AN INVESTIGATION OF CHANGES IN PRESSURE PAIN THRESHOLD DUE TO HORMONAL FLUCTUATIONS DURING THE MENSTRUAL CYCLE

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A research project submitted in partial fulfilment of the requirements for the degree of Master of Osteopathy Unitec New Zealand, 2006

ABSTRACT

The aim of this investigation was to evaluate whether there was a change in pressure pain threshold (PPT) over the course of the menstrual cycle. Changes in PPT were measured at 18 anatomical sites that are used in the diagnosis of fibromyalgia. Hypothetically, cyclical changes in PPT at these sites may influence the diagnosis of fibromyalgia. PPTs were assessed over two menstrual cycles using 11 normally menstruating women. PPTs were recorded at three different experimental sessions performed during the menstrual phase (approximately day 3 of menstrual cycle), the follicular phase (approximately day 12-13 of menstrual cycle) and the luteal phase (approximately day 21 of menstrual cycle). A hand-held spring algometer was used to apply pressure to the 18 anatomical sites. An effect size of 0.2 showed small differences between the menstrual and luteal phases in both cycles tested. The menstrual phase showed the lowest mean (standard deviation) PPT in month one and two of 3.15 kg (1.05) and 3.59 kg (1.0) respectively. The luteal phase showed the highest mean (standard deviation) PPT in consecutive cycles of 3.39 kg (1.07) and 3.72 kg (0.8) respectively. There was a general trend of increasing PPT over the six experimental sessions which is hypothesised to be a result of habituation to the experimental stimulus. The greatest variability was found when comparing the nine anatomical sites where pressure was applied. In these locations most comparisons showed large effect sizes. The PPTs found in the current study show individual variation within and between menstrual cycles, which may impact on the individual diagnosis of fibromyalgia.

DECLARATION

Name of candidate: Alenka Joy Dunnett

This research project is submitted in partial fulfilment for the requirements for the Unitec degree of Master of Osteopathy.
The regulations for the degree are set out in the Master of Osteopathy Programme Schedule and are elaborated in the course handbook.

Candidate's declaration

I confirm that:

This research project represents my own work;
The contribution of any supervisors and others to the research and to the research project was consistent with the Unitec Code of Supervision.

Candidate: Date:

Supervisors' declaration

I confirm that, to the best of my knowledge:

The research was carried out and the research project prepared under my direct supervision;
Except where otherwise approved by the Board of Postgraduate Studies of Unitec, the research was conducted in accordance with the degree regulations and programme rules;
The contribution made to the research by me, by other members of the supervisory team, by other members of staff of Unitec and by others was consistent with the Unitec code of supervision.

Primary Supervisor: Dr Dianne Roy
Date:

Secondary Supervisor: Dr Andrew Stewart
Date:

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LIST OF ABBREVIATIONS

PPT	pressure pain threshold
FSH	follicle stimulating hormone
LH	luteinizing hormone
C5-C7	cervical vertebral levels 5 to 7
T10-T12	thoracic vertebral levels 10 to 12
S2-S4	sacral vertebral levels 2 to 4

INTRODUCTION

There are many factors that could potentially influence a woman's sensitivity to pain. One such factor may be hormonal fluctuations that occur during the menstrual cycle. The potential effect of hormonal changes on pressure and pain sensitivity has particular relevance to the practice of osteopathy. The techniques used by an osteopath often induce pressure on body tissues and may generate pain. The female patient may be more sensitive to pressure and pain at certain times of the menstrual cycle. If so this variation in pain sensitivity should be considered in both the formulation of a treatment plan and in the techniques used during treatment.

One of the earliest studies to examine the effect of the menstrual cycle on the perception of experimentally induced pain was in 1933 (Riley, Robinson, Wise, & Price, 1999). Since then it has been established that there are changes in pain thresholds due to hormonal fluctuations during the menstrual cycle. However, more research in this area is needed in order to establish if there is a regular, reproducible pattern of change in pain thresholds due to fluctuations of various hormones. At present a reproducible pattern has not been found. There is conflicting evidence in the literature regarding which phase of the menstrual cycle results in the lowest pain threshold and which results in the highest pain threshold. The PPT is the moment at which the stimulus becomes painful. The results of some studies are in agreement with each other. For example, Hapidou and Rollman (1998) found that women had fewer tender sites in the luteal phase. This finding agrees with a study that reported that the highest pain threshold was measured in the luteal phase (Giamberardino, Berkley, Iezzi, deBigontina, & Vecchiet, 1997). The results of other studies conflict with each other. For example, Drobek, Schoenaers, and DeLaat, (2002) found that the highest pressure pain threshold (PPT) was in the menstrual phase, while Bajaj, Arendt-Nielsen, Bajaj, and Madsen, (2001) found the opposite result that the lowest PPT was in the menstrual phase.

In this investigation of changes in PPT over the course of the menstrual cycle, healthy female participants were tested. PPT is defined as the minimum pressure which induces pain or discomfort (Fischer, 1987). The testing was performed over the time period of two menstrual cycles. The aim of this research was to begin an ongoing investigation into the changes in PPT due to hormonal fluctuations during the menstrual cycle. This study examined whether potential changes in the first menstrual cycle tested

were reproduced in the second cycle, and if the changes corresponded to fluctuations of particular hormones.

LITERATURE REVIEW

It is clear from the literature surrounding this topic that there are variations in many areas of pain threshold investigation. There is a diversity of methodology used to investigate the effect of natural hormonal fluctuations on pain threshold. This diversity includes the operational definitions used for the phases of the menstrual cycle, methods used to apply experimental stimulation and the anatomical sites tested. These topics are discussed along with the variables that can influence the experimental measurement of pain and the 18 anatomical sites used in the diagnosis of fibromyalgia, as these are the sites at which pressure was applied in the current study.

Diversity of Methodology

In the current study it was necessary to determine which *days* of the menstrual cycle correspond to each *phase* of the menstrual cycle. It is widely accepted that the menstrual cycle consists of events occurring in the ovaries (the ovarian cycle) and events occurring in the uterus (the uterine cycle). The ovarian cycle consists of the follicular phase (pre-ovulation) and the luteal phase (post-ovulation). The uterine cycle consists of the menstrual phase (menses), the proliferative phase (pre-ovulation) and the secretory phase (post-ovulation). Ovarian changes that occur during the menstrual cycle depend completely on the gonadotrophic hormones, follicle stimulating hormone (FSH) and luteinizing hormone (LH). During the follicular phase FSH is secreted by the anterior pituitary gland. In this phase there is accelerated growth of the primary follicles each month. About two days before ovulation the secretion of LH from the anterior pituitary increases markedly and peaks 16 hours before ovulation. FSH secretion also increases at this time but not to the extent of LH. It is widely accepted that ovulation occurs approximately 14 days after the onset of menstruation. The luteal phase involves the formation of the corpus luteum after ovulation. The corpus luteum produces large amounts of progesterone and oestrogen, this production is stimulated by FSH and LH.

The menstrual cycle averages 28 days in duration. The length can range from 25-30 days (Riley et al., 1999). The interval from the onset of menses to ovulation (the follicular phase) is the most variable in duration and accounts for the range of cycle lengths observed in ovulating women. The interval from ovulation to the onset of menstrual bleeding (the luteal phase) is relatively constant (Riley et al., 1999).

Discrepancies between studies of menstrual cycle modulation of pain may be due to different procedures used in phase calculations (Hapidou & Rollman, 1998). Different studies provide different definitions of the days that correspond to each phase (Figure 2.1). Some studies provide similar but not exact definitions. For example, in one study comparing the pain thresholds for electrical stimuli, the menstrual cycle was divided into four phases (Giamberardino et al., 1997). The first day of the menstrual cycle was counted as day zero, days 2-6 were defined as the menstrual phase, days 12-16 the periovulatory phase, days 17-22 as the luteal phase and days 25-28 as the premenstrual phase. This definition is very similar to two studies investigating sensory changes during the menstrual cycle (Bajaj et al., 2001; Bajaj, Bajaj, Madsen, & Arendt-Nielsen, 2002). The differences were that Giamberardino et al. (1997) counted the first day of the menstrual cycle as day zero where Bajaj et al. (2001) and Bajaj et al. (2002) counted it as day one. The menstrual phase was defined by Giamberardino et al. (1997) as days 2-6, whereas Bajaj et al. (2001) and Bajaj et al. (2002) defined it as days 1-6. The wording used for days 12-16 was slightly different between the two studies, Giamberardino et al. (1997) called it the periovulatory phase and the other two studies called it the ovulatory phase. There was some agreement between the results of Bajaj et al. (2002) and Giamberardino et al. (1997), the former study reported the lowest PPT of women with dysmenorrhoea to be in the menstrual phase and the latter study reported the lowest pain threshold to be in the perimenstrual phase. This agreement may be due to the fact that the perimenstrual phase defined by Giamberardino et al. (1997) included the days of the menstrual phase defined by Bajaj et al. (2002).

Most of the previous studies investigating PPT used a retrospective method to decide in exactly what phase of the menstrual cycle the experimental session was performed (Bajaj et al., 2001; Bajaj et al., 2002; Drobek et al., 2002; Giamberardino et al., 1997; Hapidou & Rollman, 1998). This retrospective method could lead to a substantial difference in the phase of the menstrual cycle that each participant was tested in, producing inconsistent and inconclusive results. Hapidou and Rollman (1998) were the only researchers to include all 28 days of the menstrual cycle in their definition of the phases of the menstrual cycle. Other studies left days unaccounted for which could pose a problem if, on retrospective analysis it was found that experimental testing took place on a day that was not included in the operational definition of each phase.

Inconsistencies in assigning days to phases have been worsened by the use of different terms by different researchers. For example the *follicular phase* of the ovarian

cycle corresponds with the *menstrual* and *proliferative phase* of the uterine cycle, and can also be called the *preovulatory phase* in relation to when ovulation occurs. Most of the studies use a combination of the ovarian cycle and the uterine cycle in their definition of phases.

Direct comparisons cannot be made between the results of different studies if experimental testing is performed at different stages of the menstrual cycle. In the current study prospective analysis was used in order to schedule experimental testing times at specific stages of the menstrual cycle, rather than retrospectively assessing when the experimental sessions took place.

Another area of discrepancy in methodology was the variety of stimulation modalities that have been used to induce pain. The methods used include muscle ischemia, electrical current, thermal heat, pressure stimulation and strain-gauge. Different physiological pathways are activated depending on the type of external stimulation. For example heat and mechanical stimulation activate a different neurological pathway to that activated by electrical stimulation (Gibson & Helme, 2001). Therefore the impact of the menstrual cycle on pain sensitivity may be different for different types of stimulation. The tissue depth being stimulated will vary depending on the method and may also contribute to inconsistencies between studies (Giamberardino et al., 1997).

The anatomical site at which the experimental stimulus was applied is another variable preventing direct comparison of studies. Isselee, DeLaat, Bogaerts and Lysens (2001) and Drobek et al. (2002) were interested in the change in PPT of masticatory muscles; they tested the masseter and temporalis muscles on both sides and used the first dorsal interosseous muscle as a control site. Bajaj et al. (2001) and Bajaj et al. (2002) used two areas they considered to be sites of referred menstrual pain, which were on the abdomen at the level of the 10^{th} to 12^{th} thoracic vertebrae and the low back at the level of the 2^{nd} to 4^{th} sacral vertebrae. They also used two sites outside the area of referred menstrual pain on the arm and the thigh. Hapidou and Rollman (1998) used 13 sites bilaterally; seven of these were included on the list of Diagnostic Criteria for Fibromyalgia Syndrome (Wolfe et al., 1990). Three sites were chosen based on areas that were considered tender in other studies, and three were control sites, at the forearm, thumbnail and mid-foot.

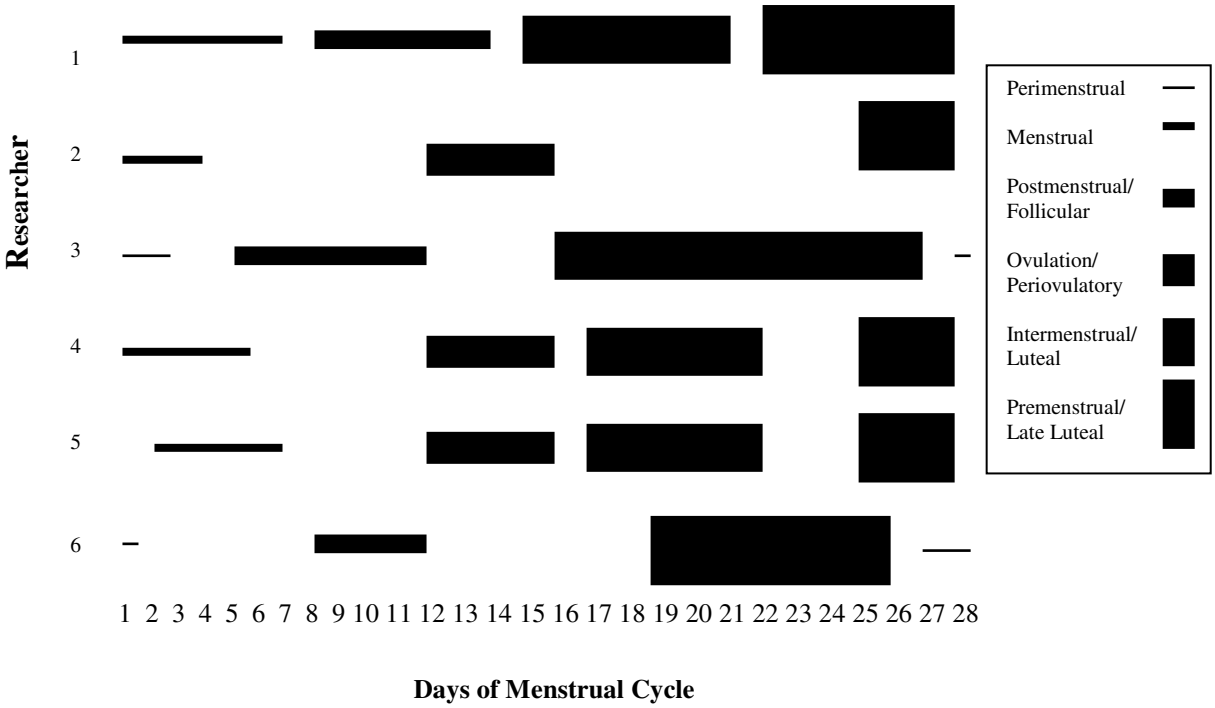

Figure 2.1: A schematic representation of the phases of the menstrual cycle defined by different researchers. 1) Hapidou and Rollman (1998). 2) Amodei and Nelson-Grey (1988). 3) Drobek et al. (2002). 4) Bajaj et al. (2001) and Bajaj et al. (2002). 5) Giamberardino et al. (1997). 6) Isselee et al. (2001).

This variation in methodology makes it impossible to directly compare studies investigating the same topic because different methods may lead to differences in results. The specific areas of significance that have been inconsistent in previous research are the definition of the phases of the menstrual cycle, the method of experimental stimulation and the sites at which this stimulus is applied.

Experimental Measurement of Pain

This research project involved the assessment of pain. When investigating experimentally induced pain many factors can influence the participant's response to the stimulus. These factors need to be kept in mind and controlled as much as possible in order to achieve consistent, reliable and ethical results.

The change in PPT could not be investigated without asking each participant to verbally indicate when pressure applied to a particular site changed from a sensation of pressure to a sensation of pain. Therefore the results are based on subjective information. The subjective nature of the current study could have allowed for a huge variation in responses. One person's idea of what is painful may be quite different to another's. Gender, age, and cultural beliefs all have an effect on how a person expresses pain and when they will report a sensation as being painful. It is now

recognized that the human pain experience is not solely due to sensory or nociceptive events but involves a complex interaction of sensory, cognitive, and behavioural processes (Melzak & Wall, 1965).

The body's system for detecting pain is not fixed and predictable as was once thought. The nociceptive system has the capacity to modify its response to the same amount of tissue damage using diverse physical and psychological factors. This means that an individual's pain can not be predicted solely by the nature of the tissue damage. Although it is likely that most people attempt to honestly report their subjective pain experience, what people tell us about pain experience is altered by their own personal experience and beliefs, therefore people experiencing the same amount of pain will respond differently (Turk & Melzack, 1992).

Gender difference may cause variations in pain expression. Levine and DeSimone (1991) investigated gender role expectations in the reporting of pain. Males holding their hand in iced water in the presence of an attractive female reported less pain than when in the presence of another male. Female participants were not significantly influenced by the gender of the experimenter (Levine & DeSimone, 1991). An investigation was conducted into gender differences in PPT (Chesterton, Barlas, Foster, Baxter, & Wright, 2003). In this study pressure was applied to the first dorsal interosseous muscle using a pressure algometer. Healthy females exhibited a significantly lower mean PPT in the first dorsal interosseous muscle than healthy males, this result was maintained for fourteen repeated measures within a one hour period (Chesterton et al., 2003). These examples demonstrate the differences found between male and female participants in experimental situations. In the current study there were only female participants, however the gender differences help to illustrate the point that there are many things influencing the reporting of pain in experimental situations. The results also highlight the importance of keeping the experimental conditions, such as the person carrying out the experiment, consistent throughout the trial in order to avoid bias in reporting pain.

Age is another influence on the reporting of experimental pain. Gagliese, Katz and Melzack (1997) have shown that age difference in pain ratings may depend on the pain assessment scale used for measurement. A sample of 79 patients with chronic arthritis showed an age-related decrease in the sensory (physical sensation) and affective (emotional interpretation) dimensions of pain using the short form McGill Pain Questionnaire, but no age difference in pain intensity as measured by a Visual Analogue

Scale or a Verbal Descriptor Scale (Gagliese et al., 1997). Studies using a mechanical form of stimulation support the notion of age differences in pain thresholds. Five of six studies reviewed by Gibson and Helme (2001) noted increased pain thresholds in adults of advanced age. In a study of 704 participants, PPT was shown to increase by about 15% in older adults, the effect was stronger in female participants (Gibson & Helme, 2001). The age of the 'older adults' was not specified in this article. In contrast to these results, studies using electrical stimulation suggest there are no age differences in pain threshold (Gibson & Helme, 2001). The different results may be due to differences in the mechanism of pain activation. Electrical stimulation activates primary afferent fibres directly, whereas heat and mechanical stimulation require mechanisms of receptor activation and energy transduction to stimulate sensory fibres (Gibson & Helme, 2001). Age-related change in receptor morphology and function could be used to explain the altered mechanical pain perception in the absence of altered electrical pain thresholds. Changes in the skin are also important factors, the thinning of the epidermis, reduction in elasticity and flattening and separation of dermal-epidermal junction may effect the energy transduction process (Gibson & Helme, 2001). According to Turk and Melzack (1992), older age may be associated with a decrease in nociceptor density. This decrease in density could produce a decrease in sensitivity to noxious stimuli with increasing age, but no convincing evidence exists. Although there is some evidence of an age-related decrease in the intensity of musculoskeletal pain, further investigation is required (Gagliese et al., 1997).

Another important factor is response bias differences in labelling events as 'pain'. Elevated pain threshold in an older adult compared with a young individual may reflect a bias against reporting an event as painful. The intention of the participant to help the experimenter may lead to artificially elevated pain thresholds (Turk & Melzack, 1992). In the current study there was a limited age range specified, one of the inclusion criteria is that participants must be between the ages of 18-35 years. Studies comparing differences in pain threshold with age usually specify groups below 60 years and over 60 years, in such studies the participants aged 18-35 would all be considered in the same age group. Using a narrow age range in the current study was intended to prevent variation in the reporting of pain due to differences in age.

There are certain influences that govern the way in which emotion is expressed. People usually conform to what they have been taught to be socially acceptable leading to cross-cultural variation in the display of emotion and pain (Turk & Melzack, 1992).

People learn in social communities, where conventional ways of interpreting, expressing and responding to pain are acquired (Bates, Edwards, & Anderson, 1993). Culturally acquired patterns may influence the processing of nociceptive information as well as psychological, behavioural, and verbal responses to pain (Bates et al., 1993). Several studies of experimental and acute pain have found that cultural or ethnic background is associated with significant variation in pain intensity reports as well as attitudes, emotions and behaviours associated with pain. Bates et al. (1993) conducted a study to examine the influence of cultural variables on chronic pain perception. It was found that there were significant differences in the attitudes toward chronic pain and in the behavioural, psychological and emotional responses to chronic pain. The six largest ethnic/cultural groups in the study area (Worcester, Massachusetts, USA) were used. The first group comprised of 'Old Americans'. These people identified with no ethnic group but defined themselves as Americans. The other groups were Hispanics, Irish, Italians, French Canadians and Polish. The group with the highest pain intensity rating (lowest tolerance for pain) was the Hispanic group, followed by the Italian group. The Polish and French Canadian groups had the lowest pain intensity rating. Members of the Hispanic group believed most strongly that as long as they had pain, their lives would remain unhappy. They reported their pain more frequently and emotionally and had significantly higher degrees of anger, worries and tension associated with their pain. Many members of the Hispanic and Italian groups indicated a belief that emotional expression was an appropriate response to pain, while members of the Old American and Polish groups generally indicated that non-expression of pain was the ideal response. This study found differences in the accepted standards for and attitudes towards pain and pain behaviour within defined ethnic groups. The study suggests that cultural back-ground is significantly related not only to differences in reported pain perception but also to total pain intensity and the description of pain. The association between pain intensity and ethnic identity suggests that experiences, beliefs, attitudes and meanings derived from growing up within these social communities may affect one's reported perception of pain intensity .

In order to attain a homogenous sample in the current study, only New Zealand European females were included. Each participant acted as her own control; the results of each participant were compared over time. This method of evaluation was intended to help to reduce the influence of external factors such as age and culture. The individual was expected to report the onset of pain consistently, based on the same

understanding of what pain is and what is culturally acceptable, in each experimental session.

Anatomical Sites Used in the Diagnosis of Fibromyalgia

In the current study pressure was applied at the 18 anatomical sites used in the diagnosis of fibromyalgia. The understanding of fibromyalgia has changed over the years and the criteria for establishing a diagnosis of fibromyalgia has undergone a process of evolution from the 1940s when fibromyalgia was a term that was applied to a diverse series of musculoskeletal complaints such as strains, bursitis and psychogenic rheumatism (Wolfe, 1986).

A standard diagnostic criteria was developed by a committee of health professionals who set out in an effort to provide a widely accepted definition for fibromyalgia (Wolfe et al., 1990). This new investigation was done based on the fact that a number of criteria sets had already been established, but were based on studies with serious methodological problems (Wolfe et al., 1990). In this study tender sites were found to be the most powerful discriminator between fibromyalgia patients and controls. Widespread pain had a sensitivity of 97.6%. The best criteria were identified when wide spread pain was combined with the presence of 11 out of 18 tender sites, which was the variable that had the best overall sensitivity, specificity, and accuracy (Wolfe et al., 1990).

The tender point sites selected by the committee for use with the 1990 criteria were chosen based on those used in other criteria sets. Three lower-segment sites (buttocks, trochanters, knees) were included to emphasise the widespread nature of the tenderness and to avoid false-positive results in patients with shoulder girdle pain and similar syndromes (Wolfe et al., 1990). Six sites (three pairs) were eliminated due to low discriminatory power. This left 18 of the original sites of tender point examination in the final diagnostic criteria. The sites on the upper part of the body were the occiput at the suboccipital muscle insertions, low cervical at the anterior aspects of the intertransverse spaces at C5-C7, the trapezius muscle at the midpoint of the upper boarder, the supraspinatus muscle at the origin above the spine of the scapular near the medial boarder, the second rib at the second costochondral junction and the lateral epicondyle of the humerus 2cm distal to the epicondyle. The sites on the lower half of the body were the gluteal region at the upper outer quadrant of the buttock, the greater trochanter, just posterior to the trochanteric prominence and the knee, on the medial fat pad proximal to the joint line, these sites are all tested bilaterally (Wolfe et al., 1990).

The onset of fibromyalgia often occurs when the levels of oestrogen and progesterone are changing, around the times of menarche, childbirth and perimenopause (Anderberg, Marteinsdottir, Hallman, & Backstrom, 1998). This pattern indicates that gonadal hormones may play a role in the development of fibromyalgia (Anderberg et al., 1998). A study was conducted to investigate the effects of hormonal changes during the menstrual cycle on the psychological and physical symptoms of fibromyalgia. It was found that of all the symptoms recorded, pain scored the highest as the most adverse symptom. Patients suffering from fibromyalgia reported more pain in the perimenstrual phase compared to the ovulatory phase. The study reported that hormonal changes in the luteal phase, especially perimenstrually, aggravate the pain of fibromyalgia syndrome (Anderberg et al., 1998). The study had a small sample size, 16 patients diagnosed with fibromyalgia and 15 healthy control participants, which limits the generalizability of the results, however it demonstrates the influence of gonadal steroids on the symptoms of fibromyalgia and on healthy control participants (Anderberg et al., 1998).

In the current study it was decided to use the 18 anatomical sites used in the diagnosis of fibromyalgia because they are wide-spread and have the potential to demonstrate a systemic effect of hormonal changes on pain threshold. It was also thought that the results of the current study might indicate if change in PPT due to hormonal fluctuations during the menstrual cycle might affect the diagnosis of fibromyalgia.

METHODOLOGY

The current study was designed to determine the extent to which PPT fluctuated over the course of the menstrual cycle and to show if any fluctuation in PPT was consistent and reproducible form one cycle to the next. A prospective, repeated-measures analysis of variance design was used. The PPT was measured repeatedly (three times) over the course of one menstrual cycle and repeated in a second menstrual cycle. The difference between the PPT at the three different experimental sessions was analysed. The analysis was of an individual's results over time therefore participants acted as their own controls. All participants received the same treatment.

Participants

Following approval from Unitec Research Ethics committee (see Appendix A) female student volunteers were recruited from Unitec New Zealand. Notices were posted on notice boards around the campus (see Appendix B), on the Unitec Blackboard™ web site and announcements were made at the beginning of lecture sessions. Snowball sampling, a type of convenience sampling, was used (Polit & Hungler, 1997). Recruited participants were asked to identify and refer other people who met the eligibility criteria for the study.

Inclusion Criteria

To be included in this study there were several criteria that had to be met:

- Participants were required to be between 18 and 35 years of age. This age range was chosen to insure that those included in the study had established regular menses and exclude women who were beginning menopause. The age range was kept small in order to select a more homogenous sample.
- Participants were required to have histories of regular, predictable menstrual cycle lengths of 25-30 days. To ensure this regularity participant's menstrual cycles were recorded by the researcher on notification by participants. Recording was carried out for two months (two menstrual cycles) after enrolment and before the commencement of the experimental sessions. This information was then used to schedule each participant individually for experimental sessions.
- Participants were required to be of New Zealand European ethnicity. This requirement was based on the strong prevalence of European usage of

osteopathy (Moore, 2003), and the importance of obtaining a homogeneous sample.

Exclusion Criteria

Exclusion from this study was based on factors that could alter a women's sensitivity to pressure or change the normal fluctuation of female sex hormones. Those excluded were:

- Women suffering from dysmenorrhoea or any other general health problem that may alter the PPT.
- Women taking oral contraceptives or receiving intramuscular injections for birth control as synthetic hormones alter the natural fluctuation of female sex hormones (Guyton & Hall, 2000).
- Women having a clinical history of major psychological problems, or taking medication for psychological problems. It has been shown that people suffering from high levels of psychological distress and high scores on depression scales had associated low pain thresholds (Chiu et al., 2005).
- Women with a diagnosis of fibromyalgia, rheumatological disease or chronic pain syndrome as these conditions have been shown to alter pain thresholds (Hendiani et al., 2003; Laursen, Bajaj, Olsen, Delmar, & Arendt-Nielsen, 2005).

Before enrolment for this study participants were asked to complete an information sheet relating to their general health at the present time and relevant medical history (Appendix C). This information was necessary in order to screen for factors that may affect the results of the study. Once enrolled, participants answered follow up questions before each experimental session to ensure there were no major changes in their health status over the course of the study (Appendix D).

Following consent procedures (Appendix E and F), participants were given a training session to acquaint them with the sensations evoked by the experimental stimuli. Participants were requested where possible to abstain from using analgesics during the two-month experimental period. Participants were asked before each experimental session if they had taken any analgesics in the previous two or three days, if they had had any changes in health status. Anything reported by participants was recorded (see page 19).

Testing Protocol

Participants were asked to attend experimental sessions six times in total, over a two month period. Sessions were held at the Unitec Osteopathic Clinic.

Experimental session scheduling

In the current study a prospective method was used to schedule participants for their experimental sessions. Each participant reported the first and last day of menses to the researcher for two menstrual cycles before the commencement of experimental sessions. The researcher then ensured that each participant's cycle length was consistently 25 to 30 days in length. Experimental sessions began in the third menstrual cycle. The researcher used the date of the first day of each participant's third menses as day one. Each participant was scheduled for three experimental sessions per menstrual cycle, on approximately the 3rd, 12th or 13th and 21st days of the menstrual cycle. The 3rd day of the menstrual cycle was chosen because it is widely reported to correspond with low levels of the hormones oestrogen and progesterone. At this time levels of follicle stimulating hormone (FSH) and luteinizing hormone (LH) are beginning to increase. The 12th to 13th day of the menstrual cycle is the time at which secretion of oestrogen is at its highest. At this point LH and FSH secretion is also increasing. The 21st day of the menstrual cycle is approximately midway through the luteal phase of the menstrual cycle and is the stage of the cycle when progesterone secretion is at its highest point. At this stage LH and FSH are at very low levels of secretion. The scheduling of these three experimental sessions was repeated in the second month of experimental testing, assessing changes in PPT with respect to fluctuations of these four key hormones.

Sites where pressure was applied

In the current study, nine anatomical sites used in the diagnosis of fibromyalgia were assessed (Wolfe et al., 1990). Each site was bilateral (left and right sides), providing a total of 18 sites to measure PPT all over the body (Wolfe et al., 1990).

1. Low cervical: at the anterior aspects of the intertransverse spaces at C5-7.
2. Second rib: at the second costochondral junctions, just lateral to the junctions on upper surfaces.
3. Lateral epicondyle of humerus: 2cm distal to the epicondyle.
4. Knee: at the medial fat pad, proximal to the joint line.

5. Occiput: at the suboccipital muscle insertions.
6. Trapezius muscle: at the midpoint of the upper boarder of the muscle.
7. Supraspinatus muscle: at origins, above the spine of the scapula near the medial border.
8. Gluteal: in upper outer quadrants of buttocks in anterior fold of muscle.
9. Greater trochanter: posterior to the trochanteric prominence.

Equipment

A spring algometer was used (Activator Methods Instruments, Melbourne) to apply pressure to the anatomical sites. The algometer consists of a force dial which reads in pounds and kilograms and a metal rod with a 1cm diameter rubber tip at the end. Pressure exerted on the rod is transmitted to the body of the algometer and moves the indicator needle in a clockwise direction. The indicator needle remains at the achieved force value until the zeroing knob is pressed.

Procedure

Participants were required to wear shorts and a singlet and to lie comfortably on a treatment table during each experimental session. Each experimental session took approximately fifteen minutes. The amount of force required to change the sensation of local pressure to the onset of local pain was measured. Experimental sessions proceeded in the following way:

1. Participants were given instructions to say "pain" as soon as the sensation of pressure changed to a sensation of pain.
2. Participants were required to lie on their backs (supine) for the first eight sites and on their fronts (prone) for the last ten sites.
3. Each site was located by palpation using anatomical landmarks.
4. The algometer was held in the palm of the researcher's hand between the thumb and index finger. The algometer was positioned perpendicular to the participant's skin with the rubber tip over the anatomical site.
5. Before applying pressure on each site the researcher would say "applying now" and then begin applying pressure. The algometer was advanced at a steady rate

of 1kg per second (Fischer, 1987). The anatomical site on the left side of the participant was tested first, followed by the corresponding right sided site. Anatomical sites were tested in the order they are described above.

6. When the participant indicated the PPT by saying "pain" the algometer was immediately removed.
7. The reading on the force dial was recorded in kilograms.
8. The needle of the gauge was reset by pressing the pressure release button before the next reading was taken.

Data Management

All the raw data collected during experimental sessions were typed into a Microsoft Excel® spreadsheet, which resulted in eleven sets of data, one set per participant. Each set consisted of PPTs recorded in kilograms. Nine anatomical sites were tested on the left and right leaving 18 values for each participant in each test. Each participant underwent six test sessions. Tests one, two and three were performed in the first menstrual cycle and tests four, five and six were performed in the second menstrual cycle. Tests one and four were performed in the menstrual phase of the menstrual cycle, tests two and five were performed in the follicular phase of the menstrual cycle, and tests three and six were performed in the luteal phase of the menstrual cycle.

Prior to statistical analysis, data were arranged in three different ways. The first data arrangement compared the differences in PPT measurements over time, within each menstrual cycle and between each menstrual cycle. The second was to compare PPT measurements at left versus right anatomical sites, and the third was to compare the nine different anatomical sites.

The mean PPT for the 18 anatomical sites in each of the six test sessions was calculated for all 11 participants. These means were used to compare tests one and two, tests one and three and tests two and three in the first menstrual cycle, and tests four and five, tests four and six, and tests five and six in the second menstrual cycle. The comparison between menstrual cycles was investigated using the same test sessions in consecutive menstrual cycles. Thus, test one was compared with test four, test two with test five and test three with test six.

Secondly data were arranged in order to compare PPT measurements on the left and right sides of the body. All the data recorded from testing anatomical sites on the

left were separated from the data recorded from testing anatomical sites on the right. The mean of the nine sites on the left was taken for each of the six test sessions, for each of the 11 participants; the same was done for the sites on the right. This approach resulted in one mean for each test on the left and each test on the right, for each participant, in each of the six tests. The means of test one on the left were compared to the means of test one on the right.

Thirdly data were arranged in order to compare PPT measurements at the nine different anatomical sites. The first four sites were anterior; these were at the intertransverse spaces at the level of the 5^{th} to 7^{th} cervical vertebra, the costochondral junction of the second ribs, the lateral epicondyle of humerus, and the medial fat pad of the knee. The next five sites were posterior; on the suboccipital muscle insertions, over the middle fibres of the trapezius muscle, at the origin of the supraspinatus muscle, on the boarder of the gluteal muscles, and over the greater trochanteric prominence. Each anatomical site was tested six times over two menstrual cycles. Eleven participants were tested left and right resulting in 22 PPTs recorded during each of the six testing sessions for each of the anatomical sites. The mean PPT of the left and right anatomical sites was calculated for each participant at each of the six test sessions. This calculation was done for each of the nine anatomical sites. This approach resulted in 11 means at each anatomical site for each of the six testing sessions. Next the mean of all 11 participants PPT was calculated at each anatomical site. The tests were then separated into menstrual cycles. Tests one, two and three were performed in the first menstrual cycle and tests four, five and six were performed in the second menstrual cycle. Previous analysis (Table 4.1) showed only a trivial or small difference between each of the three test sessions in each menstrual cycle. Based on this finding it was decided to group the three test sessions from cycle one together and the three test sessions from cycle two together for future analysis. Menstrual cycle one then had three means for each anatomical site, as did menstrual cycle two. Exactly the same analysis was performed on the data from each menstrual cycle, however they were treated individually. The resulting three means of anatomical site one were compared to those of anatomical site two, site one was then compared to site three, then four and so on to nine. Site two was then compared to each of the other eight anatomical sites as were three, four, five, six, seven, eight and nine.

Statistical Analysis

Data were analysed using a repeated-measures analysis of variance design. The individual participants PPT measurements were compared over six experimental sessions using the change scores between tests. Intra-class correlation coefficients and 95% confidence intervals were used to examine the relationship between the same participant's results at different experimental testing times. This procedure enabled an estimate of the magnitude of change in individual participants score over the course of the menstrual cycle.

Differences between corresponding test sessions in the two menstrual cycles and different test sessions within the same menstrual cycle were computed as raw (kg) force values and effect sizes. Precision of the estimates was calculated using 95% confidence intervals. Confidence limits were not adjusted to hold the overall Type O error rate to 5% (the chance that any true value in this study falls outside its confidence interval**;** Hopkins, 1997). The author is of the opinion that in publishing precision of estimates, controlling error rate is not an issue. Readers should interpret reported effects by acknowledging that the population value may be outside the confidence interval for some of the effects. In instances where differences in means were represented as multiples of standard deviations, the magnitudes of the effects were interpreted according to the criteria of Cohen, (1988) and Hopkins, (1997): trivial, 0.0; small, 0.2; moderate, 0.6; and large, 1.2.

RESULTS

Participants

Twelve women met the inclusion criteria and were recruited. One of the participants withdrew from the study before the experimental sessions began. The age of the remaining eleven participants ranged from 19 to 35 years with a mean of 26 years. Nine of the participants were osteopathy students and two were nursing students. One participant took the morning-after pill in the time between the fifth and sixth test sessions. Data analysis (an example of some of the analysis can be found in Appendix G) with and without her results showed very little difference therefore it was decided to include her data in all statistical analysis. One participant was taking oral progesterone supplements. It was decided to include this participant in the study because the synthetic hormones were designed to maintain her progesterone levels at normal concentrations.

Comparison of the Three PPT Measurement sessions within Each Menstrual Cycle

Differences between mean PPTs for all participants recorded in the first and second months were found to be trivial or small. These differences expressed as effect sizes are given in Table 4.1.

Table 4.1: Intra-cycle Test Point Comparisons

Comparison	Effect Size	Lower 95% Confidence Limit	Upper 95% Confidence Limit	Interpretation
Test 1 & 2	0.1	-0.8	1.1	Trivial
Test 1& 3	0.2	-0.7	1.2	Small
Test 2 & 3	0.1	-0.8	1.1	Trivial
Test 4 & 5	0.02	-1.0	1.0	Trivial
Test 4 & 6	0.2	-0.8	1.1	Small
Test 5 & 6	0.1	-0.8	1.1	Trivial

Comparison of PPT Measurements during the same Phase of the Menstrual Cycle in Consecutive Months

Analysis was performed to determine the degree to which the PPT measurements varied between test sessions during the same phase of the menstrual cycle in two consecutive months. Effect statistics in raw kg values were calculated and can be found in Table 4.2, mean PPT values are shown in Figure 4.1.

Table 4.2: Inter-cycle Test Point Comparisons

Comparison	Effect Statistic (kg)	Lower (95%) confidence limit	Upper (95%) confidence limit
Test 1 & 4	0.4	-0.5	1.4
Test 2 & 5	0.3	-0.6	1.3
Test 3 & 6	0.3	-0.5	1.2

Effect sizes were also calculated and showed a small difference in all three comparisons. The estimated value of the difference between tests one and four was 0.4 (likely range -0.5 to 1.3). The difference between tests two and five, and tests three and six both had an effect size of 0.4 (likely range of -0.6 to 1.3).

A raw change score was calculated to find the degree of variation in the change in PPT between tests one and two, tests two and three and tests one and three in consecutive months. The results are shown in Table 4.3.

Table 4.3: Comparison of Change Scores between Pairs of Tests in Consecutive Months

Comparison	Effect statistic (kg)	Lower (95%) confidence limit	Upper (95%) confidence limit
Test 1& 2 v test 4 & 5	0.1	-0.1	0.3
Test 2 &3 v test 5 & 6	0.1	-0.1	0.3
Test 1 &3 v test 4 & 6	0.2	-0.2	0.6

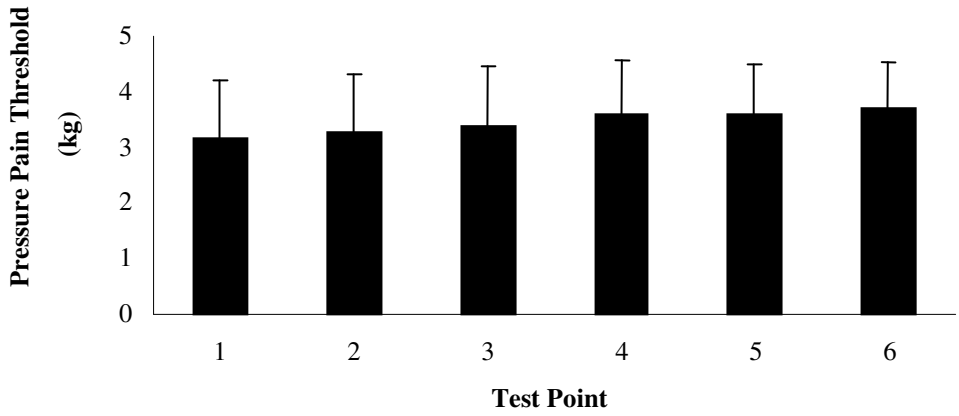

Figure 4.1: Pressure pain thresholds measured at all anatomical sites in all participants partitioned into six test sessions

Comparison of PPT at Left and Right Anatomical Sites

Analysis was performed to compare left and right anatomical sites in each of the six tests session. This resulted in raw (kg) force values that showed very small differences between left and right anatomical sites (Table 4.4). Raw force values are illustrated in Figure 4.2. Effect sizes (Table 4.5) showed trivial differences between PPT recorded on left and right sides of the body.

Table 4.4: Raw values of comparison between pressure pain threshold at left and right anatomical sites

Comparison	Effect Statistic (kg)	Lower 95% confidence limit	Upper 95% confidence limit
Test 1 left v right	0.07	-1.0	1.2
Test 2 left v right	0.06	-1.0	1.1
Test 3 left v right	0.03	-1.0	1.1
Test 4 left v right	0.06	-0.9	1.0
Test 5 left v right	0.1	-0.4	0.5
Test 6 left v right	0.06	-0.7	0.9

Table 4.5: Effect sizes of the comparison between pressure pain threshold at left and right anatomical sites

Comparison	Effect Size	Lower 95% confidence limit	Upper 95% confidence limit	Interpretation
Test 1 left v right	0.07	-0.9	1.0	Trivial
Test 2 left v right	0.05	-0.8	0.9	Trivial
Test 3 left v right	0.03	-1.0	1.1	Trivial
Test 4 left v right	0.06	-0.9	1.0	Trivial
Test 5 left v right	0.1	-0.4	0.5	Trivial
Test 6 left v right	0.08	-1.2	1.3	Trivial

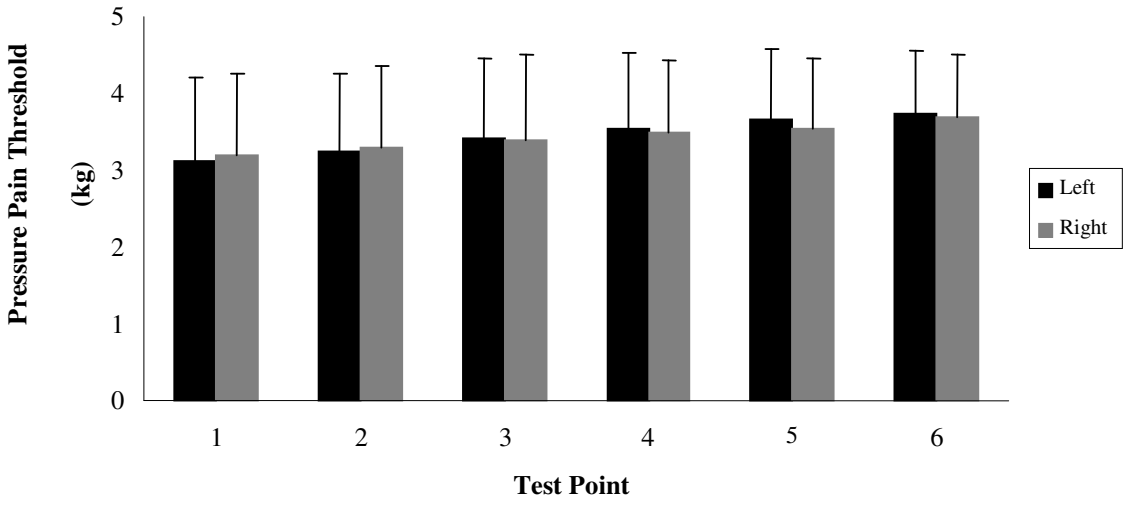

Figure 4.2: Comparison of pressure pain thresholds on left and right sides of the body

Comparison of PPT measurements at Different Anatomical Sites

Menstrual Cycle One

Comparison of PPT measurements at any two different anatomical sites showed a large effect size for most of the comparisons (Figure 4.3). The exceptions in the tests performed during the first menstrual cycle were the difference between anatomical sites four and five, four and six, five and six, and seven and nine. Comparison of PPT recorded at anatomical site four (medial fat pad of knee joint) and anatomical site five (suboccipital muscle insertion) showed a moderate effect size, as did comparison of sites five and six (upper border of trapezius muscle). The difference in PPT at sites four

and six showed only a small effect size as did comparison of sites seven (origin of supraspinatus muscle) and nine (greater trochanteric prominence of femur). All these results are shown in Table 4.6.

Menstrual Cycle Two

The majority of PPTs recorded in the second menstrual cycle also showed large effect sizes when comparing anatomical sites (Figure 4.3). However there were also some exceptions. Anatomical sites two (costochondral junction of second rib) and five (suboccipital muscle insertion) showed a moderate effect size when PPTs were compared, as did anatomical sites seven (origin of supraspinatus muscle) and eight (upper outer quadrant of gluteal muscles). A small effect size was found between anatomical sites four (medial fat pad of the knee joint) and six (upper border of trapezius muscle) and between sites seven and nine (greater trochanteric prominence of femur). Only a trivial effect size was found between anatomical sites eight and nine. All these results are shown in Table 4.7.

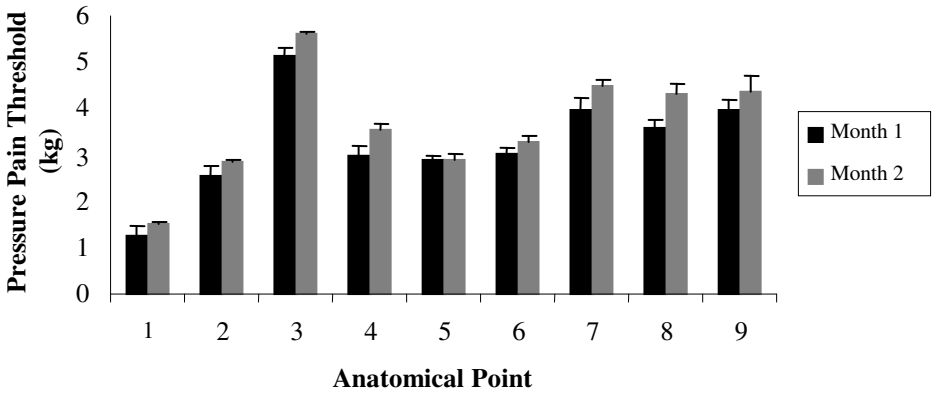

Figure 4.3: Comparison of pressure pain threshold at nine anatomical sites

Table 4.6: Comparison of pressure pain threshold at nine different anatomical sites in the first menstrual cycle tested

Anatomical Site	1	2	3	4	5	6	7	8	9
1		1.77 (0.8 to 2.7)	1.82 (1.3 to 2.3)	1.79 (1 to 2.6)	1.81 (1.1 to 2.5)	1.80 (1.1 to 2.5)	1.81 (1.1 to 2.5)	1.81 (0.8 to 2.8)	1.81 (1.1 to 2.5)
2	1.77 (0.8 to 2.7)		1.81 (1.2 to 2.4)	1.48 (0 to 3)	1.44 (-0.1 to 3)	1.56 (0.2 to 2.9)	1.77 (0.8 to 2.7)	1.75 (0.8 to 2.7)	1.76 (0.8 to 2.7)
3	1.82 (1.3 to 2.3)	1.81 (1.2 to 2.4)		1.81 (1.2 to 2.4)	1.82 (1.2 to 2.4)	1.81 (1.2 to 2.4)	1.75 (0.8 to 2.7)	1.80 (1.1 to 2.5)	1.75 (0.8 to2.7)
4	1.79 (1 to 2.6)	1.48 (0 to 3)	1.81 (1.2 to 2.4)		0.70 (-1.3 to 2.7)	0.22 (-1.7 to 2.1)	1.72 (0.6 to 2.8)	1.65 (0.5 to 2.8)	1.71 (0.6 to 2.8)
5	1.81 (1.1 to 2.5)	1.44 (-0.1 to 3)	1.82 (1.2 to 2.4)	0.70 (-1.3 to 2.7)		1.0 (-0.9 to 2.9)	1.76 (0.8 to 2.7)	1.74 (0.7 to 2.7)	1.75 (0.7 to 2.7)
6	1.80 (1.1 to 2.5)	1.56 (0.2 to 2.9)	1.81 (1.2 to 2.4)	0.22 (-1.7 to 2.1)	1.0 (-0.9 to 2.9)		1.72 (0.6 to 2.8)	1.67 (0.5 to 2.8)	1.71 (0.6 to 2.8)
7	1.81 (1.1 to 2.5)	1.77 (0.8 to 2.7)	1.75 (0.8 to 2.7)	1.72 (0.6 to 2.8)	1.76 (0.8 to 2.7)	1.72 (0.6 to 2.8)		1.38 (-0.2 to 3)	0.2 (-1.5 to 1.9)
8	1.81 (0.8 to 2.8)	1.75 (0.8 to 2.7)	1.80 (1.1 to 2.5)	1.65 (0.5 to 2.8)	1.74 (0.7 to 2.7)	1.67 (0.5 to 2.8)	1.38 (-0.2 to 3)		1.31 (-0.3 to 2.9)
9	1.81 (1.1 to 2.5)	1.76 (0.8 to 2.7)	1.75 (0.8 to 2.7)	1.71 (0.6 to 2.8)	1.75 (0.7 to 2.7)	1.71 (0.6 to 2.8)	0.2 (-1.5 to 1.9)	1.31 (-0.3 to 2.9)	

The values presented are effect sizes.

The values in brackets are lower and upper 95% confidence limits.

Table 4.7: Comparison of pressure pain threshold at nine different anatomical sites in the second menstrual cycle tested

Anatomical Site	1	2	3	4	5	6	7	8	9
1		1.82 (1.3 to 2.3)	1.83 (1.5 to 2.1)	1.82 (1.2 to 2.4)	1.81 (1.2 to 2.5)	1.82 (1.2 to 2.4)	1.82 (1.4 to 2.2)	1.82 (1.2 to 2.4)	1.81 (1.1 to 2.5)
2	1.82 (1.3 to 2.3)		1.83 (1.5 to 2.1)	1.74 (0.7 to 2.8)	0.68 (-1.3 to 2.7)	1.72 (0.7 to 2.8)	1.82 (1.3 to 2.3)	1.71 (1 to 2.4)	1.76 (0.8 to 2.7)
3	1.83 (1.5 to 2.1)	1.83 (1.5 to 2.1)		1.82 (1.3 to 2.2)	1.82 (1.3 to 2.2)	1.82 (1.3 to 2.2)	1.82 (1.2 to 2.3)	1.79 (1 to 2.6)	1.73 (0.7 to 2.8)
4	1.82 (1.2 to 2.4)	1.74 (0.7 to 2.8)	1.82 (1.3 to 2.2)		1.64 (0.4 to 2.9)	0.59 (-1.5 to 2.7)	1.80 (1.1 to 2.5)	1.74 (0.7 to 2.8)	1.68 (0.5 to 2.9)
5	1.81 (1.2 to 2.5)	0.68 (-1.3 to 2.7)	1.82 (1.3 to 2.2)	1.64 (0.4 to 2.9)		1.60 (0.3 to 2.9)	1.81 (1.2 to 2.4)	1.78 (0.9 to 2.6)	1.75 (0.7 to 2.8)
6	1.82 (1.2 to 2.4)	1.72 (0.7 to 2.8)	1.82 (1.3 to 2.2)	0.59 (-1.5 to 2.7)	1.60 (0.3 to 2.9)		1.81 (1.1 to 2.5)	1.75 (0.8 to 2.7)	1.70 (0.6 to 2.8)
7	1.82 (1.4 to 2.2)	1.82 (1.3 to 2.3)	1.82 (1.2 to 2.3)	1.80 (1.1 to 2.5)	1.81 (1.2 to 2.4)	1.81 (1.1 to 2.5)		0.96 (-0.9 to 2.8)	0.54 (-1.5 to 2.6)
8	1.82 (1.2 to 2.4)	1.71 (1 to 2.4)	1.79 (1 to 2.6)	1.74 (0.7 to 2.8)	1.78 (0.9 to 2.6)	1.75 (0.8 to 2.7)	0.96 (-0.9 to 2.8)		0.18 (-1.9 to 2.2)
9	1.81 (1.1 to 2.5)	1.76 (0.8 to 2.7)	1.73 (0.7 to 2.8)	1.68 (0.5 to 2.9)	1.75 (0.7 to 2.8)	1.70 (0.6 to 2.8)	0.54 (-1.5 to 2.6)	0.18 (-1.9 to 2.2)	

The values presented are effect sizes.

The values in brackets are lower and upper 95% confidence limits.

DISCUSSION

The current study has added another perspective to the growing body of literature investigating changes in pain threshold during the menstrual cycle. The results are discussed with reference to previous research on this topic. Limitations of the current study and future directions for research on this topic are also discussed.

In the current study trivial and small differences were found when comparing PPTs recorded during different phases of the menstrual cycle and when examining the difference between PPTs recorded on left and right sides of the body. The greatest variability of PPT was found when comparing the nine anatomical sites where pressure was applied.

Menstrual cycle

Comparison of the three test sessions within each menstrual cycle showed only a small or trivial difference in mean PPT. The biggest difference was found between the tests performed in the menstrual phase (approximately day 3 of the menstrual cycle) and the luteal phase (approximately day 21 of the menstrual cycle). In both months the effect sizes showed a small difference between these phases (Table 4.1). The menstrual phase showed the lowest mean PPT in month one and two and the luteal phase showed the highest mean PPT in consecutive cycles (Figure 4.1). This finding is in agreement with Giamberadino et al. (1997) who found that the highest threshold values always occurred in the luteal phase (days 17-22) and the lowest threshold values perimenstrually (they defined a premenstrual phase days 25-28 but no perimenstrual phase). Higher thresholds in the luteal phase may reflect the high levels of progesterone present. Progesterone has a known sedative-like effect on the nervous system (Giamberardino et al., 1997).

The results of the current study are in contrast to those reported by Drobek et al. (2002). They found that the PPT of the temporalis muscle in the menstrual phase (days not defined) was significantly higher, ($p = 0.0408$), than the follicular phase (days 5-12) in a group of participants who were taking oral contraceptives. In the current study only trivial differences were found between the menstrual and follicular phases and between the follicular and luteal phases. This finding is in agreement with Isselee et al. (2001) who found insignificant differences between the follicular and luteal phases ($p = 0.2872$, $p = 0.1857$ and $p = 0.1566$ for measurements 1, 2 and 3 respectively). Other

studies have also reported no cycle related effects for PPT (Amodie & Nelson-Grey, 1989; Hapidou & Rollman, 1998).

The results of the current study showed a general trend of increasing PPTs over the six test sessions performed during two consecutive menstrual cycles (Figure 4.1). This trend may be a result of habituation. Habituation is a decrease in the strength of a response after repeated presentation of the stimulus that elicits the response. Any elicited response can exhibit habituation but it is most evident in the body's automatic responses to new and sudden stimuli (Mazur, 1998). Habituation proceeds more rapidly with weak stimuli. The stimulus in the current study was pressure applied with an algometer; the pressure was only applied until the participant felt the sensation of pressure change to pain. This procedure may be considered to result in a relatively weak stimulus that may increase the likelihood of habituation to the pressure being applied. Isselee et al. (2001) reported no adaptation to their experimental stimulus. However other studies have reported an increase in PPT over weekly sessions (Jensen, Anderson, Olesen, & Lindblom, 1986), and testing nine to twelve weeks after a previous experimental session (Kosek, Ekholm, & Nordemar, 1993).

Small differences were found between PPTs recorded at the same time of the menstrual cycle over two consecutive months. This result may be due to habituation as discussed above. It may also be due to external influences that could affect pain sensitivity such as psychological and emotional states. Another explanation for these small differences may be discrepancies in experimental testing times. Testing sessions in the same phase of the menstrual cycle in consecutive months were not always performed on exactly the same day. Testing sessions also varied as to what time of the day they took place depending on what time was most convenient for the participant and the researcher. All of these factors could have had some influence on how sensitive each participant was to the pressure applied on any given day.

Anatomical sites

Comparison of PPTs taken from anatomical sites on the left and right side of the body showed the smallest difference in PPT of all comparisons made; all effect sizes were trivial. Drobek et al. (2002) found that the average PPTs of the masseter muscle were higher on the right in those not taking oral contraceptives, than on the left in the menstrual and follicular phases. In the luteal phase the average results were higher on the left than the right for those not taking oral contraceptives, and for all phases in the participants taking oral contraceptives. In contrast, when testing the temporalis muscle

the same study reported that the PPT of women taking oral contraceptives was significantly higher on the right in all phases. The current study tested sites all over the body so when averaged there was very little difference in PPT between anatomical sites. Perhaps if smaller anatomical areas or individual muscles were examined there would be a clear difference between left and right.

Comparison of the nine different anatomical sites where pressure was applied showed the biggest difference in PPT of all the comparisons made. The effect sizes calculated showed large differences in PPT between most of the anatomical sites. There were some exceptions of note. Anatomical sites four (medial fat pad of knee joint) and six (upper border of trapezius muscle) were found to have only a small difference in PPT in both month one and two as did anatomical sites seven (origin of supraspinatus muscle) and nine (greater trochanteric prominence of femur). Both of these pairs have one point over a muscle and one point over a relatively bony area. This finding may indicate the type of tissue over which pressure was applied is not the key in determining the sensitivity of the area. Giamberardino et al. (1997) found that absolute overall pain threshold values of skin, subcutaneous and muscle tissues did not differ significantly across the four sites that they tested. These sites were on the left and right abdomen, the deltoid muscle of one arm and the quadriceps muscle of one leg. They also reported that the pain thresholds were generally highest when testing muscle tissue and lowest when testing skin. Menstrual variations in skin thresholds differed from those of subcutaneous and muscle tissues. In the current study it was found that applying pressure over different muscles yielded different results. Anatomical point one was the most sensitive, this point is over the anterior scalene and sternocleidomastoid muscles. This sensitivity is in contrast to anatomical sites seven and eight that showed two of the highest thresholds, these were over the origin of the supraspinatus muscle and the upper outer quadrant of the gluteal muscles respectively. The variation in thresholds over the different muscles in the current study could be due to the area of the muscle over which pressure is applied. For example the sites on the supraspinatus and gluteal muscles were at the edges of the muscle bulk, if pressure had been applied to the belly of the muscle it may have shown much more sensitivity, yielding a lower PPT. Another factor that must be taken into consideration is the tissues and structures overlying the muscles. The anterior cervical site has much less subcutaneous fat than the gluteal and supraspinatus areas and many more fragile structures such as blood vessels and nerves (Kosek et al., 1993). Iseelee et al. (2001) found similar patterns of pain sensitivity for

the masseter, temporalis and thumb muscles. They reported that these results suggest a generalized menstrual cycle effect on the central nervous system.

Anatomical point three showed the highest PPT. This point was two centimetres inferior to the lateral epicondyle of the humerus. In the present study the two centimetres was measured by the researcher using two finger widths, the tip of the algometer was placed where the second finger lay. In hindsight it is likely that the algometer should have been placed next to, rather than under, the second finger. This location would be directly over the belly of the brachioradialis muscle which is very sensitive to pressure (Kosek et al., 1993). Pressure was instead applied over the much less sensitive common extensor tendon resulting in the highest PPTs recorded (Figure 4.3).

Relevance to fibromyalgia

The criteria for the diagnosis of fibromyalgia were designed to identify this syndrome from other rheumatic conditions. Sleep disturbance, fatigue, and stiffness are the central symptoms; each is present in more than 75% of fibromyalgia patients. The criteria are widespread pain in combination with pain at 11 or more of the 18 specific anatomical sites. These sites are digitally palpated with an approximate force of 4 kg. Widespread pain is classified as pain on the left and right side of the body, above and below the waist, and in the axial skeleton (Wolfe et al., 1990).

Anderberg et al. (1998) found variation in symptoms such as pain, fatigue and depression, over the menstrual cycle in healthy individuals and those suffering from fibromyalgia. They demonstrated that the hormonal changes over the menstrual cycle could aggravate pain in fibromyalgia sufferers. The results of the current study showed only small variations in the PPT over the menstrual cycle. However the raw data for the current study (Appendix H) show that 10 of the 11 participants fitted one of the criteria for fibromyalgia; that is that they had pain at 11 or more of the 18 anatomical sites at 4kg of pressure or less. Six of these participants fitted the criteria in all of the six experimental sessions, one participant only in five experimental sessions and two participants only in one experimental session. Only one participant in the current study had less than 11 sites tender at 4kg of pressure over all six experimental sessions. This finding shows there is variation in healthy individual's sensitivity to pain irrespective of the stage of the menstrual cycle they are in. Therefore hormonal fluctuations over the menstrual cycle and individual variation in pain sensitivity are likely to influence the diagnosis of fibromyalgia. This information should certainly be considered when

making the diagnosis of fibromyalgia. It will ultimately be the combination of other criteria, such as widespread pain, fatigue, sleep disturbance and stiffness that will discriminate patients who have fibromyalgia from those who do not.

Limitations

In the current study experimental testing times were based on an estimate of the phase of the cycle each participant was in. The estimate was gained by recording the participant's menses for two months before experimental sessions began and continuing to record menses during the two months of experimental sessions. There were many things that could lead to an alteration of experimental testing times, such as unavailability of the participant due to other commitments or the timing of the day estimated coinciding with the weekend when the Osteopathic Clinic was closed. Even if each participant could be tested on the exact day estimated throughout the two months there is no way of knowing if the estimate was correct. Only a small percentage of women ovulate exactly 14 days before the onset of menses, even women with regular 28 day cycles. The day of ovulation varies from day 10 of the menstrual cycle through to day 22 (Wilcox, Dunson, & Baird, 2000). About 20% of menstrual cycles are non-ovulatory and do not have the oestrogen and luteinizing hormone peak at ovulation (Bajaj et al., 2002). The current study did not use any precise measures of hormonal or ovulation status such as blood or urine testing. This lack of precise measures combined with the unpredictability of ovulation make it impossible to know exactly what stage of the menstrual cycle each participant was in when tested and therefore what level of key reproductive hormones were being secreted at the time.

The current study had a small sample size of 11 participants. The restrictive inclusion criteria, particularly the requirement that participants were not taking any oral or injectable contraceptives, appeared to be the main factor that limited the number of participants recruited. The small sample size limits the generalizability of the results and an accurate estimation of the likely true values of the comparative differences. For example the width of some of the confidence intervals (Table 4.6 and 4.7) extend beyond adjacent qualifiers for the estimated true values.

None of the anatomical sites tested in the current study were in the suggested areas of referral for menstrual pain, namely the abdomen (T10-T12) and low back (S2-S4) (Bajaj et al., 2001). These areas have demonstrated more prominent cyclical variation in PPT (Giamberardino et al., 1997). Although systemic effects have also been demonstrated (Bajaj et al., 2001; Isselee et al., 2001), the particular anatomical

areas outlined above may offer a window into the variation in pain threshold due to the fluctuation of hormones over the menstrual cycle.

Conclusion

The results of previous research show that pain sensitivity is certainly influenced by hormonal changes over the menstrual cycle. The current study adds to this evidence and also shows individual variation in pain sensitivity regardless of the menstrual cycle. The results of the current study showed small differences in PPT between the menstrual and luteal phases of the menstrual cycle, with the luteal phase showing the highest mean pain threshold and the menstrual phase showing the lowest in consecutive months. A general trend of increasing pain thresholds over the six experimental sessions was also shown. The largest differences in PPT were found when comparing the nine different anatomical sites where pressure was applied. Many of the participants in the current study found 4kg of pressure painful at 11 or more of the 18 anatomical sites. This finding adds to the literature surrounding the diagnosis of fibromyalgia and indicates that not only menstrual cycle variations in pain threshold but also individual variation should be considered when making a diagnosis of fibromyalgia.

Osteopaths and other health professionals should be aware that women may be more sensitive to pain at different times of the menstrual cycle, particularly the menstrual phase according to the results of the current study. They should also keep in mind that different individuals have different pain thresholds and may respond differently to pressure applied in exactly the same way. The results of the current study suggest that patients of any manual therapist are likely to be more sensitive to sensations evoked on the first appointment than they will be in follow up sessions when habituation may occur.

There are many studies that report results in agreement with each of these findings; there are also many studies that report contrasting results. Diversity in methodology is the main area of discrepancy among the literature surrounding this topic. In particular the definition of the phases of the menstrual cycle, the method of stimulation used to induce pain, and the sites at which stimulation is applied. Future research on this topic should aim for unity between all of these factors in order to achieve results that can be directly compared. The current study may serve as the beginning of an ongoing investigation of the changes in PPT due to normal hormonal fluctuations during the menstrual cycle. The methods used can form a template for future research and the results can be used in meta-analysis of this topic.

Appendix A

ETHICS APPROVAL

Unitec
NEW ZEALAND

Alenka Burnett
1100c New North Road
M. Albert
AUCKLAND

11th April 2005

Dear Alenka

Your file number for this application: 2004. 314
Title: **An investigation of changes in the pressure pain threshold due to hormonal fluctuations during the menstrual cycle.**

Your application for ethics approval has been reviewed by the Unitec Research Ethics Committee (UREC) and has been **approved** for the following period:

Start date: 8th December 2004
Finish date: 31 July 2005

Please note that:

1. the above dates must be referred to on the information AND consent forms given to all participants
2. you must inform UREC, in advance, of any ethically-relevant deviation in the project. This may require additional approval.

This letter has been copied to the Principal Supervisor for Unitec student research projects, and additionally to the Board of Postgraduate Studies for postgraduate student research (where applicable).

You may now commence your research according to the protocols approved by UREC. We wish you every success with your project.

Yours sincerely

Dr Andrew Stewart
Deputy Chair, UREC

RMO ref#: 503

Cc: Dianne Roy

Appendix B

ADVERTISING POSTER

Unitec
NEW ZEALAND

FEMALE STUDENTS REQUIRED FOR A RESEARCH PROJECT

I am interested in finding out if your perception of pressure changes over a month.

I am seeking New Zealand European females, aged 18 to 35, who are not taking oral or injectable contraceptives.

Your participation will help us establish if women are more sensitive to manual therapies at certain times during the menstrual cycle.

Please contact me if you are interested!

Alenka Dunnett
Master of Osteopathy student
815 3265
021 1124137
alenkadunnett@hotmail.com

Appendix C

PARTICIPANT HEALTH HISTORY

AN INVESTIGATION OF CHANGES IN PRESSURE PAIN THRESHOLD DUE TO HORMONAL FLUCTUATIONS DURING THE MENSTRUAL CYCLE

Researcher: Alenka Dunnett

Please answer the following questions in the spaces provided, please answer to the best of your ability, please print legibly and please do not hesitate to ask questions if you do not understand a question.

Participant number: _____

Date of birth: _____

Age: _____

Are you currently taking any medication or health supplements? Yes/No

If yes please record here: _____

If you have any of the following health problems please circle:

Dysmenorrhoea (difficult and painful menstrual period)

Arthritis

Fibromyalgia

Nausea

Vomiting

Chronic pain problems

Epilepsy

Heart disease

Psychological health problems (depression, anxiety, other)

List any other health problems you suffer from: _____

_____

How many hours of sleep do you get a night? _____

How would you describe your general health? _____

Appendix D

HEALTH HISTORY FOLLOW-UP QUESTIONNAIRE

Participant #:

Health History Follow Up	**Oral contraceptives?**	**Analgesics?**	**Any other medication?**	**Dysmenorrh-oea?**	**Other illnesses?**
Experimental Session #1					
#2					
#3					
#4					
#5					
#6					

Appendix E

PARTICIPANT INFORMATION SHEET

AN INVESTIGATION OF CHANGES IN PRESSURE PAIN THRESHOLD DUE TO HORMONAL FLUCTUATIONS DURING THE MENSTRUAL CYCLE

IMPORTANCE OF THE STUDY

A large percentage of osteopathic patients have musculoskeletal pain as their chief complaint. Musculoskeletal pain is due to a variety of causes. One factor influencing the experience of pain may be hormonal fluctuations during the menstrual cycle. The effect of hormonal changes on pain sensitivity has particular relevance to the practice of osteopathy. The techniques used by an osteopath may generate pain. The female patient may be more sensitive to pain at certain times of the menstrual cycle.

SELECTION OF PARTICIPANTS AND CRITERIA FOR INVOLVEMENT

New Zealand European female students at Unitec New Zealand are invited to take part in this study. If you are aged between the 18 and 35 years, and are able to communicate clearly using oral and written English language you are welcome to participate. You must have a history of regular, predictable menstrual cycles of 25-30 days and must not be taking oral or injectable contraceptives. In order to ensure this, you will be asked to inform the researcher of the first and last day of menstrual period for two months (two cycles) before the experiment begins.

REGISTRATION

Participants interested in volunteering for the study can register their interest by telephoning the researcher, Alenka Dunnett, at 815-3265 or 021 1124137. You will be asked a few questions to be sure you fulfil the criteria for involvement.

EXPERIMENTAL SESSIONS

Before the commencement of the testing sessions you will be required to answer some questions relating to your general health and relevant medical history. You will need to answer follow up questions before each testing session to ensure there are no major changes in your health status over the course of the study.

The experiment involves applying pressure to eighteen anatomical sites on the body until the sensation of pressure changes to pain. You will be required to verbally indicate when this occurs and the pressure will be removed immediately. There will be a chance for you to see exactly what the experiment involves before you agree to participate. You will be asked to attend six testing sessions at the Unitec Osteopathic Clinic, over a period of eight weeks. You will be asked to record the first and last day of your menstrual period from approximately April 2005 to May 2005 and to attend experimental sessions from approximately June 2005 to July 2005. You will be required to wear shorts and a t-shirt for the experimental session; changing rooms will be provided. The experimental session will take approximately fifteen minuets. Please

call if you are running late or need to reschedule the appointment on the following numbers: 8156794 (clinic) or 021 1124137 (Alenka Dunnett).

CONFIDENTIALITY

I will ask that you do not write your name anywhere on the health history sheet. This is important to protect your anonymity. There are numbers on these sheets so that I can correlate these anonymous results with your anonymous experimental results. A copy of the final results will be available at the School of Health and Community Studies, Unitec New Zealand. All participants are welcome to view this.

WITHDRAWAL FROM THE STUDY

Your participation in the study is voluntary so you may withdraw at any time.

FOR MORE INFORMATION CONTACT THE RESEARCHER:

Alenka Dunnett, Master of Osteopathy Student

Phone: 09 815 3265 or 021 1124137

Email: dunnea01@studentmail.unitec.ac.nz

PRIMARY SUPERVISOR:

Dr Dianne Roy

Phone: 09 815 4321 ext 8307

Email: droy@unitec.ac.nz

SECONDARY SUPERVISORS:

Dr Andrew Stewart

Phone: 09 815 4321 ext 8384

Email: astewart@unitec.ac.nz

Dr John McPartland

Email: jmcpartland@unitec.ac.nz

Thank you for your valuable contribution to this research.

This study has been approved by the Unitec Research Ethics Committee from February 2005 to July 2005. If you have any complaints or reservations about the ethical conduct of this research, you may contact the Committee through the Secretary (ph: 815-4321 ext 8041, or ethics@unitec.ac.nz). Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.

Appendix F

CONSENT FORM

AN INVESTIGATION OF CHANGES IN PRESSURE PAIN THRESHOLD DUE TO HORMONAL FLUCTUATIONS DURING THE MENSTRUAL CYCLE

Thank you for agreeing to participate in this research.

My name is Alenka Dunnett and I will be conducting the research. I will be examining changes in the pressure pain threshold due to hormonal fluctuations during the menstrual cycle. I am interested in the effect of variations in pressure pain threshold on osteopathic treatment and osteopathic diagnosis. Dr Dianne Roy, Dr John McPartland, and Dr Andrew Stewart are supervising this research project.

Name of participant (please print) ……..

I have read and understood the contents of the information sheet. I have had the opportunity to discuss with the researcher anything I was unclear about, and I have understood the explanations given. I understand that my involvement with this research is voluntary and that I have the right to withdraw at any time up until the data analysis is complete in approximately July 2005. I understand that my participation in this project is confidential and that no material that could identify me will be used in any reports on this project. I have had enough time to consider whether I want to take part. I know whom to contact if I have any questions or concerns about the project.

Signature of participant ……..... Date ….……..

Project explained by …….

Signature of researcher ……. Date ……..

The contact details of the principle researcher for this project are:

Alenka Dunnett

Osteopathic Clinic

Building 41, Entry 3

Unitec New Zealand

Carrington Rd, Mt Albert — Telephone (09) 815 6794

Private Bag 92025 — Free phone 0800 267 836

AUCKLAND — A/H (09) 815 3265 or 021 1124137

The participant will be given two copies of the consent form to sign and should retain one and return one to the researcher. This study has been approved by the Research Ethics Committee from February 2005 to July 2005. If you have any complaints or reservations about the ethical conduct of this research, you may contact the Committee through the Secretary (ph: 815-4321 ext 8041, or ethics@unitec.ac.nz). Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.

Appendix G

ANALYSIS OF DATA WITH PARTICIPANT NINE REMOVED

Table 6.1: Intra-cycle Test Point Comparison

Comparison	Effect Size	Lower 95% Confidence Limit	Upper 95% Confidence Limit	Interpretation
Test 1 & 2	0.1	-0.9	1.1	Trivial
Test 1 & 3	0.2	-0.8	1.2	Small
Test 2 & 3	0.2	-0.9	1.2	Small
Test 4 & 5	0.01	-1.2	1.2	Trivial
Test 4 & 6	0.2	-0.8	1.2	Small
Test 5 & 6	0.2	-0.7	1.1	Small

Table 6.2: Inter-cycle Test Point Comparison Showing Effect Sizes

Comparison	Effect Size	Lower 95% Confidence Limit	Upper 95% Confidence Limit	Interpretation
Test 1 & 4	0.4	-0.6	1.3	Small
Test 2 & 5	0.3	-0.7	1.3	Small
Test 3 & 6	0.3	-0.7	1.4	Small

Table 6.3: Inter-cycle Test Point Comparison Showing Effect Statistics

Comparison	Effect Statistic (kg)	Lower 95% Confidence Limit	Upper 95% Confidence Limit
Test 1 & 4	0.4	-0.6	1.4
Test 2 & 5	0.3	-0.7	1.3
Test 3 & 6	0.3	-0.7	1.3

Table 6.4: Comparison of Change Scores between Pares of Tests in Consecutive Months

Comparison	Effect Size	Lower 95% Confidence Limit	Upper 95% Confidence Limit
Test 1& 2 v test 4 & 5	0.1	-0.2	0.4
Test 2 &3 v test 5 & 6	0.2	0	0.4
Test 1 &3 v test 4 & 6	0.2	-0.1	0.5

Appendix H

RAW DATA

Table 6.5: Pressure pain thresholds for all 11 participants shown in raw kg values. The 18 values in each test are arranged from anatomical sites one to nine alternating left and right, for example the first two numbers in each column are anatomical site one, the first is the left site and the second is the right site.

Participant	Test 1	Test 2	Test 3	Test 4	Test 5	Test 6
1	2	1.75	1.8	1.6	2.5	2.1
	2	1.3	1.65	1.5	1.6	1.75
	3.9	2.5	3.8	3.75	4.3	3.7
	5	3	2.7	2.55	2.7	3.05
	5.5	7.7	8.2	10.5	8.4	8.85
	10.5	6.3	7	10.5	10.5	7.2
	2.4	4.4	2.8	5.3	2.85	4.75
	3.6	4	4	4.45	2.9	4.7
	6.6	4.9	3.4	4.1	4	5.1
	6	3.95	3	4.6	3.3	5.65
	3.4	5.95	3.45	5	5.75	5.6
	3.85	5.4	2.9	5.1	4	5.5
	6.7	5.85	4.4	6.35	6.4	7.1
	5.5	6.1	6.7	6.6	6.1	5.3
	3.1	3	3.4	4	4.25	4.05
	3.95	3.8	3.1	3.9	5.5	4.5
	3.1	5.4	3.2	3.85	3.8	4.15
	4.25	5.9	3.9	3.45	4.35	8.9
2	1.2	1.2	2.45	1.95	1.85	3
	1.15	0.5	2.5	1.7	1.7	1.9
	3	3.65	4.4	4.4	4.4	3.2
	2.2	2.6	5	4.2	3	2.9
	9.8	8.7	10.5	10.5	10.5	10.5
	9.4	6.75	9.75	8	10.5	10.5
	2.85	3	4.1	4	4.9	4.1
	4	5.3	6.8	4.8	5	4.8
	3.7	4.85	5	4.25	3.8	5.7
	3.6	6.3	6.7	5.2	4.05	4.4
	4.8	4.9	5.4	5.25	6	6.2
	3.75	5.65	7.15	5.7	7	4.9
	6.75	6.7	8.2	7.9	5.5	6.3
	5.6	8.8	7.85	6.35	7.1	5.7

	3	4.75	3.2	5.6	4.25	4.3
	2.4	3.6	3.05	5.15	4.2	4.4
	2.4	7	7.9	5.9	5.3	4.6
	2.7	7	6.7	5.5	5.3	5.3
3	1.3	1.6	1.5	1.2	1.45	1.4
	1.3	1.2	1.4	1.2	1	1.3
	2.2	1.8	2.4	1.9	2.4	3
	2.8	2.25	2.85	2.2	2.8	3.4
	5.45	3	4	4	4.8	5.9
	3.75	4.65	4.4	4.6	4.95	5.9
	2.15	1.95	2.9	3.25	3.2	3.1
	2.25	2.3	2.9	2.05	2.9	2.5
	3.5	1.85	2.6	2.2	2.6	2.8
	2.9	2.2	2.2	2.1	2.4	2.25
	2.85	3	3.7	3.9	3.25	3.95
	3.8	3.15	3.9	4.2	3.4	3.25
	3.35	3.55	3.8	3.3	3.55	3.4
	3.35	3.4	4.1	4.35	4	5.35
	2.6	3	3.1	2.15	4.05	3.3
	4.2	3.6	3.75	3.55	3.45	4.1
	3	3.1	3.4	2.4	3.15	4.3
	3.6	3	3.9	3.4	3.6	3.25
4	0.5	0.5	1.1	1.1	1	0.5
	1.1	0.5	0.5	0.5	0.5	1
	1.3	2.75	3.2	2	1.75	2.9
	1.9	1.65	1.9	2.3	1.4	2.8
	6	3.7	5.7	6	4.7	5.2
	4.8	4	3.8	6.35	5.15	4.7
	2.2	2.1	1.7	2.4	2.3	2.1
	2.6	2.1	2.3	2	1.8	3.3
	2	1.9	2.2	2.35	1.8	2.7
	1.9	1.75	2.2	1.4	1.6	2
	1.7	2	1.6	2.5	1.8	1.9
	1.8	2.2	2.45	2	2.5	1.6
	2.8	2.3	3.45	2.6	3.9	4
	3.1	2.5	2.5	2.4	2.9	3.5
	2.75	2.6	2.2	2.5	3	2.8
	2.5	2.1	1.7	2.4	3	3.05
	3.1	2.9	3.2	4.6	3.4	6.4

	3.35	3.6	5.2	4.2	2.8	4.1
5	0.5	1	1	1.7	0.5	1
	1	1	0.5	1.8	1	1.15
	1.25	2.4	1.7	2.2	2.85	2.8
	1.8	2.65	1.9	2.55	2.8	2.45
	4.9	4.7	4.3	4.7	5.1	3.9
	6.6	5.3	4.1	3.9	4.7	3.1
	3.2	3	3.3	3.7	3.1	3.85
	2.55	2.65	3.9	3.9	2.9	3.85
	3	2.8	1.9	2.7	2.6	2.2
	4.3	1.75	2.15	2	2	2.1
	2.6	1.8	2.65	2.1	1.7	2.9
	2.6	2.2	3	2.1	1.6	2.2
	3	4	3.6	3.3	3.45	3.6
	3.6	3.4	2.6	2.8	3.1	4.85
	3.7	2.95	4.6	4.6	4.85	3.9
	4.6	3.35	3.95	4.7	6.4	4.45
	5.35	5.25	6.2	6.2	7.1	6.55
	5.7	6.4	4.2	3.8	4.5	5.59
6	0.5	0.5	0.5	1.1	1.15	3.2
	0.5	0.5	1	1	1	1
	1.5	1.9	2.4	3.8	3.1	3.3
	1.4	1.6	2.45	2.8	2.55	3.9
	1.8	2.5	2.8	5.2	2.9	4.3
	1.6	3.4	3.1	3.2	4	3.45
	1.4	1.7	1.6	1.6	1.9	2.6
	1.4	1.45	1.8	1.5	2.1	2
	1.25	1.85	1.85	2.35	1.8	2.05
	0.5	1.85	2.7	2.5	2.4	2.8
	1.2	3.4	1.6	5.55	4.5	2.7
	1.05	2.1	1.15	4.7	1.6	2.9
	1.8	2.6	2.9	5.5	3.65	3.8
	1.75	2.1	2.7	4.1	3.65	4
	2.25	1.8	3.1	3.2	3.1	3.5
	1.9	2.4	2.15	4.4	5.1	2.6
	1.9	1.9	2.2	3.2	4.1	2.75
	1.7	2.8	2.7	2.9	2.55	2.55
7	1	1.05	2.3	1.5	3.7	1.8

	1.6	0.5	1.75	1.35	1.6	1.8
	3.9	2.65	2.9	2.8	2.5	2.25
	2	1.3	2.6	2	2.8	2.6
	7.5	6.2	5.15	5.5	5	7
	6	7.6	5.05	3.6	4.4	5.5
	3.9	5.7	2.8	4.15	4.1	5.1
	5.6	6	5.8	3.8	6.4	5.05
	2.8	2.3	3.2	2.5	2.6	2.4
	2.45	3.7	3	3.1	3.1	2.8
	5.2	3.7	3.15	4.8	2.7	2.65
	4	4.85	2.95	3	2.9	3.8
	4.25	4.8	4.5	3.05	4.4	4.1
	3.6	4.8	4.4	4.8	6	4.9
	5.25	3.8	4.4	5	4.3	5.15
	5.4	6	6	6.3	3.5	4.2
	6.9	5.2	2.7	8.55	5.6	3.05
	6.7	3.6	3.85	8.2	3	6.3
8	0.5	0.5	0.5	1.1	1	1.4
	0.5	0.5	0.5	1.05	0.5	1.1
	1.2	1.4	1.35	1.7	1.5	2.2
	1.1	1.6	2.1	1.9	2.05	2
	1.15	2.4	3	3	3.5	3.9
	2.15	3	3	3	3.25	4.4
	1.15	1.9	2.45	1.95	2.5	2.5
	1.5	1.55	1.85	2.1	2.9	2.8
	1.15	1.4	1.8	1.25	1.75	2.4
	1.4	1.5	1.95	1.3	1.6	2.15
	1.05	1.6	1.6	1.1	2	2.4
	1.7	1.9	2.15	1	2.15	2.9
	2.8	3.5	3.4	2.7	3.5	2.7
	2.85	2.5	3.3	2.95	3.3	3.6
	2.45	2.8	2.75	3.2	2.9	4.2
	2.35	2.4	3.1	3.1	3.4	4
	2.4	2.75	4.05	2.65	3.5	4.7
	2.3	2.2	3	2.15	2.6	4.4
9	1.5	1.9	1.85	1.35	2	1.8
	1.15	1.7	1.8	1.6	1.5	0.5
	2.3	2.8	3.85	2.45	2.7	2.6
	1.9	2.7	2.2	2.4	3	2.2

	5.2	4.55	3.8	5	5.1	4.9
	3.6	3.8	3	4	3.4	3.4
	3.4	3.6	3.7	4.2	4.2	3.55
	3.35	4	3	3	3.6	4
	3.4	2.7	4.3	3.35	4.3	3
	3.1	2.85	3.35	3.6	4.05	3.4
	2.4	1.85	2.3	2.9	3.6	2.8
	2.35	3.1	2.1	2.8	3	1.85
	4.05	3.9	3.9	4.7	4.3	4.9
	1.8	3.9	3.9	5	4	5.1
	4.25	5.95	4.45	6.75	6.75	5.2
	4	7	3.6	6.15	6.75	6.55
	3.5	3.6	4.6	3.9	6	3.5
	5.05	4.85	4	5.4	4.6	4.65
10	1.85	1.25	2.5	2.35	2.5	1.9
	2.25	1.9	2.6	1.9	2.1	1.85
	5	3.8	4.8	4.4	5.1	3.7
	3.7	3.4	2.8	3.05	3	2.5
	7.65	5.95	7.1	7.6	6.2	5.85
	6.3	6.75	7.3	7.75	7.1	6.8
	3	3.4	3.1	4.2	4.8	3.5
	3.9	3	3.1	3.5	4.9	3.1
	3.5	3.5	4.3	4.8	2.6	2.15
	2.5	3.1	2.9	3.7	3.1	3
	4.6	4.05	5	4.7	3.4	3.8
	3.9	3.7	4	4.5	3.1	2.7
	3.55	4.4	3.8	6.8	6.1	6.9
	3.3	3.6	4.6	4	5.2	5.25
	5.25	5.2	5.75	4.25	5	5.85
	4.6	4.45	4.45	3.5	5.7	4.5
	4.7	4.4	5.2	3.35	4.7	5.6
	4.7	4.4	5.15	3.8	4.4	7.1
11	1.9	1.6	1.5	1.1	1.2	1.55
	1.35	1.1	1.25	1.35	1.2	1.6
	2.1	1.95	1.8	3	2.9	3.5
	2.7	2.3	2	2.8	2.5	2.3
	2.7	5	4.9	3.85	4.4	4.5
	4.2	3.5	4.2	3.1	4.1	4
	1.9	2.5	2.6	2.9	2.4	3.2

2.6	2.35	1.75	2	1.75	2.4
1.7	2	1.8	2.2	2.1	2.2
3.6	1.8	2.1	2.6	2.9	3
3.4	3.2	2.9	3.25	3.4	2.9
2.7	2.6	2.4	2.85	3.3	2.7
3.8	2.95	3.65	3.1	3.5	2.8
4.2	4.2	3.95	4.1	5.3	3.95
1.9	2.95	4	2.65	5.15	3.9
2.4	3.5	5.25	3.45	5.95	5.2
1.9	2.25	2.55	2.85	2.1	3.3
2.1	1.85	3	2.8	3.65	3.8

REFERENCES

Amodie, N., & Nelson-Grey, R. (1989). Reactions of dysmenorrheic and nondysmenorrheic women to experimentally induced pain throughout the menstrual cycle. *Journal of Behavioural Medicine, 12*(4), 373-385.

Anderberg, U. M., Marteinsdottir, I., Hallman, J., & Backstrom, T. (1998). Variability in cyclicity affects pain and other symptoms in female fibromyalgia syndrome patients. *Journal of Musculoskeletal Pain, 6*(4).

Bajaj, P., Arendt-Nielsen, L., Bajaj, P., & Madsen, H. (2001). Sensory changes during the ovulatory phase of the menstrual cycle in healthy women. *European Journal of Pain, 5*, 135-144.

Bajaj, P., Bajaj, P., Madsen, H., & Arendt-Nielsen, L. (2002). A comparison of modality-specific somatosensory changes during menstruation in dysmenorrheic and nondysmenorrheic women. *The Clinical Journal of Pain, 18*, 180-190.

Bates, M. S., Edwards, W. T., & Anderson, K. O. (1993). Ethnocultural influences on variation in chronic pain perception. *Pain, 52*, 101-112.

Chesterton, L. S., Barlas, P., Foster, N. E., Baxter, G. D., & Wright, C. C. (2003). Gender differences in pressure pain threshold in healthy humans. *Pain, 101*, 259-266.

Chiu, Y. H., Silman, A. J., Macfarlane, G. J., Ray, D., Gupta, A., Dickens, C., et al. (2005). Poor sleep and depression are independently associated with a reduced pain threshold. Results of a population based study. *Pain, 115*, 316-321.

Cohen, L. (1988). *Statistical power analysis for the behavioural sciences* (2nd ed.). Hillsdale, NJ: Lawrence Erlbaum.

Drobek, W., Schoenaers, J., & DeLaat, A. (2002). Hormone-dependent fluctuations of pressure pain threshold and tactile threshold of the temporalis and masseter muscle. *Journal of Oral Rehabilitation, 29*, 1042-1051.

Fischer, A. A. (1987). Pressure algometry over normal muscles. Standard values, validity and reproducibility of pressure threshold. *Pain, 30*, 115-126.

Gagliese, L., Katz, J., & Melzack, R. (1997). Age differences in the quality of chronic pain: a preliminary study. *Pain Research Management, 2*(157).

Giamberardino, M. A., Berkley, K. J., Iezzi, S., deBigontina, P., & Vecchiet, L. (1997). Pain threshold variations in somatic wall tissues as a function of menstrual cycle, segmental site and tissue depth in non-dysmenorrheic women, dysmenorrheic women and men. *Pain, 71*, 187-197.

Gibson, S. J., & Helme, R. D. (2001). Age-related differences in pain perception and report. *Pain Management in the Elderly, 17*(3), 433-456.

Guyton, A. C., & Hall, J. E. (2000). *Textbook of medical physiology* (10th ed.): W. B. Saunders Company.

Hapidou, E. G., & Rollman, G. B. (1998). Menstrual cycle modulation of tender points. *Pain, 77*, 151-161.

Hendiani, J. A., Westlund, K. N., Lawand, N., Goel, N., Lisse, J., & McNearney, T. (2003). Mechanical sensation and pain thresholds in patients with chronic arthropathies. *The Journal of Pain, 4*(4), 203-211.

Hopkins, W. G. (1997). *A new view of statistics. In: sportscience. Internet society for sports science*. Retrieved January 9th, 2006, from http://www.sportsci.org/resources/stats/index.html

Isselee, H., DeLaat, A., Bogaerts, K., & Lysens, R. (2001). Long-term fluctuations of pressure pain thresholds in healthy men, normally menstruating women and oral contraceptive users. *European Journal of Pain, 5*, 27-37.

Jensen, K., Anderson, H. O., Olesen, J., & Lindblom, U. (1986). Pressure pain threshold in human temporal region. Evaluation of a new pressure algometer. *Pain, 25*, 313-323.

Kosek, E., Ekholm, J., & Nordemar, R. (1993). A comparison of pressure pain thresholds in different tissues and body regions. Long-term reliability of pressure algometry in healthy volunteers. *Scandinavian Journal of Rehabilitation Medicine, 25*, 117-124.

Laursen, B. S., Bajaj, P., Olsen, A. S., Delmar, C., & Arendt-Nielsen, L. (2005). Health related quality of life and quantitative pain measurement in females with chronic non-malignant pain. *European Journal of Pain, 9*, 267-275.

Levine, F. M., & DeSimone, L. L. (1991). The effects of experimenter gender on pain report in male and female subjects. *Pain*(44), 69-72.

Mazur, J. E. (1998). *Learning and behavior*. New Jersey: Prentice Hall.

Melzak, R., & Wall, P. D. (1965). Pain mechanisms: a new theory. *Science, 150*, 971-979.

Moore, J. (2003). Perceptions about physical therapies and attitudes towards osteopathy in a selected population. Unpublished Master of Osteopathy.

Polit, D. F., & Hungler, B. P. (1997). *Essentials of nursing research. Methods, appraisal, and utilisation* (4th ed.). New York: Lippincott-Raven Company.

Riley, J. L., Robinson, M. E., Wise, E. A., & Price, D. D. (1999). A meta-analytic review of pain perception across the menstrual cycle. *Pain, 81*, 225-235.

Turk, C. D., & Melzack, R. (1992). *Handbook of pain assessment*. New York: The Guilford Press.

Wilcox, A. J., Dunson, D., & Baird, D. D. (2000). The timing of the "fertile window" in the menstrual cycle: day specific estimates from a prospective study. *British Medical Journal, 321*(7271), 1259-1262.

Wolfe, F. (1986). Development of the criteria for the diagnosis of fibrositis. *The American Journal of Medicine, 81*(3A), 99-104.

Wolfe, F., Smythe, H. A., Yunus, M. B., Bennett, R. M., Bombardier, C., Goldenberg, D. L., et al. (1990). The American College of Rheumatology Criteria for the Classification of Fibromyalgia. *Arthritis and Rheumatism, 33*(2), 160-172.