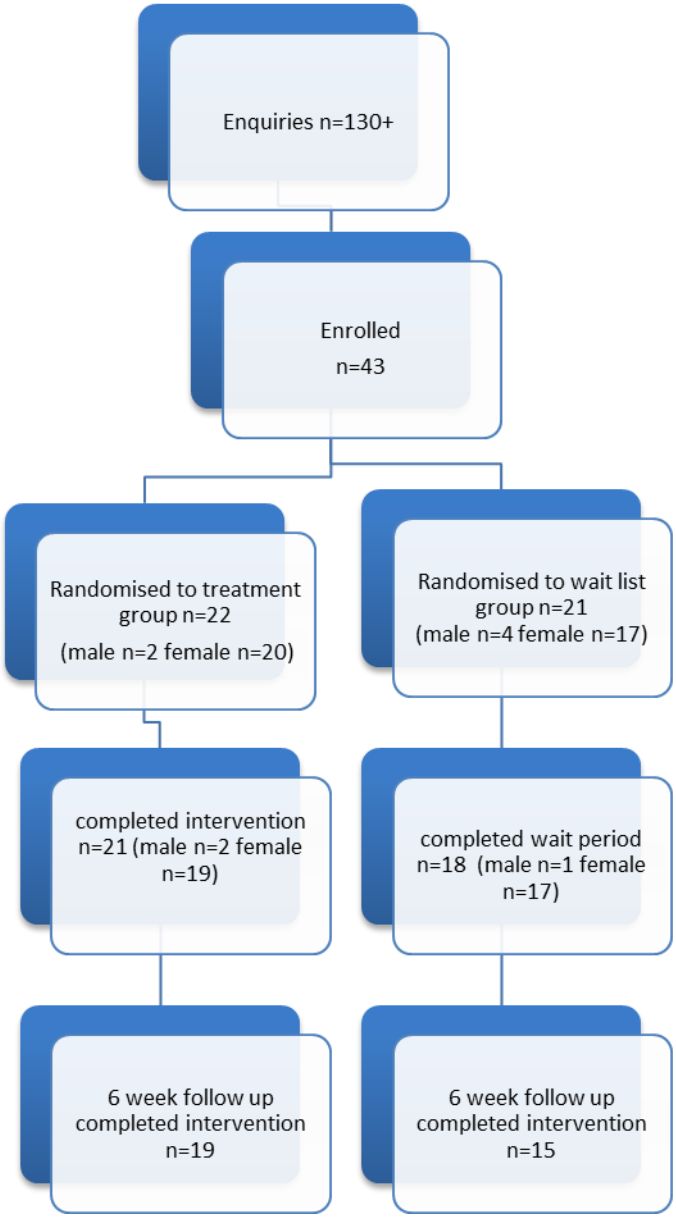
Bender et al. (2011) recommended that in studies managing pain via the internet, fuller description of all participants who chose to withdraw was desirable. In this study, a very good retention rate was achieved in both arms of the study at both study completion (95% and 81% retention in treatment and control, respectively) and 6-week follow-up (95% and 68% retention in treatment and control, respectively). A detailed description of all participants who withdrew from the study at different time points was documented and is summarised in Fig 7.1. Forty three participants who met the study eligibility criteria were given a study number and randomised to one or other group.

Prior to commencing the study, two participants withdrew. One gentleman had problems with his laptop, was unemployed and felt he could not guarantee that he would have access to the internet for the duration of the study. The second, a female, withdrew prior to commencement as she stated that her family had had a bereavement and she did not feel she would be sufficiently focused to commit to filling in the surveys each Sunday for seven consecutive weeks. Nineteen participants from the wait list group completed all seven surveys over the six weeks. The results from one participant could not be used however. Despite a letter from his doctor stating that he satisfied the eligibility criteria for the study, the gentleman wrote in the space provided for comments at the end of the final survey that he only suffered intermittently with migraine and that he had subsequently made up some of the responses. At the six week follow up a further three people did not complete their survey. One

of these contacted the researcher to explain that she was on holidays and her phone was the only internet she had access to. The survey software would not accept any responses past question three and her attempts to complete it were logged on the survey analysis software. No contact was made by the other two participants to state why they had not completed the follow up survey.

In the Intervention group, one person withdrew on day fourteen of the intervention saying that her son was getting married and she did not think she would have the time or the concentration for the study. The remaining twenty-one participants completed all surveys up to and including the follow-up survey in week six. In the six week follow up two individuals from the group did not complete the survey. One did not say why and the other contacted the researcher later to say they had been ill with a severe chest infection and had not been monitoring their emails and had forgotten about the survey.

Figure 7.1. CONSORT diagram showing participant flow through the RCT .



Baseline Measurements

Multiple participant measurements were taken prior to the intervention. To determine if there was evidence of a trend in HDI/PCS etc. prior to receiving the intervention, the change from baseline to Time 14 was calculated for each outcome of interest for each participant. Any change would have indicated a change essentially not due to treatment and that trend might have continued on.

Table 7.1: MAAS Case Summaries Days 1 and 84

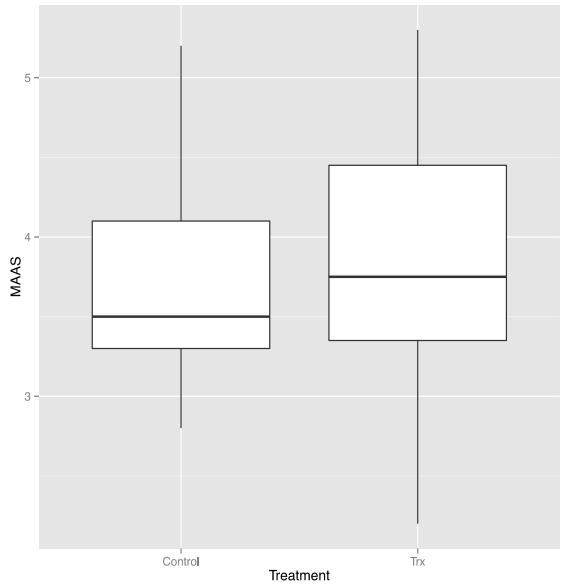
Case Summaries

Group	Time	N	Mean	Median	Minimum	Maximum	Std. Deviation
Control	1	18	3.72	3.50	3	5	.674
	84	15	3.51	3.70	1	5	.886
Treatment	1	22	3.79	3.75	2	5	.868
	84	19	3.86	3.90	2	5	.699

Mindfulness Attention Awareness Scale MAAS

At baseline, the average MAAS score of individuals in the Control group was 3.72, while the average in the treatment group was 3.79 (Table 7.1). The median MAAS score in the Control and Treatment groups was 3.5 and 3.75 respectively (Fig 7.2). There was slightly more variability in the MAAS score in the Treatment versus Control group (Std. dev = 0.868 versus 0.674). A boxplot of the MAAS scores indicated that there were no obvious outlying observations.

Fig 7.2 Median MAAS scores at baseline



The Shapiro-Wilk test of normality provided evidence that the data were normally distributed in each group.

Control:

Shapiro-Wilk normality test

W = 0.9242, p-value = 0.1537

Treatment:

Shapiro-Wilk normality test

W = 0.9528, p-value = 0.358

As a result, to test for significant differences between the average MAAS scores in both groups, a two-sample t-test was performed.

Two Sample t-test

t = -0.2787, df = 38, p-value = 0.782

95 percent confidence interval:

-0.5759936 0.4365997

The above t-test indicated that there was no evidence of a significant difference between the average MAAS scores in both groups at baseline.

MAAS Time 1 Vs Time 84:

To determine if there was a significant difference between the MAAS scores at baseline versus 6-week follow-up across groups, the changes in MAAS score at Time 1 vs Time 84 were calculated. (Table 7.2).

Table 7.2: Comparison of MAAS change in score between Time 1 and Time 84

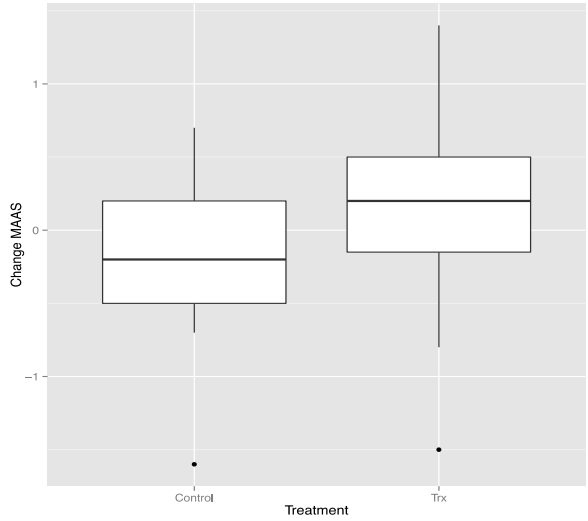
Case Summaries

Group	Time	N	Mean Change	Median	Minimum	Maximum	Std. Deviation
Control	1vs84	15	-0.21	-0.2	-1.6	0.7	0.578
Treatment	1vs84	19	0.09	0.2	-1.5	1.4	0.642

The mean change in the Control group was a decrease of 0.21 in MAAS score, while the mean change in the Treatment group was an increase of 0.09 in MAAS score.

A Shapiro-Wilk test of normality indicated that the change in MAAS scores were normally distributed in both groups and thus a t-test was carried out to test for differences between the mean change in MAAS scores across groups.

Fig. 7.3 Differences between mean change in MAAS scores across groups Time 1 vs Time 84.



Two Sample t-test

t = -1.4203, df = 32, p-value = 0.1652

95 percent confidence interval:

-0.7336494 0.1308424

The above t- test indicated that there was no evidence of a significant difference between the average change in MAAS scores in both groups between baseline and 6-week follow-up (Fig. 7.3).

Table 7.3: HDI Case Summaries Data on Days 1, 14, 28, 42 and 84

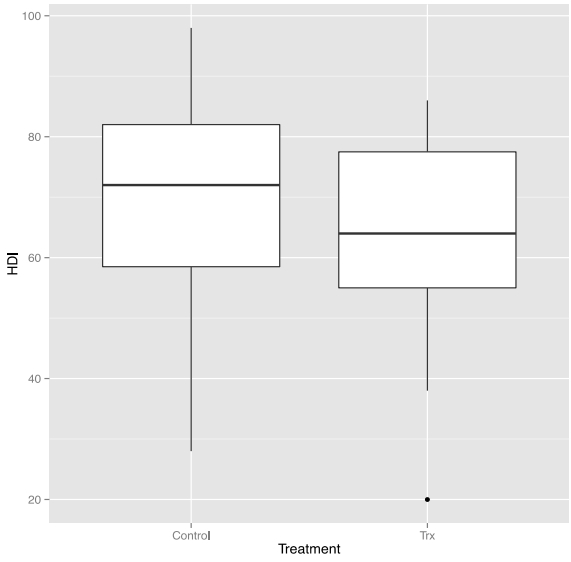
Case Summaries

Group	Time	N	Mean	Median	Minimum	Maximum	Std. Deviation
Control	1	18	68.89	72.00	28	98	19.381
	14	18	60.67	64.00	10	98	23.754
	28	18	54.78	56.00	12	98	24.754
	42	18	66.89	69.00	6	98	25.642
	84	15	61.87	60.00	22	98	24.628
Treatment	1	22	62.73	64.00	20	86	17.376
	14	22	56.64	60.00	14	94	19.434
	28	21	41.81	46.00	0	78	23.254
	42	21	40.10	50.00	0	82	26.657
	84	19	25.37	22.00	0	60	20.881

HDI

The average HDI value of individuals in the Control group at Time 1 was 68.89, while the average in the Treatment group was 62.73 (Fig. 7.4). The median HDI value in the Control and Treatment groups was 72 and 64 respectively. There was slightly more variability in the HDI values in the Control versus Treatment group (Std. dev = 19.381 versus 17.376) (Table 7.3). A boxplot of the HDI values indicated that there was a single outlying observation in the Treatment group, with a very low HDI value of 20 (Study number = 38). The outliers were included because they are real data. The mean and the median were approximately the same so removing these values would have had no impact.

Fig. 7.4 Average HDI values at Time 1.



The Shapiro-Wilk test of normality provided evidence that the data were normally distributed in each group.

Control:

Shapiro-Wilk normality test

W = 0.9592, p-value = 0.5

Treatment:

Shapiro-Wilk normality test

W = 0.9381, p-value = 0.1808

To test for significant differences between the average HDI values in both groups, a two-sample t-test was performed (assuming equal variances):

Two Sample t-test

t = 1.0594, df = 38, p-value = 0.2961

95 percent confidence interval:

-5.612656 17.935888

indicating that there was no evidence of a significant difference between the average HDI values in both groups at baseline.
The difference between HDI scores at Time 1 and Time 14 were calculated for each patient to determine if there was any change in HDI prior to receiving the intervention (Table 7.4). On average there was a drop in HDI score in both groups; a drop of 3.22 on average in the Control group and 6.09 on average in the Treatment group. A two-sample t-test indicated that there was no significant difference between the mean change in HDI from Time 1 to Time 14 across groups (Fig 7.5).

Table 7.4: Changes in HDI between Time 1 and Time 14

Case Summaries

Group	Time	N	Mean	Median	Minimum	Maximum	Std. Deviation
Control	1vs14	18	-3.22	-2	-22	20	10.957
Treatment	1vs14	22	-6.09	-2	-28	14	11.22

Two Sample t-test

t = 0.8129, df = 38, p-value = 0.4213

95 percent confidence interval:

-4.275243 10.012617

Fig. 7.5 HDI Differences Time 1 to Time 14

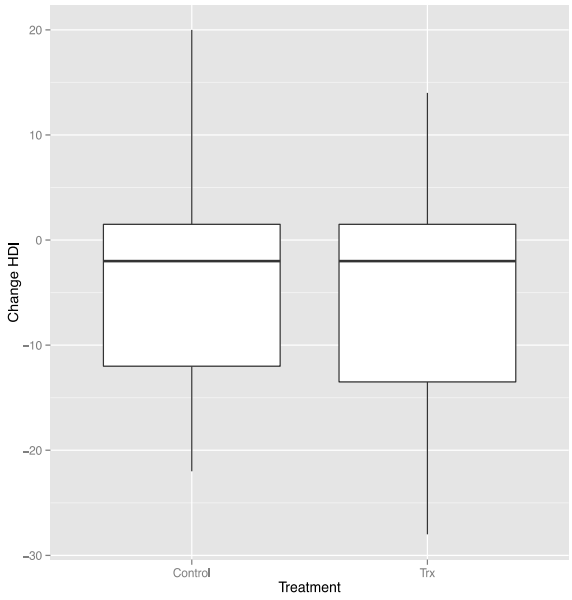


Table 7.5 PCS Case Studies Data on Days 1, 14, 28, 42 and 84

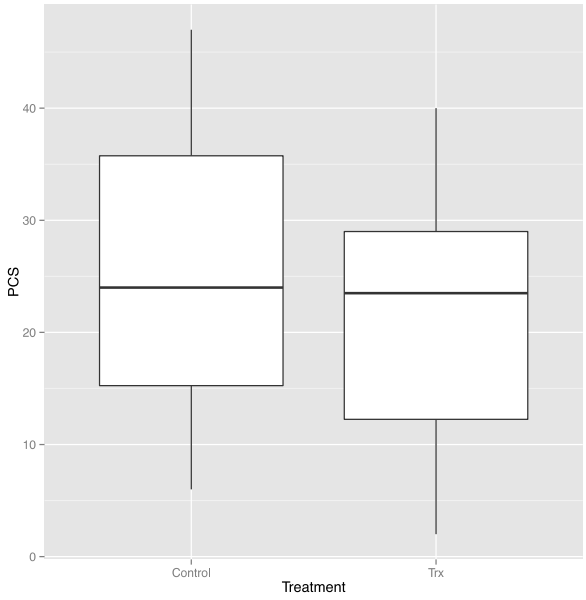
Case Summaries

Group	Time	N	Mean	Median	Minimum	Maximum	Std. Deviation
Control	1	18	24.83	24.00	6	47	12.215
	14	18	23.72	22.00	6	57	14.303
	28	18	19.83	19.00	1	44	13.391
	42	18	23.33	27.50	0	42	13.065
	84	15	25.47	33.00	5	48	17.016
Treatment	1	22	21.41	23.50	2	40	11.529
	14	22	18.86	19.00	1	36	10.701
	28	21	14.33	13.00	0	51	12.072
	42	21	11.29	9.00	0	33	10.243
	84	19	7.58	4.00	0	36	9.076

PCS

The average PCS value of individuals in the Control group at Time 1 was 24.83, while the average in the Treatment group was 21.41. The median PCS value in the Control group was 24 and in the Treatment group was 23.5. There was slightly more variability in the PCS values in the Control versus Treatment group (Std. dev = 12.215 versus 11.529) (Table 7.5). A boxplot of the PCS values (Fig 7.6) indicated that there were no outlying observations in either group.

Fig. 7.6. Average PCS values at Time 1



The Shapiro-Wilk test of normality provided evidence that the data were normally distributed in each group.

Control:

Shapiro-Wilk normality test

W = 0.9434, p-value = 0.3316

W = 0.952, p-value = 0.3451

To test for significant differences between the average PCS values in both groups, a two-sample t-test was performed.

Two Sample t-test

t = 0.9099, df = 38, p-value = 0.3686

95 percent confidence interval:

-4.194098 11.042583

which indicated that there was no evidence of a significant difference between the average PCS values in both groups at baseline.

The difference between PCS scores at Time 1 and Time 14 (Table 7.6) were calculated for each patient to determine if there was any change in PCS prior to receiving the intervention. On average there was a drop in PCS scores in both groups; a drop of 1.11 on average in the Control group and 2.55 on average in the Treatment group. A two-sample t-test indicated that there was no significant difference between the mean change in PCS from Time 1 to Time 14 across groups (Fig 7.7).

Table 7.6. Differences in PCS scores Time 1 to Time 14

Case Summaries

Group	Time	N	Mean	Median	Minimum	Maximum	Std. Deviation
Control	1vs14	18	-1.11	-1	-15	17	6.462
Treatment	1vs14	22	-2.55	-3.5	-11	5	5.012

TTwo Sample t-test

t = 0.7909, df = 38, p-value = 0.4339

95 percent confidence interval:

- 1.111111 -2.545455

Fig.7.7 Mean change in PCS from Time 1 to Time 14 prior to intervention

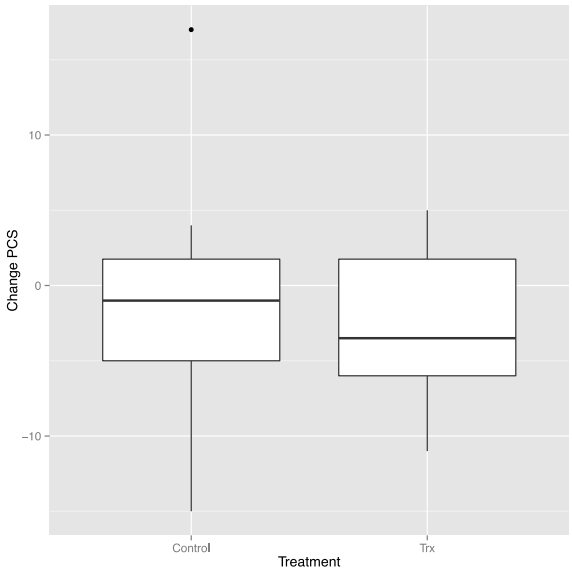


Table 7.7. Mg of Medication on days 7,14,21,28,35,42 and 84

Case Summaries

Group	Time	N	Mean	Median	Minimum	Maximum	Std. Deviation
Control	7	18	1206.11	750.00	0	5620	1660.563
	14	18	764.22	85.00	0	5040	1290.390
	21	17	1137.71	15.00	0	5840	2017.693
	28	18	1185.19	275.00	0	6165	1855.110
	35	17	1024.18	100.00	0	5000	1640.518
	42	18	1039.61	55.00	0	5800	1901.670
	84	15	471.83	50.00	0	2000	723.057
Treatment	7	22	1005.36	175.00	0	8223	1915.158
	14	22	650.05	29.00	0	4520	1288.786
	21	21	976.90	.00	0	15000	3302.226
	28	21	470.10	8.00	0	3000	865.611
	35	21	529.33	50.00	0	3000	861.993
	42	21	660.29	.00	0	5000	1452.413
	84	19	376.95	.00	0	4000	936.835

MG of Medication

Time 7:

Time 7 was the first time that the mg medication used was measured for each patient. Thus baseline for this outcome variable was Time 7 rather than Time 1 as for other outcomes of interest. The average amount of medication of individuals in the Control group at Time 7 was 1206.11mg, while the average in the Treatment group was 1005.36 (Fig 7.8). The median amount of medication in the Control group was 750mg and in the Treatment group was 175mg. 25% of participants in the control group used 34.5mg (Q1) or less of medication compared with 1.25mg or less in the Treatment group (Table 7.7). In addition, 75% of participants in the Control group used 1767.25mg or less (Q3) of medication at baseline versus 1000mg in the Treatment group. There was more variability in the amount of medication in the Control versus Treatment group (IQR = 1732.74mg versus 998.75mg). A boxplot of the amount of medication values indicated that there was a number of outlying observations in both groups, with participants 9, 14 and 28 in the Treatment group using 2875, 4000 and 8223mg of medication respectively, and participants 35 and 30 in the Control group using 5000 and 5620mg of medication respectively. Medication in mg at baseline for both groups is illustrated in Fig. 7.9.

Control

Q1	Q2	Q3	IQR
34.50	750.00	1767.25	1732.74

Treatment

Q1	Q2	Q3	IQR
1.25	175.00	1000.00	998.75

Fig. 7.8 Average medication in mg at baseline in both groups

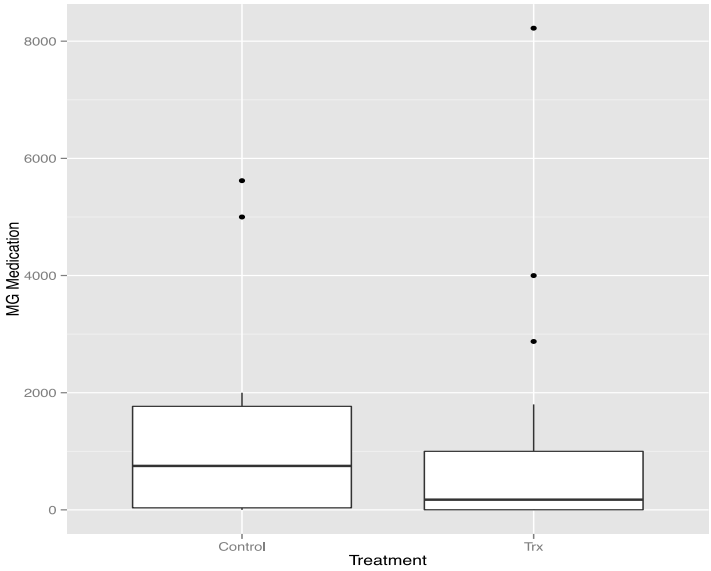
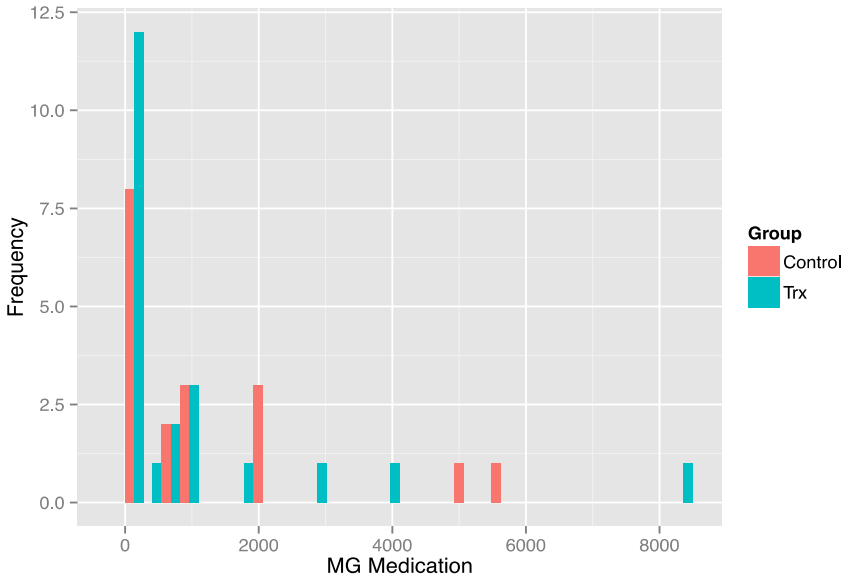


Fig. 7.9 Medication in mg at baseline for both groups



The Shapiro-Wilk test of normality provided evidence that the data were not normally distributed in each group (p-value < 0.05).

Control:

Shapiro-Wilk normality test

W = 0.7274, p-value = 0.0001

Treatment:

Shapiro-Wilk normality test

W = 0.5844, p-value = 9.055

Since the data were not normally distributed, the non-parametric equivalent of a two-sample t-test (the Wilcoxon rank sum test) was carried out to test for differences between the medians in both groups:

Wilcoxon rank sum test with continuity correction

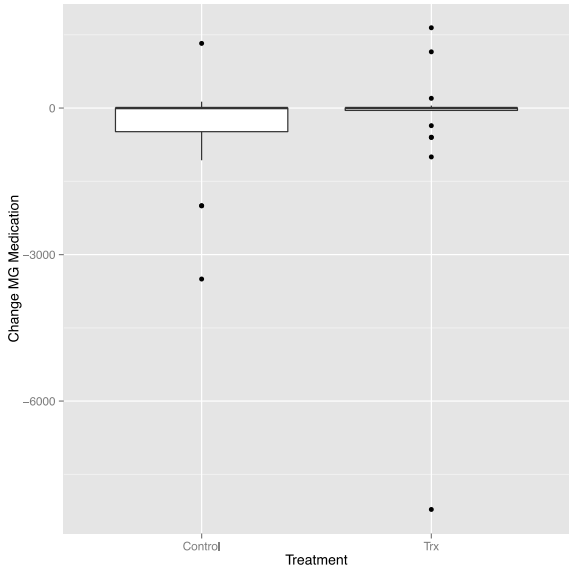
W = 232.5, p-value = 0.3514

which indicated that there was no evidence of a significant difference between the median amount of medication usage between both groups at baseline.

To examine if there were differences in the amount of medication used prior to the intervention, the changes in mg of medication used between Time 7 and Time 14 were calculated (Fig 7.10). The majority of participants exhibited small changes in the amount of medication used prior to the intervention. One patient in the Treatment group had a very large drop in mg of medication between the two time points (Study number = 28). Several participants in the Control group also exhibited a large drop in the amount of medication used; Study number 7 and 27 had a drop of 2000mg,

Study number 35 had a drop of 3500mg and Study number 39 had a drop of 1069mg from Time 7 to Time 14. The median change in mg of medication was 0 in both groups and the corresponding Wilcoxon test showed that there was no evidence of a difference between the median change in medication usage across the two groups.

Fig. 7.10 Changes in mg of medication prior to intervention



Wilcoxon rank sum test with continuity correction

W = 175, p-value = 0.53

Baseline Measurements Summary

The change from baseline to Time 14 for each outcome measure was assessed to determine if there was evidence of a trend prior to receiving the intervention across all outcomes. There was no change indicating that any changes post Time 14 were most likely due to treatment.

Table 7.8: Number of Migraines on days 7, 14, 21 28, 35, 42 and 84

Case Summaries

Group	Time	N	Mean	Median	Minimum	Maximum	Std. Deviation
	7	18	2.44	2.00	0	14	3.110
	14	18	2.06	1.00	0	14	3.171
	21	17	2.06	1.00	0	14	3.325
Control	28	18	2.06	1.00	0	12	2.711
	35	17	1.18	1.00	0	3	1.131
	42	18	1.56	1.00	0	5	1.338
	84	15	1.13	1.00	0	3	.915
	7	22	2.14	2.00	0	7	1.807
	14	22	1.73	1.00	0	7	1.609
	21	21	1.33	1.00	0	5	1.317
Treatment	28	21	1.29	1.00	0	3	.902
	35	21	1.19	1.00	0	3	1.078
	42	21	.67	.00	0	3	.856
	84	19	.95	1.00	0	3	.970

Number of Migraines

The median number of migraines at baseline is illustrated in Fig 7.11 and the number of migraines at baseline in Figure 7.12. Case summaries presented in Table 7.8 To examine if there were differences in number of migraines (Fig 7.13) prior to the intervention, the changes in the number of migraines between Time 7 and Time 14 were calculated. Six participants in the Treatment group and seven participants in the Control group had no change in the number of migraines Seven participants in the Treatment group had one less migraine at Time 14 versus Time 7, while a further four participants in that group had two less migraines. Four participants in that group had one additional migraine and one participant had two additional migraines. Similarly in the Control group, two participants had one less migraine, three participants had two less migraines and one patient had four fewer migraines. Five participants in that group had one additional migraine. A Wilcoxon test provided evidence that there was no significant difference between the change in the number of migraines between Time 7 and Time 14 across groups.

Time 7:

Control

Q1	Q2	Q3	IQR
1.00	2.00	2.75	1.75

Trx

Q1	Q2	Q3	IQR
1.0	2.00	2.75	1.75

Time 14:

Control

Q1	Q2	Q3	IQR
1.00	1.00	2.00	1.00

Trx

Q1	Q2	Q3	IQR
1.00	1.00	2.00	1.00

Fig. 7.11 Median number of migraines at baseline

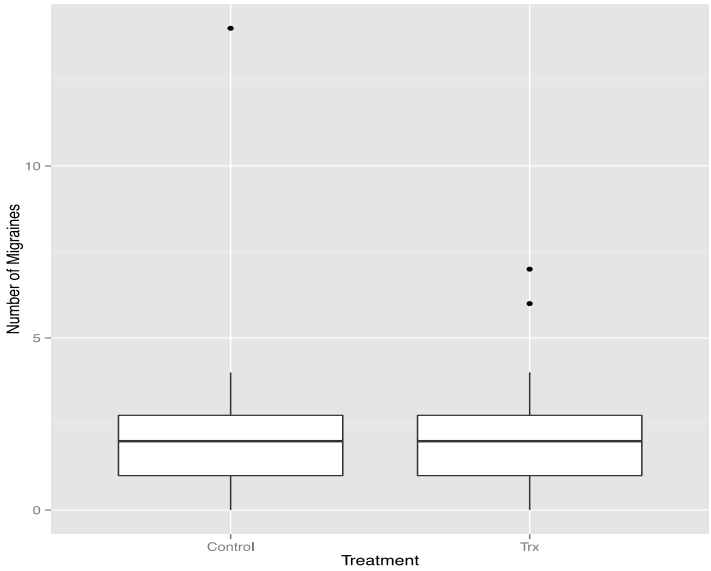
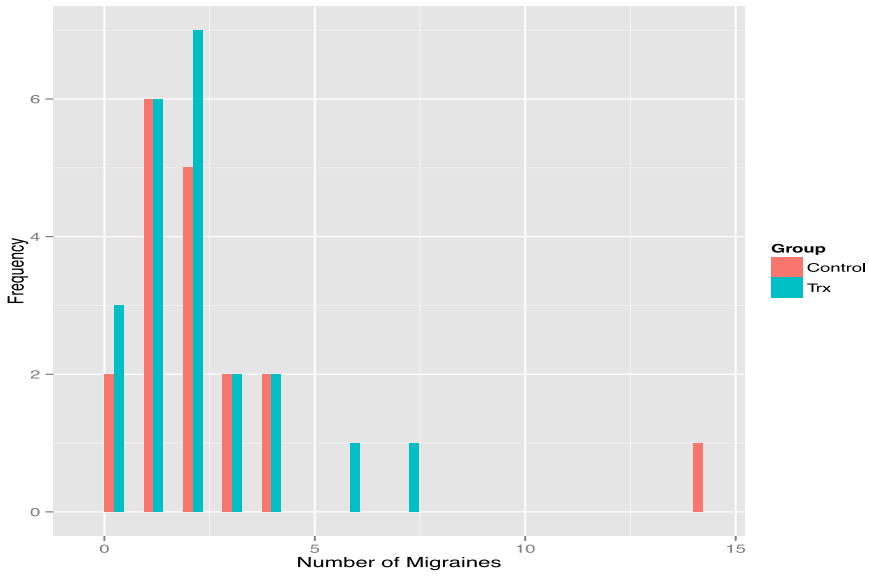


Fig. 7.12 Number of migraines at baseline



The Shapiro-Wilk test of normality provided evidence that the data were not normally distributed in each group.

Control:

Shapiro-Wilk normality test

W = 0.5939, p-value = 5.889

Treatment:

Shapiro-Wilk normality test

W = 0.8608, p-value = 0.005298

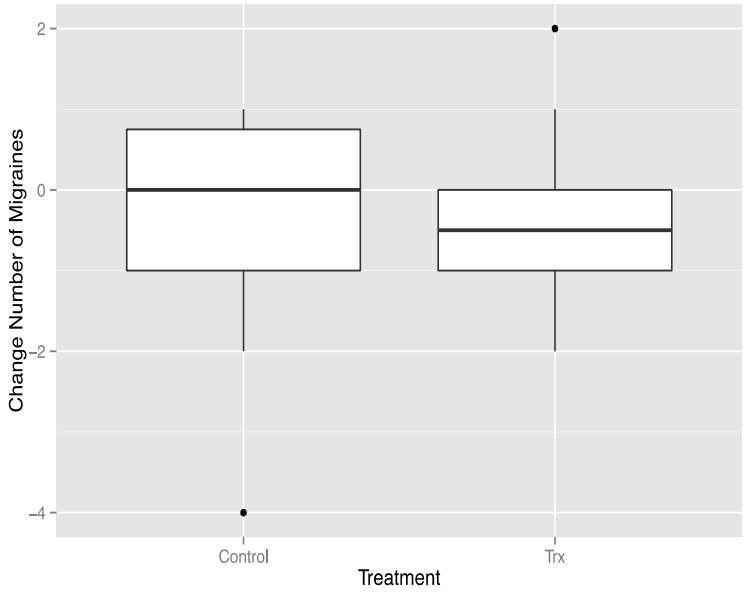
The Wilcoxon rank sum test was carried out to test for differences between the medians in both groups:

Wilcoxon rank sum test with continuity correction

W = 195.5, p-value = 0.9553

which indicated that there was no evidence of a significant difference between the median number of migraines between both groups at baseline.

Fig. 7.13 Change in number of migraines Time 7 to Time 14



Wilcoxon rank sum test with continuity correction

W = 214, p-value = 0.6635

Table 7.9: Total Hours of Migraine Days 7,14,21,28,35,42 and 84

Case Summaries

Group	Time	N	Mean	Median	Minimum	Maximum	Std. Deviation
Control	7	18	21.78	12.00	0	72	24.383
	14	18	13.94	10.00	0	48	15.795
	21	17	11.53	9.00	0	72	17.099
	28	18	12.61	7.50	0	48	13.307
	35	17	11.29	3.00	0	96	23.064
	42	18	21.72	14.00	0	72	21.616
	84	15	24.40	8.00	0	144	42.332
Treatment	7	22	21.68	12.50	0	88	24.631
	14	22	14.14	11.00	0	48	11.319
	21	21	14.29	7.00	0	70	18.612
	28	21	13.38	6.00	0	48	14.326
	35	21	13.52	4.00	0	120	25.922
	42	21	5.81	.00	0	48	11.138
	84	19	7.37	2.00	0	48	13.095

Hours of Migraine

Time 7 was also the baseline for this outcome variable (Fig 7.15). The average number of hours of migraines of individuals in the Control group at Time 7 was 21.78, while the average in the Treatment group was 21.68. Again, the median and IQR are the most appropriate measures of location and spread for these data. Case summaries for each time point are presented in Table 7.9.The median number of hours of migraine in the Control group was 12 and in the Treatment group was 12.5 (Fig. 7.14). 25% of participants in the Control group had 8 hours or fewer of migraine at baseline (Q1), compared with 6.25 hours or fewer in the Treatment group. 75% of participants in the Control group had 25.5 hours or fewer of migraine at that time, with 75% of participants in the Treatment group having 26 hours or fewer. The IQR in the Control group was 17.5 and the IQR in the Treatment group was 19.75, indicating slightly more variability in the number of hours of migraine in the Treatment group. Three participants (Study numbers 22, 42, 45) in the Control group had a very high number of hours of migraine, recording a value of 72 hours each. Three participants in the Treatment group also had very high number of hours of migraine, recording values of 88 (Study number 6), 72 (Study number 47) and 62 (Study number 32).

Time 7:

Control

Q1	Q2	Q3	IQR
8.0	12.0	25.5	17.5

Trx

Q1	Q2	Q3	IQR
6.25	12.50	26.00	19.75

Time 14:

Control

Q1	Q2	Q3	IQR
1.75	10.00	17.50	15.75

Trx

Q1	Q2	Q3	IQR
6.25	11.00	20.00	13.75

Fig. 7.14 Median number of hours of migraine at Time 7

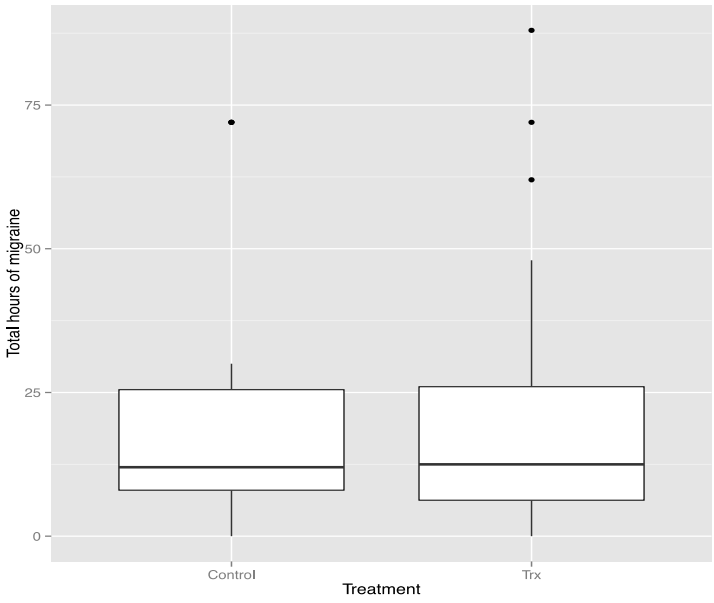
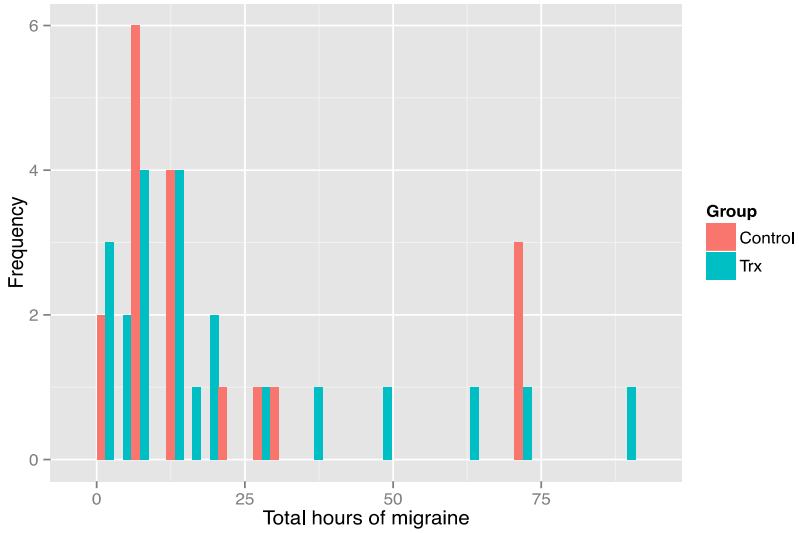


Fig. 7.15 Frequency of migraine hours at Time 7



The Shapiro-Wilk test of normality provided evidence that the data were not normally distributed in each group.

Control:

Shapiro-Wilk normality test

W = 0.7142, p-value = 0.0001172

Treatment:

Shapiro-Wilk normality test

W = 0.7858, p-value = 0.0003021

The Wilcoxon rank sum test was carried out to test for differences between the medians in both groups:

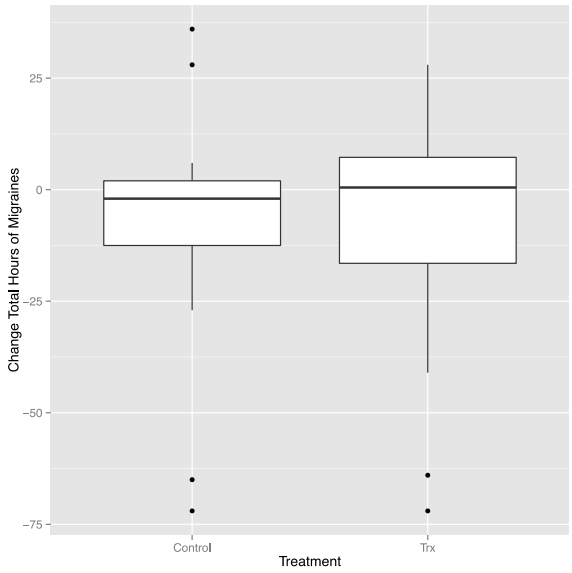
Wilcoxon rank sum test with continuity correction

W = 208, p-value = 0.7954

which indicated that there was no evidence of a significant difference between the median number of hours of migraine between both groups at baseline.

To examine if there were differences in the total hours of migraine prior to the intervention, the changes in the total hours of migraine between Time 7 and Time 14 were calculated (Fig 7.16). Nine participants in the Treatment group experienced a decrease in the total hours of migraine, while ten participants in the Control group experienced a decrease. The largest decreases were experienced by participants with study numbers 6 and 47 (Treatment group) and participants with study numbers 45 and 22 (Control group). Eleven participants in the Treatment group experienced an increase in the number of hours of migraine, while eight participants in the Control group experienced an increase. A Wilcoxon test provided evidence that there was no significant difference between the change in the total hours of migraine between Time 7 and Time 14 across groups.

Fig. 7.16 Change in hours of migraine from Time 7 to Time 14 (prior to intervention).



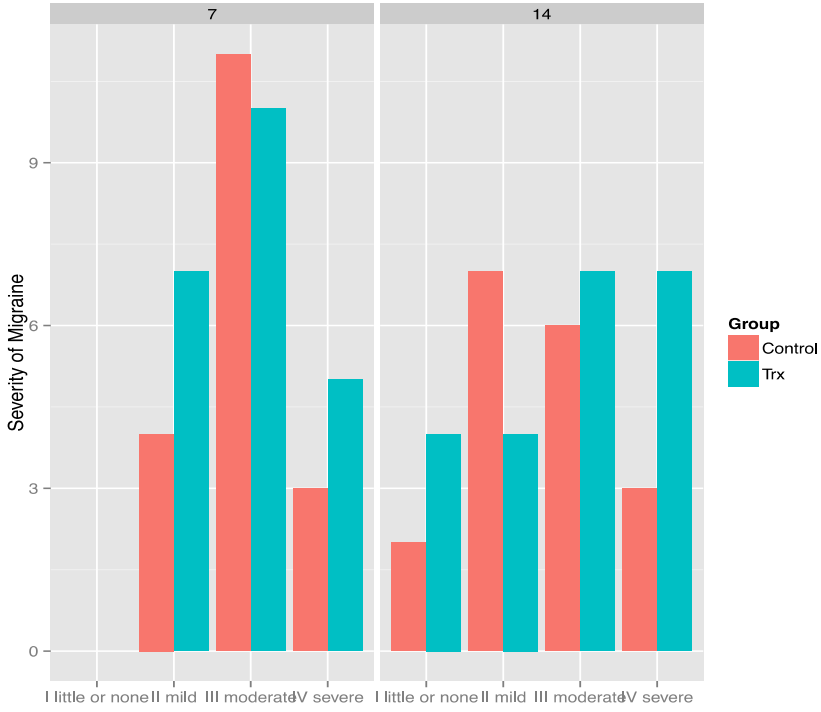
Severity of migraine

To assess whether there was a change in severity of migraines irrespective of treatment, severity of migraine at Time 7 was compared with Time 14 (Fig. 7.17). 22.2% (4 participants), 61.1% (11 participants), 16.7% (3 participants) of participants in the Control group had mild, moderate and severe migraine symptoms respectively at baseline (Time 7) compared with 31.8% (7 participants), 45.5% (10 participants) and 22.7% (5 participants) respectively in the Treatment group. At Time 14, there were changes evident in the proportions of participants with different severity of migraine in both groups. In the Control group, 11.1% (2 participants) of participants had little or no symptoms, 38.9% (7 participants) had mild symptoms, 33.3% (6 participants) had moderate symptoms and 16.7% (3 participants) had severe symptoms. In the Treatment group, 18.2% (4 participants) had little or no symptoms, 18.2% (4 participants) had mild symptoms, 31.8% (7 participants) had moderate symptoms and 31.8% (7 participants) had severe symptoms. The majority (17) of the 26 participants whose severity of symptoms changed across the two time-points had a reduction in severity (2 participants' symptoms changed from severe to moderate, 8 participants' symptoms changed from moderate to mild, 3 participants' symptoms changed from mild to little or none, 1 patient's symptoms changed from moderate to little or none and 1 patient's symptoms changed from severe to mild, 2 participants' symptoms changed from severe to little or none). 3 participants' symptoms worsened from moderate to severe, 2 participants worsened from mild to moderate, and a further 4 participants worsened from mild to severe. These results are illustrated in Table 7.10 and Fig. 7.17 .

Table 7.10 Change in severity of migraine between Time 7 and Time 14

		Time 7	Time 14
Treatment	**I little or none**	**0** **0%**	**4** **18%**
	II mild	**7** **32%**	**4** **18%**
	III moderate	**10** **45%**	**7** **32%**
	IV severe	**5** **23%**	**7** **32%**
Control	**I little or none**	**0** **0%**	**2** **11%**
	II mild	**4** **22%**	**7** **39%**
	III moderate	**11** **61%**	**6** **33%**
	IV severe	**3** **17%**	**3** **17%**

Fig. 7.17 Change in severity of migraine Time 7 (pre-treatment baseline) to Time 14 (day treatment commences)



Baseline Measurements Summary

The change from baseline to Time 14 for each outcome measure was assessed to determine if there was evidence of a trend prior to receiving the intervention across all outcomes. There was no evidence of a statistically significant change, indicating that any changes post Time 14 were most likely due to treatment.

Correlational Data

A series of analyses were undertaken to determine correlations between values to assess the strength of the relationship between variables.

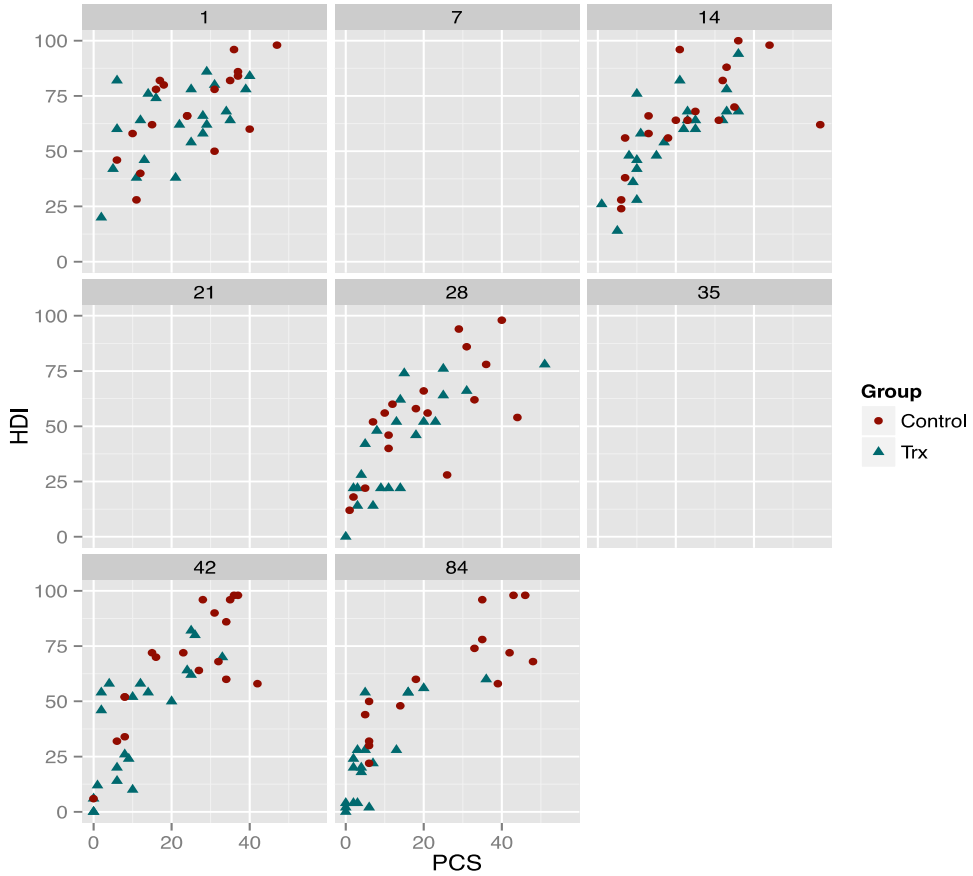
PCS and HDI

To determine if PCS was correlated with HDI (as hypothesized in thesis), a scatterplot of both scores at each time point (Time 1, 14, 28, 42, 84) for both the Control group and Treatment group was created (Fig 7.18). The scatterplot shows that there is an increasing linear trend at all time points and this trend is evident in both groups. The correlation between both scores was then calculated at each time point and the correlation coefficients and corresponding p-values are given below:

	Group	Time	cor	pvalue
1	Control	1	0.651	0.003
2	Control	14	0.645	0.004
3	Control	28	0.710	0.001
4	Control	42	0.765	0.0001
5	Control	84	0.843	0.0001
6	Trx	1	0.535	0.010
7	Trx	14	0.772	0.0001
8	Trx	28	0.777	0.0001
9	Trx	42	0.763	0.0001
10	Trx	84	0.774	0.0001

All of the correlation coefficients are positive, indicating a strong positive linear relationship between PCS and HDI (i.e. as catastrophizing score increases, the headache disability score also increases). All correlation coefficients are also highly significant (p-values < 0.05), which provides evidence that there is a significant positive linear relationship between PCS and HDI in both the Control and Treatment groups at all time points.

Fig. 7.18 HDI and PCS



PCS and MAAS:

To determine if PCS was correlated with MAAS, a scatterplot of both scores at each time point (Time 1, 14, 28, 42, 84) for both the Control group and Treatment group was created (Fig 7.19). The scatterplot shows that there is decreasing linear trend, particularly at the early time points and this trend is evident in both groups. The correlation between both scores was then calculated at each time point and the correlation coefficients and corresponding p-values are given below:

	Group	Time	cor	pvalue
1	Control	1	-0.507	0.032
2	Control	14	-0.469	0.050
3	Control	28	-0.245	0.326
4	Control	42	-0.408	0.093
5	Control	84	-0.592	0.020
6	Trx	1	-0.403	0.063
7	Trx	14	-0.383	0.079
8	Trx	28	-0.169	0.464
9	Trx	42	-0.173	0.453
10	Trx	84	-0.059	0.815

All of the correlation coefficients are negative, indicating a negative linear relationship between PCS and MASS (i.e. as pain catastrophizing score increases, the mindful awareness score decreases). Only the correlation coefficients for Time 1, Time 14 and Time 84 in the Control group are statistically significant (p-values < 0.05), which provides evidence that there is a significant

negative linear relationship between PCS and MAAS in the Control group at those time-points.

HDI and MAAS

To determine if HDI was correlated with MAAS, a scatterplot of both scores at each time point (Time 1, 14, 28, 42, 84) for both the Control group and Treatment group was created (Fig 7.20). The scatterplot shows that there is decreasing linear trend, particularly at the early time points and this trend is evident in both groups. The correlation between both scores was then calculated at each time point and the correlation coefficients and corresponding p-values are given below:

	Group	Time	cor	pvalue
1	Control	1	-0.172	0.494
2	Control	14	-0.471	0.049
3	Control	28	-0.148	0.557
4	Control	42	-0.492	0.038
5	Control	84	-0.577	0.024
6	Trx	1	-0.329	0.135
7	Trx	14	-0.488	0.021
8	Trx	28	-0.140	0.545
9	Trx	42	-0.192	0.405
10	Trx	84	0.074	0.769

Almost all of the correlation coefficients are negative, indicating a negative linear relationship between headache disability score and mindful awareness score. Only the correlation coefficients for Time 14, Time 42 and Time 84 in the Control group are statistically

significant (p-values < 0.05), which provides evidence that there is a significant negative linear relationship between HDI and MAAS in the Control group at those time-points. Similarly, the correlation coefficient for Time 14 in the Treatment group is statistically significant, indicating that there is evidence of a significant negative linear relationship between HDI and MASS in the Treatment group at that time-point.

Fig. 7.19 MAAS and PCS across time

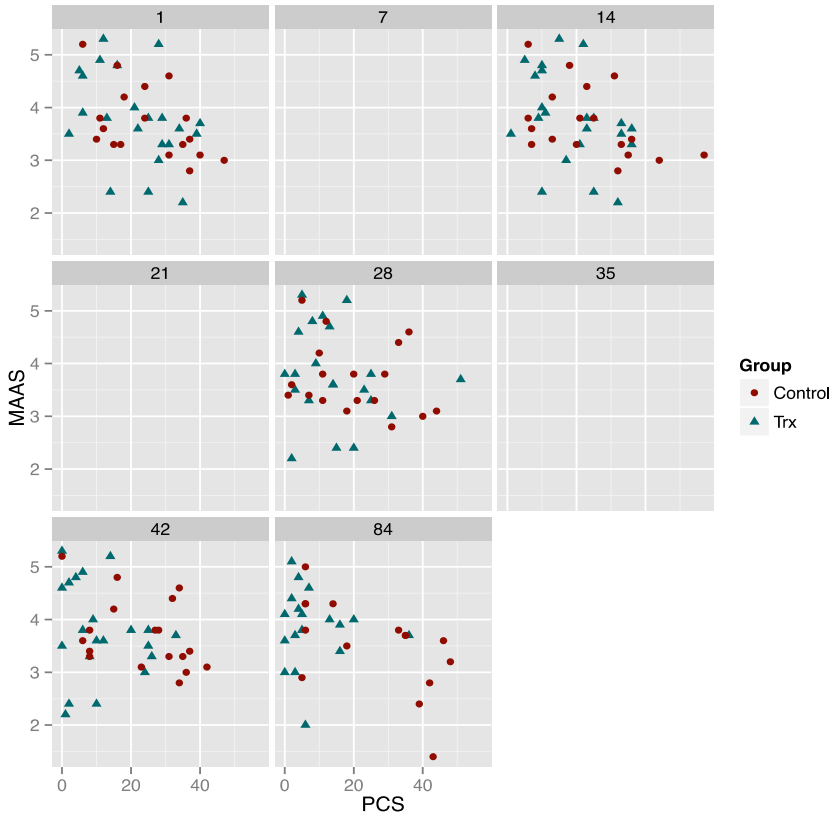
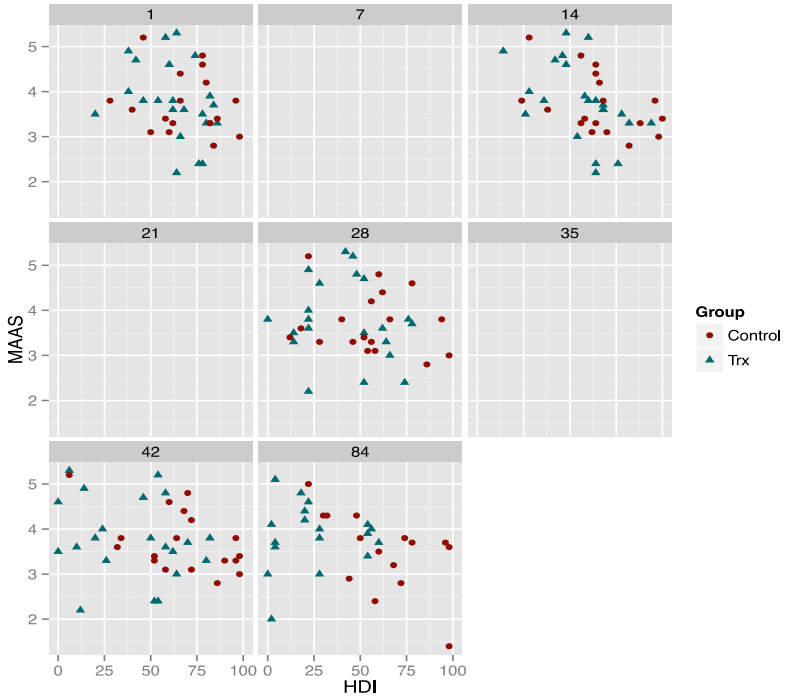


Fig. 7.20 MAAS and HDI across time



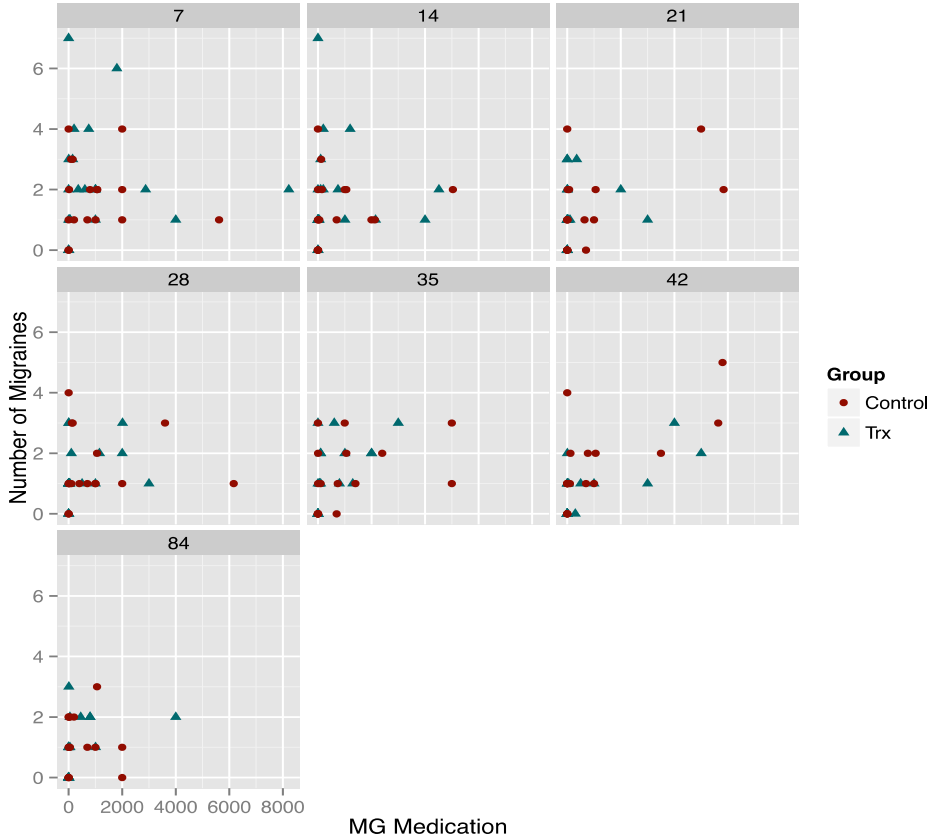
Number of Migraines and Medication Consumption

The change in the number of migraines at 6 week follow up versus Time 14 (last time point prior to intervention) was calculated (Fig 7.21). The median change in number of migraines in the Control group at 6 week follow up (Time 84) vs baseline was 0, while the median change in the Treatment group at 6 week follow up vs Time 14 was a decrease of 1 migraine per week. 11 (out of 19) participants in the treatment group experienced a reduction in the number of migraines, three subjects experienced an increase and five subjects experienced no change in the number of migraines. Five out of the 15 subjects in the Control group experienced a decrease in the number of migraines, four experienced an increase in the number of migraines and six had no change. A Shapiro-Wilk normality test indicated that the change in number of migraines in both groups were not normally distributed, thus a Wilcoxon test was performed to test for differences between the medians in both groups. This test suggested that there was no evidence of a significant difference between the change in the number of migraines between groups (p-value = 0.34).

To determine if the reduction in the number of migraines was attributed to an increase in medication usage, the correlation between the number of migraines and amount of medication consumption was investigated. A negative correlation coefficient would indicate that the number of migraines was decreasing due to an increase in the amount of medication used. Initially, it can be seen that there is a significant positive relationship between medication and number of migraines (i.e. as the number of migraines increases the mg medication also increases) at almost all time points in both groups. In addition, a number of large outliers can be seen which may affect the results (Study number 35 had 14 migraines at Time 7, 14 and 21 and 12 migraines at Time 28; Study

number 6 used 15000mg medication at Time 21). Thus, these large outliers were removed and the correlation coefficients recalculated. The results showed a significant relationship between number of migraines and amount of medication consumed at Time 42 in the Control group and Time 35 and 42 in the Treatment group. Again, these coefficients were positive indicating that any reduction in the number of migraines was not associated with the amount of medication used.

Fig. 7.21 Number of migraines and amount of medication



Total Hours of Migraine and Medication Consumption

To determine if the reduction in the total hours of migraine was associated with an increase in medication usage, the correlation between the total hours of migraine and mg medication was investigated. The full data is presented in Fig 7.22. Data with outliers removed is presented in Fig 7.23. A *negative* correlation coefficient would indicate that the total hours of migraine was decreasing due to an increase in the amount of medication used. Initially, it can be seen that there is a significant positive relationship between medication consumption and total hours of migraine at Time 28, 35 and 42 in the Treatment group. Again, a number of large outliers can be seen which may affect the results, particularly at Time 35 and 84. Study number 14 had 120 hours of migraine at Time 35; Study number 22 had 96 hours of migraine at Time 35 and 84 hours of migraine at Time 84; Study number 42 had 144 hours of migraine at Time 84 and Study number 45 had 75 hours of migraine at Time 84. Thus, these large outliers were removed and the correlation coefficients recalculated. See figure 25. The results showed a significant relationship between total hours of migraine and medication at Time 28 and 42 in the Treatment group. Again however, these coefficients were positive indicating that any reduction in the hours of migraine was not associated with the amount of medication.

Fig. 7.22 Medication consumption and hours of migraine: full data.

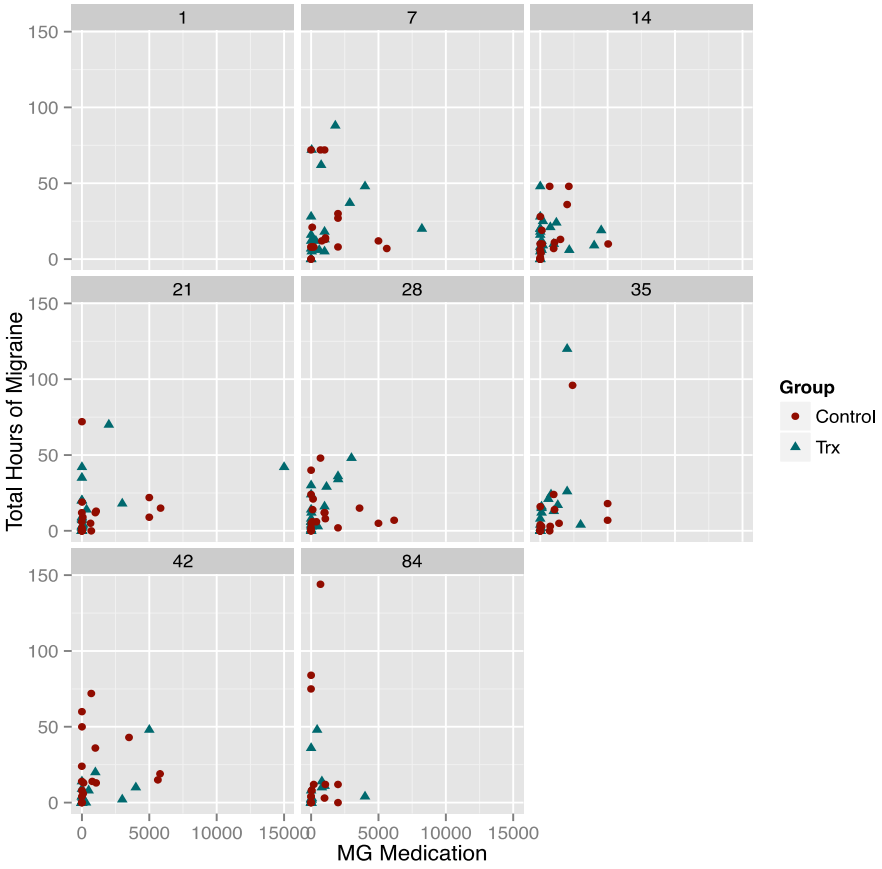
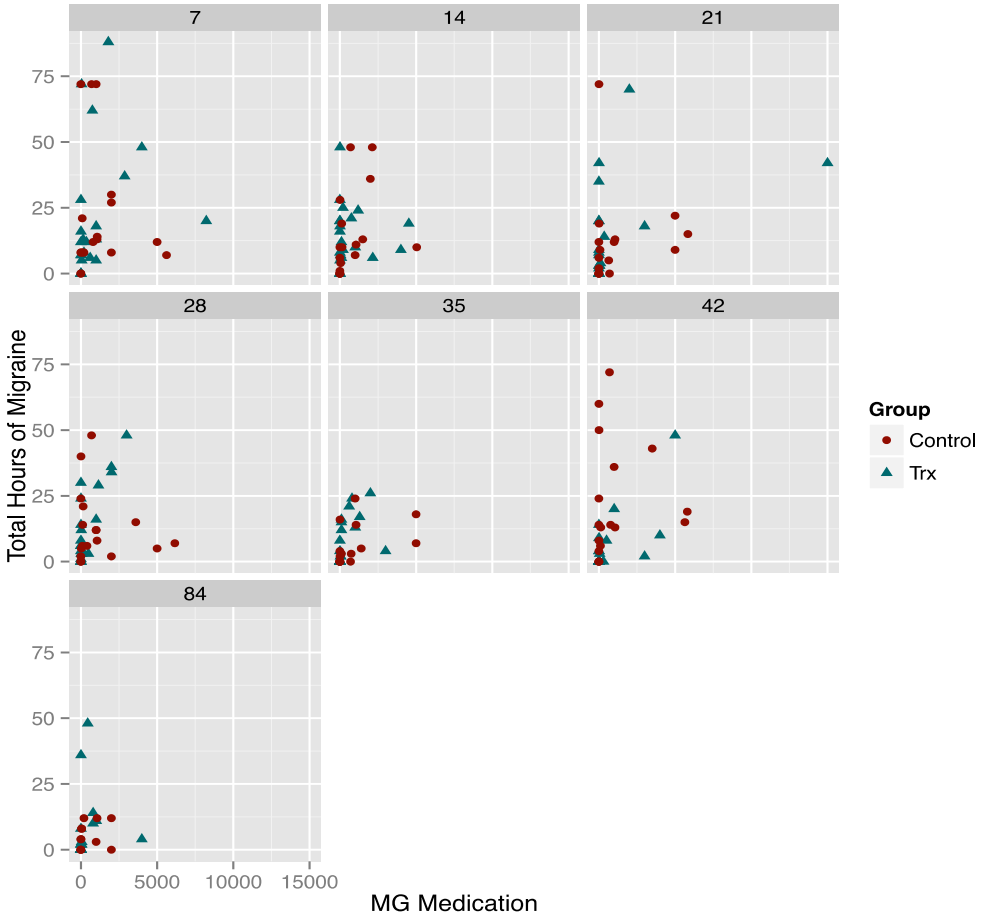


Fig. 7.23 Medication consumption and hours of migraine



Correlational Data Summary

The data indicated a strong positive relationship between PCS and HDI across all time-points in both the Control and Treatment groups, suggesting that patients with higher PCS scores also tend to exhibit higher HDI scores. There was evidence of a negative relationship between PCS and MAAS and HDI and MAAS. Thus patients with higher PCS/HDI scores tend to have lower MAAS scores. The relationships were stronger in the Control group in both cases. The data also suggested that the amount of medication used was not associated with either the reduction in the number of hours of migraine nor the number of migraines.

Mixed model analysis

To determine if there were significant changes over time between the two groups, a mixed effects model was used. Mixed effects models are appropriate for analyzing longitudinal data and account for the correlation between values measured on the same subject over time. Since these data are longitudinal, with multiple measurements made on each response variable over time for each subject, such models are the most appropriate. For each outcome of interest, the change from baseline was calculated for the remaining time points and these values were used as the response variable values. Baseline was then used as a covariate in the model to adjust for subject-specific differences at baseline and account for the fact that the change in a subject's score may be related to their starting value. For the primary outcomes (HDI, PCS), a linear mixed effects model was used. Other covariates such as education, employment status, gender, etc. were also included in the model to determine if these covariates were associated with the change in a subject's score. For both HDI and PCS, these covariates were not significantly associated with either outcome and so were removed from the final models.

HDI

From the line plot which follows (Fig. 7.24) it is clear that some subjects in both groups experience very large drops in HDI at 28 days. In general, the HDI scores for subjects in the Control group appear to exhibit little change over time (Fig 7.25) while several participants in the Treatment group appear to have a generally decreasing trend over time.

Fig. 7.24 HDI over time

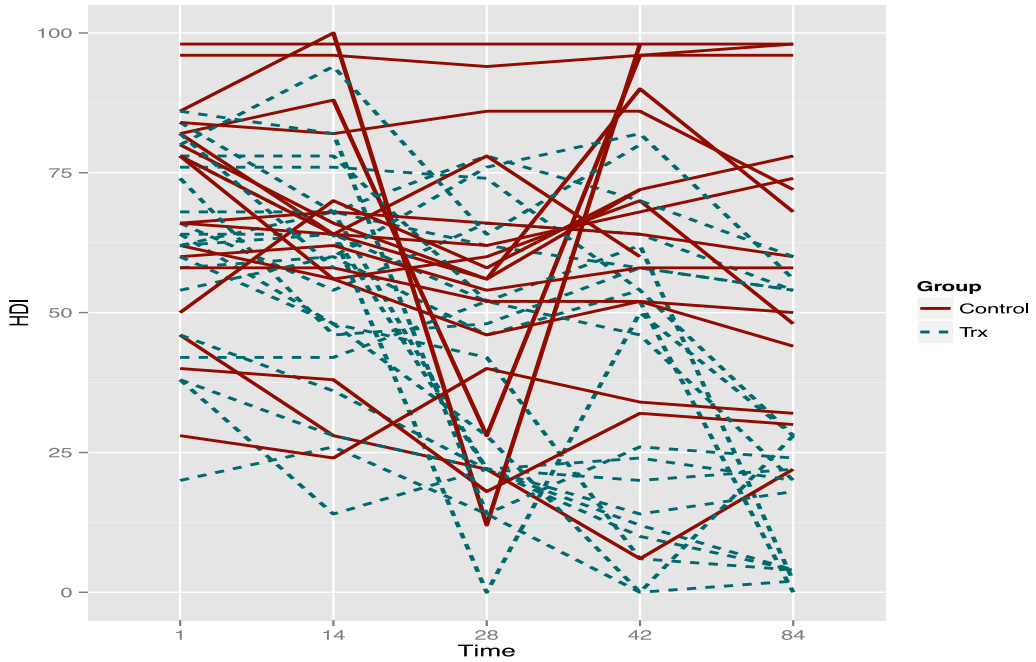
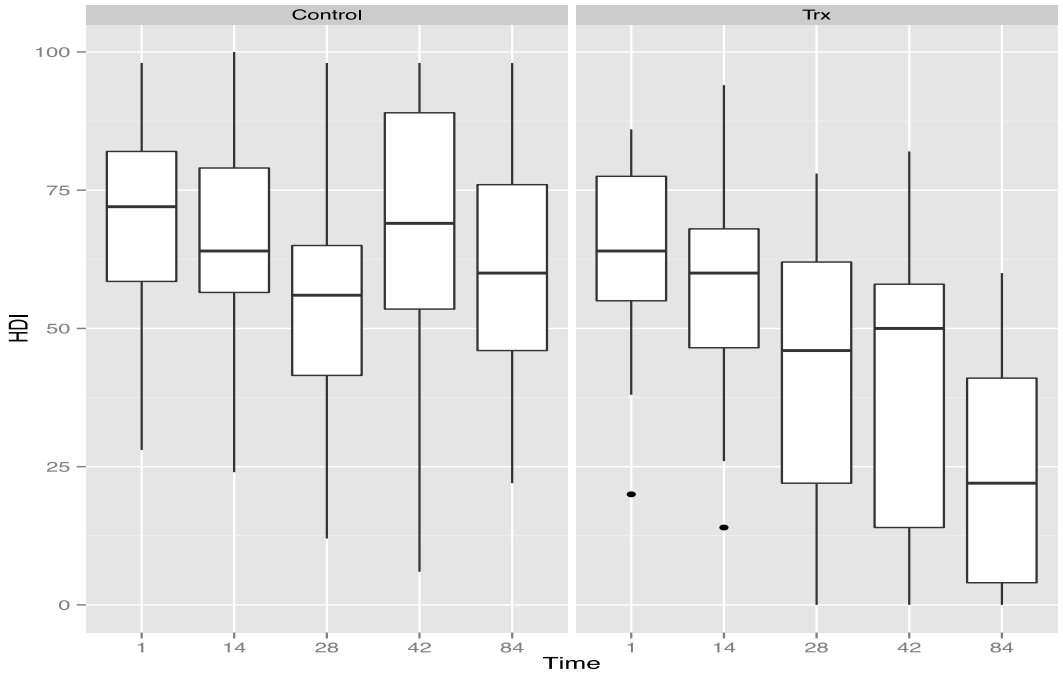
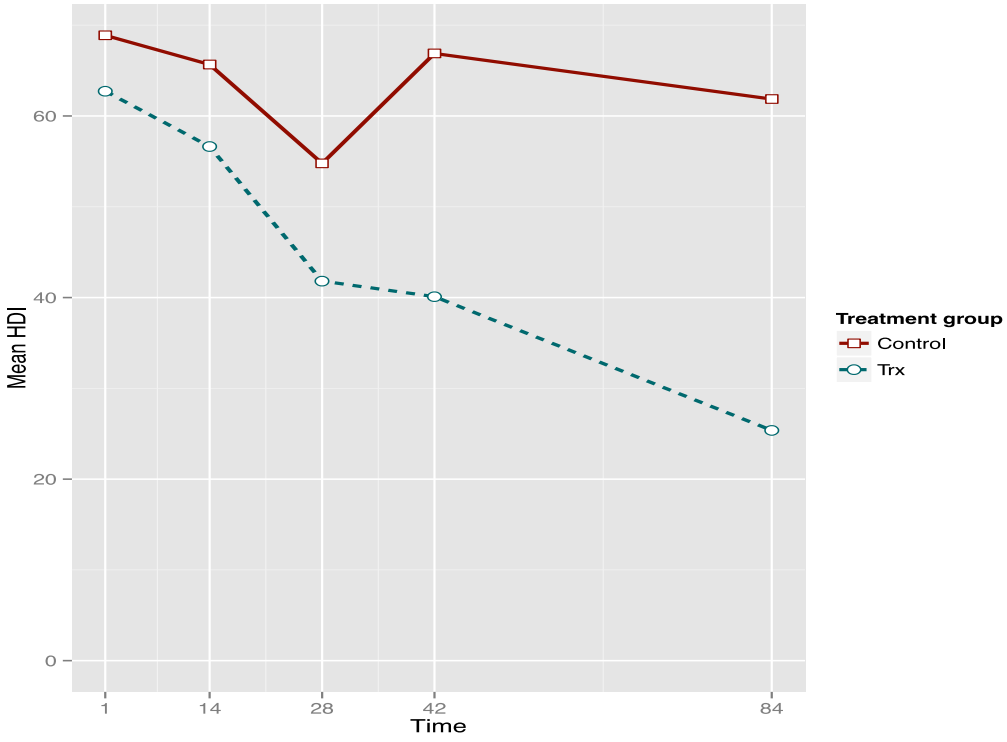


Fig. 7.25 Average HDI values over time



Examining the group means over time, it is clear that on average the HDI score of subjects in the Treatment group decreases over time, while in the Control group there is a decrease at Time 28 (possibly due to one or two participants with very large drops in HDI at that time), before increasing again at Time 42 (Fig 7.25). Participants in the Treatment group continue to exhibit a decrease in HDI levels at the 6-week follow-up (Time 84).

Fig. 7.26 Mean HDI across time



A mixed effects model was fitted using HDI as the response variable and baseline HDI as a covariate in the model. There was a significant decrease of 10.9 units on average in the Treatment group

at Time 28 versus Time 14 (p-value = 0.03). There is a significant difference between the Control and Treatment groups and Time 42 versus Time 14 and Time 84 versus Time 14. At Time 42, participants in the Treatment group had HDI levels 17.26 units lower on average than participants in the Control group (p-value = 0.012). At 6-week follow-up, participants in the Treatment group had HDI levels that were 26.26 units lower on average than participants in the Control group (p-value < 0.001). Below the values show the difference between the changes that occurred from Time 14 to Time 42 in the treatment group compared with the control group.

	Value	Std.Error	DF	t-value	p-value
(Intercept)	11.218	9.140	106	1.227	0.222
BaselineHDI	0.790	0.117	37	6.759	0.000
GroupTrx	-4.160	5.867	37	-0.709	0.483
Time28	-10.889	4.954	106	-2.198	0.030
Time42	1.222	4.954	106	0.247	0.806
Time84	-2.972	5.244	106	-0.567	0.572
GroupTrx:Time28	-3.438	6.729	106	-0.511	0.610
GroupTrx:Time42	-17.264	6.729	106	-2.566	0.012
GroupTrx:Time84	-26.269	7.040	106	-3.731	0.000

The percentage change in the mean HDI score from Time 14 (prior to intervention) to Time 84 (6-week follow-up) in the Treatment group corresponded to a 48% reduction in HDI in that group. The Control group experienced a 2% increase in HDI (Fig 7.26).

PCS

From the line plot which follows (Fig. 7.27) there is a general decreasing trend over time in PCS scores of the Treatment group. In comparison, PCS levels tend to decrease initially in the Control group up to Time 28 before increasing again at Time 42 and continuing to increase at 6-week follow-up.

Fig. 7.27 PCS scores across time

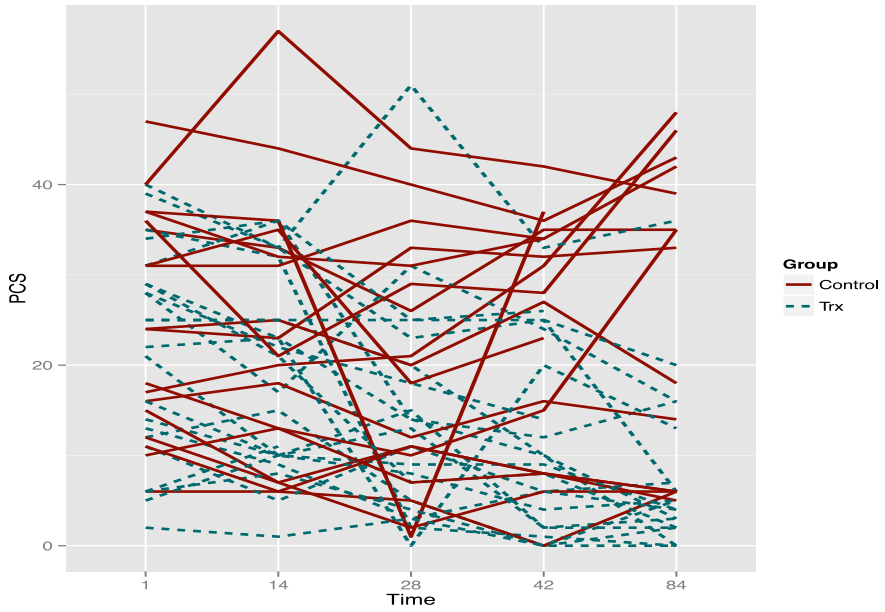
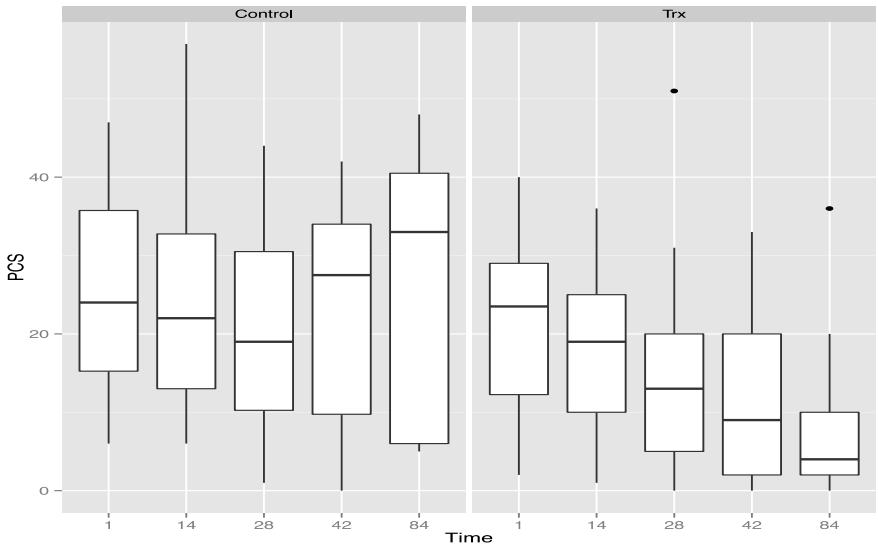


Fig. 7.28 Mean PCS scores across time



A mixed effects model was fitted using PCS as the response variable and baseline PCS as a covariate in the model. There was a significant difference between the Control and Treatment groups at Time 42 versus Time 14 and Time 84 versus Time 14 (as indicated by the significant interaction effect). At Time 42, participants in the Treatment group had PCS levels that were 7.29 units lower on average than participants in the Control group (p-value = 0.013). At 6-week follow-up, participants in the Treatment group had PCS levels that were 13.29 units lower on average than participants in the Control group (p-value < 0.001).

	Value	Std.Error	DF	t-value	p-value
(Intercept)	4.487	2.882	106	1.557	0.122
BaselinePCS	0.775	0.084	37	9.202	0.000
GroupTrx	-2.206	2.691	37	-0.820	0.418
Time28	-3.889	2.252	106	-1.727	0.087
Time42	-0.389	2.252	106	-0.173	0.863
Time84	2.918	2.385	106	1.224	0.224
GroupTrx:Time28	-1.141	3.059	106	-0.373	0.710
GroupTrx:Time42	-7.688	3.059	106	-2.514	0.013
GroupTrx:Time84	-13.915	3.201	106	-4.347	0.000

The percentage change in the mean PCS score from Time 14 (prior to intervention) to Time 84 (6-week follow-up) in the Treatment group corresponded to a 60% reduction in PCS in that group (Fig 7.28). The Control group experienced an average increase of 7% in PCS score.

PCS and Severity of Migraine

To determine if PCS was associated with severity of migraine, a linear mixed effects model was fitted using PCS as the response

variable and severity of migraine as an explanatory variable. Time and the interaction between Time and severity were also included, however there was no evidence of a difference between PCS scores over time within each severity category and so the interaction term was removed and there was no evidence of a trend over time and the time effect was removed.

	Value	Std.Error	DF	t-value	p-value
(Intercept)	13.800699	1.980130	109	6.969595	0.0000
Sev_of_MigII mild	0.434003	1.825894	109	0.237694	0.8126
Sev_of_MigIII mod	7.355091	1.828332	109	4.022842	0.0001
Sev_of_MigIV severe	10.468461	2.018483	109	5.186301	0.0000

There does seem to be an association between severity of migraine and PCS score. There is no evidence of a significant difference between PCS scores in the mild vs little or none categories on average (p-value = 0.81). Participants with moderate migraine symptoms have PCS scores that are 7.4 units higher on average than participants with little or no symptoms. Participants with severe migraine symptoms have PCS scores that are 10.5 units higher on average than participants with little or no symptoms.

Frequency, Duration and Severity of Migraine

Changes in frequency, duration and severity of migraine are outlined in turn.

Frequency (Number) of Migraines

The change in the number of migraines at 6-week follow-up versus Time 14 (last time point prior to intervention) was calculated (Table 7.11). The median change in number of migraines in the Control and Treatment group at 6-week follow-up vs Time 14 was 0 and a decrease of 1 migraine per week respectively. Eleven (out of 19) participants in the Treatment group experienced a reduction in the number of migraines, three subjects experienced an increase and

five participants experienced no change in number of migraines. Five out of 15 participants in the Control group experienced an decrease in the number of migraines, four experienced an increase in the number of migraines and six had no change.

Control

Q1	Q2	Q3	IQR
-1.0	0.0	0.50	1.50

Trx

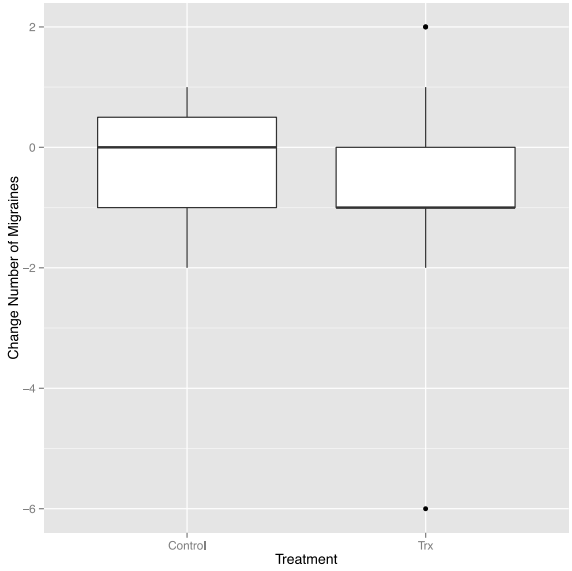
Q1	Q2	Q3	IQR
-1.0	-1.0	0.0	1.00

Table 7.11. Change in mean number of migraines prior to treatment (Time 14) and at 6-week follow up (Time 84).

Case Summaries

Group	Time	N	Mean	Median	Minimum	Maximum	Std. Deviation
Control	14vs84	15	-0.27	0	-2	1	1.100
Treatment	14vs84	19	-0.74	-1	-6	2	1.727

Figure 7.29. Median Change in number of migraines Time 14 to Time 84



A Shapiro-Wilk normality test indicated that the change in number of migraines in both groups were not normally distributed, thus a Wilcoxon test was performed to test for differences between the medians in both groups. This test suggested that there was no evidence of a significant difference between the change in the number of migraines between groups (Fig 7.29).

Control:

Shapiro-Wilk normality test

W = 0.8509, p-value = 0.01786

Treatment:

Shapiro-Wilk normality test

W = 0.8524, p-value = 0.007332

Wilcoxon rank sum test with continuity correction

W = 169.5, p-value = 0.343

Total Hours (Duration) of Migraine:

The change in the total hours of migraine per week at Time 84 (6-week follow-up) versus Time 14 (last time point prior to intervention) was calculated (Fig 7.30). The median change in the total hours of migraine in the Control and Treatment group at 6-week follow-up vs Time 14 was 0 and a decrease of 8 hours respectively (Table 7.12). The majority of subjects in the Treatment group experienced a reduction in the total hours of migraine (15/19), one subject experienced no change and three subjects experienced an increase in total hours of migraine. In contrast 7 out of 15 subjects in the Control group experienced an increase in the total hours of migraine, seven experienced a reduction in the total hours of migraine and one had no change.

Table 7.12 Change in Hours of Migraine prior to treatment (Time 14) to six week follow up (Time 84)

Case Summaries

Group	Time	N	Mean	Median	Minimum	Maximum	Std. Deviation
Control	14vs84	15	12.80	0	-36	96	37.687
Treatment	14vs84	19	-7.21	-8	-38	48	17.605

Control

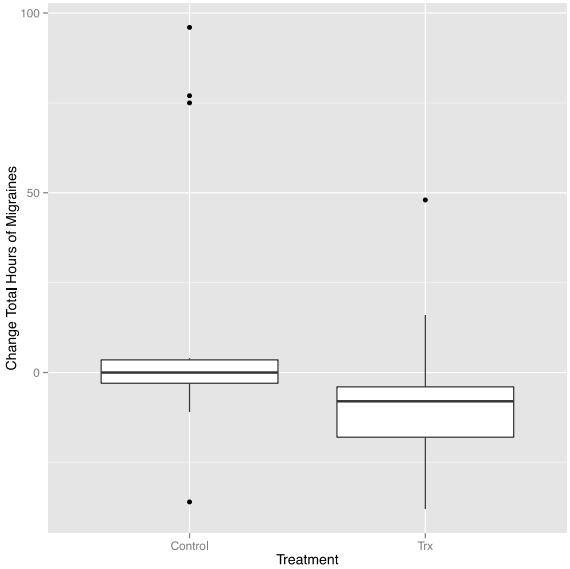
Q1	Q2	Q3	IQR
-3.0	0.0	3.5	6.5

Trx

Q1	Q2	Q3	IQR
-18.0	-8.0	-4.0	14.0

A Shapiro-Wilk normality test indicated that the change in total hours of migraine in both groups were not normally distributed, thus a Wilcoxon test was performed to test for differences between the medians in both groups. This test suggested that there was evidence of a significant difference between the change in the total hours of migraine between groups.

Figure 7.30 Change in hours of migraine Time 14 to Time 84



Control:

Shapiro-Wilk normality test

W = 0.7348, p-value = 0.000601

Treatment:

Shapiro-Wilk normality test

W = 0.8498, p-value = 0.006663

Wilcoxon rank sum test with continuity correction

W = 212.5, p-value = 0.01

Severity of Migraine

Time 42 vs Time 14:

22% of participants (4 out of 18) in the Control group experienced a decrease in the severity of migraine at Time 42 versus Time 14 (baseline) while 67% of participants (14 out of 21) in the Treatment group experienced a decrease in the severity of migraine (Table 7.13). One participant (5%) in the Treatment group experienced an increase in the severity of migraine, while 6 participants (29%) experienced no change in the severity at Time 42 vs Time 14. 8 participants in the Control group (44%) experienced an increase in severity at this time-point, while a further 6 participants (33%) experienced no change. To test for a significant difference in the proportion of subjects experiencing a decrease in the severity of migraine, a chi-square test for equal proportions was carried out. This test yielded a p-value of 0.014 indicating that there was evidence of a significant difference in the proportion of subjects experiencing a decrease in severity of migraine in the Treatment

versus Control group at Time 42 vs Time 14 as illustrated in Table 13.

Table 7.13. Changes in severity of migraine compared between pre-treatment (T14) and post-treatment (T42)

	Improve	No change/worsen
Treatment	14 67%	7 33%
Control	4 22%	14 78%

Time 84 vs Time 14:

33% of participants (5 out of 15) in the Control group experienced a decrease in the severity of migraine at Time 84 versus Time 14 (baseline) while 63% of participants (12 out of 19) in the Treatment group experienced a decrease in the severity of migraine. One participant (5%) in the Treatment group had worsened severity, while 6 participants (32%) had no change. Similarly, 5 participants (33%) in the Control group had worsened severity while a further 5 patients (33%) had no change. To test for a significant difference in the proportion of participants experiencing a decrease in the severity of migraine at these two time-points, a chi-square test for equal proportions was carried out. This test yielded a p-value of 0.16 indicating that there was no evidence of a significant difference in the proportion of subjects experiencing a decrease in severity of migraine in the Treatment versus Control group at Time 84 vs Time 14 as illustrated in Table 7.14.

Pearson's Chi-squared test

X-squared = 1.9088, df = 1, p-value = 0.16

Table 7.14. Changes in severity of migraine pre-treatment (Time14) vs six-week follow-up (Time 84).

	Improve	No change/worsen
Treatment	12 63%	7 37%
Control	5 33%	10 67%

Medication consumption

A Shapiro-Wilk normality test indicated that the change in amount of medication in both groups were not normally distributed, thus a Wilcoxon test was performed to test for differences between the medians in both groups. This test suggested that there was no evidence of a significant difference between the change in the medication used between groups (Fig.7.31). Change in the amount of medication consumed in mg between pre-treatment and follow up (T84) is illustrated in Table 7.15.

Control

Q1	Q2	Q3	IQR
-97.5	0.0	5.0	102.5

Trx

Q1	Q2	Q3	IQR
-50.0	-1.0	2.0	52.0

Control:

Shapiro-Wilk normality test

W = 0.6344, p-value = 5.36

Treatment:

Shapiro-Wilk normality test

W = 0.7037, p-value = 6.158e-05

Wilcoxon rank sum test with continuity correction

W = 140, p-value = 0.9443

Figure 7.31. Median change in medication consumed (in mg.) between pre-treatment (Time14) and follow-up (Time 84)

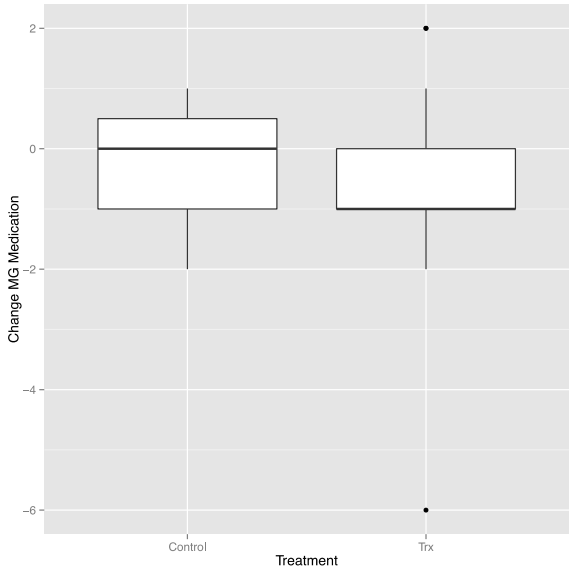


Table 7.15 Change in amount of migraine medication consumed in mg between pre-treatment (T14) and follow-up (T84).

Group	Time	N	Mean	Median	Minimum	Maximum	Std. Deviation
Control	14vs 84	15	-211.23	0	-4990	2000	1471.146
Treatment	4vs14 84	19	-354.68	-1	-4520	2800	1622.00

Mixed Model Analysis Summary

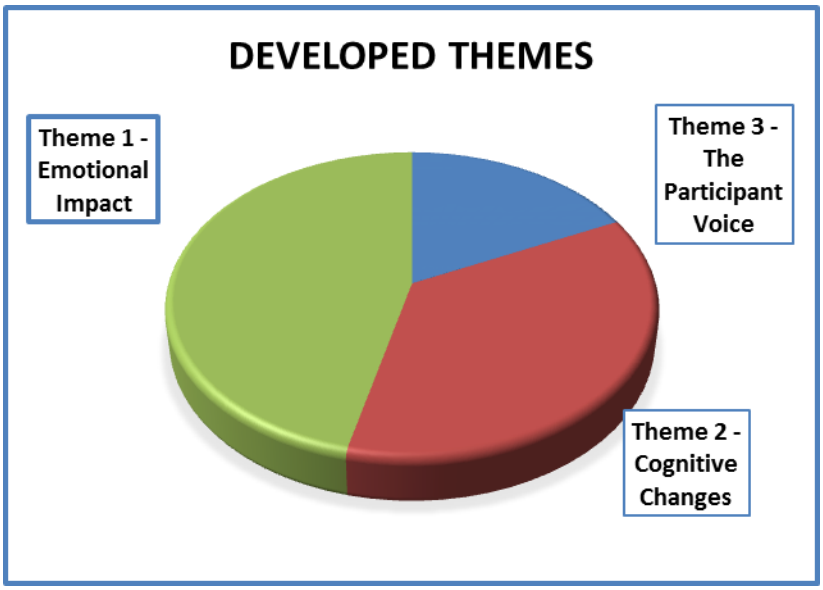
Significant improvements were found from Time 14 (pre-intervention) to Time 84 (6 week follow-up) for HDI and PCS. There was a 48% reduction in the mean HDI score in the Treatment group versus a 2% increases in the mean HDI score in the Control group. Similarly, there was a 60% reduction in the mean PCS score in the Treatment group, with a 7% increase in the mean PCS score in the Control group. There was evidence of a significant decrease in the average number of hours migraine in the Treatment group versus the Control group, with patients in the Treatment group experiencing 8 hours less of migraine on average than those in the Control group. The change in the number of migraines suffered and the proportion of patients experiencing a decrease in the severity of migraine did not differ significantly between groups, although a higher proportion of those in the Treatment group did experience a decrease in migraine severity than the Control group (67% vs 33%). The data also suggested a decrease in the medication usage for both groups, however there was no evidence of a significant difference in the change in medication usage between groups.

Qualitative Results

Fourteen people from the treatment group were available in the timeframe post intervention to take part in a semi-structured interview with a view to exploring their personal experience of the intervention and better understanding the numerical data. Their interviews were recorded on audio and then transcribed. Some questions were designed to probe further into the questionnaires used in the quantitative data, namely Headache Disability Index and Pain Catastrophizing. A final section of the interview included an open-ended question to give participants an opportunity to express their subjective opinion and discuss anything they thought was

relevant. An initial thirty-seven codes were generated from this data. These were then broken down into six categories and subsequently refined down to three categories in the data reduction phase. The three categories reflected the participants' experiences and attitudes towards the impact which migraines have on their daily activities, changes occuring in their thought patterns during and after the intervention and unprompted responses which shed light on issues for consideration in future research in this area. This breakdown is presented in Fig 8.1 below.

Fig 8.1. Developed Themes



Theme 1: Emotional Impact

Within the emotional impact category, disability in terms of emotional and functional ability as a consequence of migraine was analysed. Positive impact of the intervention on emotions emerged as the dominant theme with twenty references from eleven interviews. Within this theme, reference to improved relaxation and reduced stress was the benefit most frequently mentioned (sixteen references from ten individuals). All fourteen individuals discussed the impact migraines had on their relationships prior to intervention and how the intervention had helped improve their relationships.

Ten people noted a positive change in communication with others at work or in social situations. In terms of changes in activity, thirteen of the fourteen noted a distinct increase in activity which occured during the six weeks they were taking part in the study. These results are reflected in Fig. 8.2.

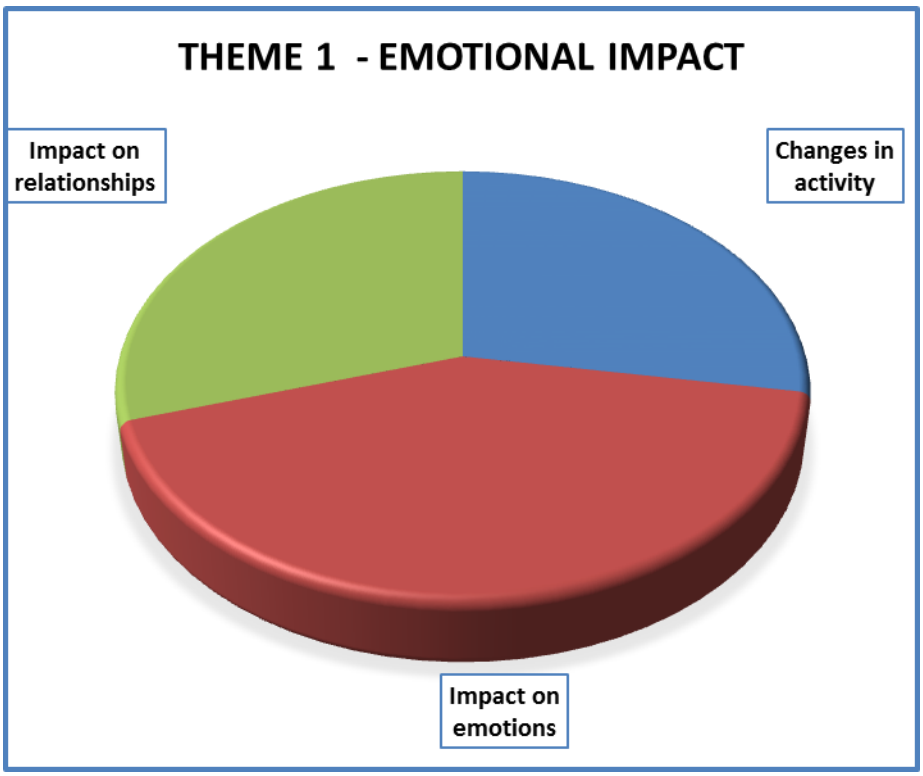
Changes in Activity

To uncover more detailed information behind the impact of the intervention on daily activity participants were asked whether they had noticed any difference in activity levels. Nine of the fourteen participants said they had noticed an increase in activity. Of these, four said they socialised more during the intervention, three commented on the fact that work benefited as a result and two people found that they were, as one participant (2) put it, 'more relaxed about everything and more positive about everything'. The same participant also mentioned that they now had 'no problems committing to doing things'. The five who reported no change in activity said that in the past they would never have allowed their migraines to stop them from doing anything and so did not find this relevant to them. For those who noticed a change in activity the pattern appears to have been associated with the fact that they experienced fewer migraines and/or their thinking around migraines had altered. As participant 9 explained, 'I would have been…, I am very careful about the effort I put in to something like a long drive and stuff like that or even something like painting but actually now I have got a lot braver and I am doing that sort of stuff because, touch wood, nothing has come back to bite me yet anyway.' It may be relevant to note that this participant had no migraines after the fourth week of the six week intervention and would have had at least two migraines each month prior to commencing the programme. This progress was maintained up to and including the six week follow up.

Impact on relationships

When asked about any changes they noticed within relationships in their lives, thirteen of the fourteen were conscious of mood changes in themselves and they reflected on what that must have meant for those around them. One participant (9) remarked that the programme had a positive effect on the people around them. 'I think people were happy when I was on it (the intervention). I would not be as dramatic. Usually coming up to these things you become very dramatic. Things look very black and bleak and then it becomes a vicious circle and one thing leads to another.' Another participant (6) reported how others had been commenting on the changes they saw in her. 'Some people have just observed that my face looks a lot better because any time I have a headache, my face reflects it. People are saying "gosh you look an awful lot better" and I am smiling saying "I don't have migraines". So people often are remarking on it and it goes back and forth a bit like a tennis ball, if someone is smiling at me I am smiling at them etc. etc..' There were other participants who were somewhat aware that the change in their mood must have had an impact on those around them. One participant (5) summed it up succinctly, responding, 'I just think I am a little more pleasant, a little less impatient.'

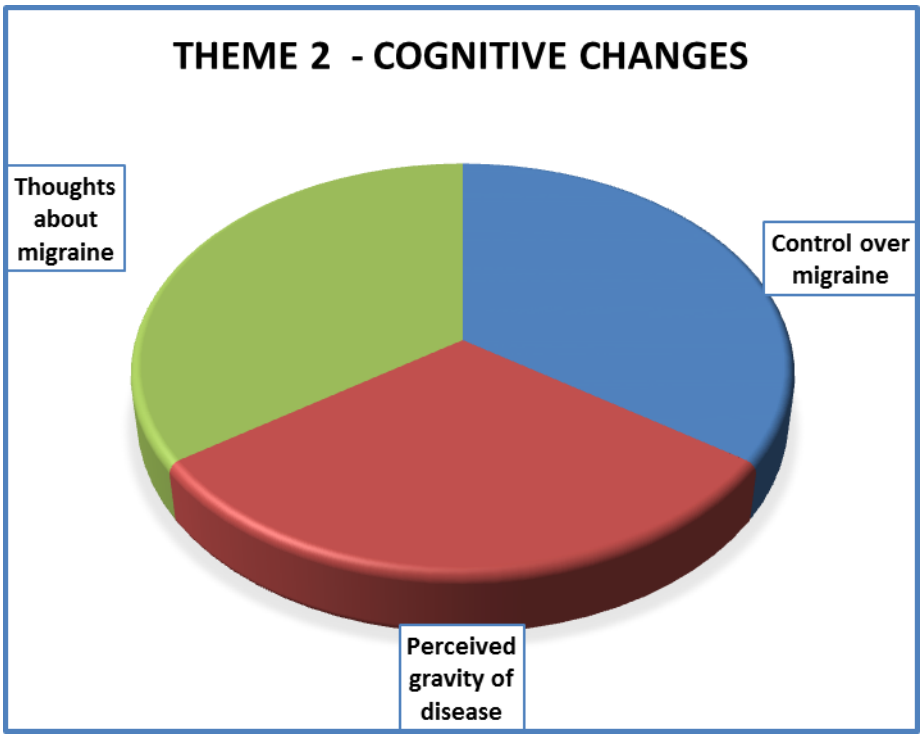
Fig 8.2 Emotional Impact



Theme 2: Cognitive Changes

Changes in thought processes were noted twenty three times by eleven participants. Of the three who did not bring up specific changes in their thought patterns, their emphasis centred around an increase in activities. Twelve participants reported a greater feeling of control over their migraines. In terms of perception of how serious their disease was, four people noticed a reduction in the gravity with which they viewed their migraines and most (n=7) reported no change. Fig 8.3 documents the breakdown of cognitive changes.

Fig 8.3 Cognitive Changes



Thoughts about Migraine

The constant comparative method employed in this qualitative evaluation in particular, highlighted the changes in cognitive processes occurring as a consequence of the intervention. The responses indicated a considerable shift in thinking which was reflected in the quantitative data regarding pain catastrophizing. Twenty one unprompted references to a positive change in thought patterns around migraine were made by eleven out of the fourteen people interviewed. Some, like participant 1, reflected, 'I notice I am getting better at observing my own thoughts going on especially with pain management' while participant 13 made more generalised comments about changes in their thought patterns 'I am thinking more clearly.' What emerged from the interviews was that specific

suggestions gave those listening to the mp3s a greater confidence in dealing with their migraine and a new perspective on the disease. One participant (10), observed a dramatic change in their thinking. 'The other thing that has been the major shift for me, has been.., and this is genuine.., as I say…., it has always been about managing the migraine when it comes and now I am thinking completely differently.... I am thinking "I am going to look at my life to see can I stop getting the migraines".' This sentiment was echoed by participant 2 who was cognisant of not thinking about them at all and how this fact alone made her think about migraines differently. 'It's funny, when you have a couple of days free or a week free and it goes in to another week you sort of relax about it and you sort of say "This is how life can be.", You can put it out of your mind. absolutely.'

Control over Migraine

The concept of taking responsibility over how participants may be contributing to their own migraines arose frequently. The thinking changed to having more control over their migraines rather than simply accepting the migraine pattern they had previously resigned themselves to. This was mentioned by six of the participants (6,7,8,10,12, & 13). As participant 7 stated, 'I found they made me analyse my life and certain things. I would sit back and say I didn't realise I did that.… So they made me think about life and just migraines and how I was making my life more stressful and there were times when I would find that I was getting stressed and I would think about the mp3 player and what was on it and it would actually chill me down and what was on it so it wouldn't even be that I felt a migraine coming on that I started to think about it.'

A similar thought process was shared by several other participants and it had a subsequent effect on the way they managed their migraines. Participant 2 made the comment, 'sometimes I could get very uptight about things but I am sort of better able to take a deep breath and start again or say "we can do this tomorrow" whereas

before I would have said, “no we are going to do this now” or “am I going to manage this that or the other thing”.’ This change in attitude and behaviour was echoed by participant 10 who was quite intrigued by the fact that after 45 years of thinking one way she was now looking at migraines in a completely different way. ‘I have been having them since I was fourteen you know and I am fifty nine so what’s that… that’s forty five years.. right.. so it has always been for me about managing the migraine when it comes and I use that term always managing and I’ve shifted using that term from looking after myself when I have a migraine so I have been managing.. take two pills then take another one and just get on with it while now I am just more “*I have a migraine, ok, that’s not a great thing to do, to be… maybe I should take it easy, maybe I should rest rather than keep going as I have always done*”.’

Some participants, like participant 7, were courageous enough to confront themselves with the question as to whether they were motivated to have a migraine in order to avoid a situation, a question which had been embedded in the suggestions on one of the hypnosis tracks. ‘But yet, there certainly were questions you have to say, *“I would never have thought that”* so I will be following that and exploring that and looking at what is going on around the time of the migraine. Is there something where I am saying “*is there something I can escape from it with a migraine?*” Just ideas that have come in to my head.’ Participant 8 had a similar experience. ‘Its nearly like…, I wouldn’t have said it was psychosomatic before. I would have said “*I am getting this pain in my head and it is going to kill me and I am going to be in bed for two days and that is my way of getting out of things*” whereas now I feel if I put the tape on where I think about some of the things I have heard on it, it is helping me to address it.’

Perceived Gravity of the Disease

Helplessness is one aspect of pain catastrophizing. To better understand the reduction in pain catastrophizing which occurred

with the intervention group, a question pertaining to feelings of control over the pain was asked in the interviews. Thirteen of the fourteen participants felt they were more in control of their migraine with one participant, (6), describing it as 'life-changing'. There was just one participant (participant 14) who felt they did not feel any more or any less in control as a consequence of the intervention. This trend was also reflected in that the majority of those interviewed tended to think about their migraines less. Participant 1 noted, 'I did have fewer thoughts because I notice, I am getting better at observing my own thoughts going on especially with pain management. So I've noticed when some pain or discomfort in my body was coming before I would have got distressed and now to know that when I relax more and I think no matter what it helps in any situation. Before I would have got stressed more. Once you are in a relaxed state the migraine is easier to bear.'

Another question included in the interview was regarding the issue of whether, when they had a migraine, they believed or had thoughts that something more serious may happen. Four participants said they were less concerned about the prospect of something serious happening as a result of listening to the hypnotic recordings and the remainder never had serious concerns to begin with. Participants put this down to having the results of an MRI (participant 4), the knowledge that migraines were in their family (participant 7) and pattern familiarity (participant 3), saying that they knew their migraine would eventually go away.

Theme 3: The Participant Voice

The most frequent, unsolicited comment made by participants was regarding the serverity and frequency of migraines after the preliminary study had finished. In fact, twenty three references were made by thirteen of the fourteen participants with all thirteen mentioning that they had fewer migraines overall and five stating that they had no migraines in the two weeks after the intervention. References to experiences which they felt were unusual for them

constituted fifteen statements made by ten of the participants. These included surprise at the profound effect of the hypnosis mp3s, descriptions of their physical experience while listening to the mp3s e.g. a feeling of floating and the fact that various triggers such as increased pressure at work or home which previously would have instigated their migraines no longer did so. Ten individuals remarked on the quality of the mp3s or on various phrases or suggestions on the recordings which resonated with them and three of the participants commented on the length of the intervention, indicating an interest in seeing whether the effects would continue over time. The breakdown of these seven areas is presented in Fig 8.4.

When asked about what worked for them, participants identified relaxation was identified as an important element in the process. Three participants mentioned that they were familiar with other relaxation strategies and nine commented about the ongoing relaxation they felt. Of those who mentioned, in passing, that they were familiar with other relaxation strategies (n=3), all were able to differentiate hypnosis from other techniques which they had used previously. One participant (10), familiar with mindfulness meditation found hypnosis easier to put into practice. 'I have done loads of mindfulness and meditation but I can't sit there, on a cushion, just looking at a candle or looking at nothing… breathing.. I can do it for five minutes but I found because I relax for twenty minutes or eighteen or whatever they are that that is helping me… I may get to the stage where I can meditate because I am now coming to the stage where I can actually relax for twenty minutes.' Another participant (13) noticed a 'profound difference' after listening to the third and fourth mp3s in the series. That difference, she felt, was down to 'becoming more consciously aware than before just how much I can control the migraine.'

The persistent relaxation which participants experienced was an added, unexpected, value for nine of the fourteen participants who stressed that the relaxation lasted beyond the time taken to listen to the mp3s even, when as one participant (5) noted, their schedules remained the same. 'They helped me relax and because, so many of my days, I get up and never stop. It seems like it is 11 O'Clock at night and I am trying to wrap things up at work and the fact that I can take time out of the day and relax and listen to that tape really made my day a lot less stressful so beyond the migraine it was a relaxing moment that I really needed and it was just very good.'

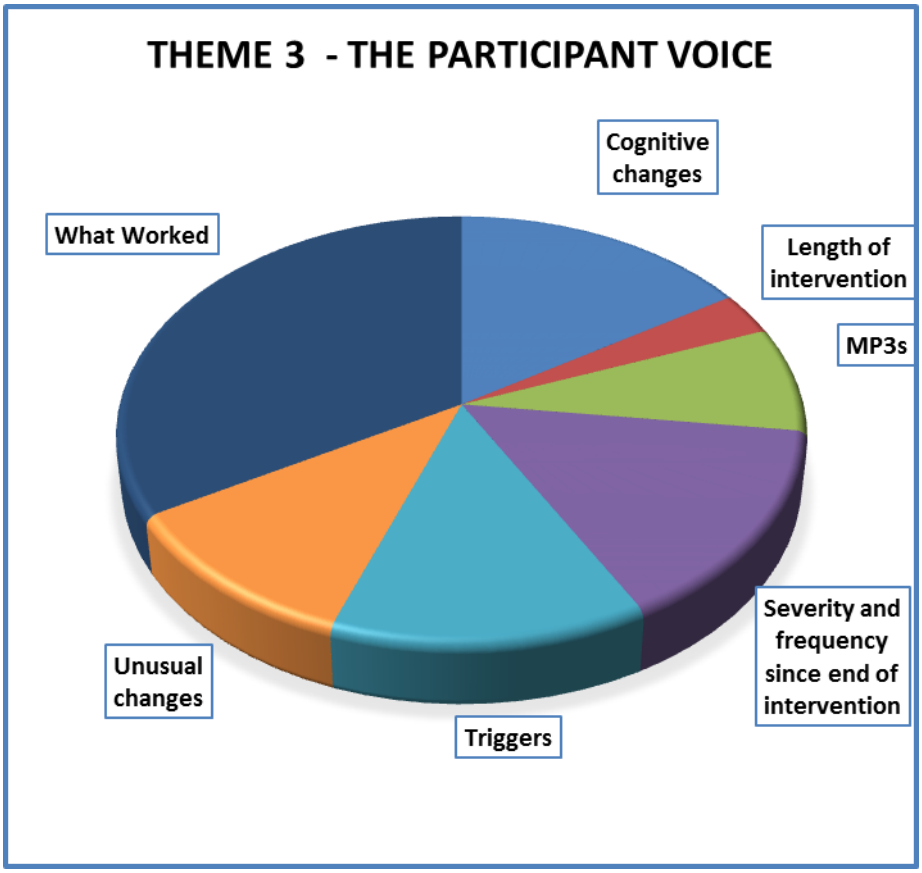
Of the nine participants who mentioned mental relaxation, three were inclined to attribute the element of taking time out as being of most value. 'The value for me they added, they required time. Therefore they gave me the opportunity to take that time for relaxation.' Other participants found an unexpected benefit of being able to handle increased pressure with work or social occasions or that it stimulated a new thought process. One of the participants remarked that, while listening to the mp3s as scheduled she was trying to juggle returning to work and having recently had a baby. 'During the trial I started going back to work and I would have been worse if it had not been for the intervention because I had a lot of pressure.'

Anecdotally, food as a migraine trigger is a frequent topic of conversation amongst migraineurs. Fasting was identified as a migraine trigger for 46.3% in a study of 182 participants aged between 14 and 58 yrs based in India and (Yadav, Kalita & Misra, 2010). Three of the present study mentioned particular foods which they believed would guarantee that they would get a migraine. Referring to one of the mp3's in the study which contained suggestions to make it easier to give up any foods specific to themselves which might be contributing to their migraines, participant 8 remarked 'well, I've changed my eating habits,

whether that is part of the process…' and followed later by saying 'I have recognized that stress is the main reason for my migraine. I'm still not quite sure what's going on but I most definitely have had a reduction in the number of migraine attacks in the last few weeks.' One of the participants (14) mentioned that she only got migraines at the week-end. When I inquired as to any differences in the length of time she would sleep during the week and at the weekend she did say that she used to sleep for longer periods at the weekend. However, this only came to light when we spoke about it and, at that point, when she was interviewed, she had not made any adjustments in her sleep patterns but she had not had a migraine for two week-ends. This was, for her, she said, highly irregular. 'Just in relation to my migraines I have not had any migraines for the past two weekends which .. I would wake up practically every weekend with a migraine. For the last two, I have not had one.'

In response to the general question regarding comments they would like to make about the intervention, thirteen of the fourteen participants mentioned, that in the two weeks following the intervention they had had fewer (n=6) or no migraines at all (n=7) in that time period. This was described by the participants as 'most unusual' (participant 12), something that they were 'very surprised at' (participant 13), and one (participant 6) had a 'disbelief' she was not getting migraines like she used to, which she says had the effect of creating 'this bubble of joy inside me that keeps coming to the surface because I don't have this pain.'

Fig. 8.4 The Participant Voice



Chapter 8: Discussion

8.1 Summary

Migraine is number seven among all diseases world-wide causing disability (World Health Organisation, 2011). This disability has both macroeconomic and personal repercussions. There are financial implications for society in terms of lost earnings and productivity as well as direct and indirect medical costs. The personal cost for individuals with migraine include disability and pain and reduced quality of life in many domains.

The present study set out to develop and evaluate the efficacy of an online hypnotherapy intervention to reduce disability associated with migraine. The effect of hypnosis, delivered via the internet, on pain catastrophizing, frequency, severity and duration of migraines was also investigated. Potential changes in medication usage was of interest too. A number of conclusions can be drawn from the results of this study. The quantitative findings, and the theoretical implications of those findings are discussed initially. Discussion of the qualitative findings follow after.

8.2 Quantitative Findings

8.2.1 Headache Disability

The primary area of interest in this study was the development and evaluation of hypnosis mp3s to address the disability incurred by migraine sufferers as a consequence of their disease. In the area of headache research, a 50% or more reduction in headache activity without a corresponding increase in medication use has been proposed for clinical significance (Blanchard & Schwarz 1988).

The findings of this study established the efficacy of using an online platform for the delivery of an hypnosis programme to reduce disability caused by migraine. The percentage change in mean HDI score from Time 14 (prior to the intervention) to Time 84 (6-week follow up) corresponded with a 48% reduction in HDI in the treatment group compared with a 2% reduction in HDI observed in the control group.

The HDI as a measure of disability was used in this research for two reasons: firstly the ability of the survey to account for affective distress and secondly, it was accessible for participants to understand and use online. Holroyd et al., (1999) looked at twenty-two headache impact measures designed to provide information about the impact of pain on functioning or quality of life. They recommended that the construct of headache impact should include three factors, namely pain, disability and affective distress. Affective distress can impair functioning and exacerbate problems created by headache (Holroyd et al., 1999). Initially the inclusion of The Migraine Disability Assessment Test (MIDAS) was considered for this study. It is a shorter inventory in terms of administration and it was designed to assess the degree of severity to which a patient's life is affected by migraine. However, use of this test would have required that participants track their migraines for three months prior to intervention and for reasons of participant retention an alternate scale was used.

Brandes (2007) examined the extent of suffering for migraineurs during and between migraine attacks. She found that, irrespective of variability among studies in terms of surveys used, the results consistently reported a 'compromised sense of well-being, mood, energy level and family and social interactions' (p.434). This, she pointed out was in addition to the findings of studies conducted internationally which found that 50% of participants reported

disability which was severe enough to cause a decrease in productivity across all areas of life, including work, home and social situations. Brandes (2007), also noted in her review that the majority of research in this area had been conducted to determine the efficacy of drugs and that statistical power may not necessarily be indicative of patient requirements. That review concluded with recommendations that any effective migraine preventive therapy should decrease the frequency, severity and duration of migraine and in doing so could potentially prevent or decrease the progression from episodic migraine to chronic migraine. These three factors were taken into consideration in the present study and findings indicated that the intervention was successful in reducing migraine duration.

The script developed for 'Living Life to the Full' (Appendix 11). targeted unhelpful congitions with respect to pain catastrophizing and disability. These cognitions were explored in the qualitative analysis undertaken in the present study. The changes included participants feeling more in control of their migraines and the associated pain and a decrease in the tendency to ruminate about migraines. The analysis facilitated a greater understanding of the decrease in disability or daily interference which occurred in the treatment group. Thirteen of the fourteen participants interviewed for example, remarked on changes in the activities they became involved in during the study such as socialising more (participants 8 and 10) despite, as one participant (8) pointed out 'I have actually socialised more, I have made a point, even though I don't have more time really.' Participants attributed changes in activity to a variety of reasons including experiencing greater energy levels, taking time out to relax and being more confident in undertaking tasks (participants 4, 8 and 9), headaches being less severe (participant 6) and having fewer migraines (participant 11). These observations were reflected in the HDI scores for the treatment group in this

study which showed a general decrease over time (Fig. 26) suggesting that there may be a cumulative effect of hypnosis.

8.2.2 Pain Catastrophizing

In spite of the considerable volume of research which involved pain catastrophizing, Scott, Wideman and Sullivan (2013) acknowledged that it was not clear how clinicians might best interpret scores on catastrophizing before and after treatment. Scott et al., (2013)'s finding that PCS reductions of 38%-44% post intervention were best associated with return to work and low pain ratings were used as a guideline in this study. The authors recommended that these percentages serve as a preliminary guideline in assessing clinical significance for interventions assessing changes in pain catastrophizing for participants with subacute pain after musculoskeletal injury. To date there are no guidelines for assessing clinical significance in pain catastrophizing for migraineurs.

In the present study the median percentage change in PCS score from Time 14 (prior to intervention) to Time 84 (6 week follow up) in the treatment group corresponded with a 60% reduction in PCS in that group. The median percentage change in the control group was 0%. The mean percentage change in PCS score from Time 14 to Time 42 in the treatment group was a 45% reduction in PCS score versus a 1% reduction in the control group.

Sullivan (2009), defined the constructs of catastrophizing as rumination, magnification and helplessness. He suggested that intervention techniques which influence any of these three dimensions may have therapeutic benefit. Suggestions were included in the hypnosis mp3s in this study to increase feelings of control and enable participants to gain perspective. The specificity of hypnotic suggestions used to target the dimensions of pain catastrophizing has provided support for the importance of direct suggestions in hypnosis and the efficacy of such an approach.

Sullivan (2009) in the Pain Catastrophizing Manual quoted Moseley (2004) and Turk (2004) who speculated that education may have permitted individuals to re-evaluate the internal monologue concerning their condition and to re-assess their perceived ability to participate in activities. The present study provided this education within the hypnotherapy scripts. Changes in perception regarding the migraine condition and alterations in the associated anticipated disability were recorded by participants during the qualitative analysis.

Hassinger, Semenchuk and O'Brien (1999) hypothesised, based on their findings, that migraineurs used more maladaptive coping strategies to manage stress than individuals without headaches and that less effective coping strategies can make conditions worse. They referred to a stress theory proposed by Lazarus and Folkman (1984) which suggested that the ways in which people cope with stress can be a determinant of health and social functioning. Hassinger et al., (1999) surmised that less effective coping strategies for pain and stress amongst migraineurs may have made the impact of that pain and stress worse. Keefe et al., (2004) also found that high levels of pain catastrophizing were linked with high levels of disability. Furthermore, changes in PCS have been shown to affect treatment outcome (Smeets et al., 2006). In the present study, the primary outcome of interest was disability and a strong positive linear relationship was identified between PCS and HDI in both the treatment and the control groups at all time points which is supportive of previous findings in the literature. Keefe et al., (2004) also suggested that the PCS score was related to severity of migraine. That finding was supported by the present study. Participants with moderate migraine symptoms had scores that were 7.4 units higher on average than participants with little or no symptoms, while participants with severe migraine symptoms had PCS scores which were 10.5 units higher on average than participants with little or no symptoms.

8.2.3 Migraine Frequency, Duration and Severity

There was no evidence of a significant difference between the change in the number of migraines from Time 14 to Time 84 between groups. However, there was a significant difference between the change in the total hours of migraine between groups. Fifteen of nineteen participants (79%) in the treatment group experienced a reduction in the total hours of migraine compared with seven of fifteen (47%) experiencing a reduction in the control group. The average reduction in the treatment group was 8 hours per week compared with 0 hours reduction per week in the control group at the 6-week follow up vs Time 14. There was also evidence of a significant difference in the proportion of participants experiencing a decrease in the severity of migraine in the Treatment Group versus the Control Group at Time 42 vs Time 14. This significance was not evident at the six week follow up versus pre-intervention. These findings may be reflective of the content of the mp3s. The suggestions on the hypnosis mp3s were primarily aimed at reducing headache disability and pain catastrophizing, the primary and secondary areas of interest in the study respectively.

8.2.4 Mindfulness

A review of hypnosis and clinical pain by Patterson and Jensen (2003), explored the relationship between hypnotizability and pain outcome for participants using hypnosis. They cited Montgomery et al., (2000) who found that although there was considerable evidence to show that those scoring higher on hypnotizability measures would achieve a better outcome, 75% of the population could obtain substantial pain relief from hypnotic analgesia irrespective of ratings on scales of hypnotizability.

A valid online assessment of hypnotizability was not available when the present study was conducted. It was, however, possible to administer a mindfulness assessment, the Mindfulness Attention

Awareness Scale (MAAS) online. While different brain plasticity changes were found for hypnosis and mindfulness (Halsband, Mueller, Hinterberger & Strickner, 2009), there were also commonalities. Hypnosis and mindfulness were believed to be related to each other in a complementary way (Harrer, 2009).

There was a negative linear relationship between HDI and MAAS in the control group of the present study. As the disability score increased, the value of mindfulness score decreased. The correlation co-efficients for Time 14, Time 42 and Time 84 were statistically significant in the control group. There was, therefore, evidence of a significant negative linear relationship between HDI and MAAS at those time points. Similarly, the correlation co-efficient for Time 14 in the treatment group was statistically significant for Time 14 indicating evidence of a negative linear relationship between HDI and MAAS in the treatment group at that time point. Higher scores of MAAS reflect higher levels of dispositional mindfulness. Given that PCS scores were related to HDI the challenge to remain mindful when feeling more disabled could be influenced by negative thoughts related to the disability.

Cassidy, Atherton, Robertson, Walsh and Gillett (2012) in a study of chronic low back pain patients found that greater mindfulness did not mediate the relationship between catastrophizing and disability but that catastrophizing could mediate the relationship between disability and mindfulness. In the present study catastrophizing scores remained unchanged in the control group over time with the exception of a 1% drop at Time 42. This had returned to 0% at Time 84. In the study by Cassidy et al. (2012) a cognitive behavioural intervention (CBT) was used. Although catastrophizing was reduced in the intervention group in the present study the only significant negative linear relationship between mindfulness and disability in the intervention group in this study was at Time 14 - prior to intervention. Thus, the *type* of intervention used to alter

catastrophizing i.e. hypnosis rather than CBT may perhaps not be as influential in mediating the relationship between disability and mindfulness.

A negative linear relationship between PCS and MAAS was observed in the findings of the present study. As PCS increased, the value of MAAS decreased. The correlation co-efficients for Time 1, Time 14 and Time 84 in the control group were statistically significant (p-values<0.05) which provided evidence for a significant linear relationship between PCS and MAAS in the control group at those time points. Analysis showed that there was no evidence of a significant difference between the average change in MAAS scores in both groups between baseline and 6-week follow up. This suggested that the hypnotic intervention for migraine did not increase or decrease mindfulness. Harrer (2009), found that hypnosis and mindfulness, albeit they are opposite ends of the same spectrum, are essentially two different states of consciousness.

8.3 Qualitative Analysis

The results of the qualitative analysis revealed three primary themes. Each of these themes is discussed in turn.

8.3.1 Theme 1: Emotional Impact

Becker and Ware (2000), investigated what it meant to have migraine. They emphasised the difference between migraine from a physician's perspective and a participants perspective. Most physicians, they pointed out, thought of migraine in terms of various head pain characteristics, associated symptoms and limitations on the duration of the headache. Most participants, on the other hand, thought of migraine in terms of reduced quality of life. The concept of quality of life has been perceived in terms of physical

functioning, social functioning, physical perception and role limitations (Terwindt, Ferrari, Tijhuis, Groenen, Picavet & Launer, 2000). The use of HDI as a measure in the present study meant that functional and emotional impact were taken into consideration.

Mood and emotions have been singled out as important considerations in the treatment of migraine given that migraine participants have twice the chance of suffering from depression and anxiety (Pozo-Rosich, 2012). The 48% drop in HDI scores for the intervention group from week 1 to the 6 week follow up at week 12 demonstrated that the hypnosis mp3s used in the study were effective in reducing headache disability. These results could, in part, be explained by the fact that more than half the participants (n=8) interviewed said that as a result of listening to the mp3s they were, in general, more relaxed. There were nineteen references to relaxation in the transcripts from eleven of the interviewees. Although the Fear Avoidance model of pain explains how patients develop chronic pain as a consequence of avoiding activity (Lethem et al., 1983) the trend in this study seemed to be that participants benefited from learning to cut back on activity. The migraineurs reported a change in the way they viewed relaxation, that is they began to accept that when they had pain that it was acceptable to take time out to rest and that by experiencing relaxation while listening to the mp3s they felt that this had a positive impact on their ability to do more on a daily basis. The suggestions in the mp3 'Reducing Stress and Eliminating Food Triggers' specifically targeted at understanding the importance of balance between work and rest and challenged the notion of driving on with work while in pain. An example of this in the mp3 is 'Balance is an integral part of life and living… rest is as important as work.. relaxing.. as important as being energised…. You do not need to justify taking time out to relax.'

8.3.2 Theme 2: Cognitive Changes

Maladaptive coping strategies should be considered in the management of migraine participants (Radat, Lanteri-Minet, Nachit-Ouinekh, Massiou, Lucas, Pardalier, et al., 2008). Pain catastrophizing was identified as a maladaptive method associated with migraine participants (Yavuz, Yvuz, Ulusoy, Alniak, & Gunes, 2013; Kolotylo & Broome, 2000). Yavuz et al., (2013) examined a variety of dysfunctional cognitive processes associated with primary headaches and found that the PCS scores of migraineurs and individuals with tension type headache were significantly higher than a group of healthy controls who had no headache complaints. The researchers suggested that the high levels of negative thought processes could explain the high frequency of depression among the population. They also recommended further investigations of the cognitive and behavioural aspects accompanying migraine and headache. This, they speculated, would contribute to reducing losses in functional ability caused by both headache and migraine. The findings of the present study which showed a strong positive linear relationship between HDI and PCS confirmed this belief.

There are many excellent meta-analyses and reviews evaluating the efficacy of hypnosis as a treatment for chronic pain in terms of quality of life measures. The importance of using specific suggestions for this purpose has been recognised and documented for a long time. Erickson and Rossi (1976), stated that when using hypnosis as a treatment for chronic pain, there were several outcomes to consider when scripting suggestions. These included decreasing pain, increasing comfort, improving one's ability to divert attention or manipulating the perception of the sensation of pain so that it was instead perceived as tingling or numbness. More recently, the neurophysiological processes occurring as a result of hypnosis and hypnotic analgesia have been investigated and brain imaging has provided evidence of the physiological changes which correspond with different suggestions (Nusbaum et al., 2011). This

study compared differences in brain activity using direct and indirect suggestions in a waking state and in an hypnotic state for participants with low back pain. The suggestions were effective in both normal alertness and in hypnosis but were more effective when using hypnosis. The direct suggestions activated cognitive processes (frontal, prefrontal and orbitofrontal cortices) while indirect suggestions activated an emotional weighted network (frontal cortex, anterior insula, inferior parietal lobule, and ACC).

Thus, suggestions are of particular importance in the delivery of hypnosis as an intervention. However, it was difficult to locate research documenting the phenomenological experience of individuals who had received hypnotherapy in the treatment of chronic pain. Literature documenting the changes in thought processes which evolve as a consequence of hypnotic intervention was lacking. To date, most of the literature has concerned itself with proving the efficacy of hypnosis as a mechanism to alleviate pain and/or the potential physiological mechanism of hypnotic analgesia e.g. Patterson and Jensen (2003), Hawkins (2001) and Accardi and Milling (2009). Given the significance of specific suggestions in hypnosis, a phenomenological investigation provided a means to provide both an insight into the thought processes before and after an hypnosis intervention. This information facilitated a platform from which future scripts could be written for a particular pain population (migraineurs) so that maximum benefit in terms of reducing losses in functional ability can be achieved.

The qualitative analysis provided evidence that specific suggestions on the mp3s stimulated a new train of thought for many of the participants. The natural corollary was a change in attitude and in behaviour such as resting instead of pushing oneself to keep going in spite of the pain. A switch in belief systems from ‘putting a stop to migraine’ to ‘managing migraine’ also emerged in the data which may reflect acceptance of the condition. These insights into

the cognitive processes may well reflect the underlying constructs which led to changes in feelings of helplessness with respect to the disease.

8.3.3 The Participant Voice

Dye, Schatz, Rosenberg and Coleman (2000), described a kaleidoscope metaphor in the constant comparative method of qualitative analysis which emphasised the importance of allowing categories to fit the data in contrast to actively fitting data to categories. These categories then facilitated an understanding of patterns emerging from otherwise individual experiences. In the present study, during the semi-structured interviews, an open-ended question encouraged participants to volunteer any information or comments which they felt were relevant or warranted extra mention or consideration. Several categories emerged as being significant to the participants. These included the experience of hypnosis as a relaxation technique, differences in duration and frequency of migraines after the intervention had finished, feedback about the content and delivery of the mp3s and the frequency with which they listened to the mp3s.

Jensen and Patterson (2006) described nine studies which compared the effects of hypnosis with one or more relaxation interventions including biofeedback-assisted and non-biofeedback assisted relaxation training. They concluded that in a few instances hypnosis was more effective than relaxation training and that it was equally as effective in some instances. They suggested that this may be due to treatments labelled as relaxation e.g. autogenic training, may actually contain elements of hypnotic relaxation such as suggestions in the experience of sensations. This clearly would make it difficult for individuals unfamiliar with the structure of hypnotic relaxation sessions to differentiate it from other relaxation strategies. Of the three participants in the present study who mentioned that they were familiar with other relaxation strategies such as autogenic training

and mindfulness, two (participants 10 and 13) highlighted a difference between the content of the hypnosis mp3s and what they had used before and one person (participant 1) associated the mp3 with a previous technique 'I am used to autogenic training. When the mp3s first kicked in I felt a warming in my body'. Overall however hypnosis seemed to be perceived as a general relaxation technique with the majority of participants (nine of the fourteen) mentioning that the hypnosis mp3s had the effect of relaxing them even beyond the time allocated to listening to them.

No consensus was found in the literature about the optimal number of times participants should receive hypnosis sessions for any particular chronic pain affliction. In this study it was recommended that participants listened to the mp3s three sessions a week. Of those interviewed, eight listened to the mp3s more than three times a week, two listened to the mp3s less than three times a week and four listened to them three times a week as suggested. One of the participants who listened to the mp3s less frequently (participant 6), still reported a considerable difference in migraine severity, frequency and duration. This person was keen to ensure that others would benefit from hypnosis stating 'if anyone suffers from migraine and could avail of this too… because it is life changing in such an amazing way.'

The majority of the research on the effect of environment on migraine and headaches indicated that, compared with the general population, migraineurs had a lower than normal threshold for light-induced discomfort, noise tolerance and olfactory sensitivity (Friedman & De Ver Dye, 2009). Whether the mp3s in this study increased tolerance or caused an alteration in sensitivity is unclear.

Two of the participants made the suggestion, based on their experience of listening to the mp3s and the effect it had afterwards

that a longer intervention would have been preferable in terms of experiencing a greater improvement. One of those participants (12) explained why. 'When I spoke to you the other day I couldn't believe that because I have suffered migraine for so long and so bad and I mentioned to you…. I go to the migraine clinic in Beaumont hospital and the neurologist in Dublin and, em, I have been on a lot of medication; prescribed medication and expensive medication, and I haven't taken any all week which is most unusual. And yeah, even at the moment, I have a lot going on and I am changing jobs and my mam is very sick and finding it very hard, and at home trying to keep everything going and I have actually been ok this week which is very unusual and that is why I do think em, it probably, actually that would be one of the suggestions to you would be to maybe have it for a longer time, so rather than the four to six weeks maybe have it for three months.' This observation by the participants was a valid one as there was a steady decrease across HDI scores from the start of the intervention to the six week follow up (Fig 26.)

Strengths and Limitations

This study was, to the best of the author's knowledge, the first to report a qualitative analysis for a randomised controlled study of hypnotic intervention in a pain population. There are many benefits associated with the provision of health care via an online platform. There are also some drawbacks. In the present study participants resident in different parts of the country and two participants from outside the country were able to participate. The distance proved a challenge following the intervention however, with respect to meeting participants. Most were unable to attend in person and it was therefore not possible to assess hypnotizability.

The population in this study was limited to a section of the pain population who had two or more migraines per month. The gender ratio in the study was not reflective of the gender ratio in the

population of migraine sufferers but it is consistent in the fact that more females were involved in the study than males. Further studies delivering hypnosis online to other pain populations would be necessary to determine the efficacy of hypnotic mp3s via this platform for other chronic pain complaints. The MRC guidelines (2008), noted that consideration needed to be given to retention of participants and delaying receipt of an intervention in order to study its health impact needed careful consideration. For these reasons it was deemed reasonable to provide the wait list group in this study with the mp3 three months post commencement of the intervention. This time period seemed acceptable as it still allowed for a six week follow up and comparison of both the treatment and the wait list group and was not too lengthy a delay in treatment for the latter. Because of the absence of hypnotizability data in this study, it was not possible to ascertain whether there was a correlation between PCS scores and hypnotizability scores. The potential association between the two has not been mentioned or investigated in the literature to date.

There was a higher than normal retention rate in this study compared with other online interventions. The researcher of this study spoke with each of the participants for approximately ten minutes prior to the study in person or on the phone and made it clear that there was an open line of communication between researcher and participants which may have helped with retention rates. The email address and phone numbers of the researcher and the supervisor were included in the participant information sheet and participants were advised that they could contact either individual if they had any questions. In a feedback section at the end of the seventh survey participants in both arms of the intervention commented on the fact that they knew they could contact the researcher at any stage. Despite this access to help the only enquiries which arose during the study were with respect to an error

in the answer format of one of the questions which was subsequently rectified once brought to the researcher's attention.

The possibility that the progression of pain could subside over time has been mentioned in the literature (Jensen & Patterson, 2006). The researchers explained that it is important to measure outcomes prior to, and after, a baseline period in order to rule out the possibility that changes seen with hypnosis are not due to passing of time. When Jensen and Patterson (2006), examined studies employing hypnosis for the treatment of chronic pain that used a no treatment baseline period, they found that little or no change in outcome was reported during this baseline period. No treatment baseline measures as well as follow up measures were employed in the current study.
A slightly longer follow up time of two months as opposed to six weeks may be useful in future studies. There was a decreasing trend in HDI over time in this study. If this trend continued as it had been from baseline and follow up had been two or three months as opposed to six weeks post intervention the 50% reduction or more in HDI recommended for clinical significance by Blanchard and Shwarz (1988), may have been recorded.

No recommendations to denote clinical significance have been made to date in relation to pain catastrophizing scores for migraineurs. In the present study, the 60% drop in PCS corresponded with a 48% drop in headache disability at Time 84. In light of the absence of these recommendations a 60% drop in PCS scores is suggested for future studies where the aim is to improve functionality and should be tested in future studies.
The systematic review included in this study has indicated that hypnosis is effective in reducing pain from migraine and chronic headache. The benefits of employing hypnosis for these conditions include it's simplicity, cost effectiveness and low risk of side effects and/or adverse reactions. Given these advantages and the encouraging outcomes which support the use of hypnosis in the

treatment of migraine and chronic headache, it provides encouraging opportunities for the pursuit of further controlled studies in this area.

The researcher conducting this study had considerable experience (11 years) working in a clinic with individuals who had presented with various chronic pain conditions, including migraine. She also met with participants prior to the present study and was aware of the phenomenological experience which those participating attributed to their migraines. In any hypnosis intervention, where a researcher is not familiar with the thought processes of a particular group of individuals whose disease category is being researched it may be useful to interview individuals prior to writing scripts and to create scripts in and around that feedback. Further qualitative documentation following intervention in future studies would facilitate insight for future researchers conducting studies in these areas.

Recommendations for Future Research

One observation which came to light and which may be of interest to future researchers is a common genetic polymorphism for catastrophizing and hypnotizability. Two studies identified the COMT gene as being associated with pain catastrophizing (George, Wallace, Wright, & Moser, 2008; Finan, Zautra, Davis, Lemery-Chalfant, Covault, & Tennen, 2010). George et al., (2008) found an association between low COMT activity and higher pain ratings and low COMT activity and higher pain catastrophizing. Finan et al., (2010) loked at the val(158)met polymorphism in the COMT gene noting that it mediated pain catastrophizing in participants with fibromyalgia. In a meta-analysis, Tammimaki and Mannisto (2012), stated that low COMT activity was not associated with migraine or chronic musculoskeletal pain conditions but was associated with increased sensitivity in participants with chronic acute widespread pain, clinical preoperative and postoperative pain. The authors

explained that the interactions of adrenergic and dopaminergic activity in parts of the nociceptive system may be an explanation for the complex effects of low COMT activity.

Hypnotizability has also been associated with polymorphisms in the COMT gene. This is an area which warrants further exploration. As outlined previously, Lichtenberg et al., (2000) found that participants in their study who had with the met/val COMT heterozygote geno-type scored highest on hypnotizability. Finan et al., (2010) found in their study of 45 females with fibromyalgia that the genetic variation in the val58met polymorphism might moderate their pain through pathways of pain related cognition.

The criticism of qualitative research is often that it is cannot be generalised. However, as Lincoln and Guba (1985) pointed out, specifics can be lost when generalisations are made. In the present study, the qualitative inquiry used semi-structured interviews. This allowed for elaboration on the raw data generated from standardised measures and permitted a phenomenological reflection from the participants' perspective. From a research context, issues such as changes in cognition, which otherwise may not have been intuited were given prominence. The constant comparative methodology also generated a number of potentially useful considerations for future studies. They include the following:

- Generation of information which reflects the general attitude of migraineurs towards their disease. This may be useful to future researchers interested in devising hypnotic suggestions for similar interventions.
- Insight into the cognitive changes stimulating behaviour changes in participants and the specific suggestions on the mp3s which stimulated the modification of those thought processes.
- Consideration of participants' desire for longer interventions.

- Information about the type of activities which migraineurs are more likely to engage in as their migraines subside.
- Acknowledgement that interpersonal relationships with others change relative to changes in the frequency and severity of their migraines and how they perceive their migraines e.g. feeling more in control, less impatient etc.
- Potential to educate migraineurs about the difference between hypnosis and other relaxation techniques.

Implications for Clinical Practice

Overall, findings from this study provide evidence for the efficacy of an online hypnosis programme to reduce headache disability and pain catastrophizing in migraineurs. There was a 48% reduction in mean HDI score and a 60% reduction in PCS in the treatment group ten weeks after commencing the intervention. A strong positive linear relationship between PCS and HDI was found in the present study. Furthermore, PCS was found to relate to severity of migraine. Both of these findings were supportive of previous findings in the literature. An observation which was made and which was beyond the scope of the present study, and which warrants further investigation, was the common genetic polymorphism for PCS and Hypnotizability. The findings of the present research offer the opportunity to broaden the research to other pain populations. The results also have implications for the way in which migraine pain can be managed via the internet. For migraineurs who do not wish to use medication or who are experiencing unpleasant side effects from medication, hypnosis is a novel, accessible option for the management of migraines with the additional benefit of having no negative side effects.This was the first study to design, deliver and evaluate a hypnosis intervention for migraineurs via the internet. The results of this study indicated that hypnosis delivered online was an effective method for reducing headache disability and pain catastrophizing for migraineurs.

References

Accardi, M.C. & Milling, L.S. (2009). The effectiveness of hypnosis for reducing procedure-related pain in children and adolescents: a comprehensive methodological review. *Journal of Behavioural Medicine*. *32,* 328-339.

Adachi, T., Fujino, H., Nakae, A. Mashimo, T., & Sasaki, J. (2013). A Meta-Analysis for Chronic Pain Problems: A Comparison between hypnosis, standard care, and other psychological interventions. *International Journal of Clinical and Experimental Hypnosis. 62(1),* 1-28.

Agee, J. (2009). Developing qualitative research questions: a reflective process. *International Journal of Qualitative Studies in Education*. 22(4), 431-447.

Anderson, J. A., Basker, M. A., & Dalton, R. (1975). Migraine and hypnotherapy. *The International Journal of Clinical and Experimental Hypnosis. 23*(1), 48-58.

Andrasik, F., Buse, D.C., Grazzia, L. (2009). Behavioural medicine for migraine and medication overuse headache. *Current Pain and Headache Reports. 13*, 241-248.

Andreychuk, T., & Skriver, C. (1975). Hypnosis and biofeedback in the treatment of migraine headache. *The International Journal of Clinical and Experimental Hypnosis., 23*(3), 172-183.

Antila, V., Winsvold, B.S., Gormley, P., Kurth, T., Bettella, F., McMahon, G., Kallela, M., Malik, R., et al., (2013) Genome-wide meta-analysis identifies new susceptibility loci for migraine. *Nature Genetics*. 45, 912-917.

Apkarian, A.V., Hashmi, J.A., & Baliki, M.N. (2011). Pain and the brain: Specificity and plasticity of the brain in clinical chronic pain. *Pain. 152(3,Suppl),* S49-64.

Baad-Hansen, L., Abrahansen, R., Zachariae, R., List, T. & Svensson, P. (2013). *Clinical Journal of Pain. 29.* 518-526.

Babel, P. (2015). Memory of pain and affect associated with migraine and non-migraine headaches. *Memory. 23(6),* 864-875.

Bajwa, Z.H., Swanson, J.W., Dashe, J.F. (2015). Acute treatment of migraine in adults. www.uptodate.com/contents/acute-treatment-of-migraine-in-adults.

Baliki, M.N., Chialvo, D.R., Geha, P.Y., Levy, R.M., Harden, R.N., Parrish, T.B., & Apkarian, A.V. (2006). Chronic pain and the emotional brain: specific brain activity associated with spontaneous fluctuations of intensity of chronic back pain. *The Journal of Neuroscience. 22;26(47),* 12165-73.

Barber, T.X. (1959). Toward a theory of pain: Relief of chronic pain by prefrontal leucotomy, opiates, placebos, and hypnosis. *Psychological Bulletin*, 56, 430.

Barber, J., & Mayer, D. (1977). Evaluation of the efficacy and neural mechanism of a hypnotic analgesia procedure in experimental and clinical dental pain. Pain. 4(1), 41-48.
Bantick, S.J., Wade, G.W., Ploghaus, A., Clare, S., Smith, S.M., Tracey. I. (2002). Imaging how attention modulates pain in humans using functional MRI. *Brain. 125*, 310-9.
Bashir, M., Afzel, M. & Azeem, M. (2008). Reliability and Validity of Operational Research Paradigm. *Pakistan Journal of Statistics and Operation Research.* 4(1), 35-45.
Battino, R. (2007). Expectation: Principles and practice of very brief therapy. *Contemporary Hypnosis. 24(1),* 19-29.
Baxter, P. & Jack, S. (2008). Qualitative case study methodology: study design and implementation for novice researchers. *The Qualitative Report.* 13(4), 544-559.
Becker, W.J., & Ware, J.E. (2000). What does it mean to have migraine? *Neurology. 55(5),* 610-611.
Bender, J. L., Radhakrishnan, A., Diorio, C., Englesakis, M., & Jadad, A. R. (2011). Can pain be managed through the Internet? A systematic review of randomized controlled trials. *Pain. 152(8),* 1740-50.
Benedetti, F. (2007) The Placebo and Nocebo Effect: How the therapists words act on the patient's brain. *Karger Gazette. Mind & Body.* 69, 7-9.
Benedetti, F. & Amanzio, M. (1997). The neurobiology of placebo analgesia: from endogenous opioids to cholecystokinin. *Progress in Neurobiology. 51*, 109-125.
Benedetti, F. (2013). Placebo and the new physiology of the doctor-patient relationship. *Physiological Reviews. 93:*1207-1246.
Benedetti, F. & Amanzio, M. (1997). The neurobiology of placebo analgesia: from endogenous opioids to cholecystokinin. *Progress in Neurobiology. 51:* 109-125.
Benham, G., & Woody, E.Z. (2006). Expect the unexpected: Ability, Attitude, and responsiveness to hypnosis. *Journal of Personality and Social Psychology. 91(2),* 342-350.
Benoit, D.P. (2009). An introduction to migraine pathophysiology. *Techniques in Regional Anaesthesia & Pain Management. 13*, 5-8.
Berman, B. M., & Swyers, J. P. (1999). Complementary medicine treatments for fibromyalgia syndrome. *Bailliere's Clinical Rheumatology. 13(3),* 487-492.
Bigal, M.E. & Ho, T.W. (2009). Is there an inherent limit to acute migraine treatment efficacy? *The Journal of Headache and Pain.* 10, 393-394.
Bigal, M.E., Borucho, S., Serrano, D., & Lipton, R.B. (2009). The acute treatment of episodic and chronic migraine in the USA. *Cephalagia. 29(8),* 891-897.
Black, A.K., Fulwiler, J.C. & Smitherman, T.A. The role of fear of pain in headache. *Headache. 55(5),* 669-679.

Blanchard, E.B. & Schwarz, S.P. (1988). Clinically significant changes in behavioural medicine. *Behavioural Assessment*. *10*, 171-188.

Blau, J.N. (1980). Migraine prodromes separated from the aura: complete migraine. *British Medical Journal*. 281, 658-660.

Blau, J.N. (1984). Migraine pathogenesis: the neural hypothesis re-examined. *Journal of Neurology, Neurosurgery and Psychiatry*. *47*, 437-442.

Boeije, E. (2002). A purposeful approach to the constant comparative method in the analysis of qualitative interviews. *Quality and Quantity*. 36, 391-409.

Brandes, J.L. (2008). The migraine cycle: Patient burden of migraine during and between attacks. *Headache.* 48, 430-441.

Breslau, N., Davis, G.C., Andreski, P. (1991). Migraine, psychiatric disorders and suicide attempts: An epidemiologic study of young adults. *Psychiatry Research*. 37:11-23.

Brigo, F. Storti, M., Tezzon. F. Manganotti, P. & Nardone, R. (2013). Primary visual cortex excitability in migraine: a systematic review with meta-analysis. *Neurological Science.* 34, 819-830.

British Psychological Society (2013). Ethics Guidelines for Internet-mediated Research. INF206/1.2013. Leicester: Available from www.bps.org.uk/publications/policy-andguidelines/research-guidelines-policydocuments/research-guidelines-policies.

Bronfort, G., Nillson, N., Haas, M., Evans, R., Goldsmith, C., Assendelft, W. & Bouter, L. (2009). Non-invasive physical treatments for chronic/recurrent headache. *Cochrane Database of Systematic Reviews*. Issue 1.

Brown, H., Newman, C., Noad, R., & Weatherby, S. (2012) Behavioural management of migraine. *Annals of Indian Neurology*. 15(Suppl 1): S78-S82.

Bryant, R.A. and Hung, L. (2013). Oxytocin enhances social persuasion during hypnosis. PLOS One. 8(4):e60711

Bubenzer, T. & Huang, H. (2014). Posthypnotic use of olfactory stimulus for pain management. *International Journal of Clincal and Experimental Hypnosis.* 62(2): 188-194.

Burrows, G.D., Stanley, R.O. & Bloom, P.B. (2001). International Handbook of Clinical Hypnosis. Chichester. Wiley.

Caldwell, K., Emery, L., Harrison, M. & Greeson, J. (2011). Changes in Mindfulness, well-being, and sleep quality in college students through Taijiquan Courses: A cohort control study. *The Journal of Alternative and Complementary Medicine.* 17(10), 931-938.

Calhoun, A.H., Ford, S., Finkel, A.G., Kahn, K.A. & Mann, J.D. (2006). The prevalence and spectrum of sleep problems in women with transformed migraine. *Headache: The Journal of Head & Face Pain*. 46(4), 604-610.

Cassidy, E.L., Atherton, R.J., Robertson, N., Walsh, D.A. & Gillett, R. (2012). Mindfulness, functioning and catastrophizing after multidisciplinary pain management for chronic low back pain. *Pain.* 153, 644-650.

Castel, A., Pérez, M., Sala, J., Padrol, A., & Rull, M. (2007). Effect of hypnotic suggestion on fibromyalgic pain: Comparison between hypnosis and relaxation. *European Journal of Pain*, 11(4), 463-468.

Cevoli, S., Giannini, G., Favoni, V., Pierangeli, G., & Cortelli, P. (2012). Migraine and sleep disorders. *Neurological Science.* 33, 43-46.

Chaibi, A., Tuchin, P., & Russell, M. (2011). Manual therapies for migraine: A systematic review. *The Journal of Headache and Pain; Official Journal of the "European Headache Federation" and of "Lifting the Burden" – the Global Campaign against Headache*". 12(2). 127-133.

Chakravarty, A.A., Mukherjee, A. & Roy, D. (2008). Migraine pain location: how do children differ from adults. *Journal of Headache Pain.* 9,375-379.

Chambless, D.L., & Hollon, S.D. (1988). Defining empirically supported therapies. *Journal of Consulting and Clinical Psychology*. 66(1), 7-18.

Chen, J. (2011). History of pain theories. *Neuroscience Bulletin.* 27(5); 343-50.

Chen, A.C. Dworkin, S.F., Drangsholt, M.T. (1983). Cortical power spectral analysis of acute pathophysiological pain. *International Journal of Neuroscience*. 18: 269-278.

Chiros, C., & O'Brien, W.H. (2011). Acceptance, appraisals, and coping in relation to migraine headache: an evaluation of interrelationships using daily diary methods. *Journal of Behavioral* Medicine, 1-14.

Colon, Y. & Avent, M.S. (2014). Medical Hypnotherapy for Pain Management. *Journal of Pain and Palliative Care Phramacotherapy*. 28:174-176.

Condello, C., Piano, Virginie, P., Dadam, D., Pinessi, L., Lanteri-Minet, M. (2015). Pain Beliefs and Perceptions Inventory: A Cross-Sectional Study in Chronic and Episodic Migraine. *Headache*. 55:136-148.

Coon, D. & Mitterer, J.O. (2008). Introduction to Psychology: Gateways to Mind and Behavior. 12thed. Wadsworth Publishing Company.

Crombez, G., Eccleston, C., Van Damme, S., Vlaeyen, J.W.S. & Karoly, P. (2012). Fear-Avoidance Model of chronic pain. *Clinical Journal of Pain.* 28(6):475-482.

Cuijpers, P., Van Straten, A. & Andersson, G. (2008). Internet-administered cognitive behavior therapy for health problems: A systematic review. *Journal of Behavioral Medicine*, 31(2), 169-177.

Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I., & Petticrew, M. (2008). Developing and evaluating complex interventions: The New Medical Research Council Guide. British Medical Journal. 337, a1667.

Creswell, J. (2002). Educational research: Planning, conducting, and evaluating quantitative and qualitative research. Upper Saddle River, NJ: Merrill Prentice Hall.

Creswell, J.W. (2007). Qualitative inquiry and research design: Choosing among qualitative approaches (2nd ed.). Thousand Oaks, CA: Sage.

D'Amico, D., Grazzi, L., Usai, S., Rigamonti, A., Curone, M., & Bussone, G. (2005). Disability Pattern in Chronic Migraine With Medication Overuse: A Comparison With Migraine Without Aura. Headache: *The Journal of Head & Face Pain*, 45(5). 553-560.

D'amico, D., Grazzi, L., Usai, S., Leonardi, M & Raggi, A. (2013). Disability and quality of life in headache: where we are now and where we are heading. *Neurological Science*. 34(S1), S1-S5.

D'Andrea, G., D'arrigo, A., Dalle, M., Leon, A. (2012). Pathogenesis of Migraine. Role of Neuromodulators. *Headache*. 52, 1155-1163.

Davis, R.E., Smitherman, T.A. & Baskin, S.M. (2013). Personality traits, personality disorders and migraine: a review. *Neurological Science*. 34(S1), S7-S10.

De Benedittis, G. (2003). Understanding The Multidimensional Mechanisms of Hypnotic Analgesia. *Contemporary Hypnosis*, 20(2), 59-80.

De Fazzano, C. (1980). *Effectiveness of hypnosis in the treatment of migraine: The role of hypnotisability*. Unpublished manuscript.

De Morton, N.A. (2009). The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. *The Australian Journal of Physiotherapy*. 55(2)129-33.

Devineni, T., & Blanchard, E. B. (2005). A randomized controlled trial of an internet-based treatment for chronic headache. *Behaviour Research and Therapy*, 43(3), 277-292.

Dickenson, A.H., Bee, L.A. & Suzuki, R. (2005) Pains, gains and midbrains. *Proceedings of the National Academy of Sciences*. 102(50), 17885-17886.

Diener, E., & Suh, E. (1997). Measuring quality of life: economic, social, and subjective indicators. *Social Indicators Research*. 40, 189-216.

Dillworth, T. & Jensen, M. (2010). The role of suggestions in hypnosis for chronic pain: A review of the literature. *The Open Pain Journal*. 3, 39-51.

Dionne, F., Blais, M.C. and Montestes, J.L. (2013). Acceptance and commitment therapy in the treatment of chronic pain. *Sante Mentale au Quebec*. 38(2):131-52.

Doherty, M. (1994) Probability versus Non-Probability Sampling in Sample Surveys, *The New Zealand Statistics Review*. March Issue. 21-28.

Donatone, B. (2013) Focused Suggestion with somatic anchoring technique: Rapid self-hypnosis for pain management. *American Journal of Clinical Hypnosis*. 55(4): 325-342.

Dowson, A.J., Lipscombe, S., Sender, J., Rees, T., & Watson. D. (2002). New Guidelines for the management of migraine in primary care. *Current Medical Research Opinion*. 18(7). 1-53.

Ducros, A. (2006). Physiopathologie et approche génétique de la migraine. (French). Mechanisms and Genetics of Migraine. (English), 20, 1-11.

Ducros, A. (2013). Genetics of migraine. *Revue Neurologique*. 169(5), 360-71.

Dye, J.F., Schatz, I.M., Rosenberg, B.A., & Coleman, S.T. (2000). Constant Comparison Method: A Kaleidoscope of Data. The Qualitative Report, 4(1/2)Available: http://www.nova.edu/ssss/QR/QR3-4/dye.html

Eccleston, C., Palmero, T.M., Williams, A., Lewandowski, A., Morley, S., Fisher, E. & Law, E. (2013). Psychological therapies for the management of chronic and recurrent pain in children and adolescents. *Cochrane Database of Systematic Reviews.* Issue 8.

Edelson, J. & Fitzpatrick, J.L. A comparison of cognitive-behavioural and hypnotic treatments of chronic pain. *Journal of Clinical Psychology*. 45(2), 316-323.

Edmeads, J. (1991). What is migraine? Controversy and stalemate in migraine pathophysiology. *Journal of Neurology*. 238(1):S2-S5.

Elkins, G., Jensen, M.P. & Patterson, D.R. (2007). Hypnotherapy for the management of chronic pain. *International Journal of Clinical and Experimental Hypnosis, 55(3),* 275-287.

Erickson, M.H. & Rossi E.L. (1976) Two level communication and the microdynamics of trance and suggestion. *The American Journal of Clinical Hypnotherapy*. *18(3),*153-171.

Ernst, W. (2004). Colonial psychiatry, magic and religion. The case of mesmerism in British India. *History of Psychiatry, 15(1),* 057-071.

Estemalik, E. & Tepper, S. (2013). Preventive treatment in migraine and the new US guidelines. *Neuropsychiatric Disease and Treatment. 9:*709-720.

Ezra, Y., Gotkine, M., Goldman, S., Adahan, H., & Ben-Hur, T. (2012). Hypnotic Relaxation Vs Amitriptyline for Tension-Type Headache: Let the patient choose. *Headache*. 52, 785-791.

Fairhurst, M., Fairhurst, K., Berna, C. & Tracey, I. (2012). An fMRI study exploring the overlap and differences between neural representations of physical and recalled pain. *PLoS ONE. 7(10):*e-48711

Feldman. (2004). The neurobiology of pain, affect and hypnosis. *American Journal of Clinical Hypnotherapy., 46*(3), 187-200.

Finan, P.H., Zautra, A.J., Davis, M.C., Lemery-Chalfant, K., Covault, J., & Tennen, H. (2010). COMT moderates the relation of daily maladaptive coping and pain in fibromyalgia. *Pain. 152(2),* 300-307.

Fingelkurts, A.A., Fingelkurts, A.A. & Kahkonen, S. (2005). Functional connectivity in the brain.. is it an elusive concept? *Neuroscience and Biobehavioural Reviews*. 28(8),827-36.

Fingelkurts, A., Fingelkurts, A., Kallio, S. & Revonsuo, A. (2007). Hypnosis induces a changed composition of brain oscillations in EEG: A case study. *Contemporary Hypnosis*. *24(1),* 3-18.

Finnochi, C., & Giorgia, S. (2012). Food as trigger and aggravating factor of migraine. *Neurological Sciences. 33.* 77-80.

Flor, H. (2014). Psychological Pain Interventions and Neurophysiology. American Psychologist. 69(2), 188-196.

Flory, N., Salazar, G.M., & Lang, E.V. (2007). Hypnosis for acute distress management during medical procedures. *International Journal of Clinical and Experimental Hypnosis. 55(3),* 303-317.

Fossey, E., Harvey, C., Mcdermott, F. & Davidson, L. (2002). Understanding and evaluating qualitative research. *Australian and New Zealand Journal of Psychiatry.* 36(6), 717-732.

Frederick, G., & Freitag, D.O. (2007) The Cycle of Migraine: Patients' Quality of Life During and Between Migraine Attacks. *Clinical Therapeutics. 29(5),* 939-949

Friedman, D., & De Ver Dye, T. (2009) Migraine and the environment. *Headache. 49(6),* 941-52.

Friedman, H., & Taub, H. (1984). Brief psychological training procedures in migraine treatment. *American Journal of Clinical Hypnotherapy*. 26(3), 187-200.

Galletti, F., Cupini, L.M., Corbelli, I., Calabresi, P., & Sarchielli, P. (2009). Pathophysiological basis of migraine prophylaxis. *Progress in Neurobiology. 89(2),* 176-92.

Gauthier, J., Cote, G., & French, D. (1994). The role of home practice in the thermal biofeedback treatment of migraine headache. *Journal of Consulting and Clinical Psychology*. 62(1), 180-184.

Gedney, J.J. & Logan, H. (2006). Pain related recall predicts future pain report. *Pain* 121(102), 69-76.

Geertz, C. (1973). The Interpretations of Cultures. New York.

Basic Books.
George, S.W., Wallace, M.R., Wright, T.W., & Moser, M.W. (2008). Evidence for a biopsychosocial influence on shoulder pain: Pain catastrophizing and catechol-O-methyltransferase (COMT) diplotype predict clinical pain ratings. *Pain.* 136(1-2), 53-61.
Gervil, M., Ulrich, V., Kaprio, J., Olesen, J. & Russell, M.B. (1999). The relative role of genetic and environmental factors in migraine without aura. *Neurology*. 22:53(5), 995-999.
Gibbs, T.S., Fleischer, A.B. Jr., Feldman, S.R., Sam, M.C., & O'Donovan, C.A. (2003). Health care utilization in patients with migraine: demographics and patterns of care in the amulatory setting. *Headache*. 43(4), 330-5.
Gilmore, B., & Michael, M. (2011). Treatment of Acute Migraine Headache. *American Family Physician*. 83 (3), 271-80.
Goadsby PJ.(2001). Pathophysiology of headache. In: Silberstein SD, Lipton RB, Dalessio DJ, eds. Wolff's Headache and Other Head Pain. 7th ed. New York, NY: Oxford University Press; 57-72.
Goadsby, P.J. (2006). Recent advances in the diagnosis and management of migraine. *British Medical Journal*. 332(7532), 26-29.
Goadbsy, P.J. (2009). Scientific Commentary. The vascular theory of migraine – a great story wrecked by the facts. *Brain*. 132, 6-7.
Goltman, A. (1936) The mechanism of migraine. *Journal of Allergy*. 7(4), 351-355.
Graffin, N., William & Lundy, R. (1995). EEG concomitants of hypnosis and hypnotic susceptibility. *Journal of Abnormal Psychology*. 104, 123-31.
Grant, C. D., & Nash, M. R. (1995). The Computer-Assisted Hypnosis Scale: Standardization and Norming of a Computer-Administered Measure of Hypnotic Ability. *Psychological Assessment*, 7(1), 49-58.
Green, J.P., Barabasz, A.F., Barrett, D., & Montgomery, G.H. (2005). Forging ahead, the 2003 APA Division 30 definition of hypnosis. *International Journal of Clinical and Experimental Hypnosis*. 53, 259–264.
Gruzelier, J.H. (2000). Redefining Hypnosis: Theory, Methods and Integration. *Contemporary Hypnosis*. 17(2):51-70.
Gustavsson, A., Svensson, M., Jacobi, F., Allgulander, C., Alonso, J., Beghi, E., Dodel, R., Ekman, M., Faravelli, C. et al. (2011). Cost of disorders of the brain in Europe 2010. European *Neuropsychopharmacology. 21,* 718-779.
Halsband, U., Mueller, S., Hinterberger, T., & Strickner, S. (2009). Plasticity changes in the brain in hypnosis and meditation. *Contemporary Hypnosis*. *26(4),* 194-215.
Hamel, E. (2007). Serotonin and migraine: biology and clinical implications. *Cephalagia. 27(11),* 1293-1300.

Hamelsky, S.W. & Lipton, R.B. (2006). Psychiatric Comorbidity of Migraine. *Headache. 46(9):* 1327-1333.
Hamington, M. (2009). Business is not a game. *Journal of Business Ethics*. 86, 473-484.
Hammond, D. (2004). Treatment with hypnotherapy reduces the sensory and motor component of gastrocolonic response in irritable bowel syndrome. *American Journal of Clinical Hypnosis.* 47(10), 70-71.
Hammond, D.C. (2007). Review of the efficacy of clinical hypnosis with headaches and migraines. *International Journal of Clinical and Experimental Hypnosis, 55(2),* 207-219.
Hardcastle, V.G. (1999) The Myth of Pain. Massachusetts. Massachusetts Institute of Technology.

Harder, B. (2005). Against the migraine. *Science News. 167(8),* 119-120.
Harrer, M.E. (2009). Mindfulness and the mindful therapist: Possible contributions to hypnosis. *Contemporary Hypnosis.* 26(4): 234-244.
Hartman, D. (2010a). A comparison of self hypnosis versus progressive muscle relaxation in patients with multiple sclerosis and chronic pain. *Journal of Heart Centered Therapies*. 13(1), 104.
Hartman, D. (2010b). Controlled trial of hypnotherapy in the treatment of refractory fibromyalgia. *Journal of Heart Centered Therapies,* 13(1), 94.
Hartman, D. (2010c) Effects of self-hypnosis training and EMG biofeedback relaxation training on chronic pain in persons with spinal cord injury. *Journal of Heart Centered Therapies,* 13(1), 128.
Hassinger, H.J., Semenchuk, E., & O'Brien, W.H. (1999). Appraisal and coping responses to pain and stress in migraine headache. *Journal of Behavioural Medicine*. 22(4), 327-340.
Headache Classification Committee of the International Headache Society (IHS) (2013). The International Classification of Headache Disorders, 3rd edition (beta version) *Cephalalgia* 33(9) 629–808.
Haythornthwaite, J. (Ed.). (2009). *It's a Belief. It's an Appraisal. It's Coping... No, It's Catastrophizing.* Glasgow Scotland: IASP Press.
Hawkins, K., Wang, S., & Rupnow, M.F. (2007). Indirect cost burden of migraine in the United States. *Journal of Occupational Environmental Medicine. 49,* 368-74.
Hawkins, R.M. (2001). A systematic meta-review of hypnosis as an empirically supported treatment of pain. *Pain Reviews. 8,* 47-73.
Hazard, E., Munakta, J., Bigal, M.E., Rupnow, M.F., & Lipton, R.B. (2009). The burden of migraine in the United States: Current and emerging perspectives on disease management and

economic analysis. *Value in Health. 12(1),* 55-64.
Henryk-Gutt, R. & Linford Rees, W. (1973) Psychological aspects of migraine. Journal of Psychosomatic Research. *17(2),* 141-153.
Headache Classification Committee of the International Headache Society (2018). The International Classification of Headache Disorders. 3rd Ed. *Cephalagia. 38(1),* 1-211.
Hershey, A.D. (2005). What is the impact, prevalence, disability, and quality of life of paediatric headache? *Current Pain and Headache Reports Journal. 9,* 341-344.
Hines, E.A. (1938). Migraine. *The American Journal of Nursing. 38(9),* 988-992.
Hoeft, F., Gabrieli, J.D.E., Whitfield-Gabrieli, S., Haas, B.W., Bammer, R., Menon, V., & Speiegel, D. (2012). Functional Brain Basis of Hypnotizability. *Archives of General Psychiatry*. *69(10),*1064-1072.
Hofbauer, R.K., Rainville, P., Duncan, G.H. & Bushnell, M.C. (1998). Cognitive modulation of pain sensation alters activity in human cerebral cortex. *Society of Neuroscience Abstract*. 24,1135. In, De Benedittis, G. (2003). Understanding The Multidimensional Mechanisms of Hypnotic Analgesia. *Contemporary Hypnosis, 20(2),* 59-80.
Hofbauer, R.K., Rainville, P., Duncan, G.H., Bushnell, M.C. (2001). Cortical representation of the sensory dimension of pain. *Journal of Neurophysiology. 86:*402-411.
Holdevici, I. & Craciun, B. (2012). The use of Ericksonian hypnosis in somatic disorders. *Procedia – Social and Behavioural Sciences. 33:*75-79.
Holland, S., Silberstein, S.D., Freitag, F., Dodick, D.W., Argoff, C. & Ashman, E. (2012). Evidence-based guideline update: NSAIDs and other complementary treatments for episodic migraine prevention in adults. *Neurology*. 78,1346-1353.
Holroyd, K. A., Drew, J. B., Cottrell, C.K., Romanek, K.M. & Heh, V. (2007). Impaired functioning and quality of life in severe migraine: The role of catastrophizing and associated symptoms. *Cephalalgia, 27(10),* 1156-1165.
Holroyd, K.A., Malinoski, P., Davis, M.K. & Lipchik, G.L. (1999). The three dimensions of headache impact: pain, disability and affective distress. Pain. 83(3): 571-578.
Hsu, L.K.G., Kalucy, R.S., Crisp, A.H., Koval, J., Chen, C.N., Carruthers, M., & Zilkha, K.J. (1977). Early morning migraine: Nocturnal plasma levels of catecholamines, tryptophan, glucose, and free fatty acids and sleep encephalographs. *The Lancet. 309(8009),* 447-451.
Huber, A., Lui, F., Duzzi, D., Pagnoni, G., & Porro, C. (2014). Structural and functional cerebral correlates of hypnotic suggestibility. *PLoS One. 9(3),* e93187.
IASP (2011), from http://www.iasppain.org/Content/NavigationMenu/GlobalYearAgainstPain/GlobalYearAgainstHeadache/Fact_Sheets4/de

fault.htm
Innamorati, M., Pompili, M. Fiorillo, M., Lala, N., Negro, A., Del Bono, S. Lester, D., Girardi, P., Martelletti, P. (2013). Overattchment and perceived disability in chronic migraineurs. *Clinical Neurology and Neurosurgery*. 115 (7), 954-958.
Jackson, J.L., Cogbill, E., Santana-Davila, R., Eldredge, C. Collier, W., Gradall, A. Sehgal, N. & Kuester, J. (2015). A comparative effectiveness meta-analysis of drugs for the prophylaxis of migraine headache. *PLOS one*. 10 (7), e0130733.
Jackson, J.L., Kuriyama, A., & Hayashino, Y. (2012). Botulinum Toxin A for prophylactic treatment of migraine and tension headaches in adults. *Journal of the American Medical Association. 307(16)*, 1736-1745.
Jacobson, G.P., Ramadan, N.M., Aggarwal, S.K. & Newman, C.W. (1994). The Henry Ford Hospital Headache Disability Inventory (HDI). *Neurology. 44(5),* 837-842.
Jacobson, G.P., Ramadan, N.M., Norris, L. & Newman, C.W. (1995). Headache disability inventory (HDI): short-term test-retest reliability and spouse perceptions. *Headache. 35(9)*, 534-539.
Jamieson, G. A., Woody, E. (2007). Dissociated control as a paradigm for cognitive neuroscience research and theorizing in hypnosis. In G. A. Jamieson (Ed), Hypnosis and conscious states: the cognitive neuroscience perspective. Oxford. Oxford University Press.
Jensen, K.B., Berna, C., Loggia, M.L., Wasan, A.D., Edwards, R.R. & Gollub, R.L. (2012). The use of functional neuroimaging to evaluate psychological and other non-pharmacological treatments for clinical pain. *Neuroscience Letters. 520(2):* 156-164.
Jensen, M.P., Ehde, D.M., Gertz, K.J., Stoelb, B. L., Dillworth, T.M., Hirsh, A.T., et al. (2011). Effects of self-hypnosis training and cognitive restructuring on daily pain intensity and catastrophizing in individuals with multiple sclerosis and chronic pain. *International Journal of Clinical and Experimental Hypnosis, 59*(1), 45-63.
Jensen, M.P., & Karoly, P. (1991). Control beliefs, coping efforts, and adjustment to chronic pain. *Journal of Consulting and Clinical Psychology*. *59*, 431–438.
Jensen, M.P. & Patterson, D.R. (2014) Hypnotic Approaches for Chronic Pain Management. American Psychologist. 69 (2) 167-177.
Jensen, M.P. & Patterson, D.R. (2006). Hypnotic treatment of chronic pain. *Journal of Behavioural Medicine* 29(1), 95-124.
Jensen, M.P., Sherlin, L.H., Askew, R.L., Fregni, F., Witkop, A.G., Howe, J.D. & Hakimian, S. (2013). Effects of non-pharmacological pain treatments on brain states. *Clinical*

Neurophysiology. 124, 2016-2024.
Johannsen, M., Farver, I., Beck, N., & Zachariae, R. (2013). The efficacy of psychosocial intervention for pain in breast cancer patients and survivors: A systematic review and meta-analysis. Breast Cancer Research and Treatment, 138(3), 675-90.
Kallio, S. & Koivisto, M. (2013). PostHypnotic suggestion alters conscious color perception in an automatic manner. *International Journal of Clinical and Experimental Hypnosis. 61(4):* 371-378.
Kelman, L. & Rains, J.C. (2005). Headache and sleep: examination of sleep patterns and complaints in a large clinical sample of migraineurs. *Headache: The Journal of Head & Face Pain*. Jul/Aug 45(7), 904-910.
Kiernan B.D., Dane, J.R., Phillips, L.H., & Price D.D. (1995). Hypnotic analgesia reduces R-III nociceptive reflex: Further evidence concerning the multifactorial nature of hypnotic analgesia. *Pain*. *60,* 39-47.
King, B., Nash, M., Spiegel, D. & Jobson, K. (2001). Hypnosis as an intervention in pain management: A brief review. *International Journal of Psychiatry in Clinical Practice*. *5,* 97-101.
Kolb, S.M. (2012). Grounded Theory and the Constant Comparative Method: Valid Research Strategies for Educators. *Journal of Emerging Trends in Educational Research and Policy Studies*. 3(1), 83-86.
Kolotylo, C.J., & Broome, M.E. (2000). Exploration of migraine pain, disability, depressive symptomatology and coping: a pilot study. *Health Care Women International*. 21, 203-18.
Kroger, W.S. (1976). Clinical and Experimental Hypnosis. 2nd ed. Philadelphiz, PA: J.B. Lippincott: 48.
Larkin, D.M. (2014). Principles of therapeutic suggestions (Part I) and clinical applications of therapeutic suggestions (Part II). *Explore*. 10(6): 380-388.
Lang E.V, Fick L.J, Lutgendorf, S., Berbaum M.L, Berbaum K.S, Logan., Spiegel D. (2000). Adjunctive non-pharmacological analgesia for invasive medical procedures: a randomised trial. *The Lancet,* 29, 1486-1490.
Latham, B. (2007). Sampling: what is it? Quantitative Research Methods. ENGL 5377. Spring. http://webpages.acs.ttu.edu/rlatham/Coursework/5377(Quant))/Sampling_Methodology_Paper.pdf
Latsko, M., Silberstein, S., & Rosen, N. (2011). Frovatriptan as preemptive treatment for fasting-induced migraine. *Headache*. 51, 369-374.
Lauwerier, E., Paemeleire, K., Van Damme, S., Goubert, L., & Crombez, G. (2011). Medication use in patients with migraine and medication-overuse headache. The role of problem-solving and attitudes about pain medication. *Pain. 152(6),* 1334-1339.

Lazarus, R. S., and Folkman, S. (1984). Stress, Appraisal, and Coping, Springer, New York.
Lethem, J, Slade, P. D. Troup, J. D., Bentley, G. (1983). Outline of a Fear-Avoidance Model of exaggerated pain perception--I". *Behaviour research and therapy 21 (4):* 401–408.
Levinthal, C. (1987). In Wilson, F.R. (Ed.), *The effects of indirect hypnosis, direct hypnosis and progressive relaxation on the primary and secondary psychological symptoms of chronic headache*. ProQuest Dissertations Publishing.
Lifshitz, M., Howells, C., & Raz, A. (2012). Can expectation enhance response to suggestion? De-automatization illuminates a conundrum. *Consciousness and Cognition. 21:*1001-1008.
Lincoln, Y., & Guba, E. (1985). Naturalistic Inquiry. Sage Publications Inc. Beverly Hills, CA.
Linde, M. (2006). Migraine: a review and future directions for treatment. *Acta Neurologica Scaninavica. 114*, 71-83.
Linde, K., Allais, G., Brinkhaus, B. Manheimer, E., Vickers, A. & White, A.R. (2009). Acupuncture for migraine prophylaxis. *Cochrane Database of Systematic Reviews*. Issue 1.
Lipchik, G.L & Penzien, D.B. (2004). Psychiatric comorbidities in patients with headache. *Seminars in Pain Medicine. 2*, 93-105.
Lipton, R.B., Cady, R.K., Stewart WF, Wilks K, & Hall, C. (2002). Diagnostic lessons from the spectrum study. *Neurology. 58*(9), S27-S31.
Lipton, R.B., & Bigal M.E. (2005). The epidemiology of migraine. *The American Journal of Medicine. 118(1),* 3s-10s.
Lipton, R.B., Stewart, W.F., Diamond, S., Diamond, M.L., & Reed, M. (2001). Prevalence and burden of migraine in the United States. Data from the American Migraine Study II. *Headache. 41,* 646-657.
Lipton, R.B., Fanning, K.M., Serrano, D., et al. Ineffective acute treatment of episodic migraine is associated with new-onset chronic migraine. *Neurology.* 84:688-695.
Littlewood, J.T., Glover, V., Davies, P.T.G., Gibb, C. Sandler, M., & Clifford, F. Red wine as a cause of migraine. *The Lancet*. 331(8585), 558-559.
Lynn, J.L., Kirsch, I. & Hallquist, N.N. (2008). Social cognitive theories of hypnosis. In: Nash, M.R., Barnier, A.J. editor. The Oxford Handbook of Hypnosis: theory, research and practice. Oxford: Oxford University Press. Pp 111-139.
Malone, C.D., Bhowmick, A., & Wachholtz, A.B. (2015). Migraine: treatments, comorbidities, and quality of life, in the USA. *Journal of Pain Research. 12(8):*537-47.
Martin, P.R. (2001). How do trigger factors acquire the capacity to precipitate headaches? *Behaviour Research and Therapy. 39.* 545-554.

Macea, D.D., Gajos, K., Daglia Calil, Y.A., & Fregni, F. (2010). The efficacy of web-based cognitive behavioral interventions for chronic pain: A systematic review and meta-analysis. *Journal of Pain, 11*(10), 917-929.

MacDonnell, J. (2013). http://www.faculty.fairfield.edu/jmac/sj/scientists/hell.htm Mathematics department. Fairfield University.

MacGregor, A. (2004). Oestrogen and attacks of migraine with or without aura. *The Lancet Neurology*. 3,June, 354-361.

MacGregor, A. (2010). Prevention and treatment of menstrual migraine. *Drugs*. 70(14), 1799-1818.

MacKillop, J. & Anderson, E.J. (2007). Further psychometric validation of the Mindful Attention Awareness Scale (MAAS). *Journal of Psychopathology and Behavioural Assessment. 29(4),* 289-293.

Maizels, M., Aurora, S., Heniricher, M. (2012). Beyond neurovascular: migraine as a dysfunctional neurolimbic pain network. *Headache*. 52(10), 1553-65.

Marc, I., Rainville, P., Masse, B., Dufresne, A., Verreault, R., Vaillancourt, L., et al. (2009). Women's Views Regarding Hypnosis for the Control of Surgical Pain in the Context of a Randomized Clinical Trial. *Journal of Women's Health. 18*(9), 1441-1447.

Martelletti, P., Birbeck, G.L., Katsarava, Z., Jensen, R.H. Stovner, L.J. & Steiner, T.J. (2013). The Global Burden of Disease survey 2010, Lifting The Burden and thinking outside-the-box on headache disorders. *The Journal of Headache and Pain*. 14:13.1-2.

Mathew, N.T. (2011). Pathophysiology of chronic migraine and mode of action of preventive medications. *Headache. 51(2),* 84-92.

Mannix, L.K., Chandurkar, R.S., Rybicki, L.A., Tusek, D.L., & Solomon, G.D. (1999). Effect of guided imagery on Quality of Life for patients with chronic tension-type headache. *Headache. 39,* 326-334.

Maykut, P., & Morehouse, R. (1994), Beginning Qualitative Research: A Philosophic and Practical Guide, London: The Falmer Press.

McCaslin, M.L. & Wilson Scott, K. (2003). The Five Question method for framing a qualitative research study. *The Qualitative Report*. 8(3): 447-461.

McGeown, W.J., Mazzoni, G., Vannucci, M. & Venneri, A. (2015). Structural and functional correlates of hypnotic depth and suggestibility. *Psychiatriy Research: Neuroimaging. 231,* 151-159.

McGuire, B.E., Henderson, E.M. & McGrath, P.J. (2017). Tranlating e-pain research into patient care. *Pain. 158*, 190-193.

Melis, P. (1991). Treatment of chronic tension-type headache with hypnotherapy: A single-blind time controlled study. *Headache*, 31(10), 686-689.
Melzach, R. (2001). Pain and the neuromatrix in the brain. *Journal of Dental Education. 65(12):*1378-1382.
Melzack, R., & Perry, C. (1975). Self-regulation of pain: The use of alpha-feedback and hypnotic training for the control of chronic pain. Experimental Neurology. 46(3), 452-469.
Meng, I.D., Dodick, D., Ossipov, M.H. & Porreca, F. (2011). Pathophysiology of medication overuse headache: insights and hypotheses from preclinical studies. *Cephalalgia. 31(7):* 7851-7860.
Merikangas, K.R., Angst, J. & Isler, H. (1990). Migraine and psychopathology: Results of the Zurich Cohort Study of Young Adults. *Archives of General Psychiatry. 47:*849-853.
Milling, L. S., Coursen, E.L., Shores, J. & Waszkiewicz, J.A. (2010). The predictive validity of hypnotizability: The change in suggestibility produced by hypnosis. *Journal of Consulting and Clinical Psychology, 78(1),* 126-130.
Migraine Association of Ireland. (2013). www.migraine.ie
Moayedi, M. & Davis, K.D. (2012). Theories of pain: from specificity to gate control. *Journal of Neurophysiology. 109(1):* 5-12.
Moseley, G.L. (2004). Evidence for a direct relationship between cognitive and physical change during an education intervention in people with chronic low back pain. *European Journal of Pain.* 8, 39-45. In O'Sullivan, M. (2009). The Pain Catastrophizing Scale. User Manual. 1-36.
Moseley, A.M., Herbert, R.D., Sherrington, C., & Maher, C.G. (2002). Evidence for physiotherapy practice: A survey of the physiotherapy evidence database (PEDro*). Australian Journal of Physiotherapy*, 48(1), 43-49.
Mogallaoglu, M. (2013). Trigger factors in migraine patients. *Journal of Health Psychology. 18(7),* 984-994.
Montgomery, G.H., Duhamel, K.N. & Redd, W.H. (2000). A meta-analysis of hypnotically induced analgesia: How effective is hypnosis? *International Journal of Clinical and Experimental Hypnosis*, *48*(2), 138-153.
Morley, S., Eccleston, C. & Williams. A. (1999). Systematic review and meta-analysis of randomized controlled trials of cognitive behaviour and behaviour therapy for chronic pain in adults, excluding headache. *Pain.* 80:1-13.
Morse, J.M. & Field, P.A. (1995). Qualitative research methods for health professionals. 2nd Edition. Thousand Oaks. California: Sage Publications.
Moseley, L. (2007). Reconceptualising pain according to modern pain science. *Physical Therapy Reviews. 12:* 169-178.
Moseley, L.G (2013) http://opensciences.org/videos/consciousness-studies/science-of-mind-forum-with-the-dalai-lama

Moseley, L. & Butler, D. (2015). 15 years of explaining pain – the past, the present, the future. Prepublication.
Munksgaard, S.B. & Jensen, R.H. (2014). Medication overuse headache. *Headache. 54(7):*1251-1257.
Munksgaard, S.B. & Jensen, R.H. (2015). Medication overuse headache: Inaccurate and overdiagnosed. *Headache. 55(1):* 206-207.
Nahman-Averbuch, H., Granovsky, Y., Coghill, R.C., Yarnitsky, D., Sprecher, E., & Weissman-Fogel, I. (2013). Waning of "Conditioned Pain Modulation": A novel expression of subtle pronociception in migraine. *Headache. 53:*1104-1115.
Nash, M.R. & Barnie, A.J. (2012). The Oxford Handbook of Hypnosis: Theory, Research, and Practice. Oxford University Press. Oxford.
National Institute for Health and Care Excellence. (NICE). (2012). http://www.nice.org.uk/guidance/CG150/chapter/1-Guidance#management-2
Negro, A. & Martelletti, P. (2011). Chronic migraine plus medication overuse headache: two entities or not? *The Journal of Headache and Pain. 12,* 593-601.
Nicholson, R.A. (2010). Chronic Headache: The role of the psychologist. Current *Pain Headache Reports. 14(1),* 47-54.
Nicholson, R.A., Houle, T.T., Rhudy, J.L., Norton, P.J. (2007). Psychological Risk Factors in Headache Headache. 47(3), 413–426.
Nolan, R. (1995). The efficacy of hypnotic and non-hypnotic response based imagery for self-managing recurrent headache. *Imagination, Cognition and Personality*. 14(3), 183-201.
Nusbaum, F., Redouté, J., Le Bars, D., Volckmann, P., Simon, F., Hannoun, S., et al. (2011). Chronic low-back pain modulation is enhanced by hypnotic analgesic suggestion by recruiting an emotional network: A PET imaging study. *International Journal of Clinical and Experimental Hypnosis, 59(1),* 27-44.
Olness, K., MacDonald, J. T. & Uden, D. L. (1987). Comparison of self-hypnosis and propranolol in the treatment of juvenile classic migraine. *Pediatrics, 79(4),* 593.
Ost, L.G. (2014). The efficacy of acceptance and commitment therapy: an updated systematic review and meta-analysis. *Behavioural Research Therapy. 61:*105-21.
Patterson, D.R. (2004). Treating pain with hypnosis. *Current Directions in Psychological Science*. 13(6), 252-255.
Patterson, D.R. (2005). Behavioural methods for chronic pain and illness: A reconsideration and appreciation. *Rehabilitative Psychology*. *50(3),* 312-315.
Patterson, D.R. & Jensen., M.P. (2003). Hypnosis and Clinical Pain. *Psychological Bulletin, 129(4),* 495-521.

Patterson, D.R., & Ptacek, J.T. (1997). Baseline pain as a moderator of hypnotic analgesia for burn injury treatment. *Journal of Consulting and Clinical Psychology*. 65(1), 60-67.

Phan, K., Wager, T., Taylor, S., & Liberzon I. (2002). Functional neuroanatomy of emotion: A meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage*. 16, 331–348.

Ploeg, J. (1999). Identifying the best research design to fit the question. Part 2: qualitative designs. *Evidence Based Nursing*. 2, 36-37.

Ploghaus, A. Becerra, L., Borras, C. & Borsook, D. (2003). Neural circuitry underlying pain modulation: expectation, hypnosis, placebo. *Trends in Cognitive Sciences. 7(5).* 197-201.

Pearce, J. (1977). Migraine: A psychosomatic disorder. *Headache: The Journal of Head and Face Pain. 17(3),* 125-128.

Peroutka, S.J. (2004). Migraine: a chronic sympathetic nervous system disorder. *Headache.* 44(1), 53-64.

Piccione, C., Hilgard, E.R., & Zimbardo, P.G. (1989). On the degree of stability of measured hypnotizability over a 25 year period. *Journal of Personality and Social Psychology*. *56(2),* 289-295.

Pietrobon, D. & Striessnig, J. (2003). Neurobiology of Migraine. www.nature.com. *Neuroscience*. 4, 386-398.

Pozo-Rosich, P. (2012) Chronic migraine: its epidemiology and impact. *Revista de Neurologia*. *10(54),* S3-11.

Quartana, P.J., Campbell, C.M. & Edwards, R.R. (2009). Pain catastrophizing: a critical review. Expert Review of Neurotherapeutics. 9(5), 745-758.

Racine, M., Tousignant-Laflamme, Y., Kloda, L.A., Dion, D., Dupuis, G., Choiniere, M. (2012). A systematic literature review of 10 years of research on sex/gender and pain perception- part 2: Do biopsychosocial factors alter pain sensitivity differently in women and men? *Pain. 153,* 619-635.

Radat, F., Lanteri-Minet, M., Nachit-Ouinekh, F., Massiou, H., Lucas, C., Pardalier, A., Mercier, F., & Hasnaoui, A. (2008). The GRIM2005 study of migraine consultation in France. III: Psychological features of subjects with migraine. *Cephalagia. 29,* 338-350.

Rainville, P. (2002). Brain mechanisms of pain affect and pain modulation. *Current Opinion in Neurobiology. 12:*195-204.

Rainville, P., Carrier, B., Hofbauer, R.K., Duncan, G.H. & Bushnell, M.C. (1999). Dissociation of pain sensory and affective process using hypnotic modulation. *Pain. 82,* 159-71.

Rainville, P., Duncan, G.H., Price, D.D., Carrier, B. & Bushnell, M.C. (1997). Pain affect encoded in human anterior cingulate but not somatosensory cortex *Science. 15;*277(5328), 968-71.

Rapoport, A.M. (2015). How to choose a preventive medication for migraine. *American Headache Society*. www.americanheadachesociety.org.
Raskin, N.H., Hosobuchi, Y. & Lamb, S. (1987). Headache may arise from perturbation of brain. *Headache*. 27(8), 416-420.
Reid, G.J., & McGrath, P.J. (1996). Psychological Treatments for Migraine. *Biomedicine and Pharmacotherapy*. 50, 58-63.
Reisman, M. & Fuller, C. (2009). Controversies in interventional cardiology. Is patent foramen ovale closure indicated for migraine? Patent foramen closure for migraine cardiovascular interventions. *Circulation Cardiovascular Interventions*. 2, 468-474.
Rippen, H. & Risk, A. (2000). E-health code of ethics. *Journal of Medical Internet Research*. Apr-Jun. 2(2), e9.
Rockett, F.C., de Oliveria, V.R., Castro, K., Chaves, M.L.F., da S Perla, A. & Perry, I.D.S. (2012). Dietary aspects of migraine trigger factors. *Nutrition Reviews. 70(6):*337-356.
Rozen, T.D. (2004). Migraine prodrome: a nose on the face. *The Lancet. 14,* 363.
Richeimer, S. (2000). The Richeimer Pain Update from http://www.helpforpain.com/arch2000dec.htm
Roberts, L., Wilson, S., Singh, S., Roalfe, A., & Greenfield, S. (2006). Gut directed hypnotherapy for irritable bowel syndrome: Piloting a primary care-based randomised controlled trial. *The British Journal of General Practice: The Journal of The Royal College of General Practitioners.* 56(523), 115.
Rockett, F.C., de Oliveria, V.R., Castro, K., Chaves, M.L.F., da S Perla, A. & Perry, I.D.S. (2012). Dietary aspects of migraine trigger factors. *Nutrition Reviews*. 70(6), 337-356.
Scott, W., Wideman T.H. & Sullivan, M.J. (2013). Clinically Meaningful Scores on Pain Catastrophizing Before and After Multidisciplinary Rehabilitation: A prospective study of individuals with subacute pain after whiplash injury. *Clinical Journal of Pain. Apr. 1. (Epub ahead of print)*
Serrano, D., Buse, D.C., Adams, A.M., Reed, M.L., Lipton, R.B. (2015). Acute treatment optimization in episodic and chronic migraine: Results of the American Migraine Prevalence and Prevention (AMPP) study. *Headache. 55(4),* 502-518.
Shapiro, R.E. & Goadsby, P.J.(2007). The long drought: the dearth of public funding for headache research. *Cephalalgia*. 27(9), 991-994.
Sharpe L, Williams AC de C, Martin PR, Nicholas M, Welgampola M, McPhee I, Baillie A, Dudeney J, McGuire B. (2016). Psychological therapies for the prevention of migraine in adults. *Cochrane Database of Systematic Reviews*. *8*. Art. No.: CD012295.
Silberstein, S.D. & Dodick, D.W. (2013). Migraine Genetics. *Headache*. 53(8), 1218-1229.

Silberstein, S.D. & Lipton, R.B. (1993). Epidemiology of migraine. *Neuroepidemiology.* 12(3),179-94.
Silberstein, S.D., Lipton, R.B., Sliwinski, M. (1996). Classification of daily and near-daily headaches. Field trial of revised HIS criteria. *Neurology. 47:871-875.*
Society, I. H. (2011). from http://ihs-classification.org/en/02_klassifikation/02_teil1/02.00.00_tension.html
Spanos, N. (1993). Hypnotic suggestion and placebo for the treatment of chronic headache in a university volunteer sample. *Cognitive Therapy and Research,* 17(2), 191-205.
Spanos, N. P., Liddy, S. J., Scott, H., Garrard, C., Sine, J., Tirabasso, A., & Hayward, A. (1993). Hypnotic suggestion and placebo for the treatment of chronic headache in a university volunteer sample. *Cognitive Therapy & Research. 17,* 191–205.
Spanos, N.P., Radtke-Bodorik, H.L., Ferguson, J.D. & Jones, B. (1979). The effects of hypnotic susceptibility, suggestions for analgesia, and utilization of cognitive strategies on the reduction of pain. *Journal of Abnormal Pyschology*. *88,* 282-292.
Spanos, N.P., Radtke-Bodorik, H.L., Ferguson, J.D. & Jones, B. (1979). The effects of hypnotic susceptibility, suggestions for analgesia, and utilization of cognitive strategies on the reduction of pain. *Journal of Abnormal Pyschology*. *88,* 282-292.
Spiegel, H. (1972). An eye-roll test for hypnotizability. *The American Journal of Clinical Hypnosis*. *15(1),* 25-28.
Spiegel, H. (1974). The grade 5 syndrome: The highly hypnotizable person. *The International Journal of Clinical and Experimental Hypnosis*. 4, 303-319.
Spiegel, H. (1977). The hypnotic induction profile (HIP): A review of its development. Annals of the New York Academy of Sciences. *296,* 129-142.
Spiegel, D. & Albert, L.H. (1983). Naloxone fails to reverse hypnotic alleviation of chronic pain. *Psychopharmacology*. *81(2),* 140-143.
Spiegel, D. King, R. (1992). Hypnotizability and CSF HVA levels among psychiatric patients. *Biological Psychiatry. 31,* 95-98.
Spiegel, H. & Spiegel, D. (2004). Trance & Treatment. Clinical Uses of Hypnosis. 2nd Edition. American Psychiatric Publishing Ltd. Washington DC.
Spierings, N. M. K., & Spierings, E. L. H. (2007). Hypnosis in the treatment of headache: Is hypnotherapy beneficial? *Headache and Pain: Diagnostic Challenges, Current Therapy, 18(4),* 140-148.
Spinhoven, P. (1992). Autogenic training and self-hypnosis in the control of tension headache. *General Hospital Psychiatry*. 14(6), 408-15.

Srikiatkhachorn, A., le Grand, S.M., Supornsilpchai, W. & Storer, J. (2014) Pathophysiology of Medication Overuse Headache. *Headache. 54(1):* 204-210.

Sroka, G., Arnon, Z., Laniado, M., Schiff, E. & Matter, I. (2015). Hypnosis-induced mental training improves performance on the Fundamentals of Laparoscopic Surgery (FLS) simulator. *Surgical Endoscopy. 29:* 1024-1029.

Steiner, T.J., Stovner, LJ. & Birbeck, G.L. (2013). Migraine: the seventh disabler. *The Journal of Headache and Pain*. 14, 1-2.

Stewart, W.F., Lipton, R.B. & Liberman, J. (1996) Variation in migraine prevalence by race. *Neurology*. Jul;47(1), 52-9.

Stoelb, B.L., Molton, I.R., Jensen, M.P. & Patterson, D.R. (2009). The efficacy of hypnotic analgesia in adults: A review of the literature. *Contemporary Hypnosis. 26(1),* 24-39.

Stovner, L.J., Hagen, K., Jensen, R., Katsarava, Z., Lipton, R., Scher, A.I., Steiner, T.J., Zwart, J.A. (2007). The global burden of headache: a documentation of headache prevalence and disability worldwide. *Cephalagia. 27,* 193-210.

Sturgeon, J.A. (2014). Psychological therapies for the management of chronic pain. *Psychology Research and Behaviour Management*. 7, 115-124.

Strom, L., Pettersson, R., & Andersson, G. (2000). A controlled trial of self-help treatment of recurrent headache conducted via the internet. *Journal of Consulting and Clinical Psychology*. 68(4), 722-727.

Sullivan, A., Cousins, S., & Risdale, LL. (2016). Psychological interventions for migraine: A systematic review. *Journal of Neurology*. Online.

Sullivan, M.J., Bishop, S.R., & Pivik, J. (1995). The Pain Catastrophizing Scale: development and validation. *Psychological Assessment, 7(4),* 524-532.

Sullivan, M.J.L., Lynch, M.E., Clark, A.J., Mankovsky, T., & Sawynok, J. (2008). Catastrophizing and treatment outcome: differential impact on response to placebo and active treatment outcome. *Contemporary Hypnosis, 25*(3/4), 129-140.

Swanson, S.A., Zeng, Y., Weeks, M. & Colman, I. (2013) The contribution of stress to the comorbidity of migraine and major depression: results from a prospective cohort study. *British Medical Journal. e002057*. doi:10.1136/ bmjopen-2012-002057.

Szekely, A., Kovacs-Nagy, R., Banyai, E.I, Gosi-Greguss, A.C., Varga, K., Halmai, Z., Ronai, Z. & Sasvari-Szekely, M. (2010). Association between hypnotizability and the Catechol-O-Methyltransferase (COMT) Polymorphism. *International Journal of Clinical and Experimental Hypnosis. 58(3),* 301-315.

Tammimaki, A., & Mannisto, P.T. (2012). Catechol-O-methyltransferase gene polymorphism and chronic human pain: a systematic review and meta-analysis. *Pharmacogenetics and Genomics*. *22(9),* 673-691.

Tan, G., Craine, M.H., Blair, M.J., Garcia, M.K., Giordano, J., Jensen, M.P., McDonald, S.M., Patterson, D., Sherman, R.A., Williams, W. & Tsao, J.C. (2007) Efficacy of selected complementary and alternative medicine interventions for chronic pain. *Journal of Rehabilitation Research and Development*. 44(2), 195-222.

Tepper, S.J. (2008). A pivotal moment in 50 years of headache history: the first American migraine Study. *Headache*. *48(5),* 730-1.

Terhune, D.B. (2015). Discrete response patterns in the upper range of hypnotic suggestibility: A latent profile analysis. *Consciousness and Cognition. 33:*334-341.

Ter Kuile, M. (1994). Autogenic training and cognitive self-hypnosis for the treatment of recurrent headaches in three different subject groups. *Pain*. 58(3), 331-340.

Terwindt, G.M., Ferrari, M.D., Tijhuis, M., Groenen, A., Picavet, J., & Launer, L.J. (2000). *Neurology. 55(5),* 624-629.

Tozer, B.S., Boatwright, E.A., David, P.S., Verma, D.P., Blair, J.E., Mayer, A.P. & Files, J.A. (2006). Prevention of migraine in women throughout the life span. *Mayo Clinic Proceedings. Mayo Clinic. 81(8),* 1086-1092.

Trautmann, E., & Kröner-Herwig, B. (2010). A randomized controlled trial of Internet-based self-help training for recurrent headache in childhood and adolescence. *Behaviour Research and Therapy, 48(1),* 28-37.

Turk, D.C. & Wilson, H.D. (2010). Fear of pain as a prognostic factor in chronic pain: conceptual models, assessment and treatment implications. *Current Pain Headache Reports. 14(2):*88-95.

Turk, D.C., Wilson, H.D. & Cahana, A. (2011). Treatment of chronic non-cancer pain. *The Lancet*. 25;377(9784), 2226-35.

Ulrich, V., Gervil, M., Kyvik, K.O., Olesen, J. & Russell, M.B. (1999) Evidence of a genetic factor in migraine with aura: a population based twin study. *Annals of Neurology*. 45(2), 242-6.

Valente, S. (2006). Hypnosis for pain management. *Journal of Psychosocial Nursing & Mental Health Services*. 44(2), 22-30.

Vanhaudenhuyse, A., Laureys, S., & Faymonville, M.(2014). Neurophysiologie de l'hypnose. *Clinical Neurophysiology. 44;* 343-353.

Vanhaudenhuyse, A., Boly, M., Laureys, S., & Faymonville, M. (2009). Neurophysiological correlates of hypnotic analgesia. *Contemporary Hypnosis, 26(1),* 15-23.

Van Hecke, O., Torrance, N. & Smith, B.H. (2013). Chronic pain epidemiology and its clinical relevance. *British Journal of Anaesthesia*. 111(1), 13-18.

Vargas, B.B. & Dodick, D.W. (2009). The face of chronic migraine: epidemiology, demographics, and treatment strategies. *Neurological Clinics.* May, *27(2),* 467-79.

Varkey, E., Cider, A., Carlsson, J., & Linde, M. (2008). A study to evaluate the feasibility of an aerobic exercise program in patients with migraine. *Headache. 49,* 563-570.

Vassalli, A., & Dijk, D.J. (2009). Review. sleep function: current questions and new approaches. *European Journal of Neuroscience. 29,* 1830-1841.

Verhagen, A.P., de Vet, H.C., de Bie, R.A., Kessels, A.G., Boers, M., Bouter, L.M., Knipschield, P.G. (1998). The Delphi list: a criteria for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. *Journal of Clinical Epidemiology. 51(12):* 1235-41.

Villemure, C., Bushnell, M.C. (2002). Cognitive modulation of pain: how do attention and emotion influence pain processing? *Pain 95:* 195-199.

Vlaeyen J.W., Kole-Snijders A.M., Boeren R.G. & van Eek H. (1995). Fear of movement/ (re)injury in chronic low back pain and its relation to behavioral performance. *Pain , 62 (3):*363-72.

Yadav, R.K., Kalita, J., & Misra, U.K. (2010). A study of triggers of Migraine in India. *Pain Medicine*. *11,* 44-47.

Yakhnitsa, V.A., Pilyavskii, A.I., Limansky, Y.P. & Bulgakova, N.V. (1996). Modulation of the activity of midbrain central gray substance neurons by calcium channel agonists and antagonists in vitro. *Neuroscience.* 70(1), 159-167.

Yavuz, K.F., Yavuz, N., Ulusoy, S., Alniak, I., Gunes, H.N. (2013). Maladaptive cognitive content and attitudes accompanying tension type headache and migraine. *The Journal of Psychiatry and Neurological Sciences. 26,* 12-21.

Waltraud, E. (2004). Colonial psychiatry, magic and religion. The case of mesmerism in British India. *History of Psychiatry. 15(1),* 057-071.

Wallen, G., Middleton, K., Ames, N., Brooks, A., & Handel, D. (2014). Randomized trial of hypnosis as a pain and symptom management strategy in adults with sickle cell disease. *Integrative Medicine Insights*. 9, 25-33.

Warren Brown, K. & Ryan, R.M. (2003). The benefits of being present: Mindfulness and its role in psychological well-being. *Journal of Personality and Social Psychology*. *84(4),* 822-848

Wiech, K., Ploner, M. & Tracey, I. (2008). Neurocognitive aspects of pain perception. *Trends in Cognitive Sciences. 12(8):* 306-313.

Wiech, K., & Tracey, I. (2009). The influence of negative emotions on pain: Behavioural effects and neural mechanisms. *NeuroImage. 47:* 987-994.
Weichman Askay, S. & Patterson, D.R. (2007). Hypnotic analgesia. *Expert review of Neurotherapeutics*. *7(12),* 1675-1683.
Weiller ,C., May, A., Limmroth, V., Jüptner, M., Kaube, H., Schayck, R.V., Coenen, H.H. & Diener, H.C. (1995). Brain stem activation in spontaneous human migraine attacks. *Nature Medicine*. 1, 658-660.
Welch, K.M. (1987). Migraine. A Biobehavioural Disorder. *Archives of Neurology*. 44(3), 323-327.
Welch, K. (2003). Contemporary concepts of migraine pathogenesis. *Neurology. 61*, 2-8.
Welch, K.M., Nagesh, V., Aurora, S.K., & Gelman, N. (2001). Periaqueductal gray matter dysfunction in migraine: cause or burden of illness? *Headache. 41(7)*, 629-37.
Wells, R.E., & Loder, E. (2012). Mind/body and behavioral treatments: The evidence and approach. *Headache*. 52(S2), 70-75.
WHO, & Lifting The Burden. (2011). Atlas of Headache Disorders and Resources in The World. Geneva.
WHO. (2001). World health report 2001 mental health: New understanding, new hope. Geneva: World Health Organization.
Wickramasekera, I. (2007). Review of the efficacy of clinical hypnosis with headaches and migraines. American Journal of Clinical Hypnosis. 50(1), 98-99.
Wickramasekera, I. (2008). Long term outcome of hypnotic analgesia treatment for chornic pain in persons with disabilities. American Journal of Clinical Hypnosis, 51(1), 86.
Williams, C. (2007). Research Methods. *Journal of Business & Economic Research*. 5(3). 65-72.
Williams, Y. (2015). Stratified Random Sample: Example & Definition. Research Methods in Psychology. Lesson 8. www.study.com
Williams, A., Eccleston, C. & Morley, S. (2012). Psychological therapies for the management of chronic pain (excluding headache) in adults. *Cochrane Database of Systematic Reviews*. Issue 11.
Wolff, H.G. (1937). Personality features and reactions of subjects with migraine. *Archives of Neurology and Psychiatry. 37(4),* 895-921.
Wretman, J. (2010). Reflections on Probability vs Nonprobability Sampling. In Carlson, Nyquist and Villani (eds), Official Statistics – Methodology and Applications in Honour of Daniel Thorburn. 29–35.
Yin, R. K. (2003). Case study research: Design and methods. 3rd Ed. Thousand Oaks, CA: Sage

Zeidan, F., Martucci, K.T., Kraft, R.A., Gordon, N.S., McHaffie, J.G., & Coghill, R.C. (2011). Brain mechanisms supporting the modulation of pain by mindfulness meditation. *The Journal of Neuroscience. 31(14),* 5540-5548.

Zitman, F.G., Van Dyck, R., Spinhoven, P., & Linssen, A. (1992). Hypnosis and autogenic training in the treatment of tension headaches. A two-phase constructive design study with follow up. *Journal of Psychosomatic Research. 36:*219-228.

http://www.physiopedia.com/Psychological_approaches to_pain_management

Appendices

Appendix 1:

Suite 29 Floor 2
The Galway Clinic
Doughiska
Galway

31/12/12

Suite 29 Floor 2
The Galway Clinic
Doughiska
Galway

Dear Dr. Jahnke,
Thank you for your interest in the PhD research study 'Development and Evaluation of an online Hypnosis Study for the Treatment of Migraines' at NUI, Galway.
Further to our previous meeting please find details pertaining to potential participants you wish to refer to the study. Participants will be required to contact the researcher (Niamh Flynn) at info@bodywatch.ie and by written correspondence to the above address enclosing a letter signed by yourself to state that that they have a diagnosis of migraine and that you are happy that they satisfy the inclusion and exclusion criteria outlined below.

Inclusion Criteria

- Adults aged 18 years of age or older
- Two or more migraines per month for the preceding three months
- Fluency in the English language
- Familiarity with the use of the internet
- Agreeable to completing a daily migraine diary and to adhere to the full protocol
- No change in prophylactic or abortive medication for at least one month prior to commencement of study

Exclusion Criteria

- Individuals with psychiatric disorder
- Migraine related to the menstrual cycle
- Women who are pregnant
- Participation in other trials while enrolled in this trial

The meeting for the initial pilot study will be held on Tuesday 16th January 2012 @10am in Galway. The meeting for those participating in the main study will be in early February 2012. I will confirm that date with you later.
Thank you very much for your interest in this study.

Kind regards,

_____

Niamh Flynn MBA MMEDSCI BA DHP CI

TEL: 091 720145 MOBILE: 086 8234337

Appendix 2: Eligibility Criteria Sheet

Copy and print this page for your GP or Neurologist

Development and Evaluation of an Online Hypnosis Intervention for the Treatment of Migraine

Researcher: Niamh Flynn MBA MMEDSCI BA DHP CI

Address for correspondence: Niamh Flynn, Suite 29 Floor 2, The Galway Clinic, Doughiska, Galway.

Fax: 091 720146 **Tel:** 091 720145 **Mobile:** 086 8234337
Email: info@bodywatch.ie

Criteria For Eligibility

Inclusion Criteria

- Adults aged 18 years of age or older
- Two or more migraines per month for the preceding three months
- Fluency in the English language
- Familiarity with the use of the internet
- Agreeable to completing a daily migraine diary and to adhere to the full protocol
- No change in prophylactic or abortive medication for at least one month prior to commencement of study

Exclusion Criteria

- Individuals with severe psychiatric disorder
- Migraine related to the menstrual cycle
- Women who are pregnant
- Participation in other trials while enrolled in this trial

Appendix 3: Participant Information Sheet

Participant Information Sheet

Development and Evaluation of an Online Hypnosis Intervention for Migraine Sufferers

Please read this leaflet before deciding whether to participate in this study. This information sheet outlines why the study is being carried out and what will be required of you if you wish to participate. It includes information about the purpose, risks and benefits of this research study. If you agree to participate you will be asked to sign a consent form. Please ask if there is anything here which you do not understand. We will be delighted to answer any questions you may have. You should only consent to participate in this study when you feel that you understand what is being asked of you and when you have had sufficient time to consider your decision.

What is the study about and why is it being carried out?
The aim of this study is to evaluate the efficacy of an online hypnosis programme for the treatment of migraines. 13-18% of women and 5-10% of men are affected by migraine. In the U.K alone 25 million days are lost annually by workers and students because of migraines at a significant cost to society. It is being carried out to evaluate the potential efficacy of an online intervention for migraines to decrease the disability caused by migraines, reduce the frequency of migraines and reduce levels of pain catastrophizing in migraine sufferers.

Who is funding the study?
This research is privately funded by the researcher, Niamh Flynn, who has an interest in chronic pain and has ten years of experience working with hypnosis.

Do I qualify to take part in the study?
Your neurologist or GP who will be referring you to the study will be able to assess whether you will qualify for the study. If you meet the requirement criteria you will be given a letter of referral and you can contact the researcher. Contact details are on the third page of this information sheet.
Requirements include being over 18 years of age, having a formal diagnosis from your pain specialist or neurologist as suffering from migraine with or without aura for at least three months with at least 2 migraine attacks per month and a willingness to complete all components of the study as outlined. Exclusion criteria include any psychiatric illness at time of enrolment, addiction, participation on other trials, migraine related to the menstrual cycle, abuse of acute medication for migraine and any other psychological disorders which would compromise adherence to the study and communication with the study co-ordinator.

If I take part in the study what will I be asked to do?
Once your neurologist or pain specialist has decided that you satisfy the criteria for migraine diagnosis and that you meet the criteria for inclusion in this study, if you agree to participate, numbers permitting, you will meet with the researcher prior to the study. At this time you will be provided with a consent form, any questions you may have regarding the project will be answered. Details of the study protocol are outlined on the next page. You will be requested not to participate in other research interventions while participating in this programme.

Prior to project	Week 1	Week 2 Day 14 Intervention commences	Week 4 Day 28 Intervention continues	Week 6 Day 42 Intervention complete	Six Week and Twelve month Follow up
Participant is required to complete each of the following online on days 1, 14, 28, and day 42 unless otherwise indicated.					
SHSS:C administered. Give participants instructions and a hard copy of diary to input details on a daily basis.	HDI	HDI	HDI	HDI	HDI
	PCS	PCS	PCS	PCS	PCS
	Mindfulness Assessment Scale				
Participant is required to complete each of these on a daily basis in their written diary and input all data online once a week.					
	MIS	MIS	MIS	MIS	MIS
	Diary frequency & duration of migraine	Diary frequency & duration of migraine	Diary frequency & duration	Diary frequency & duration	Diary frequency & duration

Prior to the intervention you will be invited to meet with the researcher so that the intervention can be discussed in greater detail. The intervention will take place over eight weeks. On day one you will be asked to complete a hard copy diary and an online diary of headache frequency and intensity and to continue to do so for 14 days. You will then be asked, on day 14 to complete an online questionnaire designed to potentially assess hypnotisability. On day 14 you will be asked to complete questionnaires online for baseline measures of:

a. Headache Disability Index (HDI)

b. Pain Catastrophizing (PCS)

c. Medication Index Score (MIS)

d. Frequency of migraines (Diary)

e. Duration of migraines (Diary)

f. Severity of migraines (Diary)

After collecting initial measurements, you will be allocated to one of two groups; hypnosis or a wait list control group. On day 15 (after allocation) you will be given access to the intervention online and you will be required to listen to your respective 15 minute mp3s three times per week for four weeks. Cookies will keep track of the number of times you log in and the length of time spent listening to each download at each visit. On day 28 (two weeks into the intervention) you will be required to complete two of the assessments online and any medication taken will be recorded. On day 42 (four weeks into the intervention) two more questionnaires will be assessed online and your online diaries will be accessed to evaluate medication consumed. An email will be sent to you each day with specific instructions on what to do on that particular day. If you are part of the wait list group you will receive access to the hypnosis mp3s two months after day 42. All participants will be invited to complete further assessments online two months and twelve months after listening to the mp3s.

Are all details collected confidential?
Yes. All information will be treated in the strictest confidence. All information collected online will be kept on a highly secure web-based electronic database. Your details will not be passed on to anyone else and participants will have access only to their own personal details.

Are there any risks associated with the study?
No. There are no risks associated with taking part in this study.

If I become pregnant during the intervention do I need to notify the researcher?
Yes. You will need to notify the researcher as soon as possible. The intervention is designed for migraines which are not linked with hormonal changes. The intervention will not affect you or the foetus in any negative manner but may have an influence on alterations in the changes being assessed such as disability as a result of migraines, Pain Catastrophizing and frequency and duration of migraines.

Do I have to take part in the study?
No. You do not have to take part in the study. You are free to withdraw from the study at any time and without giving a reason. A decision to withdraw will not affect your rights in any way.

On completion of the study what happens?
On completion of the study the results will be assessed and compiled and publications will be submitted to various journals. Your name will not appear on any of these publications.

Who can I contact if I have questions?
If you have any questions prior to or during the research programme Niamh Flynn can be contacted at info@bodywatch.ie . See below for telephone contact numbers.

Contact Details:
Niamh Flynn, Researcher Tel: 091 720145
Dr. Brian McGuire, Supervisor Tel: 091 493266

If you have any concerns about this study and wish to contact someone independent and in confidence, you may contact 'the Chairperson of the NUI Galway Research Ethics Committee'
c/o office of the Vice President for Research, NUI Galway, ethics@nuigalway.ie

Centre Number:
Study Number:
Participant Identification Number:

Appendix 4: Consent Form

Consent Form

Title of Project: Development and Evaluation of an Online Hypnosis Intervention for the Treatment of Migraines

Name of Researcher: Niamh Flynn

Please initial box

1. I confirm that I have read the information sheet dated (version) of the above study and have had the opportunity to ask questions ☐

2. I am satisfied that I understand the information provided and have had enough time to consider the information ☐

3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected. ☐

4. I agree to take part in the above study. ☐

Name of Participant Date Signature

Name of Person taking consent *(if different from researcher)* Date Signature

Researcher Date Signature

Appendix 5: Dates of Emails with Surveys

You will receive an email on each of the following days:

Day	Date	Content	Approximate time to complete	Tick List
1	07/04/13	Survey to complete		
7	14/04/13	Survey to complete		
14	21/04/13	Survey to complete		
(15)	22/04/13	Listen to mp3		
(17)	24/04/13	Listen to mp3		
(19)	26/04/13	Listen to mp3		
21	28/04/13	Survey to complete		
(22)	29/04/13	Listen to mp3		
(24)	01/05/13	Listen to mp3		
(26)	03/05/13	Listen to mp3		
28	05/05/13	Survey to complete		
(29)	06/05/13	Listen to mp3		
(31)	08/05/13	Listen to mp3		
(33)	10/05/13	Listen to mp3		
35	12/05/13	Survey to complete		
(36)	13/05/13	Listen to mp3		
(38)	15/05/13	Listen to mp3		
(40)	17/05/13	Listen to mp3		
42	19/05/13	Survey to complete		

Paper Trail:

- If you would like to keep track manually of any medication taken or the length /frequency and severity of your migraines you can download charts from the website and this may help with accuracy when completing your surveys on the days listed above.
- **Important: Completing Surveys:**
  All seven surveys must be completed. Each survey will be online for twenty-four hours after which time each survey will be closed and results collated. If one survey is missed that participant will not be involved in the remainder of the study from that point onward.
  MP3s will only be available to participants completing all seven surveys in full.

Appendix 6: Migraine Diary Month ________________ **Severity of Migraine** 1= little or no disability II = mild disability III moderate disability IV= Severe disability

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______
Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______
Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______
Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______	Date______ Migraine Start time______ Migraine Finish time______ Medication in mg_____ Severity ______ Triggers_______

Appendix 7: Approval Letter from Galway Clinic Ethics Committee

GALWAY CLINIC

'Excellence in Patient Care'

26 February 2013

Ms Niamh Flynn
Suite 29
Galway Clinic
Doughiska
Galway

Re: Research Project

Dear Ms Flynn,

I am pleased to confirm that the Medical Advisory Committee, based on the recommendation of the Galway Clinic Research Assessment Group has approved your research study '*Development and Evaluation of an Online hypnosis intervention for the treatment of Migraines'* at its February meeting.

Wishing you every success with the study.

Yours sincerely

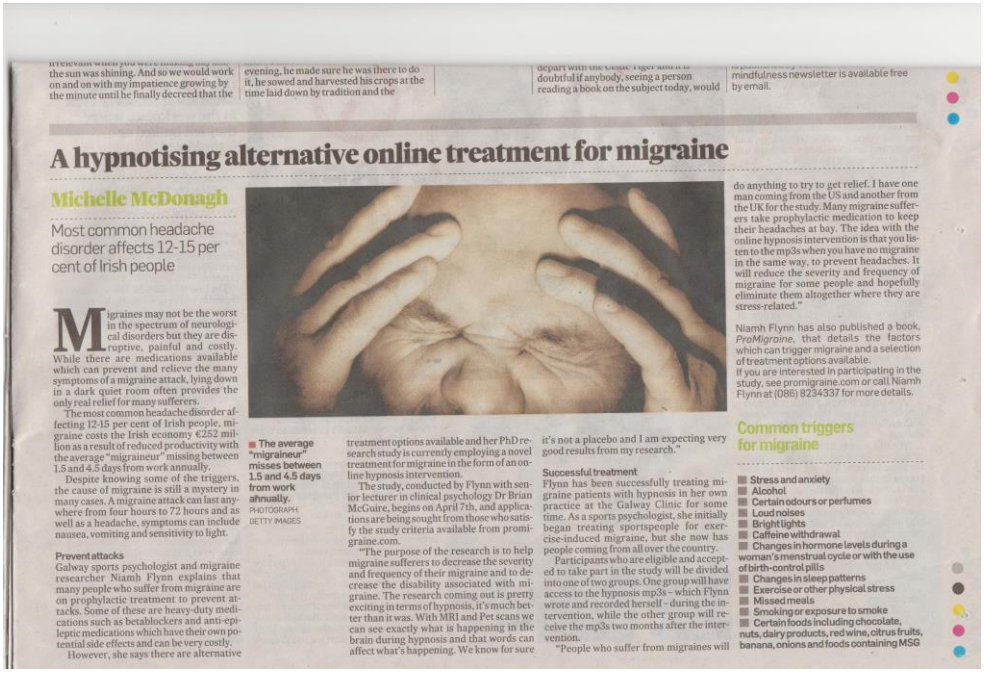
Dr John Mangan
Medical Director

Galway Clinic Doughiska Limited
Place of Registration: Ireland; Registered Number: 369921; Registered Address: Doughiska, Galway, Ireland
Directors: Ronald Bolger, Laurence J Goodman, Brendan McDonald,
Frances Sheehan, James Sheehan, Joseph Sheehan, Declan Sheeran
Tel: +353(0)91 785000 Fax: +353(0)91 785703

Appendix 8: List of Radio Interviews and Press Articles

21 January 2013	Galway Bay FM
29 January 2013	The Irish Times
7 March 2013	The Connacht Tribune
7 March 2013	Connemara Community Radio
8 March 2013	Galway City Tribune
15 March 2013	The Western People
15 March 2013	The Clare Champion
25 March 2013	Kildare FM
26 March 2013	The Irish Times

Appendix 9. Sample of Press Articles



the sun was shining. And so we would work on and on with my impatience growing by the minute until he finally decreed that the evening, he made sure he was there to do it, he sowed and harvested his crops at the time laid down by tradition and the

depart with the Celtic Tiger and it is doubtful if anybody, seeing a person reading a book on the subject today, would

mindfulness newsletter is available free by email.

A hypnotising alternative online treatment for migraine

Michelle McDonagh

Most common headache disorder affects 12-15 per cent of Irish people

Migraines may not be the worst in the spectrum of neurological disorders but they are disruptive, painful and costly. While there are medications available which can prevent and relieve the many symptoms of a migraine attack, lying down in a dark quiet room often provides the only real relief for many sufferers.

The most common headache disorder affecting 12-15 per cent of Irish people, migraine costs the Irish economy €252 million as a result of reduced productivity with the average "migraineur" missing between 1.5 and 4.5 days from work annually.

Despite knowing some of the triggers, the cause of migraine is still a mystery in many cases. A migraine attack can last anywhere from four hours to 72 hours and as well as a headache, symptoms can include nausea, vomiting and sensitivity to light.

Prevent attacks

Galway sports psychologist and migraine researcher Niamh Flynn explains that many people who suffer from migraine are on prophylactic treatment to prevent attacks. Some of these are heavy-duty medications such as betablockers and anti-epileptic medications which have their own potential side effects and can be very costly.

However, she says there are alternative treatment options available and her PhD research study is currently employing a novel treatment for migraine in the form of an online hypnosis intervention.

■ The average "migraineur" misses between 1.5 and 4.5 days from work annually. PHOTOGRAPH GETTY IMAGES

The study, conducted by Flynn with senior lecturer in clinical psychology Dr Brian McGuire, begins on April 7th, and applications are being sought from those who satisfy the study criteria available from promigraine.com.

"The purpose of the research is to help migraine sufferers to decrease the severity and frequency of their migraine and to decrease the disability associated with migraine. The research coming out is pretty exciting in terms of hypnosis, it's much better than it was. With MRI and Pet scans we can see exactly what is happening in the brain during hypnosis and that words can affect what's happening. We know for sure it's not a placebo and I am expecting very good results from my research."

Successful treatment

Flynn has been successfully treating migraine patients with hypnosis in her own practice at the Galway Clinic for some time. As a sports psychologist, she initially began treating sportspeople for exercise-induced migraine, but she now has people coming from all over the country.

Participants who are eligible and accepted to take part in the study will be divided into one of two groups. One group will have access to the hypnosis mp3s – which Flynn wrote and recorded herself – during the intervention, while the other group will receive the mp3s two months after the intervention.

"People who suffer from migraines will do anything to try to get relief. I have one man coming from the US and another from the UK for the study. Many migraine sufferers take prophylactic medication to keep their headaches at bay. The idea with the online hypnosis intervention is that you listen to the mp3s when you have no migraine in the same way, to prevent headaches. It will reduce the severity and frequency of migraine for some people and hopefully eliminate them altogether where they are stress-related."

Niamh Flynn has also published a book, *ProMigraine*, that details the factors which can trigger migraine and a selection of treatment options available.

If you are interested in participating in the study, see promigraine.com or call Niamh Flynn at (086) 8234337 for more details.

Common triggers for migraine

- Stress and anxiety
- Alcohol
- Certain odours or perfumes
- Loud noises
- Bright lights
- Caffeine withdrawal
- Changes in hormone levels during a woman's menstrual cycle or with the use of birth-control pills
- Changes in sleep patterns
- Exercise or other physical stress
- Missed meals
- Smoking or exposure to smoke
- Certain foods including chocolate, nuts, dairy products, red wine, citrus fruits, banana, onions and foods containing MSG

Pioneering Galway study seeks migraine sufferers for online hynosis treatment

Appendix 10. Hypnosis script. MP3 Track 1. Analgesia for Migraine

Induction

Now that you are comfortably relaxed, allow your eyes to close and relax the little muscles around your eyes. You may find that after a while your entire body relaxes completely. Take a deep breath in and fill your lungs with air. As you breathe out slowly close your eyes down and relax the muscles of your shoulders and arms… your legs and your feet….. And as you take another deep breath in…. notice how steady your breathing has become … breathing out gently… allowing your entire body to simply let go… and you drift down deeper and deeper and deeper relaxed.

Your attention may wander from one thought to another while listening to the recording and the sound of my voice and that is fine .. but just for a moment, focus your attention on the muscles of your legs and your feet……..they may feel heavy… almost like lead… so very comfortable… and as your mind wanders think about your breathing, take a deep breath in, and as you breathe out sink down deeper and deeper relaxed…

In a while it may feel like your body is floating and that is fine ….. for the moment let your body sink right down deeper and deeper and deeper relaxed.

Picture yourself sitting by a lake somewhere after enjoying a relaxing sunny day. Dusk is falling and the light on the lake is very beautiful… You are safe and secure… notice any towering trees with strong branches protecting you overhead. There is a gentle breeze and you feel so very comfortable. You let your feet touch the surface of the water as it glides slowly and gently by… seeming barely to move but so gentle and it feels as though you have not a care in the world.. you may even hear some birds singing in the distance… you are safe and secure… an immense sense of calm and tranquillity descends and you observe a boat in the distance.. the lake is so still and so calm. After a while the sun begins to sink on the horizon and you make your way home slowly… bringing with you the wonderful sense of peacefulness and calmness that you have absorbed from this wonderful sight.

Now, silently, in your mind, begin to go through the alphabet backwards, starting with the letter Z.. you may find that you know the alphabet in reverse as well as you know it from A to Z and that is fine and if you don't you may find that you get three or four letters in reverse and then you go from A to Z before going in reverse again but keep focused on those letters. You will still hear my voice in the background but keep focused on the numbers and if you lose your place just go back to the letter Z again and that is fine… your subconscious mind will continue to accept all of the suggestions which I am giving you which will benefit you in a way that you want… After a while those letters will simply dissolve and fade away but stay focused for now and see how far back through the alphabet you can go…

Post hypnotic suggestions

As you listen to this recording regularly you may find that from this point forward the frequency of the discomfort in your head decreases and the sensations of migraines become weaker and weaker … In fact, after a while you may find that they become less and less noticeable until they disappear completely allowing you to carry on with all of the work and leisure activities which you enjoy participating in in a calm and relaxed manner.

In time… maybe less time than you could imagine, your migraines become less and less frequent and the discomfort decreases until they may even disappear completely… and even as you become more comfortable you find that you are able to do more – you are more active. You are engaged in more activities and you feel in control. You know you are in control of

this and as the discomfort dissolves and disappears you feel happier and more relaxed… free to do all the things you would ordinarily do..
It may even feel as though a vice grip has been loosened and broken .. as though all the pressure has been released like from a valve has been opened with all pressure dissipating…
Push the letters of the alphabet from your mind now if you have not already done so… and ..

Analgesic Suggestions
Imagine now, just for a moment a warm cap made of soft comfortable material is sitting gently on your head. It is just the right temperature for you so that it feels comforting and soothing. And you could imagine that the back of it comes down so that it has a warm, soothing feeling around the back of your neck also… Adjust the temperature so that it is right for you and notice perhaps that is seems to have a warming effect on your head and neck… almost like all the discomfort dissolves and disappears.. Feel the warmth of that area around your head and neck….. how wonderful it is simply to relax. Your level of comfort increases and you may even be thinking of what it feels like to be so very comfortable .. as though you have not a care in the world.. or perhaps you are thinking and feeling what it is like to be able to do all the things you like to do…. You feel so very comfortable.. that wonderful warmth spreading to every part of your head and neck… like a soothing, relaxing, comfortably warming sensation going from your forehead, right back over the top of your head, along the sides and that warmth spreading down along the neck ..leaving you totally relaxed and perfectly at ease… you may be surprised at how comfortable you feel right now.. and how it feels to remember how balanced and relaxed your body feels, right from the top of your head to the tips of your toes.

Suggestions to reduce discomfort
Now, Picture or visualise two glass jars side by side and visualise a tap attached to ONE of those jars… the one on the left. And think about a colour, that to you is indicative of the discomfort which the migraine represented. Now imagine, think about and visualise the glass jar on the left… the one with the tap.. filling up with a liquid of that specific colour… almost as though the migraine is being transferred into that glass jar.. It may be a dark and ominous colour with a thick viscosity but you could imagine it draining away from you head and into that glass jar… and as your body and mind relax and you drift even deeper and deeper imagine another colour.. this time a very pleasant and soothing colour.. one perhaps that represents feelings of tranquillity and peacefulness and a feeling of being in control.. and imagine that glass jar on the right filling up.. slowly at first… with a relaxing and tranquil liquid in that particular colour. And then you begin to notice something.. and it is a little peculiar.. As you fill the glass jar on the right with that soothing relaxing liquid bathed in a tranquil colour the dark viscous liquid starts to drain from the tap on the side of that jar in which it was encased… slowly at first….. then steadily.. … and then another peculiar thing begins to occur.. you may feel that as that dark and viscous colour drains away your body and head begin to feel lighter … in the most pleasant way… and you begin to feel powerful and in control.. and you notice how the glass jar on the right… filled with the most beautiful soothing and relaxing colour liquid bathes your mind in feelings of relaxation… and a feeling of control…
Any time you wish to reduce feelings of discomfort and increase the levels of comfort all you need to do is find a place where you can relax completely.. and as you close your eyes down visualise and imagine those two glass jars.. the one on the left with a tap on it and the one on the right is solid and strong… and on any particular day where you wish to adjust the levels of discomfort all you have to do is first notice to what level that

dark and ominous, viscous colour liquid, which represents the migraine, is at in the glass jar on the left and as you turn the tap on watch how the positive, peaceful calming feeling permeates every cell in your head and body as that pleasant colour, that to you represents freedom, a feeling of control over the situation and a deep feeling of relaxation begins to fill the jar on the right….. and the more that drains from the tap of the jar on the left the more the jar on the right begins to fill.
The interesting thing is that you have control over the tap.. you can let the tap drain away *some*.. or all of that horrible discomfort or you can stop it at any point… and the more you turn the tap to let the discomfort escape and drain away the more of the pleasant and soothing colour liquid that fills the jar on the right… it may even fill up to the top.. The more you allow to leave from the tap on the left the more of that soothing colour that fills up on the right… … At times it may feel as though there is a valve being opened and all the pressure is being released … leaving you feeling a sense of calm and relaxation…

Deepener.
Imagine you are standing at the top of a staircase and in a moment you can walk down that staircase and with every step you take you drift further and deeper and deeper relaxed. There are ten steps…
Ten…. Feeling so very relaxed. Taking the first step down. Nine… there is a stable handrail…you are safe and secure. Eight… drifting down…Seven. It may even feel as though you are floating down…Six…. Five… Four….drifting deeper and deeper down…Three… feeling . … One… Step off the last step into a place of total relaxation and calm…….. you may even feel as though you are floating.. now or later….

Analgesic suggestions
Imagine again now, just for a moment, that warm cap made of soft comfortable material sitting gently on your head. It is just the right temperature for you so that it feels comforting and soothing. And you could imagine that the back of it comes down so that it has a warm, soothing feeling around the back of your neck also… Adjust the temperature so that it is right for you and notice perhaps that is seems to have a warming effect on your head and neck… almost like all the discomfort dissolves and disappears.. Feel the warmth of that area around your head and neck….. how wonderful it is simply to relax. Your level of comfort increases and you may even be thinking of what it feels like to be so very comfortable .. as though you have not a care in the world.. or perhaps you are thinking and feeling what it is like to be able to do all the things you like to do…. You feel so very comfortable.. that wonderful warmth spreading to every part of your head and neck… like a soothing, relaxing, comfortably warming sensation going from your forehead, right back over the top of your head, along the sides and that warmth spreading down along the neck ..leaving you totally relaxed and perfectly at ease… you may be surprised at how comfortable you feel right now.. and how it feels to remember how balanced and relaxed your body feels, right from the top of your head to the tips of your toes.

One to five awareness
In a few moments I will count from one to five. On the count of five you will be fully aware, energised, relaxed and calm. One, feeling wonderfully relaxed. Two,…. Every muscle and nerve, from the top of your head, along your neck and shoulders, right down through your back, stomach and legs, right down to the tips of your toes is completely relaxed. Three, you feel amazing. Four… on the next number, open your eyes and be fully aware and relaxed and calm. Five.. eyes open now. Fully aware, relaxed and calm.

Appendix 11. Hypnosis Script: Track 2. Living Life to the Full

Do not ever listen to this recording while driving or while operating machinery. Make sure you are listening to this recording in a place which is comfortable and where you can safely relax. If your attention is needed urgently at any point while listening to this recording you will open your eyes immediately, be fully aware and respond appropriately to the situation.

Induction

Focus your eyes now on a point in front of you and allow your body to completely relax. Take a deep breath in and hold that breath for a moment. As you breathe out close your eyes down and relax the muscles of your shoulders and arms…..

Take another deep breath in…. hold that breath….. and keeping your eyes closed… breathe out gently…. And drift down deeper and deeper relaxed. Focus your attention on the muscles of your legs and your feet……..notice how heavy or how light they feel… take a deep breath in and as you breathe out sink down deeper and deeper relaxed…

Now focus your attention on the muscles of your chest and back and take another deep breath in… hold that breath and as you breathe out sink down ten times deeper relaxed… It may feel as though your body is getting heavier or as though you are floating.. now or some time later…… as you drift and relax….

Now imagine yourself in a beautiful place.. somewhere you know of or somewhere you are creating in your imagination.. some people imagine themselves on a stunning beach with white sand and a clear blue ocean… where a gentle sun bathes in a beautiful blue sky… others go to a place they retreat to .. a place that is at once familiar and comforting…. Then there are some who like to imagine wandering through a refreshing woodland on a crisp Autumn day where it is possible to hear the sound of twigs crunching beneath your feet and feel the cool refreshing breeze meandering past. Wherever you are, notice the sense of calm and the feeling of safety and peacefulness…….

Now, silently, in your mind, begin to count backwards in multiples of three from the number 1000 and after each number say the words 'drifting and relaxing'… for example…. 997 drifting and relaxing…. 994 drifting and relaxing.. you will still hear my voice in the background but keep focused on the numbers and if you lose your place just go back to the number 1000 and that is fine… Keep focused on the numbers..

As you drift you may notice that there is a wonderful sense of relaxation from the top of your head to the tips of your toes.. in fact in a few moments… or maybe in a little more time than that … or less you may find that you drift into the deepest and most powerful state of relaxation that you have ever experienced…. Keep focused on the numbers….

As your legs and feet relax it may be that one part of your body relaxes more deeply… at first … than another part of your body … or it may be that your entire body drifts down ten times deeper relaxed so your body feels so heavy so that even if you wanted to move your arms or feet would feel so very relaxed it would be difficult even to try . … so very relaxed…..

And if you lose track of the numbers just go back to a thousand again until the numbers dissolve and disappear and you become even more relaxed… as you drift deeper and deeper down……

Catastrophizing reduction suggestions

From this point forward you feel more in control and you find that it is easier to plan the things you wish to do because you have control over the discomfort until that discomfort diminishes and may disappear entirely. You could even discover that it becomes easier and easier to accomplish

the goals and tasks which you have set for yourself. Occasionally you may find that your thoughts wander and ruminate in a negative way and if this happens occasionally then all you have to do is shout the word 'STOP' silently in your mind and instantly and immediately you feel very much in control, as your mind focuses on all the things that you *can d*o and will do… as you gain control over the discomfort and it becomes less and less frequent until it may disappear entirely. You know at subconscious level that you can overcome those challenges in a calm and relaxed manner. Think back now to a time when you felt comfortable and completely in control.. it could be in any situation .. Go back into that situation in your mind and see what you saw, feel what you felt and hear what you heard. .. … you will still hear my voice in the background but immerse yourself in that pleasant memory…

…….. relax and drift…… and as you immerse yourself in that positive experience notice how good it feels to be in control.. to be relaxed and to be able to handle the situation confidently and competently in a peaceful manner. Tap into those feelings of being in control and silently in your own mind say the word 'Power' and as you do you relax deeper and deeper and deeper relaxed.

Headache Disability Suggestions.

As you relax and drift deeper and deeper allow yourself now to focus on all of the activities that you find pleasant… for some it may be going for a walk. For others it involves reading a pleasant book.. or.. it could be something entirely different.. As you let your mind relax and wander you find it easier to drift deeper and deeper and deeper down, learning to let go and to relax deeply… Your muscles relax… in fact every muscle, every nerve and every cell in your body can relax completely now.. as you simply let go… From day to day you find it easier to do all of the things you like to do and need to do.. you feel a sense of being in control… as your muscles and nerves relax now and you drift deeper and deeper and deeper down… feel that discomfort drifting away now.. as a wave of relaxation moves from the top of your head down to the tips of your toes… it may even feel as though the discomfort in your head is gently leaving through the top of your head… almost as though someone is gently removing it as you let go and drift deeper and deeper and deeper down. Visualise or imagine yourself taking part in an activity which in the past was difficult for you because of the migraines… now imagine yourself active, relaxed and completely in control… perfectly capable of being involved in that activity….. and how great that feels… and every time you listen to this recording you may find that it becomes easier and easier to do everything you wish to do and need to do on a daily basis. You are finding it easier to plan your schedule now because, as the frequency and the intensity of your migraines subsides you are mastering the art of maintaining optimal great health.

Post hypnotic suggestions

As you listen to this recording regularly you find that the frequency of the discomfort in your head decreases and the sensations of migraines become weaker and weaker … In fact, after a while you may find that they become less and less noticeable until they disappear completely allowing you to carry on with all of the activities you desire in a calm and relaxed manner. It may feel as though a vice grip is being loosened and is then broken .. all the pressure releasing like from a valve has been opened and all pressure dissipates…

Your migraines become less and less frequent and the discomfort decreases until they disappear completely… and even as you become more comfortable you find that you are able to do more – you are more active. You are engaged in more activities and you feel in control. You know you are in control of this and as the discomfort dissolves and disappears you

feel happier and more relaxed… free to do all the things you would ordinarily do..

Deepener.

Imagine you are standing at the top of a staircase and in a moment you can walk down that staircase and with every step you take you drift further and deeper and deeper relaxed. There are ten steps… Ten…. Feeling so very relaxed. Taking the first step down. Nine… there is a stable handrail…you are safe and secure. Eight… drifting down… Seven. It may even feel as though you are floating down…Six…. Five… Four….drifting deeper and deeper down… Three… feeling fantastic.. Two… One… Step off the last step into a place of total relaxation and calm…….. you may even feel as though you are floating.. now or later….

Catastrophizing reduction suggestions

You are creating in yourself in a state of mind where, from this point forward you feel more in control. You are deciding how to perceive each and every situation you encounter and create and you are relaxed and calm.. as you drift and relax now. You know you have immense resources available to you and you are gaining more and more control over the discomfort which your migraines used to cause. In fact, in time, as that discomfort diminishes the migraines may even disappear entirely. On the very odd occasion if you notice your thoughts wander and ruminate in a negative way then all you have to do is shout the word 'STOP' silently in your mind and instantly and immediately you feel very much in control as you become aware of the incredible resources you have to deal with all circumstances in a peaceful and calm manner. You focus your mind on all the strengths you have as an individual and the positive and supportive resources in your life right now. You are creating a wonderful sense of control over the migraine discomfort which you experienced as that discomfort becomes less and less frequent and may even disappear entirely. You know at subconscious level that you can overcome all challenges in a calm and relaxed manner.

Headache disability suggestions

You are very much aware, at subconscious level, of all of the activities which you are capable of participating in. You may even be surprised how, as each day goes by you find it so easy to cope with everything and everyone in a relaxed and calm way. As you let your mind relax and wander you find it easier to drift deeper and deeper and deeper down, learning to let go and to relax deeply… Your muscles relax… in fact every muscle, every nerve and every cell in your body can relax completely now.. as you simply let go… Think about some of those activities which in the past may have been excluded from your life because of migraines.. and imagine yourself participating in those activities with an ease and a sense of enjoyment. As each day goes by you find it easier to do all of the things you like to do and need to do.. you have an increased sense of feeling that you are in control… as your muscles and nerves relax now and you drift deeper and deeper and deeper down… feel that discomfort drifting away now.. as a wave of relaxation moves from the top of your head down to the tips of your toes… it may even feel as though the discomfort in your head is gently leaving through the top of your head… almost as though someone is gently removing it as you let go and drift deeper and deeper and deeper down. As you now choose one of the activities which you would like to participate in more frequently, visualise or imagine yourself fully taking part in that activity at a time of your choosing. And every time you listen to this recording you may find that it becomes easier and easier to do everything you wish to do and need to do on a daily basis and you find your ability to do things on a daily, weekly and monthly basis increases…

One to five awareness

In a few moments I will count from one to five. On the count of five you will be fully aware, energised, relaxed and calm. One, feeling wonderfully relaxed. Two,…. Every muscle and nerve, from the top of your head, along your neck and shoulders, right down through your back, stomach and legs, right down to the tips of your toes is completely relaxed. Three, you feel amazing Four… on the next number, open your eyes and be fully aware and relaxed and calm. Five.. eyes open now. Fully aware, relaxed and calm.

Appendix 12: Hypnosis Script: MP3 3. A Metaphor for Restoring Health
Do not ever listen to this recording while driving or while operating machinery. Make sure you are listening to this recording in a place which is comfortable and where you can safely relax. If your attention is needed urgently at any point while listening to this recording you will open your eyes immediately, be fully aware and respond appropriately to the situation.

Induction
Now that you are nicely relaxed, focus your eyes on a point above eye level, take a deep breath in, hold that breath for a moment, and as you breathe out let your entire body relax.. allow your breathing to become very relaxed and concentrate your mind on my words as you allow every sound to help you to relax further and deeper and deeper relaxed.
Think about all the pleasant places you have ever visited or would like to visit that begin with the letter 'S' … any towns, cities, countries… that you have ever been to or would like to go to …. keep focused on those place names… you will still hear my voice in the background.. and you may find that your mind wanders after a while but that is fine.. Perhaps you will visualise each place in your mind as you remember it or as you imagine it to be and maybe you will hear sounds which bring back happy memories of those places or sounds which you would envision hearing in each specific place…. Maybe you will feel a sense of wandering in those places as you drift and relax… And as your mind relaxes, your body relaxes too. Your shoulders and arms relax… your legs and feet relax and you drift down deeper and deeper and deeper… into a wonderful state of relaxation.. Once you have recalled all those places you could choose another letter .. any letter.. perhaps on one day when listening to this you will choose the letter U … … on another day you may choose the letter C or E… continue to focus and recall and think of as many places as you can with any particular letter.. you will still hear my voice in the background and your mind may drift at some point or you may decide to listen to the sound of my voice.. it doesn't matter which you decide to do right now.. your subconscious will continue to hear and respond to everything that is important to you at this time.

As you drift and relax, you know at conscious level and at subconscious level too that emotions and feelings can have an effect on your physiology. When you are happy your natural inclination may be to smile. In some situations, when things are going fantastically well for you, you may even feel like you are ten feet tall. When you are sad your eyes may look downwards and your shoulders might slump.. Feelings and emotions affect the body at cellular level.. ……..sometimes that impact is visible and at other times it is there but not visible. And yet all these emotions, memories and feelings leave a trace at a much deeper cellular level.
You know at subconscious level that there may be incidences in the past which were painful or hurtful and even the memory of them at this moment in time could make you feel sad.. Similarly there may be celebrations and happy occasions in the past and merely remembering those times could bring a huge smile to your face. And it is important that we remember some things at conscious level while the subconscious mind, that very powerful part of the mind, will remember everything.. almost like a protective inbuilt mechanism, to draw us towards situations in the future which will be helpful and not harmful.. Most of the time this immense subconscious mind makes valid and helpful connections and associations but sometimes those connections and associations are no longer relevant to the current life you are leading. Then, it may be time to link back and erase those which are no longer purposeful and create new, empowering and

more positive connections and associations… And it really does not matter if you remember those events and memories, the feelings or even the emotions on a conscious level.. in a few moments your subconscious mind will direct you to those which may have contributed to your current experience of migraines and you can erase and delete any and all which are not useful to you at this moment in time… Almost like you have the ability to start afresh… to learn to live a life where migraines are an unnecessary part of your life.

Main Script

So just imagine for a moment that you are on the grounds of a magnificent castle and you are approaching the front door of that castle. The door stands almost ten feet tall and it is solid and strong.. Picture yourself with the key to that door and turn the key; and feel the weight of the door as you push it open with all your strength. You find yourself in an expansive hallway with high, high ceilings and a beautiful marble floor. The light coming through the open door is reflected on the walls and the ceiling. Close the door behind you now and hear the echo in that hallway. Your eyes light up as you scan a tall marble statue of a figure to your left. You admire the incredible craftsmanship and wonder how long it took someone to create this object of beauty. As you approach the statue and examine it in more detail you notice it is flawless. Somehow even taking in the perfection of this work of art instils a great sense of calm within you. Someone has clearly taken great care of this flawless piece which has undoubtedly brought much happiness to those who spend time in its presence. Now, notice a stairs leading downwards to your right … and begin to walk towards that stairs… There is a glossy marble handrail and you are safe and secure. The steps wind around in a curve so it is difficult to see the end of that staircase but begin to walk down that staircase now and with every step you take feel yourself drifting downwards .. further and further and deeper relaxed. .. and further and deeper down. You will still hear my voice in the background but keep focusing as you drift deeper and deeper down… you may find that after a while my voice drifts into the background and that is fine.. just let your mind drift and wander ..

At times it may feel as though one side of your body is more relaxed than the other and that's fine.. just allow yourself to relax completely. When you reach the bottom step you step off that step and into a place where you feel safe and secure. And you notice in front of you an old-fashioned blackboard. On that blackboard there are images and words.. each of these represents a part of your past which in some way contributed to or triggered the discomfort that you felt with migraines. Some of these words and images may be clear and some may be blurred. It does not really matter how vague or how vivid those images may be. Each has an emotion or feeling attached to it. These may be clear or they may be difficult to decipher. Peer closer now and see if you Can identify any of those memories, events, images, emotions or feelings. Notice how many there are on the blackboard. The entire blackboard might be covered … or it could just be a section. Whatever you are noticing now is correct. Resting on a table to the left of the blackboard is an eraser.. the old-fashioned kind which would have been used to wipe away every wisp of chalk from the board. Pick it up and feel the weight of it in your hand. Now, with that eraser, start on the left hand side of the blackboard and wipe away all feelings and emotions which are no longer helpful and which are attached to the words and images.. As you do so you may notice something strange… the memories – be they words or images, begin to change.. They might become larger or smaller.. They may even disappear entirely.. They could morph or change shape… like you are looking through a different lens… Allow your arm to reach up and wipe away more and more of the negative feelings and emotions which in the past may have contributed to your migraines… Wipe the entire blackboard and

notice how the memories… in words or images adapt and change.. all feelings and emotions which are no longer useful to you are wiped away.. completely.. Even some of those memories may become faded and after a while could disappear entirely. Dip the eraser in a bowl of water which you see on the table and wash away even the remnants of the chalky dust particles which are no longer needed. Now, Choose a piece of chalk from the table … any colour chalk you like… and begin to fill the spaces on the blackboard with happy, positive images and thoughts and words and notice how light your body feels.. almost as though a weight has been lifted from you… you could choose to leave some space on that blackboard so that any time you choose to visit this peaceful castle in the future you can record the many positive moments which have occurred in your life since your previous visit and wipe away and erase those which have contributed to anything other than your good health and happiness. It is time to leave now the castle for now but as you climb the stairs you feel wonderful… light, grounded and incredibly relaxed… and on your way out you meet the caretaker of the castle who is polishing the stunning marble statue in the hallway. He explains to you that many years ago this same statue which is now gleaming and perfect was lovingly restored after years of neglect and turbulent times. Listen as he tells you more and in a few moments I will count from one to five and on the count of five you will be fully aware, relaxed and calm. …

One to five awareness

So just relax and drift.. … and drift and relax…. One… slowly, easily and gently…..Two… every muscle in your body is so very relaxed…Three… you feel wonderful…Four… on the next number, open your eyes and be completely and fully aware. Five…. Eyes open now … fully aware, relaxed and calm…

Appendix 13. Hypnosis Script: MP3 4. Reducing Stress and Eliminating Food Triggers

Do not ever listen to this recording while driving or while operating machinery. Make sure you are listening to this recording in a place which is comfortable and where you can safely relax. If your attention is needed urgently at any point while listening to this recording you will open your eyes immediately, be fully aware and respond appropriately to the situation.

Induction

Close your eyes down….. Visualise….. Imagine…. Picture … in your mind The capital letter A…. make it larger…….. make it smaller……. Push it away…….. turn it upside down……. bring it closer……. Push it away…….. it disappears……Visualise the capital letter B……. make it larger……. Make it smaller…….. push it away……turn it upside down……. Turn it the right side up…….. bring it closer…….. push it away…… it disappears……Visualise the capital letter C……. make it larger…….. make it smaller……. Turn it upside down…… turn it the right side up…….. push it away…… it disappears……

Main script

As you drift deeper and deeper down you know at conscious level and at subconscious level, there are specific decisions which you can make which will allow you to decrease the frequency of your migraines and which may even help you to eliminate them completely from your life. You can choose to eliminate any thought processes, any and all emotional aberrations which have contributed to other than your natural good health and, if you wish, you can choose too to avoid specific foods which upset the balance of your energy and health. You are making decisions which support you so that you free up time which you can use any way you choose. You do not need to allow migraines to dictate your schedule to you anymore. You can do two things in particular to support your body's excellent good health: firstly make a decision to take quality rest each day and secondly, take decisive action to eliminate foods from your life which in the past have triggered your migraines.

Balance is an integral part of life and living.. rest is as important as work… relaxing ….as important as being energised…. You do not need to justify taking time out to relax anymore… you do not need an excuse to relax anymore. Rest is important for survival… You now choose to make rest a priority and restore the balance in your body and mind. Think about a specific time each day that you are prepared to allocate to allowing your mind and your body to really relax.. you no longer need to have a migraine in order to retreat to a place of quiet… that place of quiet .. that specific time to recharge and unwind becomes a necessity.. a protection against pain … and it is ok to simply relax and to enjoy that relaxation … you do not need to have a migraine in order to justify a need or desire to retreat for a while… Quiet, pleasant, restorative rest needs no excuses …no reasons… as you allow yourself to rest in a quiet and pleasant way each day… It may be time that you spend that time watching television or reading a book, maybe you will simply spend that time with the people whose company you enjoy..

You could choose to spend your time off each day or week or month enduring the pain of migraines or you could choose to accept that time off is essential for recovery and good health. Making and allocating time to relax and unwind is important. When you choose to prioritise relaxation time and make it a part of your daily routine you may be surprised at how

quickly you gain control over your migraines. you may even find that migraines are no longer necessary as you restore the homeostasis and balance in your body.
You do not need to justify relaxation time. You accept that, just as we need time to complete specific tasks each day and week, we also need time to relax, recover and recuperate.
Identify what purpose your migraines used to serve. Was it justification for time out? Was it a way to attract attention? Your conscious mind may not know what the purpose is or was but your subconscious mind knows and even if you don't believe that you can eliminate migraines from your life just allow yourself to imagine a life free from migraines.. pretend for a moment that you are living a life full of joy and happiness and love, free from migraines..
You have the resources to deal with and to amend all the circumstances in your life which are not as optimal as you would like them to be. You are in control of the choices you make and consequently you have control over the direction your life and your health take. You **can** choose to eat healthily if you wish to and you can choose to eliminate the foods which you know your body cannot tolerate. You can also choose to make time to rest and facilitate the restoration of balance in your body at a physical, emotional and cellular level. When you decide to allocate time to rest each day, week and month you find you are better able to deal with everyone and everything in a calm, relaxed manner and you may even find that your subconscious response may be to decrease or even eliminate migraines forever… Your subconscious mind is so powerful it will guide you in the right direction and you can take action to create the life which is supportive of your good health.

Allocate time to relax.
Make a decision this moment to make time to let your body recover. What time each day will you allow yourself to give your body and mind time to recharge? Are you choosing to meditate for an hour first thing in the morning *or* is relaxation *to you* setting aside time to read a book for an hour each day. .Treat this time as a priority. How much more pleasant it can be to relax in a pleasant way rather than a painful way. And as quality rest becomes a priority, pain can become a distant memory as you relax and drift now…

Eat properly
You can choose too to be mindful of the food you are eating. There may be particular foods which trigger your migraines. Think about those foods now.. you may even have written them down in your migraine diary. From this point forward you are going to find it very easy to avoid those foods and drinks which cause discomfort to you. You are taking control of your health and you have no interest in, no need for and no desire for foods and drinks which trigger your migraines. Go over that list in your mind right now of those foods and drinks which you know instigate migraine pain in your body. Write each word clearly in your mind….. one under the other.. like a list on a piece of paper… it may be long or it may be short… it is personal to you….. You will still hear my voice in the background and that is fine but keep focused on that list in your mind… your body may feel as though it is getting heavier or lighter … from time to time it may even feel as though you are floating… perhaps some time later. As you drift and relax… and relax and drift… make a decision to eliminate that list of foods from your eating plan. Imagine drawing a line through each and every one of the foods on that list and be decisive in your decision to eliminate each and every one of them from your eating plan.
You know that there are a large variety of other foods and drinks which you can choose instead so it does not matter if you are preparing food or drink yourself or whether you are eating out. You are very clear that you

will no longer include foods and drinks in your eating plan which your body cannot tolerate. When eating out you always find foods which are suitable for your optimal good health and you know that by making the choices which are healthy for you, you will enjoy the social occasions even more.. you are in control of your migraines and you are keeping the migraines away …. Choosing only foods and drink which you know your body can process easily and effortlessly without causing discomfort to you. It feels wonderful to socialise and enjoy the company of friends, family or colleagues in the knowledge and awareness that you will be choosing only those foods and drinks which support your good health. Consequently you are taking control over your migraines. You are relaxed and calm.

Because you are choosing only those foods and drinks which are conducive to good health from this point forward you find that you are full of energy and you feel fantastic. You are freeing up more time… time that used to be consumed by migraines .. and you are using that time any way you choose. Perhaps you are taking time out to enjoy relaxing …….. just as you are relaxing right now.. as you drift deeper and deeper and deeper down..

Focus on those foods again.. those foods on the list which you made which trigger discomfort in you.. think about how horrible they can make you feel ……

you have no interest in them, no desire for them and no need for them.. In fact when anyone offers you any one of those foods or drinks you say, confidently and in a relaxed manner, 'No thank you. I don't want that as it can cause migraines for me'. When eating out people are often happy to accommodate you. You choose healthy foods and drinks which you know that your body can process with ease you feel a wonderful sense of freedom.. freedom to decide how you are going to use your time… whether you choose to relax or something else entirely. It is your choice… always your choice. You refuse to allow certain foods and drinks to dictate your timetable. You much prefer the freedom to plan each day with confidence and reassurance now by refusing to consume the foods and drinks which in the past triggered your migraines. You are exercising your right to be healthy and to help keep migraines away. In all situations from this point forward you now identify and avoid foods and drinks which in the past contributed to the development of your migraines. you do not want them and you do not need them. In fact you refuse to consume anything which you know could trigger a migraine.

Suggestions related to blood vessel diameter (acidity e.g.- correct foods)

You are finding too that you are choosing foods and drinks which you know your body can tolerate and which allow you to have sufficient energy to facilitate your ability to do your work and also to relax. You are calm and relaxed. You refuse to have foods and drinks which you know your body does not respond well to. You are in control of the choices you make and you choose to include only those foods and drinks which your body can tolerate and which are conducive to good health.

You feel fantastic now. You have made a very powerful decision to eliminate foods and drinks which in the past contributed to the onset of migraines, so you have taken back control over this part of your health and you feel empowered. You would not ever want to force someone else to consume something which would make them unwell so when anyone offers you food or drink which in the past contributed to your migraines you will politely but firmly say 'no thank you. That would give me a migraine' and you feel so good when you say this. You are ensuring that you are taking decisive action by being in control of your good health. You are doing two things in particular to support your body's excellent good health from this point forward. firstly you are making a decision to take quality rest each day and thus allowing your body to recharge, restore and balance. Secondly, you are taking decisive action to eliminate foods from

your life which in the past have triggered your migraines. You are taking responsibility for your health and you are taking action to create a lifestyle which supports your good health and which eliminates the thoughts, emotions and foods which contributed to the onset of migraines in the past. Now drift and relax… and relax and drift…

One to five awareness

In a few moments I will count from one to five, on the count of five you will be fully aware, relaxed and feeling fantastic. One… slowly, easily and gently. Two… every muscle in your body is so very relaxed. Three… you feel wonderful… Four… on the next number, open your eyes and be completely and fully aware. Five…. Eyes open now … fully aware, relaxed and calm.

Appendix 14. Phase 1. Open Coding – 37 Initial broad participant led codes

Appendix 14 Phase 1 - Open Coding - 37 Initial broad participant led codes		
Open Codes	**Interviews Coded**	**Units of Meaning Coded**
Acceptance	1	1
Adding Value	14	15
Cognitive changes	11	23
Cognitive General Change	9	14
Cognitive Physical	3	3
Cognitive Social	3	3
Cognitive Work	1	1
Control over migraine	14	14
Equal to 3 times per week	3	3
Feeling in control	2	2
Fewer Concerns	4	4
Fewer thoughts about migraine	13	14
Frequency	14	14
Greater than 3 times per week	9	10
Impact on emotions	14	18
Impact on relationships	14	14
Increase in activity	13	13
Length of intervention	3	4
Less than 3 times per week	2	2
Mental Relaxation	10	12
More Control	13	14
MP3s	8	10
No Change	2	2
No change in activity	5	5
No change in control	1	1
No Difference	7	7
Perceived gravity of disease	14	14
Physical Relaxation	5	9
Re-evaluation of the disease	3	3
Reflection	1	1
Relaxation or less stress	10	16
Severity and frequency since end of intervention	12	20
Stress Reduction	3	4
Thoughts about migraine	14	14
Unusual changes	10	14
Yes Change	10	13

Appendix 15. Phases 2 & 3 Categorization of Codes & Coding on - 37 Open codes organized into 5 categories of codes and further broken down into a further 11 sub-codes.

Appendix 15 - Phases 2 & 3 Categorization of Codes & Coding on - 37 Open codes organized into 5 categories of codes and further broken down into a further 11 sub-codes		
Categories & Subcategories	**Interviews Coded**	**Units of Meaning Coded**
Cognitive changes	***11***	***21***
HDI	***14***	***52***
Changes in activity	13	13
Decrease in activity	0	0
Increase in activity	13	13
Impact on emotions	11	25
Acceptance	1	1
Feeling in control	2	2
Re-evaluation of the disease	2	2
Relaxation or less stress	11	19
Impact on relationships	11	14
No Change	1	1
Yes Change	10	13
Pain Catastrophizing	***14***	***56***
Control over migraine	14	14
Less Control	0	0
More Control	12	14
No change in control	1	1
Perceived gravity of disease	14	14
Fewer Concerns	4	4
More Concerns	0	0
No Difference	7	7
Thoughts about migraine	14	14
Fewer thoughts about migraine	12	13
More thoughts about migraine	0	0
No Change	1	1
Unprompted responses	***14***	***74***
Familiarity with other relaxation strategies	3	5
Length of intervention	3	4
MP3s	10	13
Severity and frequency since end of intervention	13	23
Unusual changes	10	15
What Worked	***14***	***42***
Adding Value	14	15
Mental Relaxation	10	12
Physical Relaxation	5	9
Reflection	1	1
Stress Reduction	3	4
Frequency	14	14
Equal to 3 times per week	3	3
Greater than 3 times per week	9	10
Less than 3 times per week	2	2

Appendix 16. Phase 4 - Data Reduction - Developing Themes

Phase 4 - Data Reduction - Developing Themes			
Themes Coded	**Interviews Coded**	**Units of Meaning Coded**	**Analytical Memos & Summary Statements**
Theme 1 - Emotional Impact	***14***	***47***	
Changes in activity	13	13	
Impact on emotions	10	20	
Impact on relationships	11	14	
Theme 2 - Cognitive Changes	***14***	***95***	
Control over migraine	14	28	
Perceived gravity of disease	14	25	
Thoughts about migraine	14	28	
Theme 3 - The Participant Voice	***14***	***122***	
Cognitive changes	11	20	
Length of intervention	3	4	
MP3s	8	10	
Severity and frequency of migraine since end of intervention	11	19	
Triggers	12	17	
Unusual changes	10	14	
What Worked	14	42	

Appendix 17. CD with Four Hypnosis Recordings

Appendix 18. Qualitative Questions

- What was it like listening to the MP3s?
- Did you listen to them more than three times or less than three times any of the weeks?
- Had the mp3s any value outside of the protocol?
- Were there any activities that you found you could do while you were using the mp3s that ordinarily you would not be able to do or chose not to do in the past because of your migraines?
- What impact , if any, did the intervention have on how you feel emotionally (e.g. confusion, irritability) about your migraine?
- Has the intervention had an impact on the way you relate to people around you?
- Do you notice any changes as a result of the intervention in your feelings of control over your migraines?
- Have you found any changes in your thoughts about the discomfort of migraines as a result of the intervention?
- Have you noticed any changes in how you perceive what may happen when you have a migraine?
- Is there anything I have not asked about your experience that you would like to comment on?