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The Relationship Between Pain Responsiveness And Disease Activity In Fibrositis And Rheumatoid Arthritis

Roger Alan Scudds

differences in the "Conversion V" pattern between patients with or without physical findings. They did, however, consider that these patients were depressed and theorized that, as with some conversion reactions, depression was not apparent but was masked by hypochondriasis and hysteria.

The MMPI has been the most frequently used psychometric instrument in the analysis of personality disturbance in the presence of chronic pain. The literature amassed through its use is immense. The two studies cited above give only some of the flavor of the conflicting results obtained using this instrument. Other studies have used the MMPI to predict treatment outcome (Kuperman et al, 1979; McCreary et al, 1979), surgical outcome (Oostdam et al, 1981) and for differentiating between groups of pain patients (Prokop et al, 1980). In recent years, however, the use of the MMPI in the evaluation of pain patients has been seriously questioned (Rook et al, 1981; Naliboff et al, 1982; Lamping, 1985). While some authors think that it still may be a useful adjunct in the clinical evaluation of individual patients (Cohen et al, 1983), others would deem it an invalid instrument. Lamping (1985) points out that the MMPI was developed to measure psychopathology and not disturbance in medically ill patients. In this respect, then, it may be inappropriate for chronic pain patients. Of more importance, however, is the fact that the items on some of the scales are not independent and endorsement of one item may lead to it being scored on two or more scales.

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THE RELATIONSHIP BETWEEN PAIN RESPONSIVENESS AND DISEASE ACTIVITY IN FIBROSITIS AND RHEUMATOID ARTHRITIS

by

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Abstract

The present research examined the relationship between pain responsiveness and disease activity in patients with the rheumatologic diagnoses of rheumatoid arthritis (R.A.) and fibrositis. Three studies were carried out.

In the first study, 68 R.A. subjects were assessed for levels of disease activity using 7 standard measures, plus the rheumatoid factor titre and the R.A. functional classification. The Basic Personality Inventory was used to measure anxiety, depression, hypochondriasis, and denial. Pain threshold and tolerance levels were taken in each subject using trains of electrical pulses, a constant-pressure algometer, and a variable-pressure dolorimeter. The data were analyzed by multiple regression. The results indicate that pain tolerance is best predicted by levels of disease activity, gender, hypochondriasis and rheumatoid factor titre. Significant differences were found between the sexes on pain responsiveness and disease activity.

One year later, 38 (55%) of the original subjects returned. The same measures, methodology, and analyses were used as on the previous visit. It was found that disease activity and pain responsiveness had decreased between visits. A much clearer pattern of association between the variables was evident. Disease activity was the most important single predictor, in a negative direction, of pain threshold and tolerance levels.

In the third study, 36 patients with the diagnosis of fibrositis completed a 10-week placebo-controlled, randomized double-blind crossover trial of low-dose amitriptyline. Outcome measures were local tenderness (TMS), and pain threshold and tolerance, assessed with the variable-pressure dolorimeter. The other principal measures were, depression, state anxiety, sickness impact, hypochondriasis and pain. The data were initially analyzed using multivariate statistics. Compared to placebo, amitriptyline significantly improved pain, pain threshold, TMS, depression, hypochondriasis and sickness impact. Levels of pain, and pain threshold and the TMS showed a strong negative relationship. A discriminant analysis indicated that pain and the length of symptoms were the most important variables that predicted those who responded to amitriptyline.

This research supports "hypervigilance theory" which holds that people with chronic pain become more responsive to painful stimuli as a result of their symptoms.

Dedication

This dissertation is dedicated to T. L. Shiva, for his strength, support and inspiration in my life.

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I would like to thank the individual members of my committee: Dr. P. A. Vernon for his sound advice and encouragement in looking for the simplest measures in the complex analyses of the study data; Dr. M. Harth who has guided me calmly and with insight through the clinical problems of the study population; I am also indebted to my advisor, Dr. G. B. Rollman, for his academic and personal guidance and support throughout my time at graduate school, and whose work laid the foundations for my research. To each of you I extend my gratitude. Lastly, I would like to thank Dr. G. A. McCain, whose expertise and enthusiasm was a great help throughout the research.

Table of Contents

List of Tables

Study 1

Study 2

Study 3

List of Figures

List of Appendices

"When you cannot measure it, when you cannot express it in numbers - you have scarcely, in your thoughts, advanced to the stage of science, whatever the matter may be."

Lord Kelvin.

Introduction

Chapter 1

The purpose of the present research is to examine the relationship between pain threshold and tolerance, and different levels of disease activity in two groups of rheumatologic patients. Each of these diagnostic groups, fibrositis and rheumatoid arthritis, is characterized by pain and dysfunction over a long period of time

Pain is an integral part of the human condition. Most people will experience it briefly at some point in their lives. For some, however, pain is a constant and prolonged feature of daily existence. In those cases, where it becomes chronic, pain loses its usefulness as a warning signal and leads to, what seems to be, unnecessary suffering.

Pain and suffering were viewed historically as "passions of the soul" and were essentially seen as a reflection of disharmony of the inner being and taken to be a reaction to something done wrong, either emotional or physical (Merskey, 1980). Within the last century, with its emphasis on physiological processes, pain was viewed as a natural reaction to stimulation, usually excess

stimulation, of nerves. Johannes Muller's (1840) doctrine of "specific nerve energies" stated that pain will arise as a consequence of stimulation of specific nerves, but it also implied that the intensity of the pain experienced would be directly proportional to the intensity of the peripheral stimulation or injury. In this context, pain was seen as a sensation. However, as with other perceptual processes, the experience that is aroused by afferent stimulation is based on more than the amount of stimulus energy and the strength of discharge of peripheral receptors, such as past experience, the context of the situation and the meaning of the experience to the person (Chapman, 1978). Beecher's classic observations on the experience of pain in soldiers at Anzio beach bear strong witness to this point. There, under the stress of battle, some soldiers with obviously terrible wounds did not complain of pain or said that the pain did not bother them. However, those same soldiers would react in a very painful manner to the injection of a hypodermic needle (Beecher, 1959).

Pain has gradually come to be seen in a larger context than within a straight stimulus-response paradigm. Melzack and Wall's (1965) "gate control" theory of pain pointed out the interplay of the different aspects of pain - sensory, affective and cognitive- and proposed that each aspect might modulate the other in certain ways. The resultant experience would therefore be attributable to an

interaction of those factors and serve to influence the way an individual will perceive pain at any particular time. However, it should always be borne in mind that pain is subjectively experienced by people as a unitary experience of "pain", not as a multi-dimensional experience.

The understanding of the problem of pain has advanced greatly over the last twenty years. Part of that advance has been in the development of methods to quantify or assess the different domains of the pain experience. This is important because it is only through more exact measurement of the dimensions of the individual experience that accurate and appropriate approaches to pain relief can be assessed.

The first chapter of this dissertation will deal with general issues of pain measurement and with the experimental induction of pain in the laboratory. This will lead to the application of pain assessment methods to clinical populations, with an emphasis on those used in fibrositis and rheumatoid arthritis, which will be dealt with in Chapter 2.

From the review of the literature that is presented in the first 2 chapters, certain research questions will be posed which will look specifically at the relationship between pain responsiveness, as assessed by pain threshold and tolerance levels, and disease activity combined with personality and demographic variables.

Pain assessment in the laboratory.

The definition of pain that is used by the International Association for the Study of Pain is that "pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (IASP, 1979).

This definition is not without its critics but it does give a reasonably acceptable operational definition and serves, in part, to emphasize its multi-dimensional nature. Assessment has been defined as "the act of settling, determining or fixing the amount of" some quantity (Oxford English Dictionary, 1961). Thus, pain assessment seeks to determine how much pain someone is experiencing. Methods of assessment are almost as numerous as there are researchers in the area. Each method is used in an attempt to quantify and define more clearly the individual's experience of his pain. Further, there is a need for attempts at accurate quantification in order to understand such factors as individual and group differences of pain perception and to assess response to treatment. However, it must be remembered that most methods seek to measure only a small part of the complexity of the pain experience. This is especially true of experimental measures that are used in the laboratory.

Experimentally produced pain has the advantage that it is possible to deliver, and reproduce, an exact amount of stimulus energy. The response of the subject can then be

examined. As well, the laboratory context serves to control the intrusion of extraneous variables (Procacci et al, 1979). An obvious disadvantage in the use of experimental pain in the laboratory is that there is little of the affective component that is present in organic pain and that the subject knows that the stimulus is unlikely to cause tissue damage and will be of a limited duration. As well, for ethical reasons, studies do not usually manipulate such factors as anxiety and depression within the experimental design. Allowing for these factors, experimental pain in the laboratory does have a place in the overall context of pain assessment as it will be seen that some of the methods currently employed in clinical assessment were first developed in the laboratory. It should be remembered, however, that experimentally induced pain more closely mimics the characteristics of acute pain than those of chronic pain.

The pioneers in the area of laboratory pain assessment were Hardy, Wolff and Goodell (1952). They employed a radiant heat stimulus to induce pain and asked their subjects to indicate the painfulness of the particular stimulus. The measures that they were most interested in were the pain threshold and the pain tolerance levels. Pain threshold may be defined as the point at which pain is just perceived. Pain tolerance is the point at which pain is no longer tolerated voluntarily (Jacox, 1977).

Apart from the radiant heat method, other thermal

stressors, such as the cold pressor test (Hilgard, 1971) the contact thermode and laser have been used (Wolff, 1978). The use of modifiable trains of electrical pulses is also common (Rollman, 1983; Schalling, 1970). This has the advantage of being able to deliver fine gradations of stimulus intensity but has the disadvantage that many subjects associate these stimuli with previous experiences, or expectations, of electric "shock", even though the stimulus bears little relationship to the "all or none" nature of "shock". Chemical methods such as the injection of intramuscular saline or the use of the sub-maximum effort tourniquet test are also in use. These are claimed to more closely resemble clinical pain in that they produce a deep muscular aching which slowly increases in intensity and which does not cease immediately (Chapman et al, 1986).

The final most common method of applying a painful stimulus is the use of pressure. This can be either a constant pressure as with the Forgione-Barber pressure algometer (Forgione and Barber, 1971) or through a variable pressure dolorimeter (Keele, 1954; Merskey and Spear,1964). Constant pressure has the characteristic of a slowly rising (tonic) pain but has the disadvantage, when pain tolerance levels are being measured, that the slope of the increase in the perceived intensity tends to plateau after a certain time. Thus, for some subjects, no "true" tolerance level is reached. This same criticism is also true for the cold-pressor test.

One of the problems in the cross-comparison of results of pain perception studies is that different research groups use different means of inducing pain which may have different properties inherent in the stimuli. It might reasonably be expected that the use of different painful stressors may lead to a different pattern of responses both within and between subjects. Thus, a phasic stimulus like electrical pulse trains may not be comparable to a tonic stimulus such as constant pressure or the sub-maximum effort tourniquet test.

Difficulties, more germane to perceptual measurement in general, also arise in making judgments of any perceptual experience. This is even more apparent in the area of pain measurement. Classical psychophysical techniques such as the method of limits, the method of constant stimuli and the method of adjustment may be acceptable in the laboratory measurement of pain threshold but are inappropriate for pain tolerance measures. Further, measures which require the repeated application of the stimulus are unethical in the context of patients who are already in pain and are therefore questionable for use in clinical trials of treatment effectiveness except in exceptional research conditions (Sternbach, 1978). Frequently, in the clinical context, a single run of an ascending method of limits is used. This may lead to inaccuracy in the measures and to the questionable lack of sensitivity in individual and group measures. However, a

recent review of pain measurement concluded that both threshold and tole·ance measures could produce valid outcomes under conditions where extraneous variables are carefully controlled (Chapman et al, 1985).

A few studies have addressed the question of whether pain threshold and tolerance measures are generalizable across different stressors (Davidson and McDougall, 1969; Brown, Fader and Barber, 1973; Harris and Rollman 1983). These studies, in general, indicated that there were significant correlations between different stressors in normal healthy subjects. However, Harris and Rollman (1983), using trains of electrical pulses, a cold pressor test and a constant pressure algometer, found that although significant positive correlations were found between the measures, these tended to be low (between .3 and .5). They also found that the different measures satisfied the requirements for convergent and discriminant validity (Campbell and Fiske, 1959). Thus, the measures were assessing the same traits (threshold and tolerance) but there were enough differences in responses to the stressors to satisfy the requirements of discriminant validity between the stressors, i.e. they produced a distinct pattern of responses from each other. Scudds (1984), using 3 different stressors to assess pain threshold and tolerance, found a slightly higher order of correlations across stressors for tolerance (between .44 and .74) but lower for threshold (between .22 and .32). All correlations

were significant but these data did not completely satisfy the requirements for discriminant validity.

Signal detection theory (SDT) has also been applied to the area of pain measurement. Conceptually, SDT allows the separation of the purely sensory aspect of the stimulus (sensitivity, or d') from the subject's criterion or response bias. An implicit assumption of SDT is that there is no absolute threshold but that thresholds will vary according to the criterion set by the subject. This criterion can be altered in many ways to increase or decrease the probability of the subject reporting the presence of the stimulus (Green and Swets, 1966). This is attractive to pain researchers because it might provide a technique that separates the purely sensory factors from the cognitive factors of the pain response. SDT has been used by many investigators to examine responses to such factors as drugs, placebo and transcutaneous electrical nerve stimulation (TENS) (Wolff, 1978). In general, it has been claimed that psychological modulators tend to change the criterion level, leaving sensitivity unchanged while physical modulators, such as drugs or TENS alter sensitivity. Rollman (1977) questioned, on both theoretical and methodological grounds, whether SDT procedures were applicable to experimental pain research. The methodological problems can be overcome by improving techniques but the theoretical problems remain. The main criticism is that in supra-threshold pain studies it is not

clear exactly what d' measures in this context. Rollman concluded that it measured the ability to separate two stimuli and not pain, per se, and was therefore unsuitable for supra-threshold pain research.

Various other factors, such as age, sex, ethnicity, culture, affective state, demand characteristics and situational context have all been found to influence threshold and tolerance measures to experimentally induced pain. However, in assessing the influence of these factors, problems are encountered in the comparison of studies that employ different stressors. It might reasonably be expected that different stressors may produce different patterns of response. Thus, Wolff and Jarvik (1963), using deep somatic pain found that pain tolerance increased in men with age but not with women. Clark and Mehl (1971) found that pain tolerance increased with age to radiant heat. Contrary to this, it has been reported that pain tolerance decreased with increasing age in response to a deep pressure stimulus (Woodrow et al, 1972). This finding was supported by Scudds (1984), using two pressure stimuli and electrical pulse trains who found that age was significantly negatively correlated with pain threshold for all three stressors.

Similar problems are encountered in the literature dealing with sex differences. Here again, different stressors may confound comparisons across studies. Thus, various studies have reported no sex differences using

radiant heat (Clark and Mehl, 1971); men have been reported to have significantly higher tolerance but not threshold to trains of electrical pulses (Nottermans and Tophoff, 1967); male athletes are reported to have higher tolerance than female athletes to cold and to muscle ischaemia (Jaremko et al, 1981). Finally, Rollman and Harris (1983) found that males had higher threshold and tolerances to shock, constant pressure and a cold-pressor test.

If conclusions can be drawn from the studies reported above, then it might seem that men are less responsive to painful stimulation and that sensitivity increases with age. However, this may not be true in the clinical context where the meaning of the situation and previous experience with pain may more profoundly influence pain report behavior.

In a related manner, Dworkin and Chen (1982) demonstrated that subjects were significantly more sensitive to dental tooth-pulp pain in a clinical setting, which is associated with anxiety, when compared to their responses in the laboratory. Other affective states have been found to influence pain responsiveness, although these are more relevant to endogenous pain rather than experimental pain (Turk and Kerns, 1983).

Summary.

Various pain induction methods have been examined and factors that might influence pain responsiveness within an experimental context have been presented. The generality of

pain responses to different stressors is still in question. Therefore, in experimental studies it is advisable to use more than one stressor to control for individual differences in response. This may not be possible in the clinical context, with the result that studies using only one stressor should be interpreted with caution. Further, wherever possible, such factors as age, sex and the situational context should be controlled for in the study design or in subsequent data analysis.

Adaptation-level and hypervigilance effects.

The context in which stimuli are delivered within an individual experimental session has also been demonstrated to affect the intensity of pain experienced. Rollman (1979) used electrical pulses in an SDT paradigm with healthy subjects and found that the subject's estimate of the intensity of the stimulus was influenced by the magnitude of the paired stimulus within that session. If the accompanying stimulus was high then the subject's estimate of the less intense stimulus was lower than would have been expected if the stimuli had been delivered in a steadily increasing fashion. It was reasoned that the subjects used the stronger stimulus as a reference point on which to base subsequent judgments of intensity. He called this finding the "adaptation-level effect", after the work of Helson (1964) who proposed that when a person is asked to estimate some quantity, the estimate will be made with reference to past experiences, by the presence or absence

of standards and also by the range of stimuli that are presented. This position has gained some recent experimental support from Chen and Treede (1985) who used a tonic pain stressor (muscle ischaemia) and phasic pain (electrical intracutaneous stimuli) to evaluate different pain responses. They found that, when the two stimuli were applied simultaneously, the perceived magnitude of the phasic pain was significantly lower than when it was delivered separately. No change was found in tonic pain estimates.

On theoretical grounds, Chapman (1978, 1986) stated that an effect opposite to the "adaptation level effect" might be expected, that is the person may become more sensitive or "vigilant" to stimuli when faced with repeated stimuli. The subjects might therefore be expected to overestimate the magnitude of the intensity of the stimulation in this context. Further, subjects might be influenced by intolerant models to pain or by the instructional "set" of the experimenter.

Scaling procedures.

Various scaling procedures have been used in the laboratory to obtain subjective estimates of the pain experience. These have mainly been directed at the intensity of the sensation but have more recently also attempted to gauge the unpleasantness of the experience. Simple category scales which employ such verbal descriptors

as no pain, mild pain, moderate pain and severe pain are easy to understand and are simple to use as measures of pain intensity. Words, such as mild, discomforting, distressing, horrible and excruciating have been used to scale the affective component of the pain (Melzack, 1975). However, these scales lack the sensitivity, when used on their own, to detect fine changes in pain or to differentiate small increments in the intensity of the stimulus (Chapman et al, 1985). Further, the categories imply a rank ordering which can presuppose equal intervals of the experience which are often assumed but rarely derived experimentally.

Numerical rating scales, with numbers ranging from 0 to 10, or 0 to 100 may seem to increase the range of possible choices for the subjects but are confounded by subject preference for particular numbers and for reticence to use the extreme ends of the scale (Scott and Huskisson, 1976).

By far the most common rating procedure in use is the visual analogue scale (VAS). It is simple to use, has face validity and is highly reproducible, although the reproducibility varies at different positions along the line. Dixon and Bird (1981), using a 10 cm. line, found that subjects tended to overestimate line length at a length of less than 6.2 cm. and underestimated the length beyond this point.

The VAS usually consists of a 10 or 15 cm. horizontal

line, the ends of which are bounded by word descriptors which signify the end-points of the experience to be measured. Seymour and colleagues (1985) found, using dental pain, that a line demarcated by the words "no pain" at one end and "worst pain imaginable" at the other, was the most suitable and that lines of 10 and 15 cm. had the highest sensitivity to change.

The use of the VAS seems to be a "simple" magnitude estimation procedure. Estimation of line length has an exponent of one and might therefore be assumed to be a straightforward procedure (Stevens, 1975). Unfortunately, it is not as simple as some researchers take it to be. It has been argued, on both theoretical and experimental grounds, using cross-modality matching procedures, that the VAS can be used as a ratio scale and the results treated as parametric data (Gracely et al, 1978). However, most researchers approach the VAS as if it is a given assumption that it is a ratio scale without providing a rationale for this assumption. Non-parametric procedures of data analysis as well as parametric should therefore be considered when analyzing these data.

Measures of pain behavior are more applicable to the clinical setting than the experimental one. However, it could be argued that any vocalization is a behavioral measure and thus some of the measures mentioned previously could be classified as behavioral in nature. The "true" behaviorist might argue that the only way we can know

anything about a person is through his behavior (Lazarus et al, 1980). This is an extremely limited viewpoint when taken within the context of pain because it assumes that, if taken to the extremes that it implies, if no pain behaviors are displayed by the subject or patient then that person is not in pain. This position is highly questionable and will be returned to in the section dealing with the assessment of clinical pain.

Pain behaviors are important, however, in the overall assessment of pain but few validated measures have been developed in the experimental setting. Vocalizations, limb movements, clutching or rubbing a part, and facial expressions are all possible sources of behavioral measures but are generally gross and difficult to quantify for the laboratory (Craig and Prkachin, 1983). Some interesting attempts have been made in the area of facial expressions in reaction to experimental pain where there have been attempts to grade different types of expression in response to painful stimuli (Patrick et al, 1986). Results are promising but, as yet, the procedure is time consuming and it is difficult to foresee immediate applications for it in clinical settings.

Physiological reactions, such as heart rate, blood pressure, respiratory rate, skin palor, galvanic skin response, electromyography and evoked cortical potentials, although they do change in response to pain and give "hard" measurements, are not good indicators of pain. This is due

to the fact that they are covariant with arousal and tension in general rather than pain alone (Chapman et al, 1985). The use of evoked cortical potentials is, perhaps, more promising and is receiving much attention from some investigators but it is still not yet fully developed to make exact predictions about the nature of the response (Bromm and Treede, 1987).

Conclusion.

Pain measurement in the laboratory has led to an increased understanding of the nature and dimensions of the pain experience. Individual measures give insight into particular aspects of pain but these are usually unidimensional measures. It was also seen that, even in the laboratory, pain responsiveness can be influenced by many factors and it will be shown that the assessment of the many-faceted nature of clinical pain will require a more multi-dimensional approach to encompass all the domains of the pain experience.

Chapter 2

Chronic pain may be viewed as a syndrome in its own right or it may be concomitant with some other chronic disease process, such as arthritis or cancer. Chronic pain is difficult to manage but it is a requirement of effective management that the full impact of the condition on the patient be assessed.

Pain complaints are prevalent in society. In a survey of the prevalence of pain complaints in a general population in industrial Ontario, it was found that 16% of the individuals sampled randomly from a family practice had experienced pain within the previous 2 weeks. More than twice as many people reported persistent pain than temporary pain (Crook et al, 1984). Pain is therefore a frequent symptom, sometimes the most important symptom, of many complaints that may arise in a normal population.

Many measures have been developed to assess pain which has become severe and long lasting. These are similar to, but are generally more extensive than, those which are employed in the laboratory. This chapter will stress the multi-dimensional nature of pain measurement. Firstly, general pain populations will be examined briefly in terms of the measurement of pain perception, scaling of subjective report, behavior, personality and multi-dimensional indices. Next, two groups of patients frequently encountered in rheumatology clinics - patients

with rheumatoid arthritis and those with fibrositis - will be examined in more detail.

Assessment in chronic pain populations

As with experimentally induced pain, the most common method of pain assessment in the clinic is visual analogue scaling. It has been used with many different patient populations and under diverse circumstances, such as for back pain and joint pain (Linton and Gotestam, 1983), cancer pain (Ahles et al, 1984), and headache (Philips and Hunter, 1982). It has also been used to assess pain relief from analgesics after such procedures as meniscectomy and in post-operative dental pain (Quiding and Haggquist, 1983; Seymour, 1982).

Various scales have been used with different lengths, word delimiters, with and without numbers (numerical rating scales) and with different orientations. In general, the correlations between the scales are high, a correlation as high as .99 being reported in a study using a clinical population and horizontal and vertical visual analogue scales (Scott and Huskisson, 1979). Further, there are high correlations reported between the VAS, graphic rating scales (GRS) and ordinal scales of simple word descriptors (Huskisson, 1974). However, the VAS has been shown to be more sensitive to change than the ordinal scales. As well, it has been shown that the VAS with word delimiters at either end provides a more even distribution of scores than

the graphic rating scale. Berry and Huskisson (1972) found that the majority of patients used only the levels indicated by the descriptive terms of the GRS, whereas this problem did not occur with the VAS.

Scores are not evenly distributed along the VAS, however. In an analysis of pain at gynecological surgery, it was shown that the VAS provided a skewed distribution of scores (Grossi et al, 1983). The same authors tested an analog chromatic continuous scale which provided a more even distribution of scores. They also pointed out some of the common problems with the VAS in surgical populations, such as imprecise marking by the subject, inaccurate measurement by the experimenter and the inability of the patient to carry out the task consistently due to post-operative lethargy.

Another problem with the VAS in clinical populations is that commonly it is used to assess change in pain as a response to some intervention. If the patient originally marks at the top end of the scale and then his pain gets worse, there is no further range in which he can mark. Huskisson (1983) advocates the use of a pain relief VAS, the ends of which are marked by no relief and complete relief. An advance on this would be the use of a comparative VAS as compared to the usual absolute scale. Carlsson (1983) concluded, in the evaluation of pain relief after trans-cutaneous nerve stimulation, that the comparative VAS was more valid and reliable than the

absolute type of VAS. This type of VAS is a 10 cm. line with the mid-point marked as "unchanged" and the extreme ends of the line are marked less severe and more severe.

Summary

The VAS has been shown to be a valid and reliable method of estimating pain in clinical populations. It is easy to use and to understand by most patients and is easy to score by the clinician and experimenter.

Pain responsiveness in chronic pain populations

Attempting to bridge the gap between experimental and clinical pain, various pain induction methods have been used with different populations of pain patients to obtain a clearer understanding of the nature of pain responsiveness as it relates to changes in disease processes. As early as 1943, Sharman analyzed pain threshold data obtained with 2 pressure techniques from a large number of pain patients and healthy controls (Sharman, 1943). Although his methodology was imprecise and his split of patients into "functional" and "organic" categories is not fully explained, the data presented give some interesting insights into pain responsiveness and to future directions in research. Like Keele (1954), he split his normal subjects into hyper-, hypo- and normo-sensitive subgroups with an approximate normal distribution. In his patient groups, however, it was found that there were many more hypersensitive patients than expected in the "functional" pain group and more hypo-sensitive patients

than expected in the "organic" pain group. The "functional" group contained patients in whom no organic disease could be identified and were characterized by "nervousness, chronic exhaustion, anxiety neurosis and vague and ill-defined pains". He concluded that "patients with organic disease usually have a higher threshold to pain than those with functional complaints".

Differential alterations in pain thresholds have also been found in headache patients in response to a noxious sound stimulus (Philips and Hunter, 1982), in patients with myocardial infarctions (Keele, 1968), in psychiatric and neurological patients to the pressure algometer (Merskey and Evans, 1975) and in diabetic polyneuropathy to trains of electrical pulses (Morley et al, 1984). Taken together, these studies indicate that pain sensitivity can differ depending upon psychological state and type of condition. For example, it was demonstrated that patients with "functional" pain (with depression, anxiety, hysterical or hypochondriacal reactions) had lower pain thresholds than those with "organic causes for their pain" (Merskey and Evans, 1975). Further, headache prone patients have been shown to be more sensitive to a sound stimulus than normal controls. This hypersensitivity to the stimulus was even more marked during periods of headache attacks (Philips and Hunter, 1982). It has also been demonstrated that patients with diabetic peripheral neuropathy have lower pain thresholds than normal subjects but that a similar group

thresholds than normal subjects but that a similar group of patients who were being successfully managed for their condition had no difference in pain sensitivity than that of healthy subjects (Morley et al, 1984).

Pain sensitivity has also been assessed in myofascial pain syndromes (MPS) (Reeves et al, 1986) and in myofascial pain dysfunction syndrome (MPDS) (Malow and Olson, 1981). Both of these conditions are characterized by chronic pain which is accompanied by areas of acute tenderness throughout the body (in MPS) and around the temporo-mandibular joint (in MPDS). The dolorimeter has been found to be a reliable instrument in testing the sensitivity of these tender points, an alteration in which may be used as an indicator of treatment success (Reeves et al, 1986). In MPDS, it has been shown that patients have lower pain thresholds than age and sex-matched controls to a constant pressure stimulus (Malow et al, 1980), which the authors classed as "hypervigilance". However, this returned towards normal values after successful treatment of the condition (Malow and Dougher, 1979; Malow and Olson, 1981). These findings in MPDS are supported by a recent study using a variable pressure dolorimeter (Fricton and Schiffman, 1987).

In the past, both MPS and MPDS have been thought of as having "functional" components and both have been associated with anxiety, depression and hypochondriasis (Lupton, 1969). Jimenez and Lane (1985), using the

muscle pain patients had an increase in both threshold and tolerance measures after successful treatment of their pain.

However, not all studies indicate that pain patients have an increase in pain sensitivity as compared to healthy controls. Some studies have indicated that pain patients may demonstrate an "adaptation-level" response, that is, they demonstrate decreased responsiveness to pain. Callaghan and co-workers (1978) demonstrated that low-back pain patients with radiating pain in one limb had significantly decreased sensitivity to heat and shock in that limb compared to the non-painful limb. This decrease in sensitivity returned towards normal values after treatment with TENS.

Chronic low back pain patients have also been shown to have raised radiant heat thresholds when compared to normal controls (Naliboff et al, 1981). Interestingly, a control group of chronic respiratory disease subjects also had higher thresholds than the normal controls in this study. These findings were supported in a more recent study, also with low back pain patients and heat thresholds (Yang et al, 1985). It was found that the pain patients had higher pain thresholds and were poorer discriminators than healthy cortrols. The authors discussed their results in terms of adaptation-level phenomenon.

Summary.

It is interesting that both the hypervigilance and the adaptation-level theories have found clinical support. However, this has been largely in different patient populations with different stressors. Further, it seems that alterations in pain sensitivity in either direction away from the normal may be reversed on successful treatment of the painful condition. It is unclear what makes one patient, or group of patients, obey one paradigm and not the other. Possibilities might include the level and duration of ongoing pain, the psychological profile of the subject or the "organic" versus "functional" background to the pain complaint.

Behavioral Measurements.

Behavioral measurements of pain are valuable in both in-patient and out-patient clinical settings. Such measurements are sometimes taken as being complete and sufficient in their own right and sometimes are used to augment those of self-report. Commonly reported variables include: specific activities of daily living, measures of the amount of time spent standing, sitting or lying down, sleep patterns, performance on prespecified tasks, medication demand or intake, household activities and recreation activities (Bradley et al, 1981).

While individual indicators of pain behavior may give valuable information, attempts have been made to develop inventories of pain behavior either for general use

(Fordyce, 1988, Pilowsky and Spence, 1976) or for specific pain populations, such as headache sufferers (Philips, 1983). Both self report measures and direct observation have been used to assess pain behaviors. Thus, Keefe and Block (1982) have used an observational system for scoring back-pain behaviors which includes bracing, rubbing, sighing and guarded movements. Others have also used observational ratings of pain behavior because it has been pointed out that patient self report of behavior is often inaccurate (Kremer et al, 1981) and is often at variance with observational ratings by observers, even when there was high inter-rater reliability (Teske et al, 1983). Apart from the inaccuracy of self-report data, two other serious problems are encountered with behavioral data. The first is that they quantify pain behaviors and not pain itself. Thus the targeted behaviors may improve, the patient may become more functionally independent, but this may say little or nothing about the nature of change in the pain. Thus, the validity of these measures as indicators of pain has not yet been confirmed.

The second and, perhaps, more serious problem is that if it is accepted that some pain clinic programs use predominantly behavioral data to evaluate the efficacy of their treatments, and these "pain behaviors" are targeted for treatment, then "success" may be taken as the eradication of the pain behaviors. However, this may leave

the other components of the pain experience virtually untouched. Perhaps a true behaviorist might deny that subjective experience is open to assessment but to base treatment solely on observational data is to deny the accepted definition of pain as an experience.

Personality Factors

Personality factors and mood states are other important areas that must be considered in the overall evaluation of the effect of pain on the patient. As with behavioral measures, they are not the concern of direct pain measurement but they may have an influence on the onset, course and general effect of the pain on the patient's well-being and adjustment.

Certain relationships between personality traits and the nature and course of chronic pain have been established, but the exact nature of the relationship has been the subject of much disagreement. Hanvik (1951), using the Minnesota Multiphasic Personality Inventory (MMPI), reported that acute and chronic low back pain patients without physical findings could be distinguished from low back pain patients with organic findings. Patients without a firm physical diagnosis showed elevations on the "neurotic triad", that is, elevation of the hypochondriasis and hysteria scales with depression relatively low. Patients with physical findings showed normal personality profiles. Sternbach and co-workers (1973) found no

differences in the "Conversion V" pattern between patients with or without physical findings. They did, however, consider that these patients were depressed and theorized that, as with some conversion reactions, depression was not apparent but was masked by hypochondriasis and hysteria.

The MMPI has been the most frequently used psychometric instrument in the analysis of personality disturbance in the presence of chronic pain. The literature amassed through its use is immense. The two studies cited above give only some of the flavor of the conflicting results obtained using this instrument. Other studies have used the MMPI to predict treatment outcome (Kuperman et al, 1979; McCreary et al, 1979), surgical outcome (Oostdam et al, 1981) and for differentiating between groups of pain patients (Prokop et al, 1980). In recent years, however, the use of the MMPI in the evaluation of pain patients has been seriously questioned (Rook et al, 1981; Naliboff et al, 1982; Lamping, 1985). While some authors think that it still may be a useful adjunct in the clinical evaluation of individual patients (Cohen et al, 1983), others would deem it an invalid instrument. Lamping (1985) points out that the MMPI was developed to measure psychopathology and not disturbance in medically ill patients. In this respect, then, it may be inappropriate for chronic pain patients. Of more importance, however, is the fact that the items on some of the scales are not independent and endorsement of one item may lead to it being scored on two or more scales.

Further, chronic pain patients, indeed chronic illness patients in general (Naliboff et al, 1982), will almost invariably score high on the scales of the "neurotic triad" due to the fact that many items in these scales are the symptoms of common pain complaints. Thus, there is inadequate content validity as well as construct validity in the MMPI, at least as far as pain patients are concerned. Therefore, instruments should be chosen that are both valid and applicable to pain patients.

Depression, anxiety, helplessness, denial, neuroticism, extroversion/introversion and low self esteem have all been found to be associated with chronic pain syndromes (Sternbach, 1978; Lupton, 1969; Skevington, 1983; Woodforde and Merskey, 1972; Elton et al, 1979). For depression and anxiety, at least, there has been some question as to whether the pain is the "chicken or the egg". Does chronic depression predispose to pain a "pain prone disorder" as Blumer and Heilbronn (1981) infer? The question of causality has not yet been resolved but certainly there is a relationship between pain and depression. However, in treatment, some cases of pain may be relieved without relief of depression, in some both may be relieved, and in others depression may be relieved without relief of pain (Feinmann, 1985). In a similar manner, anxiety has been associated with muscle tension which has been linked to pain, such as in headache or MPDS

(Lupton, 1969; Philips, 1983). However, it is unclear whether the pain causes the anxiety or the anxiety predisposes to pain.

Summary.

Many personality and mood disturbances have been found to be present in chronic pain populations. These can be largely seen as being reactive to the onset of the pain and disability and therefore need to be assessed in any total evaluation of pain. However, care must be taken with the choice of instrument, as what may be a "normal" profile for a chronic pain patient may be interpreted as "abnormal" when examined with such psychometric instruments as the MMPI.

Multidimensional Instruments.

Possibly the most important advance in the area of pain assessment in the last ten years has been the introduction of various instruments which treat pain as the complex multi-dimensional experience that it has been shown to be and attempt to assess the different domains of that experience. These have been developed, generally, from a social science background with attempts made to satisfy the requirements of validity and reliability for either specific (such as low back pain or arthritis) or general pain populations.

The McGill Pain Questionnaire (MPQ) (Melzack, 1975) was one of the first instruments to be introduced that attempted to assess the multidimensional nature of pain. It

is the most widely used and evaluated method of assessment. It has been used with such disorders as dental pain (Van Buren and Klienknecht, 1979), cancer pain (Graham et al, 1980) and low back pain (Prieto et al, 1980), amongst many others. The MPQ was empirically derived and has been examined for construct, concurrent and discriminant validity as well as for reliability (Reading, 1979). The Present Pain Intensity (PPI), a 5-word verbal rating scale, has been criticized as lacking in sensitivity, in common with all verbal rating scales. However, the Pain Rating Index (PRI), an attempt to organize verbal descriptors of pain into distinct, ranked categories, has been found to be reliable and to have good concurrent and discriminant validity. Its construct validity is more open to question due to the fact of the heavy loading of words on the sensory-discriminative aspect of the inventory, with fewer words on the motivational-affective dimension and even fewer on the cognitive-evaluative domain. Further, factor analysis has revealed 4 factors instead of 3 with the fourth being a mixed sensory and affective dimension (Prieto et al, 1980; McCreary et al, 1981). The widespread use of the MPQ, and the continued analysis of its properties, however, should enable further improvement to be carried out on this very important instrument.

Two other methods of multidimensional pain measurement will be described to contrast their methods with the MPQ. Firstly, there is the computerized chronic

pain profile developed by Duncan, Gregg and Ghia (1978). This attempts to classify each patient based on a mathematical comparison of the behavioral, psychological and pathophysiological (organic) aspects of chronic pain. The ensuing classification would provide the clinician with the relative importance of each dimension as a guide to suitable treatment. This is a very comprehensive instrument which has been used for research purposes but has not yet been widely tested by other researchers. It is truly multidimensional, however, as it contains within it (a) a complete rating of organic dysfunction (although it is unclear how this rating is derived), (b) a psychosocial index which contains, amongst other measures, a scale of significant recent life events, anxiety, depression and the MMPI and (c) a pain behavior index which contains the MPQ, a global estimate of pain severity and a cross-modality matching of ischaemic tourniquet pain. Such a massive instrument as this would be lengthy to complete but would yield a very complete picture of the patient's pain and disability. An attractive feature of this inventory is that it is computer based and can be "easily" updated to give details of the changing profile of the patients across time and throughout treatment.

The West Haven-Yale Multidimensional Pain Inventory (WHYMPI) (Kerns et al, 1987) is another broadly-based instrument which, unlike the computer-based pain profile, is empirically derived and is quick and easy to score as

all scales use either 6- or 7-point scales. It consists of 3 sections:- (a) an evaluation of the perceived pain intensity and its impact on different areas of the patient's life including mood, control and interference with various activities, (b) the responses of significant others to the patient's expressions of pain and (c) the evaluation of the frequency of performance of various activities. The advantage of this instrument is its brevity and comprehensiveness, especially in the areas of psychosocial and interpersonal adjustment. Due to its recent introduction, however, it is not yet possible to say how useful it will prove to be.

Various instruments have been developed which attempt to assess the functional disability that is a consequence of chronic illness or chronic pain. The Sickness Impact Profile (SIP) is an example of these instruments (Follick et al, 1985). This is a behaviorally based, self-report measure of global disability which generates 3 general dimension scores (physical, psychosocial and general activities) and 12 specific category scores. The SIP has been used with arthritis populations (Meenan et al, 1984) and chronic low back pain patients (Follick et al, 1985). It has been found to be sensitive to pre- and post-treatment changes, to be reliable, and to have good concurrent validity. While not evaluating pain itself, this would appear to be a promising instrument in assessing the

magnitude of the effect that chronic pain may have on patients' lives.

Summary.

Three multidimensional inventories were presented in this section, each with a different emphasis on pain, functional impairment and psychological status. The type of instrument chosen for research would depend on the nature of the study populations and the depth of the information required to answer the hypotheses.

General summary of pain assessment in chronic pain populations.

The complexity of the chronic pain experience may sometimes demand that extensive measures be used to assess all the domains of that experience in clinical populations. Obviously, more detailed measures may be needed in the research milieu rather than the clinical situation. However, such factors as subjective report, pain responsiveness, pain behaviors, personality and mood state, and functional limitations should all be taken into account. A global picture is required because a patient may appear normal on one dimension, for example in the subjective report of pain and yet show abnormal characteristics in other domains such as pain responsiveness or personality measures. These measures may not all be required in strictly experimental situations, such as in the assessment of pain responsiveness, but

multidimensional instruments should always be used when the aim is to assess the effect of treatment on chronic pain.

Pain assessment and related measures in rheumatoid arthritis

Rheumatoid Arthritis (R.A.) is a progressive systemic disease which is present in approximately one percent of the population and is found more often in women than men (Anderson et al, 1985). The age of onset is variable but usually starts in early adulthood (O'Dell, 1977). It is a chronic inflammatory condition that is characterized by immunological abnormalities and is associated with peri-articular and intra-articular changes (Ropes et al, 1958; Harkness et al, 1982). Pain is one of the main complaints in R.A., along with increasing joint and muscular disability. The amount of pain that the patient experiences is variable but has been directly related to the amount of disease activity present at the time and to previous destructive changes within the joint complex (Kazis, et al, 1983; Pinals et al, 1981). Disease activity is subject to fluctuations over time through periods of acute exacerbation and remission.

Various methods have been designed to assess the different components of disease activity in R.A. (Pinals et al, 1981; Mallya and Mace, 1981). An important feature of this is the assessment of pain, firstly in its own right and secondly in the performance of analgesic, anti-inflammatory and remittive agents (Hansen et al, 1979) and

lastly in the effectiveness of other pain relieving modalities such as heat, cold and TENS (Kumar and Redford, 1982). In an evaluation of the various components that are used to assess health status, it was found that pain was the single most important predictor of health assessment by both physician and patient (Kazis et al, 1983).

However, two recent studies used the MPQ to compare pain in different rheumatic disease populations. One found that the MPQ could reliably discriminate between R.A. patients, those with localized osteo-arthritis and those with generalized osteo-arthritis (Wagstaff et al, 1985). The other examined pain properties in R.A. patients and fibrositis patients with a modified MPQ. It was found that the fibrositis patients used more words than the R.A. patients but that the intensity of the pain was not significantly different between the two groups. However, it is difficult to draw firm conclusions about the results of this study as the MPQ data were not scored in the normally accepted manner.

Behavioral measures of pain have also recently been employed with R.A. (Anderson et al, 1987). This study used a previously validated observational method developed by Keefe and Block (1982) in an effort to establish the concurrent validity of the instrument with rheumatology fellows' estimates of patient pain. They found significant positive correlations between pain behavior scores and the rheumatologists' estimates. Behavioral measures are also

included in instruments that are used in arthritis research to examine health status. Some of these, for example the Functional Status Index (Jette, 1980), the Health Assessment Questionnaire (Fries et al, 1982) and the Arthritis Impact Measurement Scales (AIMS) (Meenan et al, 1982), have been developed specifically for arthritis research. These are multidimensional instruments whose main categories attempt to assess the domains of pain, mobility, social activity and various activities. The AIMS also includes a depression sub-scale.

Little work has been carried out into the nature of pain responsiveness in rheumatoid arthritis and other destructive joint conditions. Keele (1954), in the development of a spring-loaded variable pressure algometer (the dolorimeter), established normative values for pain thresholds in healthy subjects. Since then, the dolorimeter has been used with other conditions and has been found to be a reliable instrument in the measurement of pain thresholds (Merskey and Spear, 1964; Reeves et al, 1986).

Huskisson and Hart (1972) found that R.A. patients did not have significantly different pain thresholds than those of normal control subjects. However, they did report that pain threshold was inversely related to a measure of pain - the number of analgesics taken by the patient. Scudds and co-workers (1987) also did not find significant differences in pain thresholds between R.A. subjects and normal controls. However, they did find lower pain tolerance

levels to the dolorimeter in the R.A. group compared to the normal group.

In a related condition, osteo-arthritis, it has been demonstrated that patients with enough hip pain to warrant joint-replacement surgery have lower pain thresholds than normal subjects. These thresholds returned towards normal values after successful surgical intervention. It was also found that those patients who had equally severe joint changes as shown by x-ray, but who did not require surgery, had significantly raised thresholds when compared to normal subjects (O'Driscoll and Jayson, 1974).

Psychological factors have often been associated with R.A. but the prevailing opinion at present is to reject the notion of a pre-morbid "rheumatoid personality" as a predisposing factor to the onset of the disease (Achterberg-Lawlis, 1982; Spergel et al, 1978). Anxiety, depression, denial, hostility and anger have all been found in R.A. patients, with the most consistent pattern being that of depression, denial, somatization and a high degree of bodily concern. None of these factors is particularly surprising, however, due to the chronicity of the condition and the sometimes extensive interference with normal physical and emotional well-being. As well, psychological "disturbances" that are present in R.A. can also be found in other chronic pain and chronic illness populations.

Crown and Crown (1973) found that patients with early

rheumatoid disease did not differ from a normal population in psychological profile, but that their results differed from other studies which showed changes in psychological state in subjects with advanced R.A.. They suggested that it may not only be the length of the disease that is important but also the severity of the symptoms. This position is supported by Viney and Westbrook (1981) who found, with a mixed group of patients, that severity of disability was a greater predictor of anxiety, depression and anger than was diagnostic category. However, a recent study has shown that current depression in R.A. patients is more related to higher levels of pain than to disease activity (Frank et al, 1988). As well, Hawley and Wolfe (1988) have shown that levels of anxiety and depression are more associated with socioeconomic factors than disease activity.

A sub-group of R.A. patients has been reported by some authors (Rimon, 1973; Alarcon et al, 1982; Solomon, 1981; Vollhardt et al, 1982). Sero-negative R.A. patients (i.e., patients who test negative for serum rheumatoid factor) generally tend to have milder disease levels than their sero-positive counterparts (Rimon, 1973; Alcaron et al, 1982). Interestingly, it has also been suggested that sero-negative R.A. patients have higher levels of psychological disturbance, such as somatization, anxiety, and depression (Solomon, 1981, Vollhardt et al, 1982). However, it has not been shown yet whether these psychological

factors predate the onset of physical symptoms, rather than develop subsequent to the onset of the disease.

It would now seem reasonable to accept the concept that personality differences reported in long-standing R.A. patients are similar to those of other chronic diseases, painful and not painful, and that the previously held idea of a predisposing "rheumatoid personality" is unacceptable (Spergel et al, 1978; Cassileth et al, 1984).

Summary.

Pain is an important feature of R.A.. The VAS is the most commonly used method used to assess the pain although recently the MPQ and more global methods of measurement have also been employed. Personality and mood disturbances have been found with these patients but these can largely be attributed to the extensive symptomatology and chronicity of the condition.

Pain responsiveness in R.A. has been found to be largely similar to that of normal populations. However, no study has yet examined the effect of the state of disease activity on pain perception in these patients. From the data examined in other pain populations, it might reasonably be expected that pain responsiveness would alter in reaction to change of disease state as the patients go through periods of exacerbation to periods of quiescence. It would be interesting to examine a large population of R.A. patients to ascertain if this relationship exists.

Pain assessment and related measures in Fibrositis.

Fibrositis is a very interesting and complex condition that has been classified under the broad heading of "non-articular rheumatism". It is found with much greater frequency in women than in men and is mostly present in early middle-age (McCain, 1983). Fibrositis has been reported to be present in 14.6% of the out-patient population of a rheumatology clinic. It is characterized by a diffuse, chronic muscular pain which is associated with multiple areas of extreme tenderness in predictable areas throughout the body (Payne et al, 1982, Wolfe et al, 1985). Other diagnostic features of fibrositis include disturbed sleep patterns and tenderness of the upper back (Smythe and Moldofsky, 1977).

Recent evidence indicates that fibrositis patients may have some underlying pathogenic abnormalities in muscle (Bengtsson et al, 1986), substance P (Vaeroy et al, 1988) and muscle tissue oxygen pressure (Lund et al, 1986). However, these research findings have not yet been accepted as "diagnostic" of the presence of fibrositis. Therefore, at the present, fibrositis shows an absence of any routine radiographic and serological abnormalities (Smythe, 1979). Thus, unlike R.A. which has "firm" physical signs to account for the symptomatology, no obvious biological markers of the condition have yet been found in fibrositis.

Personality and mood variables have been examined as both possible causative factors and as a consequence of the

condition in fibrositis. Payne et al (1982) found that a group of hospitalized patients with fibrositis scored generally higher on some of the MMPI scales than a group of matched R.A. patients. They suggested that psychological factors might play a large part in fibrositis. Another study found that patients with fibrositis had 8 significantly elevated scores on the MMPI when compared to normal controls and 4 when compared to subjects with R.A. (Ahles et al, 1984). These investigators later re-analyzed these data, controlling for some of the response biases that are inherent in the MMPI in chronic pain populations (Ahles et al, 1986). Although the magnitude of the scores of the elevations was reduced, the same number of fibrositis patients as before remained classed as "psychologically disturbed". Two other reports, comparing fibrositis and R.A. patients found that the fibrositis group had significant elevations on anxiety and depression scales (Wolfe et al, 1984a; Wolfe et al, 1984b). These studies indicate that patients with fibrositis, in common with other chronic pain groups, have significant elevations on some personality and mood scales and that this disturbance is greater than in patients with R.A.. However, none of these studies imply causality, nor do they look at change in psychological profile in response to treatment.

Fibrositis has been claimed to be a disorder of pain modulation or "pain amplification" (Smythe, 1979). However, the experimental data do not fully support this statement.

Although the dolorimeter has been used to measure pain responsiveness in the common areas of tenderness in fibrositis, only three studies have examined the nature of pain responsiveness in non-painful areas in these patients. Campbell and co-workers (1983) reported that fibrositic patients did not differ significantly in "pain threshold and tolerance" values from clinic-matched patients with musculo-skeletal complaints. However, they chose multiple, poorly specified areas to obtain their measures. Further, they did not use the stringent Smythe (Smythe and Moldofsky, 1977) criteria in their diagnosis of fibrositis. As well, their control group had unspecified musculo-skeletal complaints and were presumably not a homogeneous sample. In a companion report to this study, Clark et al (1985) found that there was no difference in psychological status between their two groups. They concluded that fibrositis patients are not different in either psychological status or in pain perception from other patients with chronic musculo-skeletal pain.

Scudds et al (1987) examined pain responsiveness and personality variables in fibrositis patients as compared to two age- and sex-matched control groups. These were a group of patients with R.A. and a group of healthy controls. This study used three stressors, a visual analogue scale of present pain intensity and personality measures on the Basic Personality Inventory (BPI) (Jackson, 1989). It was found that the subjects with fibrositis had significantly

lower pain threshold and tolerance levels and were also significantly raised on the hypochondriasis, depression, anxiety and social introversion scales of the BPI when compared to the healthy control subjects. The R.A. subjects only showed significantly lower tolerance to the dolorimeter and had raised hypochondriasis scores compared to the normal subjects. Hypochondriasis scores, however, were significantly lower for the R.A. group than the group with fibrositis. It was concluded that fibrositis subjects were "hypervigilant" to pain and that this might be associated with an elevation of the personality scores.

The results of the previous study are supported by a recent report which examined pain threshold and tolerance levels in fibrositis patients compared to normal controls using a pressure algometer (Tunks et al, 1988). This study found that fibrositis patients had significantly lower generalized pain threshold and tolerance levels than the healthy control group. It is interesting that they also found, testing typical fibrositic tender points in the normal controls, that these points were more sensitive to pressure than other "non-tender" points. However, the magnitude of the increased sensitivity at these points was significantly less than that of the sensitivity of the tender points in the fibrositis patients. This latter finding is supported by another study which found a similar pattern of response in "tender" and "non-tender" points in healthy subjects (Arbegg, 1985, cited in Campbell, 1986).

Therefore, the studies above indicate that patients with fibrositis may be more sensitive to painful pressure than other patient groups. If this is true, it may well be associated with other reports that indicate that fibrositics showed loudness intolerance and a hyperactive vestibular response (Gerster and Hadj-Djilani, 1984), and oculomotor abnormalities which were concluded to be as a result of brainstem dysfunction (Rosenhall et al, 1987).

A few studies used the dolorimeter to assess whether the sensitivity of the fibrositic tender points would change in response to medication. However, none of these studies measured generalized pain responsiveness as a function of treatment efficacy. Carette and co-workers (1986), in a study of the effects of the antidepressant amitriptyline against placebo, found that there were no significant differences in sensitivity at the tender points between the amitriptyline and placebo groups at the end of the study even though other measures showed significant improvements. However, in a similar study, Goldenberg et al (1986), did find that the tender point score improved significantly in response to a combined medication regimen of amitriptyline and naproxen. As well, dothiepin which is also a tricyclic anti-depressant, has been shown to improve the sensitivity of fibrositic tender points after an 8-week period.

A further study used dolorimeter scores, amongst other measures, to gauge the effectiveness of strong

exercise on the symptoms of fibrositis (McCain, 1986). This study found, for those patients who responded well to the exercise program, that there was a significant elevation in scores at the tender points after treatment.

It would seem, then, that tender point scores are a common, and consistent, indicator of disease activity in patients with fibrositis and that they improve, in most studies, in response to treatment.

In an interesting series of studies, Moldofsky and co-workers found that patients with fibrositis have disturbances in sleep patterns and that this disturbance may be related to the sensitivity of tender points (Moldofsky and Scarsbrick, 1976; Moldofsky and Warsh, 1978; Moldofsky and Lue, 1980; Moldofsky et al, 1984). They also found that tender point sensitivity became more marked in normal subjects by depriving them of level 4 sleep. Further, they have demonstrated that tender point sensitivity can be decreased in fibrositis patients by administering dietary tryptophan which is a precursor of 5-hydroxytryptamine (serotonin). This is very interesting because alterations in endogenous serotonin levels are implicated in sleep disturbances, chronic pain and depression (Feinnman, 1985). Each of these factors may be present in fibrositis and it is possible that the success of amitriptyline, which blocks the re-uptake of serotonin at the synaptic terminals, is dependent on its action on one, or all, of these factors.

Summary.

Pain is one of the dominant diagnostic features of fibrositis. The VAS and the dolorimeter are used to gather subjective and objective measures of pain. Fibrositis patients have been shown to have lower generalized pain threshold and tolerance levels than normal subjects. Further, they are very responsive to pressure stimuli at the fibrositic tender points. This sensitivity may improve in response to treatment but this has not yet been fully established. As well, these patients generally have elevated profiles on anxiety, depression and hypochondriasis measures. If these are secondary to the disease status of the patient, then it could be expected that these and the pain measures would return towards normal values on "successful" treatment of the condition.

Conclusions.

Pain is a very complex and unpleasant experience about which our knowledge has grown immensely within the last 20 years. It is no longer viewed as being purely a sensation to be measured along a unitary dimension of intensity, but as being multifaceted in nature. This demands that many different measures be used to fully assess the pain and its impact in experimental and clinical subjects. Subjective measures, as well as personality factors, pain responsiveness, pain behaviors and functional impact must all be taken into account.

The present research.

Pain responsiveness has been previously demonstrated to differ between individuals and between patient groups, with some displaying an adaptation-level response and others conforming to a hypervigilance paradigm. It is possible that this is purely reflective of a normal range of individual, and group, differences in responsiveness. However, the consistent findings that pain responsiveness returns towards normal values after successful treatment runs contrary to that position.

The purpose of the present research is to examine two different clinical populations and determine whether state of disease activity and response to treatment can be predictors of the subjects' pain responsiveness. This will be achieved in 3 studies.

The first study will examine pain responsiveness in a large number of subjects with the diagnosis of rheumatoid arthritis who display different levels of disease activity along a continuum from no disease activity to acute exacerbation of the condition. It has previously been demonstrated that the responsiveness of patients with RA is not different from that of normal healthy controls. However, it is an expectation of this study that those patients with high levels of disease activity will display a hypervigilant response and those patients with low disease activity will display an adaptation level response. It is further expected that those patients with higher

levels of disease activity will display higher levels of psychological disturbance which might, in turn, be associated with altered levels of pain responsiveness.

The second study will re-examine the same sample of rheumatoid arthritis patients after a period of one year has elapsed. It is expected that some of the subjects will show alterations in disease activity levels after this time and that these alterations will be associated with corresponding changes in pain responsiveness.

The third study will examine changes in pain responsiveness in fibrositis patients after treatment. Previous research has demonstrated that these patients may conform to the hypervigilance paradigm. If this is so, then those patients who respond well to treatment should show a decrease in pain responsiveness, that is a raising of pain threshold and tolerance levels. Further, those patients who remain unchanged by treatment should demonstrate no change in pain responsiveness. It is also expected that changes in mood state, and functional capability would alter only in those patients who respond to treatment.

A major problem in the examination of these questions is the fact that fibrositis is a difficult condition to treat. However, Carette et al (1986) found that a significant number (55%) of fibrositis patients respond well to treatment with the antidepressant amitriptyline when given in low doses. The third study will therefore

attempt to replicate the clinical results of that study and to extend those results to examine changes in generalized pain responsiveness as a consequence of treatment.

Chapter 2

Study 1

Method

Subjects.

Sixty eight subjects participated in this study. All subjects had the diagnosis of classical or definite rheumatoid arthritis (see Appendix A for the diagnostic criteria for classical or definite rheumatoid arthritis). These patients were drawn from the in-patient and out-patient populations of Dr. D. Bell, Dr. M. Harth and Dr. G. McCain of the Department of Medicine, Rheumatology Service, University Hospital, London, Ontario. Ninety two potential subjects from the out-patient population were approached initially by letter and then by follow-up telephone call, to request their participation in the study. Fifty four subjects entered the study in this way. Five out-patient subjects were admitted to the study by direct referral from the out-patient clinic, that is, they were not first contacted by letter and telephone but were requested by the attending physician to enter the study.

Nine subjects were admitted to the study while under care as in-patients at the rheumatic diseases unit at the University Hospital. These subjects were referred to the experimenter by the attending physician for potential inclusion in the study and were then contacted directly by the experimenter. Nine of the 15 subjects contacted in this way entered the study.

Both in-patients and out-patients were fully informed of the nature of the study and were free to refuse to take part, with the understanding that refusal would not prejudice their treatment in any way. Subjects were not paid for participation in the study but traveling expenses were payable on request.

The age range of all subjects was from 21 yrs to 74 yrs with a mean of 52.5 yrs and a standard deviation of 12.8 yrs. Forty four subjects were female and 24 were male.

Consent Forms.

One consent form was used for all subjects. This form outlined the procedures to be used in the study (see Appendix B). Subjects were given the opportunity to ask questions before signing the form. No subjects needed to be excluded from the study for having taken analgesics in the previous 12 hours.

Apparatus.

1. Electrical stimulation: A Fredrick Haer and Company constant current stimulator delivered trains of 35, one-millisecond (msec) monophasic square wave pulses, separated by 10 msec to the skin over the first dorsal interosseous muscle of the hand. Current was applied through a pair of Grass silver electrodes filled with electrode paste. The area was first cleaned with a mildly abrasive compound (Brasivol) and then washed with alcohol, to minimize skin resistance. Electrodes were held in place by hypo-

allergenic tape. Current was increased gradually from 0 to a maximum of 7.5 milliamperes (ma).

2. Constant pressure: a modified Forgione-Barber (Forgione and Barber, 1971) constant pressure algometer was used. Modification was required because this device is normally used to exert pressure on the middle phalanx of one finger. Such a procedure was not suitable in this study due to possible finger joint symptoms in some of the subjects. The device, largely conforming to the original design, was made to apply a 3000 gm weight through a dull lucite wedge to a point above the wrist on the lateral surface of the radius, at the junction of the middle and lower thirds (Appendix C). A 3000 gm weight was chosen because in a recent study 27.5% of the subjects went to the maximum time limit using a 2000 gm weight (Harris and Rollman, 1983).

3. Dolorimeter: A Chatillon Company (Kew Gardens, N.Y.) variable pressure dolorimeter was used to apply gradually increasing pressure to a point on the forearm which lay mid-way between the styloid process of the radius and the lateral epicondyle of the humerus with the arm pronated and supported (Appendix D). The range of the device was from zero to 9.1 Kg. The head of the dolorimeter had a surface area of 1.54 cm^2.

4. Visual Analogue Scale: A fifteen centimeter line with word delimiters at either end of the line was employed to obtain objective measures of the pain experience. Two scales were employed. The first was used to measure present

pain intensity (P.P.I.) and to rate the intensity of the stressors at threshold and tolerance levels. The second was used to rate the unpleasantness of the stressors at threshold and tolerance levels.

5. Basic Personality Inventory (BPI): This is a 240 item inventory consisting of 11 clinical scales and 1 critical item scale (Reddon et al, 1983; Holden et al, 1983). Each scale has 20 items, 10 true-keyed and 10 false-keyed, except for the deviation scale which has 20 true-keyed items (See Appendix E). The BPI is based on a construct-oriented approach to test development and emphasizes: 1) the role of psychological theory in selecting potential items, 2) convergent and discriminant validity in item selection procedures and 3) scale homogeneity and generalizability (Holden et al, 1983). The psychometric properties of the BPI have been recently established for use in medical settings (Holden et al, 1988).

To retain the "completeness" of the test, all questions in the inventory were administered, although there was a specific a priori interest in the anxiety, denial, depression and hypochondriasis scales.

6. A modified sphygmomanometer pressure cuff: this was developed and tested as an objective assessment for grip strength in rheumatoid arthritis and other patient groups. (Giles, 1984). The instrument is a modified aneroid sphygmomanometer in which the bladder has been removed from

the cuff, folded and placed in a cotton bag. The bag is first inflated to 100 mm/Hg. and then deflated to 20 mm/Hg. The subject is then required to grip the bag as hard as possible to a maximum of 300 mm/Hg.

Measures employed.

Pain threshold:

(a) For electrical pulses, pain threshold was taken as the point (in ma) at which the stimulus first became painful.

(b) For the constant pressure algometer, pain threshold was taken as the time (in secs) between the weight being first applied and the subject reporting the feeling of pain. Two stop watches were started when the pressure was first applied and one of them was stopped immediately after the subject reported pain. The other was stopped at tolerance.

(c) For the dolorimeter, pain threshold was taken as the reading, in kg or part of a kg, that was indicated on the scale at the time when the subject first reported pain.

For each stressor, the subject was asked to mark on a visual analogue scale (VAS) the point that best corresponded to the experience when the feeling of pain was reported. Estimates were made of intensity and unpleasantness of the stimuli on separate analogue scales.

Pain tolerance:

(a) For electrical pulses: tolerance was taken as the

intensity reading at the point at which the subject indicated that he was not willing to take a further increase in current. A ceiling level of 7.5 ma was set but the subject was not informed of this before the stimulation began.

(b) For constant pressure: tolerance was taken as the time elapsed between the first application of pressure and the point at which the subject indicated that he did not wish to tolerate the pressure any longer. The maximum time was set at 3 min but, again, the subjects were not informed of this.

(c) For the dolorimeter: tolerance was taken as the point at which the subject indicated that he did not wish to take a further increase in pressure. The upper limit was 9.1 kg. As before, subjects were not informed of the upper limit.

VAS ratings of intensity and unpleasantness were recorded for each of the 3 tolerance levels in the same manner as Harris and Rollman (1983) and Scudds (1984).

Indices of Disease Activity:

Each of the following indices of disease activity is a standard measure in the assessment of rheumatoid arthritis (Buchanan and Tugwell, 1985).

(a) Time to fatigue: was taken as the time in hours, or fraction of an hour, between the subjects' first rising from bed in the morning and the onset of fatigue that would necessitate them to rest. The subject was asked to estimate

this time, taken on average, over the previous week. Times in excess of 12 hours were taken as normal.

(b) Joint count: was taken as the number of "active" joints in the patient as determined by systematic examination by the experimenter. A joint was classified as "active" when there was the presence of either (i) pain on passive motion within the normal range of joint movement for that patient, (ii) tenderness on the application of firm digital pressure to the joint margins, or (iii) inflammatory joint swelling.

(c) Lansbury articular index: this is a weighted index of the number of active joints as found in the joint count. Weighting is based upon joint size, as determined by the area of the articular surface (Lansbury, 1958). (See Appendix F for details of the relative weighting of individual joints).

(d) Length of morning stiffness: was taken as the length of time, in minutes, between the subject first awakening, starting to move around in bed and the disappearance of subjective feelings of stiffness. The subject was asked to estimate this time, taken on average, over the previous week.

(e) Wintrobe erythrocyte sedimentation rate (ESR) is taken as reflecting the severity of joint inflammatory processes. Normal values range form 0 to 6.5 mm/hr in healthy young adult males and 0 to 16 mm/hr in healthy young adult females. Patients were referred to the

University Hospital haematology department for sampling and analysis if they had not had previous ESR analysis within the previous 2 weeks.

(f) Grip strength: was taken with the previously described sphygmomanometer cuff. Three trials were given to each hand and the grip strength for each hand was based on the mean of the maximum score recorded over each of the 3 trials. The range was from 20 to 300 mm/Hg.

(g) Present pain intensity (P.P.I.): was recorded on a VAS as previously described.

(h) Rheumatoid factor: this was not taken as a measure of disease activity, per se, but was used as an indicator of sero-positivity or negativity. Rheumatoid factors are defined as "antibodies specific to antigenic determinants on the Fc fragments of human or animal immunoglobulin G" (Carson, 1981). Subjects were referred to the haematology unit for rheumatoid factor titre testing at the same time as testing for ESR, as described above. Rheumatoid factor titration was carried out by the method of Singer and Plotz (1956).

(g) Functional Classification: was assessed by the experimenter and follows the American Rheumatism Association guidelines for classification (from Steinbrocker et al, 1949). Subjects are graded on their ability to perform routine tasks and are then classed into ordinal grades from Levels 1 to 4 (See Appendix G). As with the rheumatoid factor, the functional classification is not

being used primarily as a measure of disease activity, but as a descriptive aid in the classification of patients.

Procedure

All 68 subjects took part in the experiment. The data were collected between the months of April and November, 1984, between the hours of 8.30 a.m. and 7.00 p.m.. Subjects were all tested by the same experimenter and in the same environment at the Rheumatic Diseases out-patient unit of University Hospital.

Each subject read and signed the consent form, after having the procedures explained, and then answered the questions in the personality inventory. An opportunity was given for any questions to be asked. The subject's P.P.I. was then recorded on a visual analogue scale. This also offered the experimenter the opportunity to explain the use of the VAS for subsequent measures of intensity and unpleasantness for each stressor.

Each subject was tested with each of the 3 stressors, delivered in random order, allowing for 1 of 6 possible orders for each subject. The side of delivery of each stressor was also randomized. None of the points chosen for stimulation was spontaneously tender to touch before testing. Threshold and tolerance measures were gathered in the manner outlined above.

Immediately after threshold and tolerance levels were measured for one stressor, VAS ratings of the 2 measures

were obtained with a different recording sheet being used for each stressor. After each procedure was completed, the stimulus site was examined for any possible damage to the skin. Measures of disease activity were then taken with the subject seated for each measure except for the joint count and the two haematological tests. For joint count, the subject was examined in the prone lying position. For the two laboratory tests, the patients were referred to the intravenous section for blood collection immediately after the session was completed.

At the end of the session the subject was given more information about the aims of the study and was afforded another opportunity to ask questions. The length of each each session ranged from 75 to 120 minutes.

Results

The main aim of this study was to examine the relationship between pain responsiveness and disease activity. A secondary objective was to examine the effect of personality and other factors, such as age, sex and length of disease on the main study variables. Where such an analysis seems meaningful, the data will be presented for all subjects as a whole group first, and then the data will be broken down into separate groups by sex.

The results are presented in the following manner. Descriptive data are presented first. Next, the threshold and tolerance findings are reported and the relationship between the rating measures are examined. Then the measures of disease activity are presented and their inter-relationship is analyzed. This is followed by the scores on the main personality variables. Lastly, the relationships between the main study variables are explored and regression equations are presented with pain threshold or tolerance as the dependent variables and the other study variables as the independent variables, with the main focus being on the amount of disease activity present.

Throughout the results of this study, no attempt is made to control statistically for the number of comparisons in related measures, e.g. within the 3 measures of pain threshold, those of pain tolerance, and the 7 measures of disease activity. For each of these variables, one overall Z-score (e.g. of pain threshold) is calculated

for subsequent comparisons in a similar manner to that of Smythe and co-workers (1982). This approach to data analysis is adopted because it is the overall measures of pain responsiveness and disease activity that are of prime interest in this study. Further, the anticipated wide range of individual differences in disease activity and pain responsiveness normally lead to low levels of statistical significance even in the presence of large mean differences. Thus, it is the normal practice, in reporting data of this type, not to make Bonferroni adjustments for the number of comparisons (for example, Davidson and McDougall, 1969; Brown, Fader and Barber, 1973; Smythe et al, 1982). For the present results, the $p < .05$ level is taken as the minimum level of statistical significance.

Descriptive Data

As can be seen from Table 1, there were more females than males in the study, with a ratio of approximately 2:1. The subject population had a mean age in the early fifties and had been suffering from their condition for a mean length of approximately 8 years. There were no significant differences for age or length of time since diagnosis between the male and female subjects. More subjects had rheumatoid factor titre (RHF) positive than negative. Subjects were unevenly distributed between levels of functional classification, with more subjects being in classes 1 and 2 than class 3. No subjects fell into functional class 4. A proportionally larger number of males

Table 1.

Descriptive data of the experimental population.

		ALL SUBJECTS	MALE	FEMALE
		$\bar{X}$	$\bar{X}$	$\bar{X}$
N		68	24	44
AGE	(yrs)	52.5	56.1	50.6
	(S.D.)	12.8	10.7	13.6
LENGTH	(yrs)	8.2	9.0	7.8
	(S.D.)	8.9	7.5	7.3
RHF -	pos.	46	19	27
	neg.	22	5	17
FUNCTIONAL CLASS	1	32	14	18
	2	27	6	21
	3	9	4	5

Legend : Length = Length of time with RA; RHF = Rheumatoid factor titre; Functional Class = RA Functional classification.

than females were in functional class 1. However, overall, no statistically significant differences were found between the sexes for functional classification (X^2 (2 df) = 4.47, p > .05). For RHF, 80% of all males were in the RHF positive group, but no statistically significant difference was found between males and females on RHF classification (X^2 (1 df) = 2.24, p > .05).

Painful Stressors

The data for the values of the pain threshold and tolerance to the three physical stressors - electrical pulse trains (shock), constant pressure algometer (pressure) and the dolorimeter - are shown in Table 2. It can be seen that males had significantly higher pressure pain threshold than females (t = 2.42, p < .05). No other significant differences were found for the threshold values. For pain tolerance, however, males were significantly higher than the females for each of shock, pressure and the dolorimeter (t = 2.30, 2.05 and 2.05 respectively, with p < .05 for each).

Pearson product moment correlations among the physical stressors show considerable variability between the stressors (Table 3). Correlations between the measures at threshold levels were low, but significant, in 2 out of 3 instances (all less than r = .29). The correlations of tolerance measures were higher (values between r = .34 and r = .68) and all were statistically significant beyond the p < .01 level. Further, threshold measures correlated more

Table 2.

Pain Threshold and Tolerance Values for the Three Stressors

	ALL SUBJECTS	MALE	FEMALE	
THRESHOLD	$\bar{X}$ (S.D.)	$\bar{X}$ (S.D.)	$\bar{X}$ (S.D.)	
SHOCK (ma)	1.11 (0.73)	1.29 (0.85)	1.00 (0.63)	
PRESSURE (sec)	8.79 (8.66)	12.27 (10.1)	6.97 (6.75)	*
DOLORIMETER (kg)	2.07 (1.00)	2.05 (0.86)	2.08 (1.32)	
TOLERANCE				
SHOCK (ma)	3.99 (2.64)	5.10 (3.43)	3.36 (1.86)	*
PRESSURE (sec)	67.62 (65.5)	90.15 (72.7)	55.52 (58.7)	*
DOLORIMETER (kg)	5.37 (2.35)	6.15 (2.49)	4.95 (2.19)	*

* = $p < .05$ (t-test between males and females)

Table 3.

Correlation matrix of values for Shock, Pressure and the Dolorimeter at Threshold and Tolerance levels.

	THSH	THPR	THDOL	TOLSH	TOLPR
THSH	-				
THPR	.29**				
THDOL	.15	.20*			
TOLSH	.35**	.42+	.18		
TOLPR	.16	.64+	.29*	.34**	
TOLDOL	.13	.43+	.54+	.38**	.68+

Legend : Thsh = Pain threshold for shock· Thpr = Pain threshold for constant pressure; Thdol = Pain threshold for the dolorimeter; Tolsh = Pain tolerance for shock; Tolpr = Pain tolerance for constant pressure; Toldol = Pain tolerance for the dolorimeter.

* = p < .05
** = p < .01
\+ = p < .001

highly with tolerance levels to the same stressor than with the other stressors at threshold levels.

Visual analogue scale ratings of unpleasantness and intensity show no significant differences in ratings between the sexes for either rating threshold or tolerance levels to any stressor (see Table 4). Taking all subjects together, pain intensity for the dolorimeter at threshold was rated significantly higher than unpleasantness ($t = 3.61$, $p < .01$) (Table 4). No other significant differences in ratings were found at threshold levels of stimulation. For ratings at pain tolerance, intensity was rated significantly higher than unpleasantness for constant pressure ($t = 2.35$, $p < .05$). Differences between ratings for threshold and tolerance between the 3 stressors were also examined. No significant differences were found for intensity ratings between stressors at either threshold or tolerance levels. For unpleasantness, however, tolerance of shock was significantly higher than that of dolorimeter ($t = 2.21$, $p < .05$). At threshold, both shock and pressure were rated as being significantly more unpleasant than the dolorimeter ($t = 2.14$, $p < .05$ and $t = 2.61$, $p < .01$).

Pearson product moment correlations for the rating measures for intensity and unpleasantness at threshold and tolerance were calculated and are shown in Table 5. In general, unpleasantness ratings between stressors for either threshold and tolerance are more highly correlated than those for intensity. Similar measures, for example

Table 4.

V.A.S. Ratings of Intensity and Unpleasantness for Threshold and Tolerance to the Three Stressors

MEASURE	INTENSITY	UNPLEASANTNESS	
THRESHOLD	$\bar{X}$ (S.D.)	$\bar{X}$ (S.D.)	
SHOCK	3.3 (2.6)	2.8 (2.8)	
PRESSURE	3.0 (2.3)	2.8 (2.6)	
DOLORIMETER	3.2 (2.4)	2.3 (2.3)	**
TOLERANCE			
SHOCK	10.1 (3.4)	9.5 (3.3)	
PRESSURE	10.3 (3.0)	9.5 (3.5)	*
DOLORIMETER	9.4 (2.9)	8.9 (3.4)	

* = $P < .05$
** = $P < .01$

Table 5.

Correlation matrix of visual analogue scale ratings for intensity and unpleasantness at threshold and tolerance levels.

	INTENSITY						UNPLEASANTNESS				
	THRESHOLD			TOLERANCE			THRESHOLD			TOLERANCE	
	SH	PR	DOL	SH	PR	DOL	SH	PR	DOL	SH	PR
ITHSH											
PR	.45+										
DOL	.48+	.51+									
ITOSH	.39+	.16	.24*								
PR	.09	.37+	.26*	.21*							
DOL	.10	.22*	.49+	.36**	.53+						
UTHSH	.53+	.58+	.52+	.20	.26*	.24*					
PR	.34**	.61+	.56+	.16	.38+	.34**	.62+				
DOL	.35**	.39+	.52+	.19	.17	.29**	.53+	.58+			
UTOSH	.21*	.26*	.35**	.53+	.38+	.57+	.47+	.29**	.29**		
PR	.05	.17	.27*	.28*	.73+	.49+	.17	.44+	.31**	.46+	
DOL	.15	.24*	.33**	.43+	.47+	.76+	.30**	.41+	.46+	.72+	.56**

Legend : Ithsh = Perceived intensity at shock threshold; Pr = constant pressure; Dol = dolorimeter; Itosh = perceived intensity at shock tolerance; Uthsh = Perceived unpleasantness at shock threshold; Utosh = Perceived unpleasantness at shock tolerence.

* = $p < .05$
** = $p < .01$
\+ = $p < .001$

intensity threshold for shock and unpleasantness threshold for shock (r =.53), are more highly correlated than different measures within the same stressor, for example, intensity threshold for shock and intensity tolerance for shock (r = .39). Correlations between different measures and different stressors are generally low and non-significant, for example between intensity tolerance for shock and unpleasantness threshold for pressure (r = .16). The two pressure stressors showed a more significant pattern of correlations between each other than either of these ratings have individually with shock.

Disease Activity

The values for the measures of disease activity for all subjects combined, and for males and females individually, are shown in Table 6. Grip strength was, not surprisingly, significantly higher in men than in women ($t = 3.13$, $p < .01$). No other significant differences were found between the sexes. However, although these differences were not significant, the males showed a pattern of lower disease activity on all measures except present pain intensity. It can be seen from Table 7 that there is a moderate, but significant, pattern of correlations between most of the measures of disease activity. The main exception to this is for present pain intensity which is significantly correlated only with the number of active joints ($r = .22$, $p < .05$) and the Lansbury articular index ($r = .20$, $p < .05$). The number of active joints shows the strongest

Table 6.

Values of Measures of Disease Activity.

	ALL SUBJECTS	MALE	FEMALE	
MEASURE	$\bar{X}$ (S.D.)	$\bar{X}$ (S.D.)	$\bar{X}$ (S.D.)	
NUMBER	10.2 (8.1)	7.7 (7.4)	11.5 (8.2)	
GRIP (mm/Hg)	132.6 (73.0)	172.5 (89.0)	110.5 (51.9)	**
STIFF (hrs)	0.96 (1.2)	0.68 (0.9)	1.1 (1.4)	
TTF (hrs)	8.5 (3.3)	9.4 (2.9)	8.1 (3.5)	
LANSBURY	42.3 (37.4)	34.2 (36.1)	48.1 (37.6)	
ESR (ml/min)	28.7 (15.5)	23.8 (12.7)	31.4 (16.5)	
PPI	2.8 (2.5)	3.2 (2.8)	2.6 (2.4)	

Legend : Number = number of active joints; grip = grip strength stiff = length of morning stiffness; TTF = time to fatigue; Lans = Lansbury articular index; ESR = erythrocyte sedimentation rate; PPI = present pain intensity.

** = $p < .01$

Table 7.

Correlation matrix of measures of disease activity.

	PPI	NUMBER	GRIP	STIFF	T.T.F.	LANS.	E.S.R.
PPI	-						
UMBER	.22*	-					
GRIP	-.11	-.49+	-				
STIFF	.11	41+	-.44+	-			
T.T.F.	-.17	- .39+	.36+	-.27*	-		
LANS.	.20*	.83+	-.39+	.32**	-.40+	-	
E.S.R.	.00	.44+	-.45+	.34**	-.14	.45+	-

Legend : Number = number of active joints; grip = grip strength; stiff = length of morning stiffness; TTF = time to fatigue; Lans = Lansbury articular index; ESR = erythrocyte sedimentation rate; PPI = present pain intensity.

* = $p < .05$
** = $p < .01$
\+ = $p < .001$

pattern of correlations with the other measures of disease activity.

Basic Personality Inventory (BPI)

The four main personality variables, which were selected a priori to be of importance to this study, are hypochondriasis, depression, anxiety and denial. The scores for these, along with the scores of the other BPI scales, are shown in Table 8 and Figures 1 and 2. It can be seen that only for the denial scale was there a significant difference between the two sexes, with males responding higher than the females ($t = 2.31$, $p < .05$). However, with the exception of hypochondriasis, all the scales fall within the normative values established for the BPI (Jackson, 1989). For hypochondriasis, men scored 1 standard score above the published values. No other scales of the BPI revealed significant differences between the sexes.

Relationship between the main study variables

The main objective of this study was to examine the relationship between pain responsiveness and disease activity. Three measures of pain threshold and tolerance, and seven measures of disease activity were gathered. In order to decrease the variability of response pattern to the individual stressors and to simplify the initial examination of the relationship between the main variables, each of the measures of pain threshold, tolerance and

Table 8.

Basic Personality Inventory Scores

	ALL SUBJECTS		MALE		FEMALE		
	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D.)	
HYPOCHONDRIASIS	9.3	(3.0)	8.7	(3.2)	8.0	(3.0)	
DEPRESSION	3.7	(2.9)	3.7	(3.7)	3.7	(3.3)	
DENIAL	7.4	(3.0)	8.5	(3.4)	6.8	(2.6)	*
ANXIETY	6.7	(3.3)	6.7	(4.2)	6.8	(2.7)	
INTERPERSONAL PROBLEMS	6.3	(2.9)	6.6	(3.3)	6.1	(2.7)	
ALIENATION	3.0	(2.2)	3.1	(2.3)	2.9	(2.2)	
PERSECUTORY IDEAS	3.5	(2.2)	3.6	(2.3)	3.5	(2.2)	
THINKING DISORDER	2.8	(1.9)	3.2	(2.1)	2.5	(1.8)	
IMPULSE EXPRESSION	5.2	(3.2)	5.5	(3.5)	5.1	(3.1)	
SOCIAL INTROVERSION	4.1	(3.2)	3.7	(2.2)	4.4	(3.6)	
SELF DEPRECATION	2.3	(2.5)	2.3	(2.6)	2.3	(2.0)	
DEVIATION	1.9	(2.0)	1.9	(2.2)	1.9	(1.8)	

* = $p < .05$

Legend : Main study variables above the dotted line.

Figure 1

Basic Personality Inventory Scores for the Women

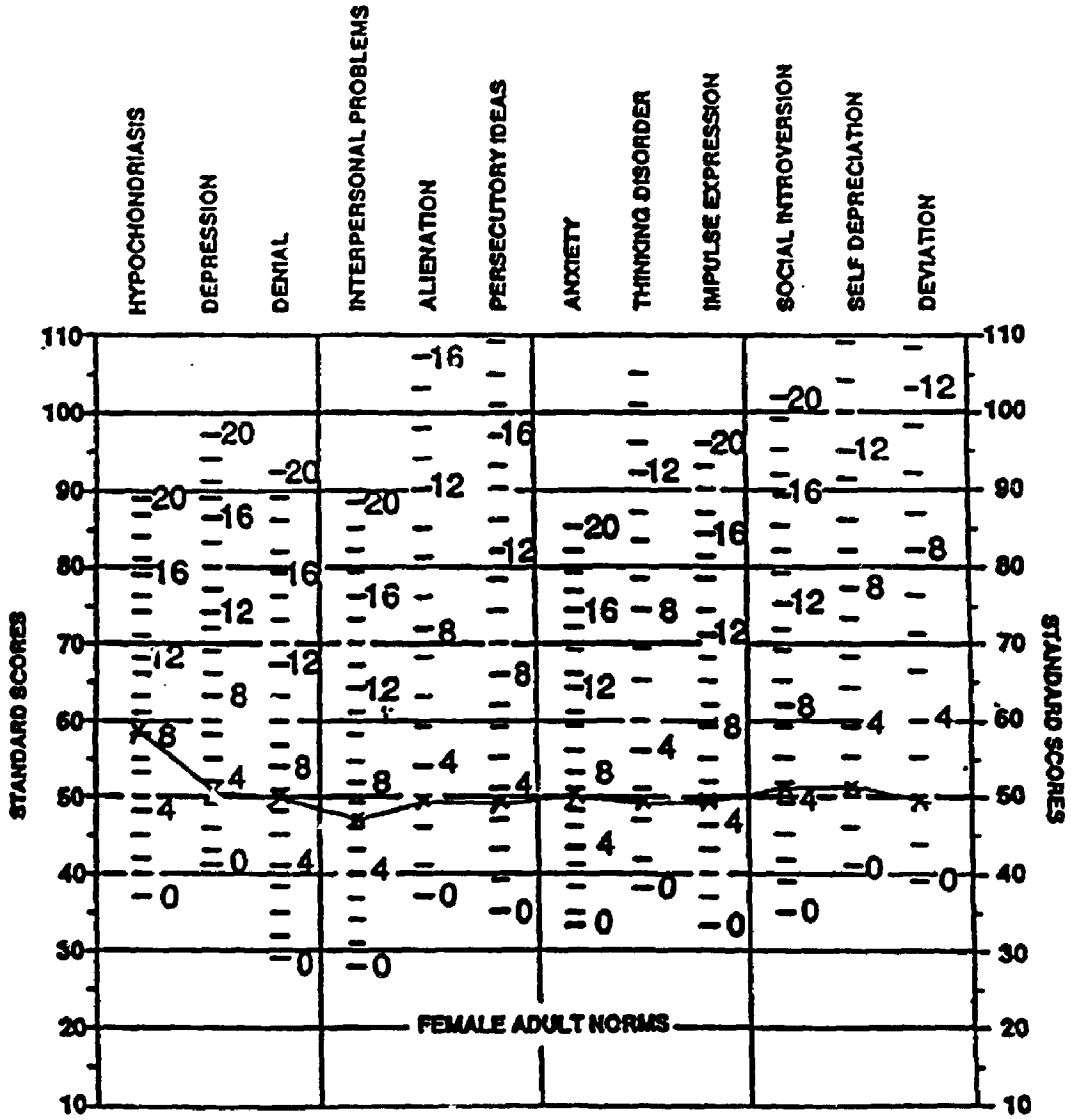
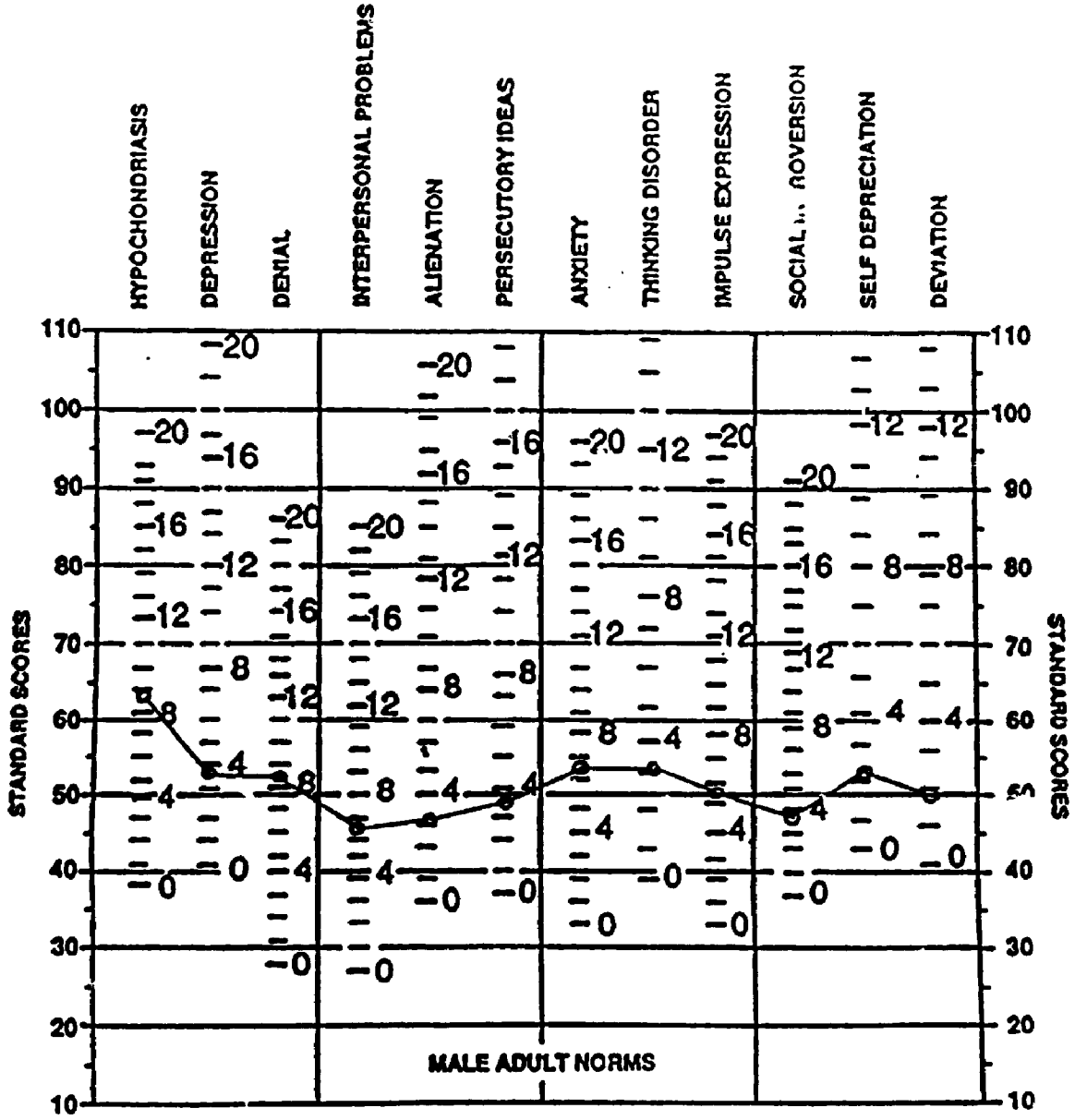


Figure 2

Basic Personality Inventory Scores for the Men



disease activity was standardized and compounded to yield one measure each of pain threshold, pain tolerance and disease activity. They were compounded in the following manner:-

1. Pain threshold = (Zthrshock + Zthrpress + Zthrhdol) / 3
where Zthrshock, Zthrpress and Zthrdol represent the standard scores of pain threshold to shock, pressure and the dolorimeter respectively.

2. Pain tolerance = (Ztolshock + Ztolpress + Ztoldol) / 3
where Ztolshock, Ztolpress and Ztoldol represent the standard scores of pain tolerance to shock, pressure and the dolorimeter respectively.

3. Disease activity = ((ZNUMB + (-ZTTF) + ZPPI + ZLANS + ZESR + (-ZGRIP) + ZSTIFF) / 7

where ZNUMB, ZTTF, ZPPI, ZLANS, ZESR, ZGRIP and ZSTIFF represent the standard scores of the number of active joints, time to fatigue, present pain intensity, Lansbury articular index, ESR, grip strength and length of morning stiffness respectively. The inverse of time to fatigue and grip strength were taken because both these measures represent a decrease in disease activity as their scores increase. The others show increasing disease activity as scores increase. Single measures of disease activity have previously been standardized and reported in a similar compounded manner (Smythe et al, 1982).

The values for the compounded and standardized scores of disease activity, pain threshold and pain tolerance for

both men and women are shown in Table 9. It can be seen that men had significantly higher pain tolerance and lower levels of disease activity than women ($t = 2.89$, $p < .01$, and $t = 2.42$, $p < .05$ respectively). For pain threshold the values for men were higher than the women, but this did not reach statistical significance ($t = 1.87$, $p < .06$). All these statistics were two-tailed t-tests with pooled variance estimates.

The correlations of the main study variables for all subjects taken together are shown in Table 10. Present pain intensity is included separately in the correlation matrix because, from previous research, it has been shown to have an effect on personality and pain responsiveness. It can be seen that pain threshold (PTH) is not significantly correlated with disease activity (DIS) but that pain tolerance (TOL) shows a low, but statistically significant negative correlation with disease activity ($r = -.26$, $p < .05$). Of the personality variables, hypochondriasis (HYP) shows the largest number of significant correlations with the other non-personality variables. It is positively correlated with age, present pain intensity, and disease activity, as well as with denial (DEN) and depression (DEP) and is negatively correlated with pain tolerance. Anxiety shows only one significant correlation, being negatively correlated with the length of time of disease (LEN). Depression is only significantly correlated with hypochondriasis. In general the strength of association

Table 9.

Z-Score values for pain threshold, pain tolerance and disease activity for men and women

	THRESHOLD		TOLERANCE		DISEASE	
	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D.)
MEN	0.20	(.72)	0.35 **	(.88)	-0.23 *	(.53)
WOMEN	-0.11	(.62)	-0.19	(.61)	0.12	(.46)

* = $p < .05$, t-test between males and females.
** = $p < .01$ t-test between males and females.

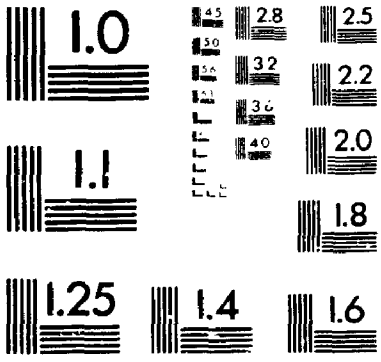


Table 10.

Correlation matrix of the main study variables for all subjects

	HYP	DEN	DEP	ANX	DIS	PPI	PTH	TOL	AGE	LEN
HYP	-									
DEN	.25*	-								
DEP	.22*	.03	-							
ANX	.09	.04	.17	-						
DIS	.24*	.07	.00	-.02	-					
PPI	.50+	.31**	-.01	.04	.39+	-				
PTH	.15	.07	-.15	-.13	.02	.22*	-			
TOL	-.21*	-.10	-.10	-.01	-.26*	-.04	.64+	-		
AGE	.28**	.51+	.16	-.03	.24*	.17	.01	-.18	-	
LEN	.10	.14	-.16	-.33**	.31**	.20	.06	-.11	.25*	-

Legend : Hyp = Hypochondriasis; Dep = Depression;
Den = Denial; Anx = Anxiety, Dis = Disease activity;
PPI = Present pain intensity; Pth = Pain threshold;
Tol = Pain tolerance; Length = Length of time of condition.

* = $p < .05$
** = $p < .01$
\+ = $p < .001$

between the variables, although significant in some cases, is low.

Correlation matrices were formed for the same variables and are displayed separately for women and for men in Table 11a and 11b. It can readily be seen that there are different patterns of association between the variables for the two sexes. Pain tolerance is significantly negatively cor elated with disease activity for men but not for women ($r = -0.54$ and $r = 0.02$ respectively). Neither sex shows a significant relationship between disease activity and pain threshold. Pain tolerance is significantly negatively correlated with hypochondriasis and present pain intensity for men but not for women. For women, hypochondriasis is significantly correlated with pain threshold but this relaticnship does not exist for the men. For both sexes, age is positively correlated with denial and negatively correlated with anxiety.

Regression equations of pain threshold and pain tolerance on the main study variables.

A series of stepwise multiple regression equations were next developed to see how much of the variance of pain threshold or pain tolerance could be accounted for by the main study variables (Table 12). Because gender was previously shown to have a significant effect on pain threshold and tolerance, the initial equations were carried out firstly controlling for sex and then not controlling for sex. In Table 12, only those equations that reach

Table 11a.

Correlation matrix of main study variables - Females

	HYP	DEP	DEN	ANX	DIS	PPI	TH	TOL	AGE	LEN
HYP	-									
DEP	.32*	-								
DEN	.33*	.16	-							
ANX	.23	.24	-.13	-						
DIS	.15	-.06	.23	-.12	-					
PPI	.37**	.00	.29*	.00	.51+	-				
PTH	.30*	-.24	.17	-.05	.13	.23	-			
TOL	.06	-.16	-.11	.15	.02	.10	.63+	-		
AGE	.26*	.21	.46+	-.04	.34*	.13	.09	-.18	-	
LEN	.07	-.11	.13	-.37**	.36**	.27	-.05	-.14	.24	-

Table 11a.

Correlation matrix of main study variables - Males

	HYP	DEP	DEN	ANX	DIS	PPI	PTH	TOL	AGE	LEN
HYP	-									
DEP	-.01	-								
DEN	.11	-.23	-							
ANX	-.05	.08	.22	-						
DIS	.52**	.20	.05	.07	-					
PPI	.66+	-.06	.27	.09	.35*	-				
PTH	-.12	.07	-.18	-.22	-.02	.08	-			
TOL	-.66+	-.01	-.31	-.16	-.54**	-.36*	.60+	-		
AGE	.28	.00	.55**	-.03	.26	.13	.09	-.18	-	
LEN	.13	-.34*	.12	-.30	-.32	.16	.19	-.15	.23	-

* = p < .05
** = p < .01
+ = p < .001

Legend : Hyp = Hypochondriasis; Dep = Depression; Den = Denial; Anx = Anxiety, Dis = Disease activity; PPI = Present pain intensity; Pth=Pain threshold; Tol = Pain tolerance; Length = Length of time of condition.

Table 12.

Summary of Stepwise Multiple Regressions of Threshold and Tolerance measures on the predictor variables - including Hypochondriasis.

VAR	SEX	R^2	ADR^2	F	SIG	VARS IN EQUATION (Rsq CHANGE)
TH	C	.15	.09	2.67	.04	RHF(9),DEP(2),HYP(2),SEX(1)
TH	NC	.14	.10	3.20	.03	RHF(9),DEP(2).HYP(2)
TOL	C	.27	.20	4.30	.002	SEX(11),AGE(7),HYP(3),RHF(3),DIS(2)
TOL	NC	.20	.15	3.78	.008	RHF(9),DIS(7),HYP(3),AGE(1)
TH	1	-	-	-	NS	
TH	2	.32	.25	4.35	.006	HYP(12),RHF(10),DEP(7),LEN(2)
TOL	1	.61	.49	5.33	.004	HYP(44),AGE(8),ANX(5),DIS(3),RHF(1)
TOL	2				NS	
THSH	C	-	-	-	NS	
	NC	-	-	-	NS	
PR	C	.09	.12	2.69	.03	SEX(8),DEN(5),DEN(5),HYP(1),ANX(1)
	NC	.09	.06	3.10	.05	RHF(6),DEN(3)
DOL	C	-	-	-	NS	
	NC	-	-	-	NS	
TOSH	C	.24	.20	6.13	.001	SEX(10),DIS(9),RHF(4)
	NC	.21	.18	8.17	.001	RHF(12),DIS(9),
PR	C	.18	.13	3.18	.02	SEX(7),HYP(6),RHF(3),DEN(2)
	NC	-	-	-	NS	
DOL	C	.21	.14	3.13	.01	DIS(7),AGE(6),SEX(4),HYP(2),RHF(1)
	NC	.16	.10	2.85	.03	DIS(7),AGE(3),RHF(3),HYP(1)
THSH	2	-	-	-	NS	
PR	2	-	-	-	NS	
DOL	2	.19	.13	2.96	.05	RHF(8),DEP(7),HYP(4)
TOSH	2	-	-	-	NS	
PR	2	-	-	-	NS	
DOL	2	-	-	-	NS	
THSH	1	-	-	-	NS	
PR	1	-	-	-	NS	
DOL	1	.51	.43	6.71	.003	AGE(32),DEP(16),HYP(3)
TOSH	1	.52	.33	2.85	.05	DIS(25),RHF(10),ANX(4),LEN(4),DEN(4),AGE(4)
PR	1	.57	.50	7.99	.001	HYP(39),DEN(11),LEN(6)
DOL	1	.59	.46	4.81	.006	HYP(44),AGE(8),RHF(2),DEN(2),DIS(1)

Legend : Th = Combined Z-score of threshold; Tol = Combined Z-score of tolerance; Dol = Dolorimeter; Anx = Anxiety; RHF = rheumatoid factor; Dep = Depression; Hyp = Hypochondriasis; Dis = Z-score of disease activity; Length = Length since diagnosis; Den = Denial; C = Sex included in the equation; NC = sex not included in the equation; Sex (1) = male; Sex (2) = female; ADR^2 = Adjusted R^2; R^2 Change = R^2 change accounted for by the addition of the variable preceding the parenthesis.

statistical significance are reported. Also, only those variables that account for at least one percent of the explained variance are reported in the tables. No adjustment has been made statistically for the number of multiple regression equations that are reported.

The first series of equations were all statistically significant beyond the $p < .05$ level, but account for only a small percentage of the variance (between $R^2 = .14$ and $R^2 = .27$). Adjusting for the number of variables in the equation resulted in even less of the variance being accounted for (adjusted R^2 between .09 and .20). The equations for tolerance showed greater statistical significance than those for threshold. Controlling for sex made little difference to threshold but it did for pain tolerance as it accounted for eleven percent of the variance. Rheumatoid factor is the most important single predictor for pain threshold while sex and rheumatoid factor, followed by disease activity were the most important for pain tolerance.

Next, regression equations were developed for pain threshold and tolerance for each sex taken alone. For women, only the equation for pain threshold was significant, accounting for 32% of the variance (adjusted $R^2 = .25$). Here, hypochondriasis, rheumatoid factor and depression were all important predictors, accounting for 29% of the variance between them. For men, only the equation for pain tolerance reached statistical

significance. This equation accounted for 61% of the variance (adjusted R^2 = .49) and the largest single predictor was hypochondriasis.

In order to further examine the effect of the predictor variables on pain threshold and tolerance, regression equations were next developed for individual measures of pain threshold and tolerance to each of the three stressors taken separately. The same strategy as before was adopted, that is, firstly controlling and not controlling for sex, and then looking at the sexes individually. In this next series of equations, controlling and not controlling for sex, the magnitude of the variance accounted for in the individual stressors is less than that of the compounded variables of pain threshold and pain tolerance. As well, for pain threshold, only the equations for pressure reached statistical significance. For these, sex and rheumatoid factor were the most important predictor variables.

In the equations for pain tolerance to the individual stressors, 5 of the 6 regression equations reached statistical significance, with the equations for shock showing the highest significance levels. For each of these equations, sex, rheumatoid factor, and disease activity were the most important predictor variables. Disease activity came first or second as a predictor in four of these equations.

Taking women alone, only the equation for dolorimeter threshold reached statistical significance. The variance

accounted for by the regression equation was 19% (adjusted R^2 = .13) with rheumatoid factor and depression being the important predictors. None of the regression equations for the stressors at pain tolerance reached statistical significance.

Taking men alone, the strength of the equations are much stronger, with between 51% and 59% of the variance being accounted for (adjusted R^2 between .33 and .50). The regression equations for the stressors at pain tolerance accounted for a higher percentage of the variance than those of pain threshold. At threshold, only the equation for the dolorimeter threshold reached statistical significance, with age and depression being responsible for most of the variance that is accounted for in the regression equation. At tolerance, either disease activity or hypochondriasis is the largest single predictor in the equations for tolerance to shock, pressure and the dolorimeter.

Due to the fact that rheumatoid factor titre showed up as an important variable in the regression equations, the main study variables were examined for differences between the groups, i.e. Rh factor positive or negative. No significant differences were found (by t-test) on any of the demographic variables, on any of the pain rating measures, or any of the 12 dimensions of the Basic Personality Inventory. However, the Rh factor negative group showed significantly lower overall levels of disease

activity ($t = -2.15$, $p < .05$). Although none of the individual measures of disease activity showed statistically significant differences between the groups, the rheumatoid factor negative group had consistently lower scores on the measures of disease activity.

The other important difference between the groups lay in the pain threshold and tolerance measures. Here, the Rh factor negative group had significantly lower overall pain threshold levels ($t = -3.31$, $p < .01$) and pain tolerance levels ($t = -2.49$, $p < .05$), than the Rh factor positive group. Within pain threshold, both pain threshold to shock ($t = -2.08$, $p < .05$) and to constant pressure ($t = -2.81$, $p < .01$) showed significant differences. At the tolerance level, only pain tolerance for shock showed significant differences between the groups ($t = -2.85$, $p < .01$). As well, it is interesting to note that, in the series of multiple regression equations, only in two equations (both for pain threshold) did Rh factor come first as a predictor when sex (gender) was also included in the equation.

In the regression equations reported in Table 12, when either hypochondriasis or disease activity is the largest single predictor in an equation, the other variable does not account for a large percentage of the variance in that particular equation. For example, in the equation for dolorimeter tolerance for men only, hypochondriasis is responsible for 44% of the variance in the equation whereas disease activity is responsible for only one percent. In a

similar manner, for the compounded variable of pain tolerance for men, hypochondriasis accounts for 44% of the variance with disease activity accounting for only three percent. From Table 11b it can be seen that both hypochondriasis and disease activity are significantly negatively correlated with pain tolerance and that both of these variables are positively correlated with each other.

As the main objective of this study was to examine the relationship between disease activity and pain responsiveness, it was decided to run the same regression equations as shown in Table 12, but to omit the predictor variable of hypochondriasis and to examine any major changes that result from this omission.

The results of these equations are shown in Table 13. Generally, the strength of the predictor equations is slightly lower without hypochondriasis in the equation. In two equations, where hypochondriasis was the largest single predictor, for pain tolerance for men and for dolorimeter tolerance for men, disease activity became the largest single predictor when hypochondriasis was eliminated from the regression equation. However, for two of the other statistically significant equations in Table 12 which have hypochondriasis as the main predictor, i.e. for Z-threshold for women and tolerance to pressure for men, disease activity does not replace hypochondriasis.

Table 13.

Summary of Stepwise Multiple Regressions of Threshold and Tolerance measures on the predictor variables - excluding Hypochondriasis.

VAR	SEX	R^2	ADR^2	F	SIG	VARS IN EQUATION (R^2 CHANGE)
TH	C	.13	.09	3.14	.03	RHF(9),DEP(2),SEX(2)
TH	NC	.11	.08	4.05	.02	RHF(9),DEP(2)
TOL	C	.24	.19	4.80	.002	SEX(11),AGE(7),RHF(3),DIS(3)
TOL	NC	.18	.14	3.52	.03	DIS(7),RHF(9),AGE,(1)
TH	1	-	-	-	NS	
TH	2	.19	.12	2.89	.05	RHF(10),DEP(7),LEN(1)
TOL	1	.49	.34	3.30	.03	DIS(30),AGE(10),RHF(4),ANX(3),DEP(2)
TOL	2	-	-	-	NS	
THSH	C	-	-	-	NS	
	NC	-	-	-	NS	
PR	C	.18	.13	4.06	.01	SEX(8),RHF(5),DIS(4)
	NC	.09	.06	3.10	.05	RHF(6),DEN(3)
DOL	C	-	-	-	NS	
	NC	-	-	-	NS	
TOSH	C	.24	.20	6.13	.001	SEX(10),DIS(9),RHF(4)
	NC	.21	.19	8.17	.001	RHF(12),DIS(9)
PR	C	.13	.08	2.80	.05	SEX(6),RHF(3),DEN(3)
	NC	-	-	-	NS	
DOL	C	.20	.13	2.90	.02	DIS(7),SEX(4),AGE(6),RHF(1),DEN(1)
	NC	.14	.10	3.27	.03	DIS(7),AGE(4),RHF(3)
THSH	2	-	-	-	NS	
PR	2	-	-	-	NS	
DOL	2	-	-	-	NS	
TOSH	2	-	-	-	NS	
PR	2	-	-	-	NS	
DOL	2	-	-	-	NS	
THSH	1	-	-	-	NS	
PR	1	-	-	-	NS	
DOL	1	.49	.41	6.18	.004	AGE(32),DEP(16),DIS(3)
TOSH	1	.52	.33	2.81	.05	DIS(25),RHF(10),ANX(3),DEN(4),AGE(4),DEP(4)
PR	1	-	-	-	NS	
DOL	1	.37	.27	3.80	.03	DIS(24),AGE(11),DEN(2)

Legend: Th = Combined Z-scores of pain threshold; Tol = Combined Z-scores of pain tolerance; Sh = shock; Pr = constant pressure; Dol = dolorimeter; Anx = Anxiety; RHF = Rheumatoid factor titre; Dep = Depression; Hyp = hypochondriasis; Dis = Z-score of disease activity; Len = length of time since diagnosis; Den = Denial; C = Sex included in the regression; NC = Sex not included in the regression; Sex (1) = male; Sex (2) = female; ADR^2 = adjusted R^2; R^2 change = R^2 change accounted for by the addition of the variable preceding the parenthesis.

Discussion

The major aim of this study was to investigate the relationship between pain responsiveness and varying levels of disease activity in rheumatoid arthritis. The results of the study indicate that there is only a weak, but statistically significant, negative correlation between pain tolerance and disease activity. However, no significant relationship was found between disease activity and pain threshold.

Multiple regression analyses, with pain threshold and tolerance as the dependent variables, both confirmed and extended these findings. The patterns of association between the independent and dependent measures varied across the different stressors. Gender, disease activity, hypochondriasis and, surprisingly, rheumatoid factor titre, were the most important predictor variables of pain threshold and pain tolerance.

The sample of subjects in this study conform to normally expected parameters for a population of patients with rheumatoid arthritis in their middle age (O'Dell, 1977). More subjects were rheumatoid factor (RhF) positive than negative, a typical finding (Alarcon et al, 1982). In this study, the rheumatoid factor titre was taken because it is a routine diagnostic measure, not as a measure of disease activity, per se. It was included as a variable in the regression equations because previous research had pointed to the presence of differing personality styles

between patients who were RhF positive and those who were RhF negative. However, as subsequent analyses showed, it turned out to be an important predictor variable in the regression of pain threshold and tolerance on the other variables. Therefore, the possible importance of the rheumatoid factor will be addressed later in this chapter.

More subjects fell into functional class 1 or 2, than in the other two categories. As well, although this was not statistically significant, there were more men than women in functional class 1.

Pain threshold and tolerance measures.

When the data from the males and the females are considered together, it can be seen that there is a wide range of individual difference of response to each stressor at both threshold and tolerance levels. In fact, for the constant pressure algometer, the standard deviation of the scores at threshold and tolerance levels almost equaled that of the mean scores (approximately 97% of the mean scores). The variability for shock (65% of the mean) and the dolorimeter (46%) were less than that of constant pressure, but were still large. These results are in general agreement with previous data (Scudds, 1984; Harris and Rollman, 1983; Davidson and McDougall, 1969; Clark and Bindra, 1956). For example, using the same 3 stressors, Scudds (1984) found standard deviations equal to, or greater than, mean values for each of shock and constant

pressure, but smaller standard deviations for the dolorimeter (approximately 50% of the mean values).

The strength of the correlations between the 3 physical measures was low at pain threshold levels and moderate at tolerance levels. Generally correlations were higher within stressors than within measures; that is, threshold to shock was more highly correlated with tolerance to shock than with threshold to either constant pressure or threshold to the dolorimeter. These results agree with those of Clark and Bindra (1956), and Davidson and McDougall (1969), but differ from those of Harris and Rollman (1983). Therefore, the characteristics of each stressor - shock, constant pressure or the dolorimeter - seem to be more associated within themselves in this study than the actual measures, i.e. pain threshold and pain tolerance levels across stressors. The low correlations between the measures indicate that the data from one stressor may not always be used to predict responses to another stressor.

These findings reinforce the differential utility of using more than one physical stressor in experimental studies. The smaller range of individual difference in responsiveness to the dolorimeter makes it a useful tool for finding statistically significant differences between groups. As well, the nature of each stressor is different. Trains of electrical pulses produce a "phasic", or, fast growing pain, whereas constant pressure produces a "tonic" pain which is presumed to more adequately mimic that of

clinical pain. Each stressor might alter differently in response to intervening therapies. The dolorimeter, having both phasic and tonic components, could well be expected to change in a different manner to the other two stressors while capturing some of the qualities of each.

In the present sample of patients, the men had significantly higher pain thresholds to constant pressure than the women. Neither of the other two stressors showed statistically significant differences between the sexes. However, men had significantly higher pain tolerance levels than the women to each of the three stressors. These results are interesting because they lend further support to a growing body of data which points to higher pain threshold and/or tolerance levels in men when compared to women (Harris and Rollman, 1983; Nottermans and Tophoff, 1975; Jaremko et al, 1981). However, Clark and Mehl (1971) did not find differences in responsiveness between the sexes using a radiant heat stressor.

It is possible that sex differences may result from the demands of the experimental situation, with men wishing to appear more stoical in the presence of the experimenter. This is not an entirely adequate explanation, however, as none of the other subjects was present at the testing or knew the results of any of the other subjects. As well, each subject was given exactly the same instructions about the experimental procedures.

The notion of men having higher pain threshold and tolerance levels runs somewhat contrary to the commonly held view that women can "put up with" pain more than men in the normal, daily context. However, as Archer (1976) concluded, "women show lower thresholds than men to touch, pain, hearing, pressure and rod vision". They are more sensitive to a wide variety of stimuli, not just pain.

The presence of different pain tolerance levels between the sexes is more problematic, but the answer may lie in the actual measure of responsiveness. In the experimental context, physical measures are used. In the clinical milieu, behavioral measures, e.g. pain complaint levels, are used. It may well be that, when men are placed in a painful clinical situation, they complain louder and longer than women. In short, they may complain more. However, this hypothesis has yet to be validated.

The physical stressors were not highly correlated with each other. However, visual analogue score ratings of intensity and unpleasantness of each measure did not differ significantly from each other at either threshold or tolerance levels. For example, no significant differences were found between ratings of intensity or unpleasantness to each of the 3 stressors at threshold levels. This also held true at tolerance levels. This indicates a consistency of ratings across stressors for both the intensity and unpleasantness ratings.

Across ratings of intensity and unpleasantness, the

situation is a little different. All mean ratings of unpleasantness were lower than those of intensity. However, only two of these differences, the ratings at threshold for the dolorimeter and at pain tolerance to constant pressure, reached statistically significant levels. This is in partial agreement with Scudds (1984) who, using the same measures, found significant differences between all ratings except pain tolerance to shock.

The correlations between the ratings of intensity and unpleasantness were higher than the correlations between the physical stressors. They also demonstrated a consistent and logical pattern in their intercorrelations. Thus, the rating of intensity at threshold to shock was more highly correlated with its most similar measure - unpleasantness at threshold to shock - than with any other measure. Further, the strength of the correlations with the other rating measures followed a consistent pattern, i.e., in descending order, the perceived intensity for shock at threshold was next most highly correlated with intensity ratings at threshold to pressure and the dolorimeter, then unpleasantness ratings at threshold, then tolerance ratings of intensity and lastly tolerance ratings of unpleasantness. This pattern of ratings is also evident with and between ratings of the other stressors.

These findings certainly satisfy the requirements of convergent and discriminant validity for these measures and stressors (Campbell and Fiske, 1959). Thus, although the

original ratings are very similar in absolute values, they are sensitive enough to discriminate between small differences in these values. This means that ratings, although quite similar, are appropriately different across rating measures and stressors. Therefore, the perceived quality of the stressors is different in each case.

Indices of Disease Activity.

The indices of disease activity showed that, as a whole group, the patients were experiencing mild to moderate levels of disease activity (Lansbury, 1958, Bombardier et al, 1982). Although mean values of disease activity were higher in women than in men for most of the individual measures, only for grip strength was there a statistically significant difference ($p < .01$) between the sexes. However, the composite Z-score of disease activity showed that women had a significantly higher ($p < .05$) level of disease activity than the men. The standard score of disease activity was adopted in this study because single measures of disease activity may not truly reflect fine differences between patients over time. As well, there is a need to control statistically where multiple outcome measures are involved (Smythe et al, 1982). The standard score that is used in the present study does not assume any preferential weighting of individual variables with regards to the "clinical meaningfulness" of each individual measure (Buchanan and Tugwell, 1985,.

The measures employed were all standard indices of

disease activity, commonly used in practice. However, when the intercorrelations amongst the variables are examined, not all the measures of disease activity show significant correlations with each other. As well, the strength of the correlations is generally in the mild to moderate range (most between r = .22 and r = .49). This is in agreement with previous reports (Mallya and Mace, 1981; Grindulis et al, 1983; Rhind et al; 1987). The strongest pattern of associations is between the number of active joints and the other variables. However, the present pain intensity showed the fewest number of correlations with the other variables, with only two weakly significant correlations.

It is not surprising that the strength of the correlations between the various measures is not high. This presumably reflects the fact that each variable measures a different aspect of disease activity and reinforces the necessity of using multiple measures. However, as pain is one of the most important symptoms of active disease in rheumatoid arthritis (Anderson et al, 1985; Kazis et al, 1983), it might reasonably be expected to correlate well with other measures of disease activity.

The measure for pain used in this study was a 15 cm visual analogue scale, which has been used successfully in many other studies. But the specific instructions for its use may be different from other studies. Huskisson, alone and with others (1972, 1974, 1982), has shown that the VAS pain scale is a reliable and valid measure for pain. As

well, he has pointed out that the instructions given to the patient, and the end points of the scale, can make a considerable difference to the results. In the case of this study, the subjects were asked to rate their pain as they were experiencing it "at this moment", that is, sitting and at rest. The sample of patients in this study were, on average, suffering from only mild to moderate levels of disease activity. As such, it might reasonably be expected that they would not report much pain when at rest. This is borne out by the mean pain score of 2.8 on a 15 cm scale, which is a low level of pain.

The results of a very recent study with R.A. patients lend support to this argument (Badley and Papageorgiou, 1989). Using visual analogue scales, they found very low correlations between scores of pain at rest and on movement. As well, they found low correlations between overall levels of pain and ratings from individual joints. The authors concluded that overall estimates of pain may be made on the basis of other factors, such as fatigue and stiffness, as well as individual joint pain.

The other measures of disease activity reflect different aspects of the disease; for example, pain on compression of the joint, length of time to fatigue, and grip strength, all contain an active or temporal component to the measurement. The pain score did not. If the patients had been instructed to report their pain "on movement", or their pain level "over the last 24 hrs", the correlation

between the pain measure and the other measures might well have been higher.

Basic Personality Inventory.

All the scores on the Basic Personality Inventory, with the exception of Hypochondriasis for the males, lay within the normal published values for the instrument (Jackson, 1989). As well, men had significantly higher scores than women on the Denial scale. However, the difference in the mean values between the sexes on denial was small (1.7) and may only reflect a slight tendency in the men to underestimate the effects of the disease on their daily lives. Conversely, it may be viewed in a positive light as a constructive coping mechanism.

A previous study, using the BPI, showed that a sample of 20 RA patients did not differ significantly from an age- and sex-matched population of normal healthy subjects on anxiety, depression or denial but were significantly higher than the normals on the Hypochondriasis scale (Scudds et al, 1987). The authors, in agreement with Pincus and co-workers (1986), reasoned that the significantly higher levels found on the Hypochondriasis scale might well be due to the wording of some of the questions which asked specifically about pain and dysfunction. The scale, then, was partly reflective of disease activity as well as psychological disturbance. This may not completely account for the fact that the males in this study lay one standard

score above normal values of hypochondriasis. Men had significantly less disease activity than women, and yet the women's scores lay within normal limits. However, as the elevation in the male scores is not high, the outcome of the present study needs to be replicated before any firm conclusions should be made about its significance.

The personality scores from the present study support the results of Scudds et al (1987) and agree with those of others (e.g. Spergel et al, 1978; Frank et al, 1988; Hawley and Wolfe, 1988) which indicate that most people with rheumatoid arthritis do not display high levels of psychological disturbance in normal levels of disease activity.

Relationship between the main study variables.

It was an expectation of this study that there would be significant negative correlations between disease activity and each of pain threshold and pain tolerance. That is, those subjects with high levels of disease activity would have low pain threshold and tolerance levels, and those with low levels of disease activity would have high pain threshold and tolerance levels. The results of this study lend only partial support to this position. Taking all the subjects, men and women, as a whole group, a significant negative correlation was found between disease activity and pain tolerance ($r = -.26$, $p < .05$). However, no significant relationship was found between pain threshold and disease activity.

It is difficult to account for the finding that, when the sexes were considered separately, only the males showed a significant negative correlation ($r = -.54$, $p < .01$) between pain tolerance and disease activity, whereas the females did not ($r = .02$). This may be viewed in the light of the overall sex differences in the patterns of association between disease activity and the other study variables. Thus, for men, disease activity was significantly correlated with hypochondriasis, pain intensity and pain tolerance, but for women disease activity was significantly correlated with pain intensity, length of disease and age. Therefore, only for present pain intensity was the correlation with disease activity significant for both the sexes. Further, pain intensity was negatively correlated with pain tolerance for men but positively correlated for women. Only three correlations show significant relationships for both men and women, positive correlations between age and denial, negative correlations between length of disease and anxiety, and positive correlations between pain threshold and tolerance levels.

Except for anxiety, little relationship was found between the personality variables and disease activity. These findings are in broad agreement with Bishop et al (1987) and Gardner (1980) who did not find any association between fluctuations in disease activity and psychological state in R.A. patients over a period of months. Further,

McFarlane and Brooks (1988) found that psychological measures were much more closely related to disability as a result of R.A., rather than the disease activity itself.

The data seem to indicate inconsistencies in responses between the two sexes. In order that these differences could be further explored, a series of multiple regression analyses were performed with pain threshold and tolerance levels as the dependent variables.

Some caution must be observed in attempting to interpret the series of multiple correlations that are presented. Firstly, while the overall ratio of sample size ($n = 68$) to the number of independent variables ($n = 7$) is adequate for this type of analysis, when the sexes are taken as separate groups, the sample sizes are decreased and the power of the test is reduced. Secondly, in calculating the overall R^2, the number of variables is not taken into account. Thus, the R^2 may be an over-inflated estimate of the actual population estimates. The adjusted, or shrunken, R^2 should therefore be examined before attempting to make interpretations of the strength of the multiple correlations. The adjusted R^2 takes into account both the sample size and the number of independent variables that are entered into the equations (Cohen and Cohen, 1983, pages 105-107). Further, the shrunken R^2 reported in Table 12 and Table 13 is adjusted using only the number of variables that account for at least 1% of the variance. If the total number of variables originally

entered into the equation was controlled for, then the shrunken R^2 would be considerably smaller in most cases. Therefore, for the reasons given above, only the adjusted R^2 will be referred to in this discussion section.

With these caveats in mind, the overall pattern of the multiple correlations will be examined, rather than the strength of the individual variables within a particular regression equation. First, taking males and females together, regressing pain threshold and tolerance on the other measures, the equations reached statistical significance, but account for only a small percent of the variance (from adjusted R^2 = .09 to AR^2 = .27).

The regression equations for pain tolerance show higher levels of statistical significance than those for pain threshold. This holds true for both the compounded variables of threshold and tolerance as well as the individual measures, e.g. pain threshold to pressure. In these 13 significant regression equations, either rheumatoid factor (5 times), sex (4 times), disease activity (twice), or hypochondriasis (twice) appears first in the equations and accounts for the largest amount of the variance in each equation. It is interesting to note that in 4 of the 6 significant equations in which sex (gender) was included in the equation, it accounted for the greatest proportion of the variance. These data reinforce the notion that there are significant differences in the patterns of responsiveness between males and females.

The second interesting finding, when considering the sexes together as one group, was that the RhF titre accounted for the largest proportion of the variance in 5 of the 11 significant equations. It will be remembered that the rheumatoid factor, as employed in this study, was used as a means of classification rather than as a continuous variable. This resulted in two groups, one of RhF positive and another of RhF negative. However, the adjusted R^2 for the overall equations in which RhF appeared first was very low (between 0.06 and 0.18). Therefore, it may have statistical relevance but its overall influence may be small.

It is difficult to account for this surprising result. Previous research (Alarcon et al, 1982; Vollhardt et al, 1982; Rimon 1973) has shown that RA patients with rheumatoid factor negative have different patterns of disease and possibly different personality styles than those of patients who are rheumatoid factor positive.

The data from this study partially support these results, in that the RhF negative patients had lower pain threshold and pain tolerance levels, and lower levels of disease activity than the patients with positive titres. However, no significant differences were found on any of the personality variables between the two groups. It may be that, as with the gender differences, the presence of significant differences in pain responsiveness between the groups led to the chance finding that rheumatoid factor

accounted for the largest proportion of the variance in these equations. As well, the step-wise regression procedures employed in the analysis would capitalize on chance findings (Cohen and Cohen, 1983). Therefore, firm conclusions on the importance of the rheumatoid factor should not be made at this stage.

No previous data exist on differences in pain responsiveness between groups of patients with either positive or negative rheumatoid factor titres. The present study indicates that those patients with RhF negative have lower levels of disease activity and are more responsive to painful stimuli. This is contrary to the general results of this study which indicate that lower levels of disease activity are associated with higher levels of pain tolerance.

However, an explanation for these apparently contradictory findings may lie in the distribution of males and females in the RhF positive and negative groups. Although this was not statistically significant, a high proportion of males (80% of all males) were in the RhF positive group. This may have artificially inflated the pain threshold and tolerance levels of the RhF positive group and, because men had significantly lower levels of disease activity than women, led to higher levels of disease activity in the RhF negative group. These sex biases, in turn, may have led to the apparent differences in pain threshold and tolerance levels between the serum

positive and serum negative R.A. patients. Therefore, the outcomes may have largely arisen from the uneven distribution of males and females in the groups.

Apart from the results of the previous paragraphs, the most important data from the series of multiple regression equations resulted when both the sexes and stressors were considered separately. For women, the regression equation for pain threshold, but not pain tolerance, reached statistical significance ($p < .01$) and accounted for 25% of the variance. Hypochondriasis was the most important variable followed by rheumatoid factor and depression. For the individual variables, only the equation for pain threshold to the dolorimeter achieved statistical significance ($p < .05$), but accounted for only 13% of the variance. In this equation, rheumatoid factor, depression and hypochondriasis were the most important variables, in that order. For the individual variables, hypochondriasis was positively correlated with pain threshold.

For men, the pattern of association was quite different to that of the women. The regression equation for pain tolerance, but not pain threshold, reached statistically significant levels ($p < .01$) and accounted for 49% of the variance. In this equation, hypochondriasis was by far the most important predictor variable, followed by age, anxiety and disease activity. It will be remembered that hypochondriasis was significantly negatively correlated with pain tolerance for men, but not for women.

For the individual regression equations at threshold levels for the men, only that of the dolorimeter was statistically significant ($p < .01$) (adjusted $R^2 = .43$) with age being the most important variable followed by depression and then hypochondriasis. At tolerance levels, however, each of the three equations, to shock ($p < .05$), pressure ($p < .001$) and the dolorimeter ($p < .01$), reached statistical significance. For each of these equations, either hypochondriasis or disease activity was by far the most important variable.

Further analysis of the data without the inclusion of hypochondriasis shed more light on the differences in response between the sexes. For men, disease activity took the place of hypochondriasis in two of the three equations in which hypochondriasis appeared as the most important predictor variable. The other equation, that of pain tolerance to pressure, did not achieve statistical significance with hypochondriasis removed from the equation. For women, the removal of hypochondriasis from the equation had no effect but to lower the significance level. It was not replaced by disease activity.

These results again show the differences of response between the sexes. For the women, disease activity was not a significant contributor to pain responsiveness. For men, however, disease activity is an important contributor to the prediction of pain tolerance levels. The higher the disease activity the lower the levels of pain tolerance to

shock and the dolorimeter. As well, for men, the contribution of disease activity to the regression equations can be masked by the inclusion of hypochondriasis in the analysis. Thus, to a certain extent, hypochondriasis and disease activity may be measuring a similar dimension. However, the hypochondriasis scale of the BPI does not seem to be acting merely as a symptom check list in this case because of its inclusion first in the regression equations. It adds more than just the amount of physical symptomatology due to the disease itself.

Limitations of this study.

The sample of R.A. patients in this study was one of convenience. Initial contact with the potential subjects was mostly by letter. All subjects who fulfilled the entry criceria and consented to take part in the study were accepted. No records were kept of the demographic characteristics of those subjects who declined to participate. It is possible, therefore, that this sample of R.A. patients may not be representative of all R.A. patients. Therefore, these data should be replicated before the generalizability of the present results can be fully accepted.

As well, the experimenter in the study was not blinded to the patients' condition. The same experimenter took all the measures of pain responsiveness, as well as the measures of disease activity. Experimental bias, however,

was minimized by having the stressors applied before the measures of disease activity were assessed.

It is also relevant to point out that, although the series of multiple regression equations provide statistically significant and thought provoking data, in many instances the equations account for only a small part of the variance in pain threshold and pain tolerance. Thus, a large proportion of the variance is not accounted for. Therefore, some of the variables which can influence pain responsiveness were not included in the analyses. Future research is needed to identify and evaluate the influence of other factors on pain responsiveness.

Summary.

The most interesting data from this study point to important differences between the sexes in pain responsiveness as they relate to disease activity. These differences are augmented by the different patterns of association between the measures of pain threshold and pain tolerance and the other main study variables. For men, but not for women, a significant negative relationship was found between pain tolerance and disease activity. Further, a surprising finding is the relationship of rheumatoid factor titre to pain responsiveness. The possible importance of each of these issues will be dealt with further in the general discussion section.

Chapter 4

Study 2

Method

Due to the wide range of individual difference of response to the stressors in Study 1, it was decided to recruit as many as possible of the original subjects and use them as their own controls after a period of time when disease activity could reasonably be expected to have changed in many of the subjects.

Subje ..

38 of the original 68 subjects returned to participate in the study. All subjects were approached first by letter and then by follow-up telephone call to request their participation again. Five of the original 68 subjects could not be contacted after repeated attempts to contact them. Twenty five of the remaining original subjects were either unable or unwilling to return for further testing. No overt pressure was put on the potential subjects to return for further testing and, as before, refusal to participate did not prejudice their further treatment in any way. All subjects who returned did so as out-patients.

The age range of the returning subjects was from 21 yrs to 71 yrs with a mean of 52.9 yrs and a standard deviation of 11.6 yrs. Twenty four subjects were female and 14 subjects were male. Consequently, the mean age and the

proportion of male to female subjects was very similar in Studies 1 and 2.

Consent Forms

One consent form, which outlined the procedures to be used in the study, was used for all subjects (See Appendix H). Subjects were given the opportunity to ask questions before signing the form. No subjects were excluded from the study for having taken analgesics within 12 hours of testing.

Apparatus

The apparatus used in this experiment was exactly the same as that used in experiment 1a. That was:

1. A constant current stimulator.
2. A modified pressure algometer.
3. A dolorimeter.
4. A 15 cm visual analogue scale.
5. The Basic Personality Inventory.
6. A modified sphygmomanometer cuff.

Measures taken.

These were also exactly the same as in study 1a. That is:

1. Pain threshold.
2. Pain tolerance.
3. Indices of disease activity.
4. Present pain intensity and unpleasantness.
5. Anxiety, depression, denial and hypochondriasis.

Procedure.

The procedure conformed exactly to that of Experiment 1a. The data were collected between the months of March and December, 1985, between the hours of 8.30 a.m. and 7.00 p.m. An attempt was made to match the time of day of testing in this experiment to that of Study 1.

Results

The purpose of this study was to expand upon the results of study 1 and to re-examine the relationship between pain responsiveness (pain threshold and tolerance measures) and disease activity after time and treatment interventions may have altered levels of disease activity in the patients. As well, the inter-relationships between the main personality, disease activity, and pain variables are examined for stability and variability.

In a similar manner to that of study 1, where it is deemed meaningful, the results will be presented for the group as a whole and then for male and female subjects separately, and comparisons will be drawn between the data from study 1 and study 2.

The results are presented in the following manner. Descriptive data are presented first, followed by the data relating to the physical stressors and pain ratings. Next, the BPI scales are presented and then measures of disease activity are examined. Lastly, the inter-relationships of the main study variables are examined with emphasis on the disease activity and pain responsiveness data. Throughout the text of this chapter, the data that are referred to as originating from study 1 are taken only from those subjects who returned for study 2, not the whole original sample of 68 subjects.

In the same manner as in Study 1, the same strategy is adopted in the presentation of these results with regard to

the analysis of multiple comparisons, i.e. Bonferroni adjustments have not been carried out where similar measures such as pain threshold to shock, pressure and the dolorimeter are involved.

Descriptive data.

Of the original 68 subjects in study 1, 38 returned for examination for study 2. In comparison with the study 1 data, none of the major descriptive variables - age, length of time since diagnosis, rheumatoid factor titre, and functional classification - showed significant differences between those subjects who returned and those who did not return (Table 1). The ratio of women to men was approximately 2:1 (Table 2). The males were significantly older than the females ($p < .05$) and the length of time since diagnosis for both sexes was approximately 8 years. No significant differences were found between the sexes on rheumatoid factor titre (X^2 (1 df) = 0.18, $p > .05$) or functional classification (X^2 (2 df) = 1.19, $p > .05$).

Painful Stressors.

The data for the values of pain threshold and tolerance to the 3 physical stressors - trains of electrical pulses (shock), the constant pressure algometer (pressure), and the dolorimeter - are shown in Table 3. No significant differences were found between the men and the women at threshold levels of stimulation. For pain tolerance, however, the men had significantly higher mean values for

Table 1.

Descriptive data of the experimental population who returned at time 2 compared to those who did not return.

		DID NOT RETURN	RETURNED
		$\bar{X}$	$\bar{X}$
N		30	38
AGE	(yrs)	51.86	52.97
	(S.D.)	14.71	11.92
LENGTH	(yrs)	9.22	7.77
	(S.D.)	7.83	7.04
RHF -	pos.	20	26
	neg.	10	12
FUNCTIONAL CLASS	1	14	20
	2	12	13
	3	4	5

Legend: Length = length of time since diagnosis, RHF = rheumatoid factor, Functional class = RA functional classification.

Table 2.

Descriptive data of the experimental population.

		ALL SUBJECTS	MALE	FEMALE
		$\bar{X}$	$\bar{X}$	$\bar{X}$
N		38	14	24
AGE	(yrs)	52.9	58.5	49.7 *
	(S.D.)	11.6	8.9	11.9
LENGTH	(yrs)	7.7	7.8	7.7
	(S.D)	7.0	8.5	6.1
RHF -	pos.	26	9	17
	neg.	12	5	7
FUNCTIONAL CLASS	1	20	8	12
	2	13	4	9
	3	5	2	3

Legend: Length = length of time since diagnosis, RHF = rheumatoid factor, Functional class = RA functional classification.
* $t = 2.36$, $p < .05$ between men and women

Table 3.

Pain threshold and tolerance values for the three stressors

	ALL SUBJECTS		MALE		FEMALE		t	p
THRESHOLD	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D)		
SHOCK (ma)	1.42	(0.88)	1.80	(1.11)	1.21	(0.67)	1.73	NS
PRESSURE (sec)	14.72	(13.74)	21.29	(17.73)	11.30	(9.36)	1.82	NS
DOLORIMETER (kg)	2.68	(1.04)	2.73	(1.05)	2.65	(1.05)	0.20	NS
Z-SCORE			0.19	(0.90)	-0.20	(0.57)	1.45	NS
TOLERANCE								
SHOCK (ma)	4.83	(3.09)	6.65	(3.24)	3.81	(2.54)	2.91	**
PRESSURE (sec)	98.87	(67.40)	125.95	(63.8)	78.65	(64.4)	2.07	*
DOLORIMETER (kg)	6.83	(2.03)	7.19	(2.25)	6.61	(1.91)	0.81	NS
Z-SCORE			0.27	(1.00)	-0.25	(0.63)	2.10	*

Legend: t = t-test between men and women; NS = not statistically significant.
* = $p < .05$
** = $p < .01$

shock ($p < .01$), constant pressure ($p < .05$), and the overall Z-score of pain tolerance ($p < .05$).

A comparison of the data for threshold and tolerance between study 1 and study 2 (Table 4) showed that the threshold measures for constant pressure and the dolorimeter were significantly higher at study 2 ($p < .05$, and $p < .001$ respectively). The pain tolerance measures of constant pressure and the dolorimeter were also higher at study 2 (both $p < .01$). No significant differences were found for shock at threshold or tolerance values between study 1 and study 2.

Values for all of the physical stressors, although not all significant, increased from study 1 to study 2. However, the magnitude of the variability, as shown by the standard deviations, varied between stressors. Thus, the largest percentage increase in mean values was for the constant pressure algometer at threshold and tolerance levels (67% and 47% respectively). But, the standard deviation values for the constant pressure algometer were also very large, almost equaling the mean values. For the dolorimeter, the percentage increase was smaller, but the ratio of standard deviation to mean score was also a lot smaller (e.g. a mean value of 5.37, and a standard deviation of 2.35 for dolorimeter tolerance at study 1).

All the stressors at threshold and tolerance levels showed significant correlations within measures from study 1 to study 2 (all $p < .01$). In general, the strength of the

Table 4.

Pain threshold and tolerance values, and correlations between stressors for study 1 and study 2, for all subjects

	STUDY 1		STUDY 2		% INC.	t	p	CORRELATION	
THRESHOLD	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D.)				r	p
SHOCK (ma)	1.11	(0.73)	1.42	(0.88)	27	1.39	NS	.48	**
PRESSURE (sec)	8.79	(8.66)	14.72	(13.47)	67	2.68	*	.47	**
DOLORIMETER (kg)	2.07	(1.00)	2.68	(1.04)	47	3.73	***	.53	**
Z-SCORE	-0.29	(0.52)	0.14	(0.76)		4.40	***	.70	***
TOLERANCE									
SHOCK (ma)	3.99	(2.64)	4.83	(3.09)	21	0.41	NS	.77	***
PRESSURE (sec)	67.62	(65.5)	98.87	(67.4)	47	2.77	**	.62	***
DOLORIMETER (kg)	5.37	(2.35)	6.83	(2.03)	27	4.99	***	.66	***
Z-SCORE	-0.23	(0.76)	0.19	(0.80)		4.41	***	.80	***

Legend: Correlation = Pearson product moment correlation;
% Inc = % increase in values from study 1 to study 2: Z-score = Score standardized against all values at time 1 and time 2: t = t-test between time 1 and time 2.

* = $p < .05$
** = $p < .01$
*** = $p < .001$

correlations was higher for pain tolerance measures (all between r = .62 and .77) than for threshold (all between r = .47 and .53). The highest correlation was between the tolerance measures for shock ($r = .77$, $p < .001$), which did not alter significantly from study 1 to study 2.

The standard scores of pain threshold and pain tolerance were calculated and compounded in a similar manner to that of study 1. However, for the data reported as the Z-score for study 2, the standardization was accomplished using the range of all data rrom all the 38 subjects who returned. Thus, 76 values were considered for each standard score, being the data from each subject from study 1 and study 2, with a mean Z-score of zero resulting. From the standardized data of pain threshold and pain tolerance to shock, constant pressure and the dolorimeter, single standard scores of pain threshold and of pain tolerance were calculated for study 1 and study 2 and are shown in Table 4. It can be seen that both standard scores of pain threshold and tolerance were significantly higher for study 2 than for study 1 ($p < .001$). As well, both showed significant positive correlations within measures between the values at study 1 and study 2 (both $p < .001$).

Visual analogue scale ratings of unpleasantness and intensity show no significant differences in any ratings within measures from study 1 to study 2 (Table 5). All ratings were positively correlated, but only 5 out of the 12 possible comparisons reached statistically

Table 5.

Pain rating data of Intensity and Unpleasantness for Threshold and Tolerance, and correlations, for study 1 and study 2.

	STUDY 1	STUDY 2	t	CORRELATION	
I. THRESHOLD	$\bar{X}$ (S.D.)	$\bar{X}$ (S.D.)	p	r	p
SHOCK (ma)	3.55 (2.84)	3.16 (2.35)	ns	.53	<.001
PRESSURE (sec)	2.71 (2.40)	3.01 (2.10)	ns	.28	ns
DOLORIMETER (kg)	3.27 (2.53)	3.26 (2.23)	ns	.27	ns
I. TOLERANCE					
SHOCK (ma)	10.18 (3.72)	10.09 (3.97)	ns	.15	ns
PRESSURE (sec)	9.44 (3.93)	9.76 (4.04)	ns	.61	<.001
DOLORIMETER (kg)	9.81 (3.01)	10.01 (3.23)	ns	.50	<.001
UNP. THRESHOLD					
SHOCK (ma)	2.93 (2.96)	2.56 (2.14)	ns	.46	<.01
PRESSURE (sec)	2.77 (2.67)	2.12 (2.15)	ns	.25	ns
DOLORIMETER (kg)	2.21 (2.40)	1.81 (1.68)	ns	.05	ns
UNP. TOLERANCE					
SHOCK (ma)	9.60 (3.38)	10.01 (4.12)	ns	.26	ns
PRESSURE (sec)	8.78 (4.22)	8.53 (4.44)	ns	.56	<.001
DOLORIMETER (kg)	9.07 (3.49)	8.61 (3.22)	ns	.22	ns

Legend: I = Intensity; UNP = Unpleasantness; t = t-test between groups at time1 and time2.

significant levels. If a conservative adjustment is made for the significance level, considering 12 possible contrasts and taking alpha at less than .004, then the correlation for shock unpleasantness threshold would not be significant. Three of these significant correlations were for intensity ratings (threshold to shock, and tolerance to pressure and the dolorimeter), and 1 out a possible 6 was for unpleasantness (pressure tolerance).

Basic Personality Inventory.

Of the four main personality variables, only denial revealed significant differences between males and females (Table 6). Denial was significantly higher for men than women ($p < .05$). When all the subjects were considered together, none of the main personality variables displayed significant differences from study 1 to study 2 (Table 7). Only one variable, anxiety, altered significantly when the sexes were considered separately. Women, but not men, showed a statistically significant decrease in anxiety at study 2 ($t(23) = 2.39$, $p < .05$). Each of hypochondriasis, depression and anxiety showed highly significant positive correlations between scores at study 1 and study 2 (all $p < .001$), whereas the scores on the denial scale were significantly correlated at the $p < .05$ level.

Disease Activity.

Males were found to show significantly lower levels of disease activity than females on 2 of the 7 measures, which

Table 6.

Basic Personality Inventory scores for the important variables

	ALL SUBJECTS		MALE		FEMALE		t	p
	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D.)		
HYPOCHONDRIASIS	7.94	(3.17)	9.00	(2.70)	7.13	(3.52)	1.75	NS
DEPRESSION	3.17	(2.30)	3.84	(3.76)	2.72	(2.94)	0.92	NS
DENIAL	7.54	(2.73)	9.76	(3.11)	7.31	(2.49)	2.56	*
ANXIETY	6.11	(3.23)	7.00	(4.76)	4.77	(3.90)	1.50	NS

Legend: t = t-test between men and women
* = $p < .05$

Table 7.

Basic Personality Inventory scores, and correlations between the scores for study 1 and study 2, for all subjects

	STUDY 1	STUDY 2	t		CORRELATION	
	$\bar{X}$ (S.D.)	$\bar{X}$ (S.D.)		p	r	p
HYPOCHONDRIASIS	7.94 (3.17)	7.82 (3.33)	0.23	NS	.59	<.001
DEPRESSION	3.17 (2.30)	3.14 (3.20)	0.06	NS	.53	<.001
DENIAL	7.54 (2.73)	8.22 (2.95)	1.21	NS	.30	<.05
ANXIETY	6.11 (3.23)	5.60 (4.31)	1.00	NS	.71	<.001

Legend: Correlation = Pearson product moment correlation;
t = t-test between study 1 and study 2.

were the number of active joints ($p < .05$) and grip strength ($p < .001$) (Table 8). However, no statistically significant difference was found between the males and females on the overall Z-score of disease activity ($p>.05$).

A comparison of the values for study 1 and study 2 (Table 9), showed that 5 of the 7 measures of disease activity decreased significantly from study 1 to study 2. However, only for the number of active joints ($p < 0.001$) was that decrease greater than at the $p < .05$ level. Neither the ESR nor time to fatigue changed significantly from study 1 to study 2.

Males had a statistically significant decrease in disease activity on only one measure, present pain intensity ($t(13) = 2.41$, $p < .05$). Females showed statistically significant decreases in disease activity on the measures of present pain intensity ($t(23) = 2.10$, $p < .05$, the number of active joints ($p < .01$), the length of time of morning stiffness ($p < .05$) and the Lansbury articular index ($p < .05$).

Six of the 7 measures of disease activity showed significant positive correlations between the values measured at each time. However, only grip strength and erythrocyte sedimentation rate had correlations significant beyond the .001 level. The measure of time to fatigue was not significantly correlated between studies ($r = .04$).

The standard scores of measures of disease activity were calculated and compounded in the same manner as for pain

Table 8.

Measures of disaease activity

	ALL SULJECTS		MALE		FEMALE		t	P
	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D.)		
NUMBER	4.78	(5.32)	3.92	(4.06)	5.92	(1.21)	2.26	*
GRIP (mm/Hg)	155.10	(73.0)	206.92	(78.5)	124.87	(49.9)	3.95	***
STIFFNESS (hrs)	0.56	(0.67)	0.66	(0.77)	0.50	(0.61)	0.70	NS
FATIGUE (hrs)	8.57	(4.07)	8.28	(4.34)	8.75	(4.00)	0.33	NS
LANSBURY INDEX	25.22	(24.02)	20.06	(18.87)	23.62	(26.9)	0.40	NS
ESR (mm/hr)	27.70	(20.02)	23.64	(13.59)	30.41	(22.5)	1.15	NS
VAS PAIN (cms)	1.80	(1.92)	1.39	(1.57)	2.05	(2.09)	1.06	NS
Z-SCORE			-0.18	(0.65)	0.10	(0.68)	1.29	NS

Legend: Number = the number of active joints; Grip = grip strength; Stiffness = length of time of morning stiffness; fatigue = length of time until the onset of fatigue; Lansbury index = Lansbury articular index; ESR = erythrocyte sedimentation rate; VAS Pain = present pain intensity measured on the visual analogue scale; T-TEST = t-test between males and females

* = $p < .05$
*** = $P < .001$

Table 9.

Measures of disease activity, and correlations between the measures for study 1 and study 2, for all subjects

	STUDY 1		STUDY 2		t		CORRELATION	
	$\bar{X}$	(S.D.)	$\bar{X}$	(S.D.)		p	r	p
NUMBER	9.13	(8.31)	4.78	(5.32)	3.53	***	.46	**
GRIP (mm/Hg)	133.07	(71.62)	155.10	(73.0)	2.42	*	.70	***
STIFFNESS (hrs)	1.09	(1.58)	0.56	(0.67)	2.24	*	.39	*
FATIGUE (hrs)	8.51	(3.50)	8.57	(4.07)	0.07	NS	.04	NS
LANSBURY INDEX	36.42	(34.63)	25.22	(24.02)	2.46	*	.33	*
ESR (mm/hr)	27.43	(17.21)	27.70	(20.02)	0.11	NS	.66	***
VAS PAIN (cms)	2.77	(2.87)	1.80	(1.92)	2.38	*	.29	*
Z-SCORE	0.13	(0.75)	-0.16	(0.57)	2.65	*	.39	*

Legend: Correlation = Pearson product moment correlation; r = rho; Number = the number of active joints; Grip = grip strength; Stiffness = length of time of morning stiffness; fatigue = length of time until the onset of fatigue; Lansbury index = Lansbury articular index; ESR = erythrocyte sedimentation rate; VAS Pain = present pain intensity measured on the visual analogue scale; Z-score = score standardized against all values at study 1 and study 2. t = t-test between study 1 and study 2

* = $p < .05$
** = $p < .01$
*** = $p < .001$

threshold and tolerance, to give one compounded score of disease activity at study 1 and study 2. Disease activity decreased significantly from study 1 to study 2 ($p < .05$) and was significantly positively correlated between the studies ($p < .05$).

Relationship between the main study variables.

A correlation matrix of the personality, disease activity and pain measures was calculated and is shown in Table 10. From a total of 21 correlations, only 5 reached statistical significance. Depression was positively correlated with anxiety ($p < .01$) and hypochondriasis ($p < .05$). There were no other significant correlations between the personality measures and any of the other variables.

Of the other significant correlations, one was between pain threshold and pain tolerance ($p < .001$). Pain threshold and pain tolerance were also negatively correlated with disease activity ($p < .01$ and $p < .05$ respectively).

The data of study 1 revealed a differing pattern of associations between the variables for men and women. However, it should be remembered that the sample sizes are much reduced in this study. Therefore, only the most important data of this study will be considered. For both men and women, disease activity was negatively correlated with pain threshold ($r = -.35$ and $r = -0.43$ respectively).

Table 10.

Correlations of the main study variables - all subjects

	HYP	DEN	DEP	ANX	DIS	PTH	TOL
HYP	-						
DEN	.11	-					
DEP	.31*	-.09	-				
ANX	.03	-.09	.46**	-			
DIS	.11	-.03	.20	.03	-		
PTH	.12	.01	.09	-.16	-.41**	-	
TOL	.04	.08	.21	-.06	-.29*	.69+	-

Legend: Hyp = Hypochondriasis;Den = Denial; Dep=Depression;Anx = Anxiety;Dis = Z-score of disease activity; Pth = Z-score of pain threshold; Tol = Z-score of pain tolerance.

* = $p < .05$
** = $p < .01$
\+ = $p < .001$

For women, this reached statistical significance at the $p < 0.05$ level. As well, disease activity was negatively correlated with pain tolerance for both women and men ($r = -0.20$ and $r = -0.31$ respectively), but neither of these correlations reached statistically significant levels (Tables 11a and 11b).

From their standard scores, difference scores of pain threshold, pain tolerance and disease activity were calculated for each variable based on their score at study 1 minus the score at study 2. Both pain threshold and pain tolerance increased significantly from study 1 to study 2 (Table 12a, Table 4). As well, disease activity decreased significantly over the same time (Table 12a, Table 9). Inter - correlations between the difference score of disease activity and those of threshold and tolerance are shown in Table 12b. It can be seen that, although they are all in a negative direction, none reaches statistical significance. This is true of all the subjects taken together, and for the sexes treated separately.

Regression equations of pain threshold and tolerance on the main study variables .

In a similar manner to the results of Study 1, a series of stepwise multiple regression equations were developed to examine the relationship between the measures of pain responsiveness (pain threshold and tolerance) and the other main study variables, as a whole (Table 13). The initial

Table 11a.

Correlations of the main study variables - females

	HYP	DEN	DEP	ANX	DIS	PTH	TOL
HYP	-						
DEN	-.30	-					
DEP	.29	-.05	-				
ANX	-.03	-.02	.50**	-			
DIS	.06	.01	.13	.09	-		
PTH	.16	.01	.04	-.16	-.43*	-	
TOL	.00	.06	.00	-.05	-.20	.59+	-

Table 11b.

Correlations of the main study variables - males

	HYP	DEN	DEP	ANX	DIS	PTH	TOL
HYP	-						
DEN	.26	-					
DEP	.28	-.32	-				
ANX	.39	-.45	.37	-			
DIS	.40	-.06	.38	.01	-		
PTH	-.11	-.09	.04	-.03	-.35	-	
TOL	-.12	-.14	.32	-.18	-.31	.71**	-

* = p < .05
** = p < .01
\+ = p < .001

Legend: Hyp = Hypochondriasis; Den = Denial; Dep=Depression; Anx = Anxiety; Dis = Z-score of disease activity; Pth = Z-score of pain threshold; Tol = Z-score of pain tolerance.

Table 12a.

Standardized difference scores of disease activity, pain threshold and tolerance from study 1 to study 2.

	Disease Activity	Threshold	Tolerance
Z-SCORE	- 0.291	+ 0.459	+ 0.358

Table 12b

Correlations between standardized difference scores of disease activity, pain threshold and tolerance.

	All subjects	Males	Females
	r	r	r
Dis. with Pth.	-.18	-.14	-.28
Dis. with Tol.	-.22	-.11	-.29

Legend: Dis = Z-score of disease activity; Pth = Z-score of pain threshold; Tol = Z-score of Pain tolerance.

Table 13.

Summary of multiple regressions of pain threshold and tolerance measures on the predictor variables

VAR	SEX	R^2	ADR^2	F	SIG	VARIABLES IN EQUATION - (R^2 CHANGE)
TH	C	.26	.16	2.77	.04	DIS(17),SEX(3),RHF(3),DEP(2)
TH	NC	.25	.15	2.65	.04	DIS(17),RHF(4),DEP(2),DEN(1),AGE(1)
TOL	C	.31	.19	2.42	.05	SEX(10),RHF(7),DEP(7),DIS(6),ANX(1)
TOL	NC	.26	.18	3.00	.03	DIS(9),DEP(8),RHF(7),ANX(1)
THSH	C				NS	
	NC				NS	
PR	C	.38	.27	3.27	.01	DIS(18),DEP(11),RHF(6),SEX(1),DEN(1),LEN(1)
	NC	.37	.28	3.24	.01	DIS(18),DEP(11),RHF(6),DEN(1),LEN(1)
DOL	C	.16	.11	3.35	.05	DIS(12),DEN(4)
	NC	.16	.11	3.35	.05	DIS(12),DEN(4)
TOSH	C	.21	.21	3.05	.04	SEX(14),ANX(4),RHF(2)
	NC				NS	
PR	C	.39	.26	2.85	.02	DIS(16),RHF(9),DEP(8),HYP(5),SEX(1)
	NC	.38	.27	2.81	.02	DIS(16),RHF(9),DEP(8),HYP(5)
DOL	C	.24	.16	2.70	.05	DIS(9),DEP(7),RHF(5),HYP(2)
	NC	.24	.16	2.70	.05	DIS(9),DEP(7),RHF(5),HYP(2)

Legend: Th = Combined Z-scores of pain threshold; Tol = Combined Z-scores of pain tolerance; Sh = Shock; Pr = Constant pressure; Dol = dolorimeter; Anx = Anxiety; RHF = Rheumatoid factor titre; Dep = Depression; Hyp = Hypochondriasis; Dis = Z-score of disease activity; Len = Length of time since diagnosis; Den = Denial; C = Sex included in the regression; NC = Sex not included in the regression; Sex (1) = male; Sex (2) = female; ADR^2 = Adjusted R^2; R^2 change = R^2 change accounted for by the addition of the variable preceding the parenthesis.

equations were regressed on pain threshold, then pain tolerance controlling for sex and then not controlling for sex. Only the equations that reach statistical significance, and those variables that account for at least 1 percent of the explained variance, are reported. Unlike study 1, due to the small sample size for men (n = 14) and women (n = 24), no regression equations are reported for the sexes separately.

With sex included in the equation, for the combined Z-score of pain threshold, the equation was significant at the $p < .04$ level. However, the variance accounted for by the equation was small, with $R^2 = 0.26$ (adjusted $R^2 = .16$). Disease activity accounted for the largest proportion of the variance. For the combined Z-score of pain tolerance, the equation was also significant at the $p < .04$ level. Here, however, sex was the most important variable in the equation.

With sex not included in the equation at pain threshold, the equation was significant at the $p \leq .04$ level and accounted for 25% of the variance of pain threshold (adjusted $R^2 = .15$). Again, disease activity was the most important variable.

For the regression equation on the Z-score of pain tolerance, with sex not included, the equation was significant at the $p < .03$ level and accounted for 26% of the variance (adjusted $R^2 = .18$). Disease activity,

depression, and rheumatoid factor contributed predominantly to the variance accounted for by the equation.

Next, regression equations were developed for the individual measures of pain threshold and tolerance to each of the three stressors taken separately, controlling and then not controlling for sex. For threshold to shock, both with sex included and not included in the equation, the equations did not reach statistical significance. For threshold to pressure, with sex included, the regression equation was significant at the $p < .01$ level and accounted for 38% of the variance (adjusted $R^2 = .27$). Of this, disease activity was the most important variable. Other important variables were depression and rheumatoid factor. The equation developed for pressure threshold, with sex not included, was also significant at the $p < .01$ level and differed very little from the equation with sex included.

For dolorimeter threshold, the regression equation was significant at the $p < .05$ level, but accounted for only 16% of the total variance (adjusted $R^2 = .11$). Only 2 variables contributed to this 16%, with disease activity being the most important followed by denial. Sex did not make a contribution to the equation.

Five of the 6 regression equations on the individual stressors at the pain tolerance level were statistically significant. In only one of these, shock tolerance, did sex contribute to more than 1% of the variance accounted for.

The regression equation on shock tolerance was significant at the $p < .04$ level and accounted for 21% of the variance. Sex accounted for most of this variance, with anxiety and rheumatoid factor accounting for the rest. The regression equation did not reach statistical significance when sex was not included in the equation.

The equation for tolerance to pressure was significant at the $p < .02$ level and accounted for 39% of the variance ($R^2 = .26$). Disease activity contributed most to the variance accounted for, with rheumatoid factor, depression, and hypochondriasis, being the other important variables.

For dolorimeter tolerance, the regression equation that was developed was very similar to that for pressure tolerance but accounted for a lower percent of the variance - 24% ($R^2 = .16$). Disease activity, depression, and rheumatoid factor were the most important predictors, in that order.

Discussion

The present study aimed to further explore the relationship between disease activity and pain responsiveness and to compare those results with the data obtained one year earlier with the same patients. It was found that the overall levels of disease activity had decreased significantly between the two studies, and that pain threshold and tolerance levels had increased significantly. However, a significant relationship was not found between the difference scores of disease activity and those of pain threshold and tolerance levels. In contrast to this, a significant negative relationship was found between the level of disease activity and each of pain threshold and pain tolerance at the time of study 2.

In a similar manner to the first study, multiple regression equations expanded upon the results of the simple correlations. It was found that disease activity was the most important predictor in all but two of the significant regression equations. Unlike the first study, the rheumatoid factor titre had much less importance in the regression equations.

In the discussion of the results that follows, emphasis will be placed on the differences in the data between the first and second studies, as well as the relationship between disease activity and pain responsiveness.

Thirty-eight (55%) of the original 68 R.A. patients

returned to take part in the present study. It would have been desirable to have a larger returning sample. However, as it was decided a priori to conform to the original study's methodology, all the participants from study 1 were first approached by letter and then by follow-up telephone call to request them to return for further testing. Seven of the 68 subjects could not be contacted due to changes of address. One subject was deceased. For ethical reasons, no overt pressure to return was placed on the other 30 subjects, nor was any attempt made to ascertain why they would not take part on the second occasion.

Demographically, the subjects who returned did not differ significantly from those who did not, i.e. no significant differences were found on the variables of age, gender ratio, length of time since diagnosis, rheumatoid factor titre classification, or functional class. These data suggest that the present sample may well be representative of the original subject population. However, unlike the first study, the women of study 2 were significantly younger than tne men ($p < .05$).

In this chapter it should be borne in mind that, although the ratio of females to males is similar to that of study 1 (22 males to 44 females), the number of males (14) and females (24) is much less than in the original study. Therefore, with a small sample size, it may not be as possible to make generalizations about the results, particularly when the sexes are considered separately. As

well, due to the reduced power, some analyses that may have reached statistical significance in the first study may not do so in the second, even though the strength of the association, or differences between the groups, are of a similar magnitude.

Pain threshold and tolerance levels.

The pattern of male to female differences in response to the physical stressors was similar to that of study 1. For each stressor, at both threshold and tolerance levels, men showed higher values than the women. However, at the threshold level, no significant differences were found between the sexes on any of the measures. The magnitude of the percentage difference at threshold to constant pressure is almost identical between the studies (55%), but unlike study 1, this did not reach statistically significant levels in study 2.

At the tolerance level, men had significantly higher values than the women on each of shock and constant pressure. Men also had higher values than women for dolorimeter tolerance but, unlike study 1, this did not reach statistically significant levels. The overall Z-score for pain tolerance was statistically significant at the $p < .05$ level, with men having higher overall pain tolerance levels than women. These results are in agreement with those of study 1.

From study 1 to study 2, the overall Z-scores of pain threshold and pain tolerance both increased significantly

($p < .001$). This upward alteration of values may merely have been the result of previous exposure to the experimental stimuli which resulted in a decrease in pain responsiveness. This is unlikely. However, it is difficult to compare the results of the present study to those of previously published literature, due to slight differences in the stimulation parameters of the stressors and the body part to which the stressors were applied.

Harris and Rollman (1983), with very similar stimulus parameters, employed the Forgione-Barber pressure algometer and trains of electrical pulses in a study involving 40 normal, healthy, young adult subjects. The absolute values of threshold and tolerance levels that they obtained were considerably higher than those of study 1 for constant pressure (21.4 sec at threshold and 112.1 sec for tolerance). The results of study 2 much more closely approximate their data, although they are still higher (see table 4 of study 2). For shock, their results are much more in agreement with the present research (1.6 ma for threshold and 4.12 ma for tolerance).

As well, the results of the present research are in close agreement with the values obtained by Scudds et al (1987) who used predominantly middle-aged subjects and identical stimuli to this research. Pain threshold values of 1.47 ma (shock) and 7.16 sec (constant pressure), were found for that study. These are very close to the values obtained in study 2. At tolerance levels, they found values

of 3.94 ma (shock) and 104.4 sec (constant pressure), which are also close to those of study 2.

In comparing the results of these studies, it would seem that the results obtained from study 1 are indeed lower than might well have been expected from previous research. However, the values of study 2 more closely approximate earlier results. Therefore, the change in pain responsiveness from study 1 to study 2 is likely due to the low values obtained at the first session and a normalization of the results at study 2.

There is very little published data on changes in pain responsiveness over time in normal subjects. Contrary to the results of this study, Rollman and Clohosey (1984) found that pain threshold and tolerance levels increased for shock, but not pressure or the cold pressor, on repeated exposure over days. The results of that study were interpreted to mean that "shock" carries with it an affective/anxiety component that the other stressors do not. After the subjects had been exposed to trains of electrical pulses the first time, the apprehension to their notion of "shock" was decreased, which resulted in an upward change of values. The other 2 stressors, for which the subjects had no previous expectations, did not change their values over time.

Another possible explanation for the upward shift in the pain threshold and tolerance values found in the present study might be that the values for pain threshold

and tolerance levels simply regressed towards the mean. However, a more likely account for the change in responsiveness lies in its relationship with disease activity. This will be dealt with later in the chapter.

Even though there were large changes in the values obtained from the stressors between the two studies, highly significant correlations were found between the repeated measures after a period of one year had intervened. The magnitude of the correlations was greater at the pain tolerance level, but all correlations were significant beyond the .01 level. This is an important finding and attests to the reliability of the individual measures.

Previous studies on the test-retest reliability of measures of pain responsiveness have usually been taken after a short period of time, with variable results. For example, Wolff (1978) found an immediate test-retest reliability for intra-muscular hypotonic saline of 0.96 which was reduced to 0.79 after an intervening 2-week interval. Merskey and Spear (1967) found an immediate test-retest of reliability of 0.69 for a pressure algometer. As well, Clark and Bindra (1956) found immediate test-retest reliabilities of 0.81 for shock, 0.91 for constant pressure, and 0.88 for radiant heat at threshold levels. More recently, Jensen et al (1986), in the evaluation of a new pressure algometer, took repeated measures at weekly intervals of one week for a five week period, and found that there was a gradual elevation in threshold

measurements over the period. They also found a 1-week test retest reliability of 0.77. The results of the present data extend these findings, and show that, despite the presence of an overall change in the scores, highly significant correlations are still present between the measures across time.

The results obtained from the subjective ratings of pain stand in marked contrast to the values obtained from the physical stimuli. No statistically significant differences were found on any of the ratings of either intensity or unpleasantness to any of the stressors, between studies. On average, therefore, subjects tended to rate threshold and tolerance level stimuli just as painful, or unpleasant, the second time as they did in the first instance. However, of 12 possible correlations between ratings at study 1 and study 2, only 5 reached statistically significant levels. Therefore, the majority of correlations between rating measures (e.g. the intensity ratings of threshold to shock at study 1 and at study 2) were not statistically significant. These data can be interpreted to mean that group ratings to stimuli are highly stable over time, but that individual ratings may vary widely. Further, these results suggest that the subjects' criteria for threshold and tolerance remained stable and that the differences in the physical measures are, therefore, likely to be reliable and important ones.

Basic Personality Inventory.

For the whole group, the scores on the main personality variables of hypochondriasis, depression, denial and anxiety did not change between the two studies. These findings are not surprising, as all the values on the BPI scales, except the Hypochondriasis scale for men, lay within normal limits at study 1. Hypochondriasis scores for men remained one standard score above normative values at the time of study 2.

When the males and females were considered separately, the females were significantly lower ($p < .05$) on anxiety than they were at study 1. However, they remained within normal published values on the Anxiety scale. It is unlikely that this change in anxiety for the women was related to changes in disease activity, as no significant association was found between anxiety and disease activity at either study 1 or 2. It is possible that the anxiety decrease in women was due to familiarity with the experimental situation which served to reduce apprehension of their approaching visit for testing.

In agreement with previous authors, (Frank et al, 1988; Hawley and Wolfe, 1988) and the results of the BPI scales of study 1, the present results emphasize the fact that the present population of subjects with R.A. were not experiencing psychological disturbance. Only the Hypochondriasis scale showed any significant positive correlations with disease activity. For the reasons

discussed in the previous discussion section, this positive correlation may have been caused by the BPI Hypochondriasis scale acting, in part, as a symptom check list.

Measures of disease activity.

Significant changes were present in overall levels of disease activity at the time of study 2. Unlike study 1, there were no significant overall differences between the sexes in disease activity. For the individual measures, however, men were still significantly higher on grip strength ($p < .001$) and lower on the number of active joints ($p < .05$) than the women, which might indicate that women still had more active disease. Of course, it should also be expected that men would normally have higher grip strength than women.

Taking all the subjects together, 5 of the 7 measures of disease activity improved significantly from study 1 to study 2. The exceptions were time to fatigue, and erythrocyte sedimentation rate. These overall changes in disease activity mask differences between the males and females. For males, only the level of present pain intensity improved at study 2 ($t= 2.42$, $p < .05$). Women, however, improved significantly on the measures of pain ($t= 2.18$, $p < .05$), the number of active joints ($t = 3.38$, $p < .01$), the length of time of morning stiffness ($t = 2.18$, $p < .05$), and the Lansbury articular index ($t = 2.14$, $p < .05$), as well as an overall change in disease activity ($t = 2.41$, $p < .05$). Therefore, the statistically

significant decrease in disease activity found in all the subjects arose largely from improvements in the female subjects.

It was not necessarily expected that levels of disease activity would change from study 1 to study 2. No active treatment interventions were recorded, but most would have been receiving some form of treatment and it is quite likely that some of the patients received some alteration in treatment in the intervening period which might account for the changes. It also possible that the original sample was biased towards patients who were initially higher in levels of disease activity than a normal population of R.A. patients. The patients who were accepted into study 1 were a sample of convenience which was drawn from the referring rheumatologists' case lists. It is reasonable to assume that patients who had recently seen the rheumatologist because of some alteration in disease state would be more likely to agree to enter the study.

It is worthy of note the ESR and the time to fatigue did not alter significantly over time while the other measures did. Each of these is a common measure, one physiological and the other functional, of disease activity. Both are often used in studies with R.A. patients (Mallya and Mace, 1981: Grindulis et al, 1983; Rhind et al, 1987) and each was significantly positively correlated with other measures of disease activity. As was the case with study 1, these data again point to the necessity of taking

multiple measures when assessing the state of disease activity in R.A. patients.

The inter-relationship between the main study variables.

There were few statistically significant correlations between the main study variables when the data of the subjects were taken together. Of the personality variables, depression was positively correlated with anxiety and hypochondriasis. However, none of the personality variables was significantly correlated with any of the other study variables.

Taking all the subjects together, both pain threshold and pain tolerance were significantly negatively correlated with levels of disease activity ($p < .01$ and $p < .05$, respectively). The direction of the correlations was in a similar manner when the sexes were considered separately, but only the correlation between disease activity and pain threshold for women reached statistically significant levels.

The significant negative relationship between disease activity and pain threshold and tolerance means that as disease activity decreases, pain responsiveness also decreases. These data are more consistent with hypervigilance theory (Chapman, 1978) than adaptation-level theory (Rollman, 1979a). Hypervigilance theory predicts that people in high levels of disease activity would become more attentive to painful stimuli, and thus, have low pain

threshold and tolerance levels. Conversely, people in low levels of disease activity would have higher pain threshold and tolerance levels. In this view, pain responsiveness is not a static phenomenon but may swing about some homeostatic set point, in an inverse relationship with disease activity. The question of whether this "swing" is modulated at peripheral or central levels will be addressed in the general discussion section.

Due to the fact that disease activity decreased over time, and pain threshold and tolerance increased over time, correlations were calculated on the difference scores of these changes. Although all the correlations were in a negative direction, none of these reached statistically significant levels. This is unfortunate, because a change in disease activity which was significantly correlated with a change in pain responsiveness would have shed further light on the hypervigilance model. However, problems exist with the use of difference scores. Gardner and Neufeld (1985), on mathematical and theoretical grounds, argue that the "simple" change score is not all that simple. This is especially so if correlations are drawn between change scores. They advocate that the elements of the change scores, for example the relationships existing between the variables at each specific measurement session, be examined and their meaning interpreted. This is the approach that has been adopted in the present study.

All the main study variables were entered into a series of multiple regression equations in a manner similar to study 1. However, unlike study 1, 13 of the 16 equations reached statistically significant levels. In 11 of these significant equations, disease activity contributed the largest percentage of the variance accounted for in the equations. Sex came first in the other 2 equations.

Due to the small sample size, the sexes were not considered separately in the equations. However, gender contributed much less to the regression equations than in the first study. As well, the rheumatoid factor titre did not appear first in any of the equations as it did in study 1. Two factors may have led to the overall differences in the regression equations in the two studies. The first is that there were significant differences in disease activity between the sexes in the first study that were not present in the second. The second is that, in study 2, patients with RhF positive or negative were more evenly distributed between the sexes than in study 1. The study population in the present sample was therefore more homogenous in terms of disease activity and RhF.

The absence of these possible biases in the present study makes the pattern of results much easier to interpret. Firstly, although the equations reached statistically significant levels, none of them was significant beyond the $p < .01$ level. As well, the variance in pain threshold and tolerance levels that was accounted

for is generally low (between .16 and .39). Further, when the R^2 was adjusted to control for the sample size and the number of variables in the equations, the adjusted R^2 was considerably lower (between .11 and .28).

The equations for the constant pressure algometer at threshold and tolerance levels showed the highest values for statistical significance levels, R^2 and adjusted R^2. In each of these equations, disease activity was responsible for the greatest proportion of the variance, followed by depression or RhF.

The equations for the dolorimeter at threshold and tolerance levels were also statistically significant but less variance was accounted for than in the equations for constant pressure. Again, disease activity was the most important predictor, followed by depression and rheumatoid factor titre.

The equations for trains of electrical pulses were quite different to those of the other 2 stressors. Only 1 of 4 equations reached statistically significant levels. This was at the tolerance level, with sex included in the equation.

These are interesting results which illustrate some important points. Firctly, each method of pain induction, not only has different physical characteristics, but is also predicted to different degrees by the variables used in this study. The variability of response to shock, a phasic stressor, was the most difficult to predict.

Second, the pattern of predictors to the two pressure stressors was similar, but was significant to different degrees. The variance that was accounted for in the constant pressure algometer, a tonic stressor, was greater than that of the dolorimeter which has both the characteristics of a phasic and a tonic stressor.

It is difficult to view these data within the context of previously published work as no studies have examined the influence of multiple factors on pain responsiveness. Thus, Jimenez and Lane (1985) reported that both pain threshold and tolerance levels increased over time in a group of chronic pain patients and stated that these paralleled a decrease in reported levels of pain. This paper, however, was reported in abstract form and no accompanying statistics were supplied. Jaeger and Reeves (1987) found that trigger point sensitivity improved to pressure with the dolorimeter after treatment. They also found that pain decreased. However, although the correlation between pain and sensitivity was in a negative direction, this did not reach statistical significance. Huskisson and Hart (1972), in a study of 106 R.A. patients, found that disease activity was not significantly correlated with pain threshold to the dolorimeter. But, a significant negative correlation ($r = -.25$) was found between the number of analgesics taken on demand and pain threshold levels. As analgesic intake can be used as an indicator of endogenous pain, it was concluded that pain

levels and pain threshold values may be negatively associated.

The influence of psychological factors on pain responsiveness has been discussed extensively in the past. For example, Merskey and Evans (1975) showed that patients with organic disease had higher pain thresholds than those with psychiatric complaints, such as anxiety, depression and hysteria. Dworkin and Chen (1982) suggest that anxiety provoking situations will reduce pain tolerance levels. However, Craig (1986) reports a much clearer influence of anxiety and its effects on reducing pain threshold levels. This position is supported by the data of Forgione and Clark (1974) who, using the constant pressure algometer, also found a negative relationship between pain threshold levels, and the fear and apprehension of dental pain.

Most reports of an association of pain and either depression or anxiety deal with endogenous pain, not exogenously induced pain. Thus anxiety and depression have both been often reported to be concomitant with pain (Sternbach, 1978; Lupton, 1969; Skevington, 1983). As well, hysteria and hypochondriasis have often been reported to be present. But their influence on pain responsiveness is not clear.

The third important factor to come out of the data from the regression equations was that the rheumatoid factor titre again showed up as an important predictor, in the same equations as disease activity. Therefore, its

effect may be seen as separate from disease activity. Its contribution to the equations was much less than in study 1, but was still high when compared to some of the other variables. Due to its presence in both studies as a significant predictor of pain responsiveness, it would be instructive to conduct a prospective study which might further examine the different patterns of pain responsiveness, personality styles and other factors, in patients who are negative to rheumatoid factor titre. Such an investigation might serve to identify the factors that lead those patients to be different from the normally larger number of RhF positive patients.

Limitations of the present study.

The limitations of the first study, such as the non-random sampling of the subjects, and the blinding of the experimenter to the study data, are also applicable to the present study. As well, the reduced sample size of the present study means that the results need to be replicated on a larger sample before definite conclusions can be made.

Summary

A reduced sample size returned to participate in the present study. No differences were found between the sexes on overall levels of disease activity. However, men had higher overall pain tolerance levels than women.

Disease activity had decreased, and pain threshold and tolerance levels had increased at study 2, when compared to

study 1. Simple correlations between these measures found a significant negative association between disease activity and each of the overall pain threshold and tolerance levels. However, multiple regression analyses revealed a different pattern of association between the main study variables and each of the 3 physical stressors. In the regression equations, disease activity was the most important predictor of pain responsiveness, followed by depression and rheumatoid factor titre.

The results of the present study show clearly that there is a negative relationship between pain responsiveness and disease activity. Pain threshold and tolerance levels are not static but change predictably in response to different levels of disease state. Patients become generally more sensitive, or vigilant, in higher levels of disease activity.

The meaning of the main findings of study 1 and study 2 will be further explored in the general discussion section following Study 3.

Chapter 5

Study 3

Preview

It will be remembered from Chapter 2 that patients with fibrositis come under the broad heading of "soft-tissue rheumatism". Fibrositis is an interesting condition but is difficult to treat, although some success has been reported after treatment with low-dose amitriptyline. Unlike the R.A. patients of the previous chapters, fibrositis patients have chronic generalized pain in the absence of any "hard", routine diagnostic test. However, in common with most chronic pain patients, the pain has a profound influence on different areas of their lives. Therefore, the outcome measures adopted in any treatment study that expects a positive effect on the symptoms associated with the condition, must sample all the domains of the experience. Thus, in the present study, measures of pain responsiveness, pain, mood, personality and function will all be included as outcome measures. Each of these has been demonstrated in the past to be associated with the symptoms of fibrositis.

Method

Subjects.

Thirty-nine subjects entered the study. These subjects had all been diagnosed a minimum of 6 months previously as having primary Fibrositis/Fibromyalgia (FS/FM) syndrome.

(See Appendix I for the diagnostic criteria of FS/FM syndrome adopted by this study). Thirty-six of these patients were referred for possible participation in the study by Dr. G. McCain and 3 were referred by Dr. M. Harth. Potential subjects were approached by letter and then by follow-up telephone call to request their participation. Patients were free to refuse to take part in the study with the understanding that refusal would not prejudice their treatment in any way. Eighty-nine potential subjects were initially approached. Of these, 39 agreed to take part.

Thirty-six subjects completed the study. The age range of the subjects was from 24 yrs to 59 yrs with a mean of 39.9 yrs and a standard deviation of 10.2 yrs. Thirty-two of the subjects were female and 4 were male.

Exclusions.

Potential subjects who fell into the following categories were excluded from the study:

(1) Those who had been treated with amitriptyline within the previous year.

(2) Those who had previously demonstrated a hypersensitivity to amitriptyline.

(3) Those who had a previous history of glaucoma, urinary retention, congestive cardiac failure or cardiac arrythmia.

Non-steroidal anti-inflammatory medication, hypnotics, anti-depressant agents and anxiolytics were discontinued for a minimum of 3 weeks prior to entry into the study. All

subjects who wished to take analgesic medication were requested to take only ordinary Tylenol (acetaminophen). No medication was to be taken within 12 hours prior to each testing session.

Consent Forms.

One consent form was used for all subjects. This form outlined the design of the study and the procedures to be used. (See Appendix J). Subjects were given the opportunity to ask questions before signing the form.

Apparatus.

1. Dolorimeter: A Chatillon Company (Kew Gardens, New York) variable pressure dolorimeter, as used in Study 1, was employed.

2. The McGill Pain Questionnaire (MPQ): This scale uses verbal descriptors which attempt to measure 3 different dimensions of pain, Sensory, Affective and Evaluative (Melzack, 1975) (See Appendix K). There are 10 groups of words in the sensory dimension, 5 groups in the affective and 1 group of words in the evaluative. The questionnaire was administered in written form. Subjects were required to underline a maximum of 1 word in each group of words that best described their pain "at the present moment". Scoring was based on (a) the total number of words chosen in all dimensions (NWC), (b) the sum of the rank values of the word descriptors chosen in each dimension. This yielded 1 score for each of the 3 different dimensions - Sensory (PRI (S)), Affective (PRI (A)) and Cognitive (PRI (C)), and

(c) the sum of the ranked scores from all dimensions (PRI (T)). For all analyses, the PRI (T) total is the value that is presented and is referred to in the subsequent text simply as the PRI.

3. The Sickness Impact Profile (SIP) : This is a self-report measure of health status and disability (Berger et al, 1981) which has been validated and used in other clinical populations (for example, Follick et al, 1985). It consists of 136 items in check-list format. These items are sub-classed into 12 different categories. However, only 7 of the categories were administered in this study. These were:- sleep and rest, domestic activities, recreation and pastimes, mobility, social interaction, alertness behavior, and emotional experience. Scores were based on (a) individual category scores and (b) the Total Impairment Score (TIS) which is the sum of the individual category scores. (See Appendix L for a description of the Sickness Impact Profile).

4. The Basic Personality Inventory (BPI) : This Personality test has been described in Study 1. In the present experiment, only the Hypochondriasis scale data are reported.

5. The Spielberger State/Trait Anxiety Inventory (STAI): This questionnaire measures both state (" How you are feeling right now") and trait ("How you generally feel") anxiety (Speilberger et al, 1970). Each dimension consists of 20 items answered on a 4-point scale of intensity to

yield a single score for each of state and trait anxiety. Only the State portion of the inventory was administered (See Appendix M).

6. The Beck Depression Inventory (BDI) : This is a 21 item self-report measure of depressed mood (See Appendix N). The reliability and validity of this instrument have been repeatedly confirmed (Beck and Baemesderfer, 1974). Scores on the individual questions are summed to yield one total score.

Two important principles guided the selection of the measures that were employed in this study. The first was conceptual, i.e. that the variables would adequately reflect the multi-faceted nature of the experience of pain. The second was largely statistical, in that each measure could be used in a manner that would yield sufficient information from the one overall score from the test, or inventory. Therefore, it was an a priori intention of this study to use only the summary statistic of the overall measures in the analysis of the data.

Measures employed.

Pain threshold.

Pain threshold measures were taken with the dolorimeter in the same manner as in Study 1. However, in this experiment, four points were tested. These were:

(a) a point on each arm mid-way between the styloid

process of the radius and the lateral epicondyle of the humerus with arm pronated and supported.

(b) a point on the shin which lay at the mid-point of the anterior surface of each tibia, with the subject in the supine position and the leg extended and supported.

Pain threshold was taken as the mean of these four points. No points were spontaneously tender to palpation before testing.

Pain tolerance

Pain tolerance was measured using the dolorimeter in the same way as in Study 1, except that the same four points were tested as for pain threshold as described above.

Total Myalgic Score (TMS).

The total myalgic score was taken as sum of the pain thresholds readings from eight "tender points". These points were taken as being representative of normally present "fibrositic tender points" (Carette et al, 1986). These measures were gathered in the same way, using the dolorimeter, as for the more generalized pain threshold measures. The points tested were:

(a) a point on each side of the neck, at the middle of the upper border of the upper fold of the trapezius muscle.

(b) a point on each side of the anterior surface of the chest wall which lay at the second costo-chondral junction.

(c) a point on the extensor aspect of each forearm which lay 2 cm. distal to the lateral epicondyle of the humerus.

(d) a point on each leg which lay over the medial fat pad of the knee.

Points (a) and (b) were tested in sitting. Points (c) and (d) were tested in the prone lying position.

All the points that were tested for pain threshold, tolerance and the total myalgic score were randomized for order and side of delivery.

Patient Global Assessment of Well-being.

This is an ordinal scale that has been used previously in clinical studies as an estimate of treatment efficacy (Carette et al, 1986). After each treatment period the subject was asked, based on how they felt at the start of the study, whether they felt : (1) Worse, (2) Unchanged, (3) Minimally improved, (4) Moderately improved or, (5) Markedly improved.

Pill Count.

All patients were asked to keep a record of the number of analgesics (acetaminophen, "ordinary Tylenol") that they took each day. This was the only analgesic medication allowed for all subjects for the course of the study. Patients, as an indicator of compliance during the treatment periods, were also asked to record that they had taken their study medication (either amitriptyline or placebo). As a further measure of compliance, patients were asked to return their medication bottles at the end of each treatment period to let the investigator count the number of pills remaining.

The Design of the Study.

A completely randomized double-blind cross-over design was employed. Patients giving informed consent were randomized into two groups, either an amitriptyline first group or a placebo first group. Prior to the inception of the study, randomization procedures for a total possible sample size of 50 patients had been carried out by the research pharmacist. The amitriptyline was in capsules that were identical to the placebo capsules.

A sample size of 35 was calculated to be needed to yield a power of 80% with alpha set at .05. The study was designed so that all data would be collected within one year and all available subjects, up to a maximum of 50, would be included within that time period.

Each group had a period of four weeks on the placebo and on the amitriptyline (10 mg/day for the first week, 20 mg/day for the second week and 50 mg/day for the final 2 weeks).

There was a "wash out" period of two weeks between the cross-over. This has been shown to be an adequate time from previous research to clear the effects of amitriptyline between treatment and placebo periods (Watson et al, 1982).

All subjects who wished to continue on the medication after the study were given an opportunity to do so. Measures were therefore taken at:

(a) baseline, on the first day of the study.

(b) 4 weeks, after the initial "treatment" period.

(c) 6 weeks, after the two week wash-out period.

(d) 10 weeks, after the second "treatment" period.

Procedure.

Thirty-nine subjects entered the study. The data were collected between the months of February, 1986 and February, 1987 between the hours of 8.00 a.m. and 7.00 p.m.. All subjects were tested by the same experimenter, in the same quiet environment at the Rheumatic Diseases outpatient unit of University Hospital.

Each subject read and signed the consent form, after having the procedures explained. An opportunity was given to ask questions about the study.

The subject's pain level was recorded first on the McGill Pain Questionnaire. The subject was then tested, in turn, for measures of pain threshold, pain tolerance and total myalgic score with the dolorimeter. After these measures were gathered, the stimulus points were examined for possible damage to the skin. No damage ever occurred but mild reddening of the stimulated area was a frequent finding.

The various inventories were then administered after explanation of their use by the experimenter. The inventories were administered in the following order: (1) state anxiety, (2) the Beck Depression Inventory, (3) the BPI and (4) the Sickness Impact Profile.

Global assessments of well-being were taken at the second, third and fourth visits, directly before the McGill Pain Questionnaire was completed.

Lastly, a further opportunity was given to ask any questions. After a further appointment had been made, the patient was given a prescription to be taken to the pharmacy department at University Hospital. Each testing period lasted approximately 90 minutes on the first session and 60 minutes on subsequent sessions.

Results

The main purpose of this study was to examine changes in pain responsiveness in patients with fibrositis after they had been treated with amitriptyline. Three measures of pain responsiveness were taken - pain threshold, pain tolerance and the total myalgic score. The other dependent measures were pain, anxiety, depression, hypochondriasis and sickness impact.

It was expected that a large proportion of patients would not display a clinically significant response to treatment. Therefore, after initial data analysis was completed on all subjects as a whole group, the subjects were split into two groups on the basis of their subjective estimate of well-being after the amitriptyline (Am) treatment period.

The results are presented in the following manner. Descriptive data are presented first. This is followed by the initial analysis which was by multivariate analysis of variance (Manova) with repeated measures on the 8 study variables with two groups. The groups consisted of patients who received Am first and those who received placebo (Pl) first. All variables were entered directly into the analysis as no a priori assumption was made on the relative clinical importance of each variable in the analysis.

Next, each variable is analyzed in turn with repeated measures analysis of variance (Anova). Post-hoc multiple comparisons are then presented with particular emphasis on

the measures of pain responsiveness. Planned a priori contrasts are also presented for each variable between the post-Am period and the post-Pl period. Lastly, for the group as a whole, the inter-relationship of all the main study variables is presented, as well as the relationship within each main variable across time.

The second phase of the analysis followed the division of all the subjects into two groups on the basis of their subjective response to Am as measured by their subjective estimate of well-being. The first group was classed as not improved, or "unchanged", by the active treatment. The second group was classed as "improved". There were 16 patients (45%) in the unchanged group and 20 (55%) in the improved group. This subdivision was based on the study of Carette et al (1986) who, using the same 5-point scale, defined a meaningful improvement as a "moderate or marked improvement by the patient's overall assessment".

Initial analysis was by repeated measures Manova with the 2 groups, followed by repeated measures Anova for each variable and post-hoc comparisons. The analysis was then repeated for each group, improved or unchanged, taken separately to examine the change of the variables within groups across time. Post-hoc multiple comparisons as well as a priori planned contrasts are presented in a manner similar to that of the initial analysis.

Finally, 2 step-wise discriminant function analyses are presented. The first examines the extent to which the main

study variables at baseline can predict response to treatment. The second examines the relative contribution of each variable after the Am period to the improved or unchanged classification.

In presenting the results of each of the major analysis sets, the main research question of interest will be stated first, then the results.

Thirty-six of the the original 39 subjects completed the study. Of these, 32 were female and 4 were male, with a mean age of approximately 40 yrs. They had been experiencing their condition for a mean of 5.1 yrs (Table 1). Two males were in each group. Three subjects withdrew from the trial: 2 withdrew for reasons that were believed to be drug-related (one in the Am-first group, one in the Pl-first group): one subject, in the Pl first group, withdrew because of insufficient therapeutic effect. The data of the 3 subjects who withdrew are not included in the analyses.

First Set of Analyses

Taking all the subjects as a group, is there a significant change in the dependent measures across time in response to treatment?

A between groups Manova with repeated measures was performed for the effects of group, group by time and time (Table 2). There was no significant effect for group (placebo or amitriptyline first), or group by time.

Table 1.

Descriptive data of the study population.

Female:Male ratio		8:1
N of subjects		36
Age (yrs)	$\bar{X}$	39.9
	SD	10.2
	Range	24-59
Duration of pain (yrs)	$\bar{X}$	5.1
	SD	4.6

Table 2.

Multivariate analysis over time for all subjects

2a. Multivariate analysis of variance for group - placebo first or amitriptyline first.

	Value	Exact F	Hypoth df	Error df	Sig of F
(a) Pillais	.2340	0.84	8.00	22.00	0.578

2b. Multivariate analysis of variance for (a) group by time, and (b) time.

	Value	Approx F	Hypoth df	Error df	Sig of F
(a) Pillais	.3036	1.16	24.00	232.63	0.277
(b) ''	.6998	3.12	24.00	236.00	0.0001

2c. Univariate F tests for time for main study variables.

Variable	Hypoth SS	Error SS	Hypoth MS	Error df	F	Sig of F
TMS	1132.28	2863.99	377.43	32.92	11.47	0.0001
PTH	202.07	2449.97	67.35	28.16	2.39	0.074
PTOL	113.99	7604.44	37.99	87.40	0.43	0.729
PAIN	407.86	2567.07	135.95	29.51	4.61	0.005
HYP	46.38	322.41	15.46	3.70	4.17	0.008
SIP	553.69	1413.72	184.56	16.25	11.36	0.0001
ANX	479.06	2293.83	159.69	26.37	6.06	0.001
DEP	595.81	1308.86	198.60	15.04	13.20	0.0001

Legend: TMS = total myalgic score; PTH = pain threshold; PTOL =Pain tolerance; HYP = hypochondriasis; SIP = sickness impact; ANX = anxiety; DEP = depression.

However, there was a highly significant effect for time across the four testing sessions (Table 2b). The Pillais trace criterion is used to improve the robustness of the test throughout the analyses and to compensate for any deviations from normality and homogeneity (Tabachnick and Fidell, 1983; Olson, 1979). Univariate F tests showed that all the variables except pain threshold and tolerance levels showed significant effects for time (Table 2c).

The more powerful Anova for the individual variables was used to examine the effects for group, group by time, and for time (Table 3). No significant group effects were found for any of the variables. For each of total myalgic score, pain, hypochondriasis, depression, anxiety and sickness impact, highly significant effects were found for time but not group by time (Tables 3a, 3d, 3e, 3f, 3g and 3h). Mean values are presented in Figures 3 to 10, with error bars representing one standard error of the mean.

Two further analyses were carried out in order that the relationship between depression and pain could be more fully explored. First an Anova was performed on levels of pain controlling for depression, and then an Anova was performed on levels of depression controlling for levels of pain. Each of these analyses reached statistically significant levels; $F = 4.01$, $p < .01$ for pain, and $F = 4.28$, $p < .01$ for depression. In both cases, the significance levels are reduced from the values reported in Table 3.

Table 3.

Multivariate analyses by time for the individual variables.

3a. Averaged multivariate test for total myalgic score

	SS	DF	MS	F	SIG
Within cells	3109.01	102	31.40		
Time	1090.27	3	363.42	11.57	0.0001
Group by Time	40.68	3	13.56	0.43	0.731

3b. Averaged multivariate test for pain threshold

	SS	DF	MS	F	SIG
Within cells	2826.72	102	28.55		
Time	224.75	3	74.92	2.62	0.055
Group by Time	21.98	3	7.33	0.26	0.856

3c. Averaged multivariate test for pain tolerance.

	SS	DF	MS	F	SIG
Within cells	8089.18	102	87.71		
Time	150.04	3	50.01	0.61	0.609
Group by Time	817.76	3	272.59	3.34	0.022

3d. Averaged multivariate test for pain

	SS	DF	MS	F	SIG
Within cells	2586.67	102	28.74		
Time	400.65	3	133.55	4.65	0.005
Group by Time	33.40	3	11.13	.39	0.762

3e. Averaged multivariate test for hypochondriasis

	SS	DF	MS	F	SIG
Within cells	364.51	102	4.05		
Time	51.90	3	17.30	4.27	0.007
Group by Time	6.71	3	2.24	0.55	0.648

3f. Averaged multivariate test for sickness impact

	SS	DF	MS	F	SIG
Within cells	1413.32	102	16.25		
Time	553.69	3	184.56	11.36	0.0001
Group by Time	69.18	3	23.06	1.42	0.243

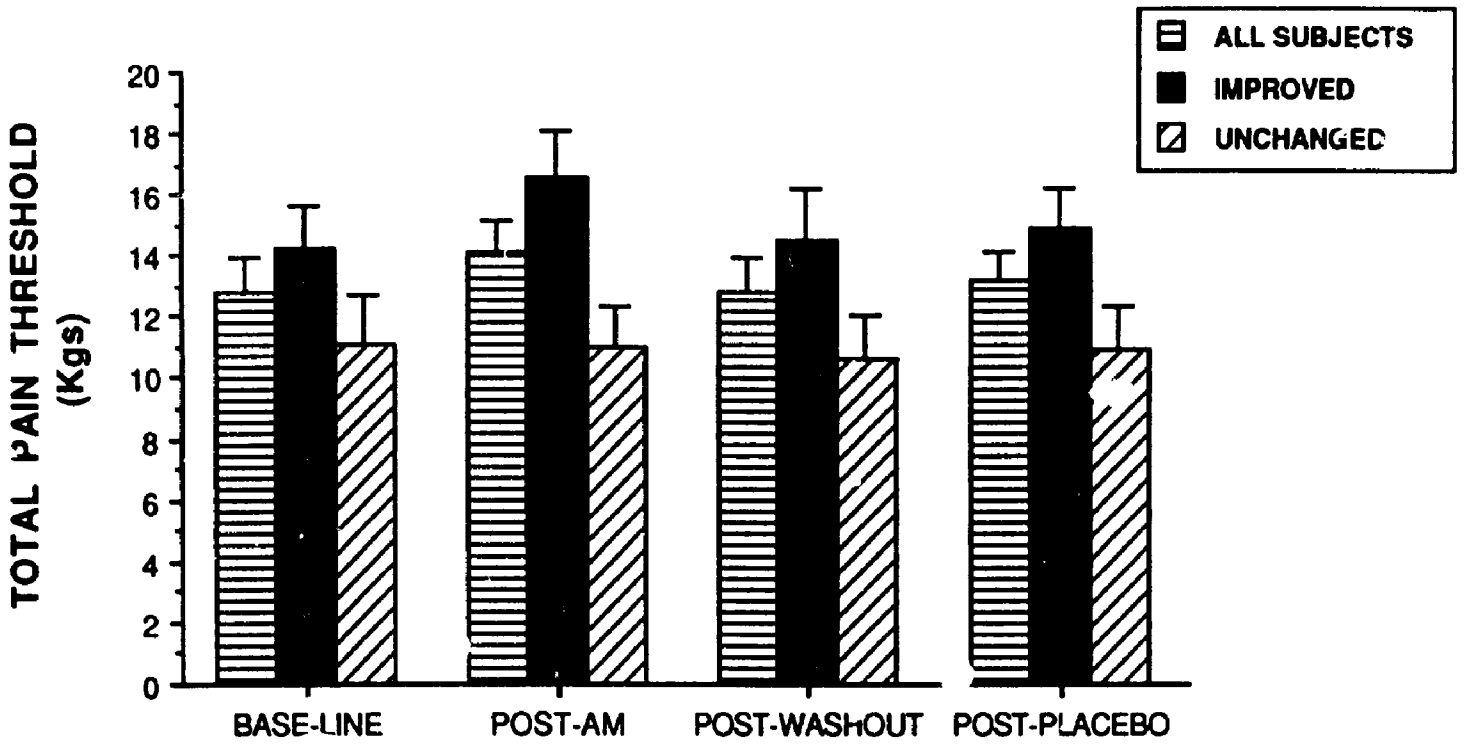
3g. Averaged multivariate test for anxiety

	SS	DF	MS	F	SIG
Within cells	2367.24	102	26.31		
Time	436.85	3	145.62	5.53	0.002
Group by Time	156.79	3	52.26	1.99	0.122

3h. Averaged multivariate test for depression

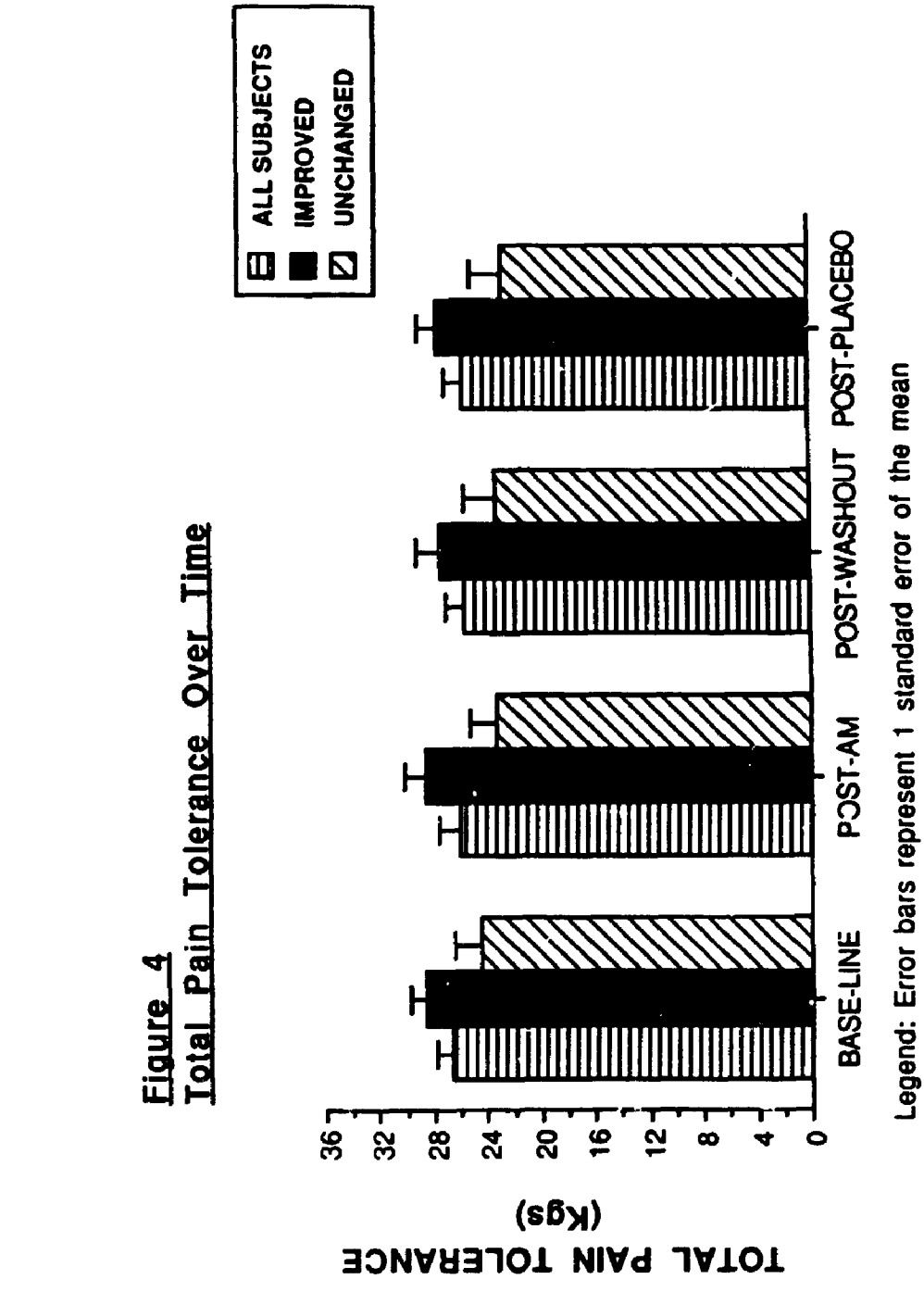
	SS	DF	MS	F	SIG
Within cells	1595.45	102	17.73		
Time	659.49	3	219.83	12.40	0.0001
Group by Time	54.40	3	18.13	1.02	0.386

Figure 3
Total Pain Threshold Over Time



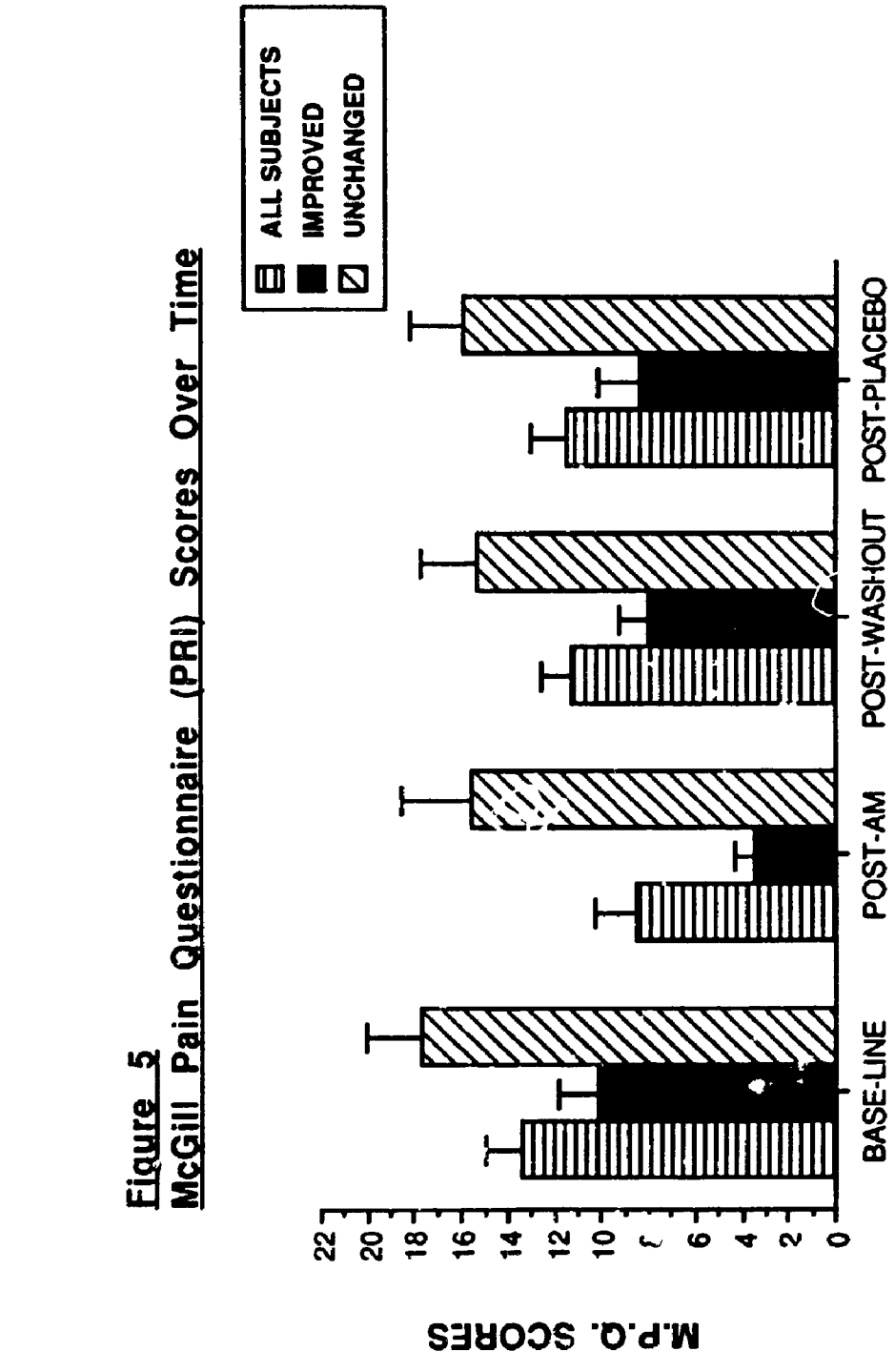
Legend: Error bars represent 1 standard error of the mean

Figure 4
Total Pain Tolerance Over Time



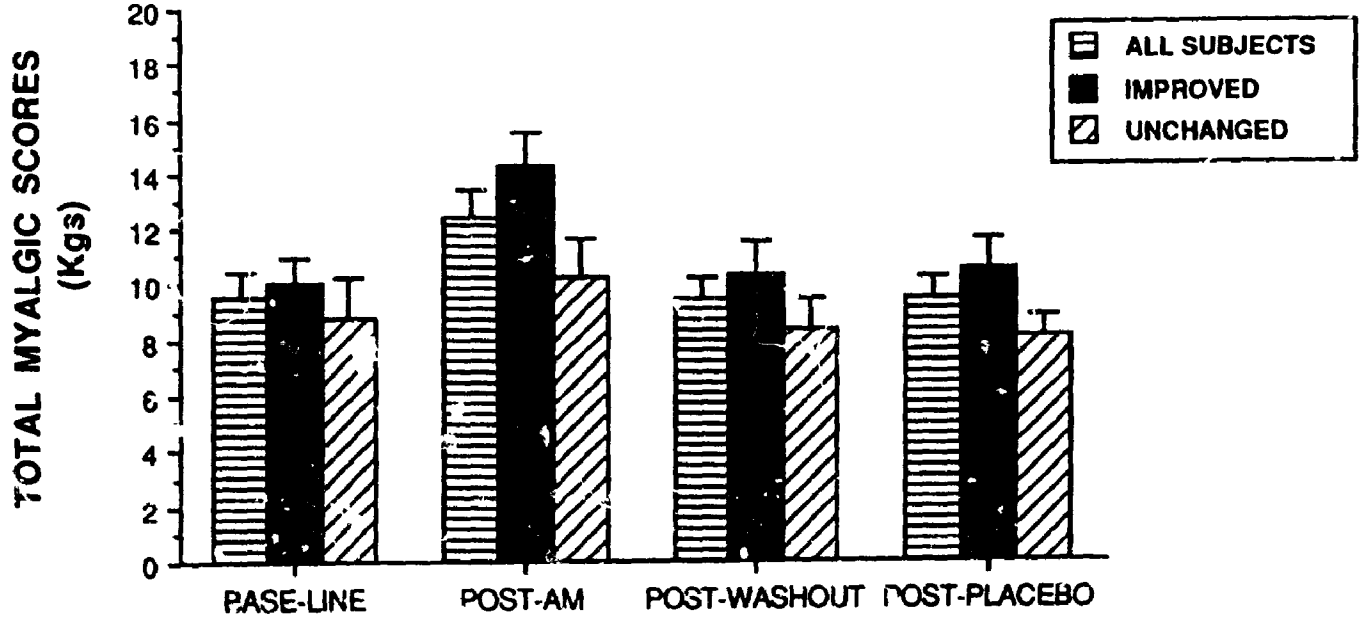
Legend: Error bars represent 1 standard error of the mean

Figure 5
McGill Pain Questionnaire (PRI) Scores Over Time



Legend: Error bars represent 1 standard error of the mean

Figure 6
Total Myalgic Scores Over Time



Legend: Error bars represent 1 standard error of the mean

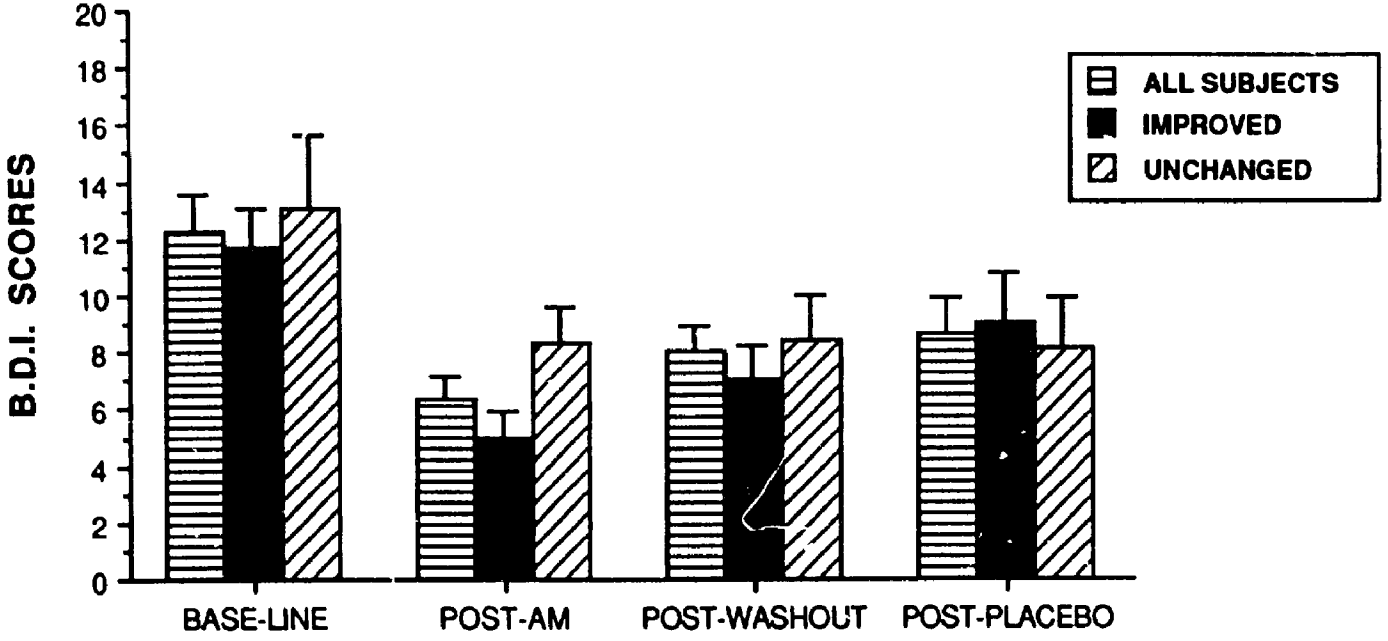

3
1.0
1.1
1.25
1.4
1.6
1.8
2.0
2.2
2.5
2.8
3.2
3.6
4.0
4.5
5.0
MicroD

Table 7.

Descriptive data of the improved and unchanged groups

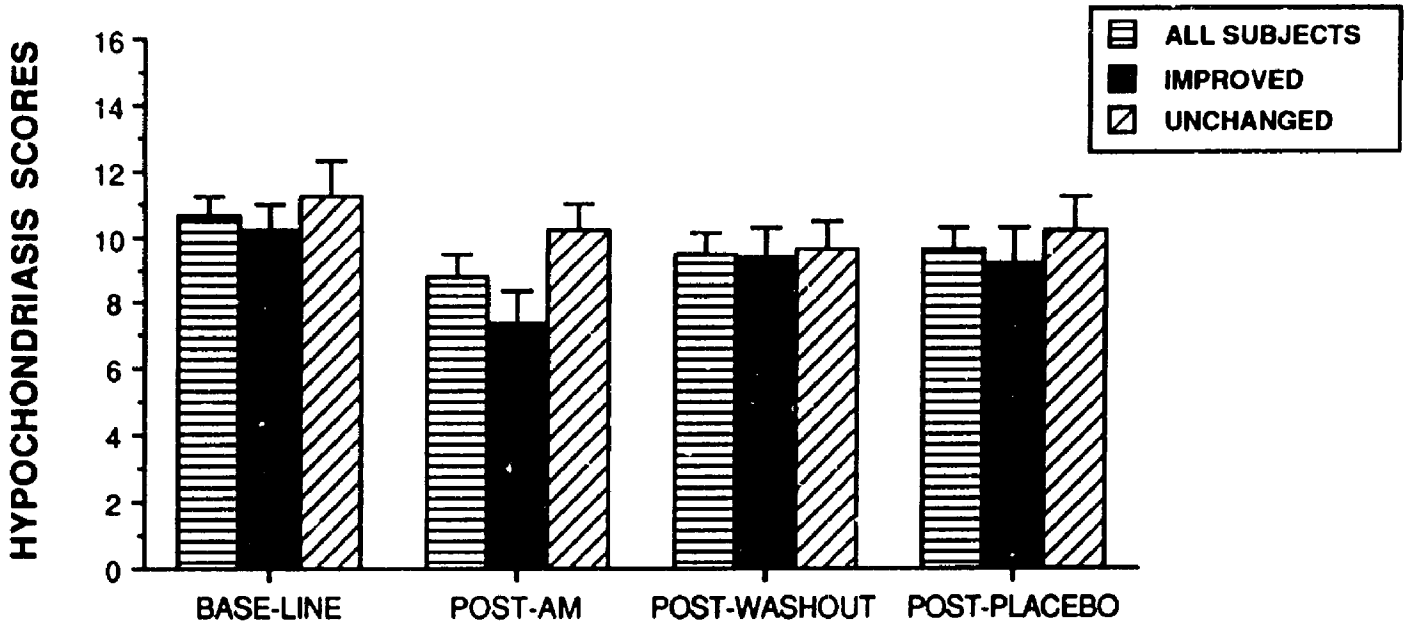
		Improved	Unchanged
Female:Male ratio		18:2	14:2
N of subjects		20	16
Age (yrs)	$\bar{X}$	40.6	39.4
	SD	10.5	10.1
Duration of pain (yrs)	$\bar{X}$	5.6	4.7
	SD	5.5	3.8

Figure 8
Beck Depression Inventory Scores Over Time



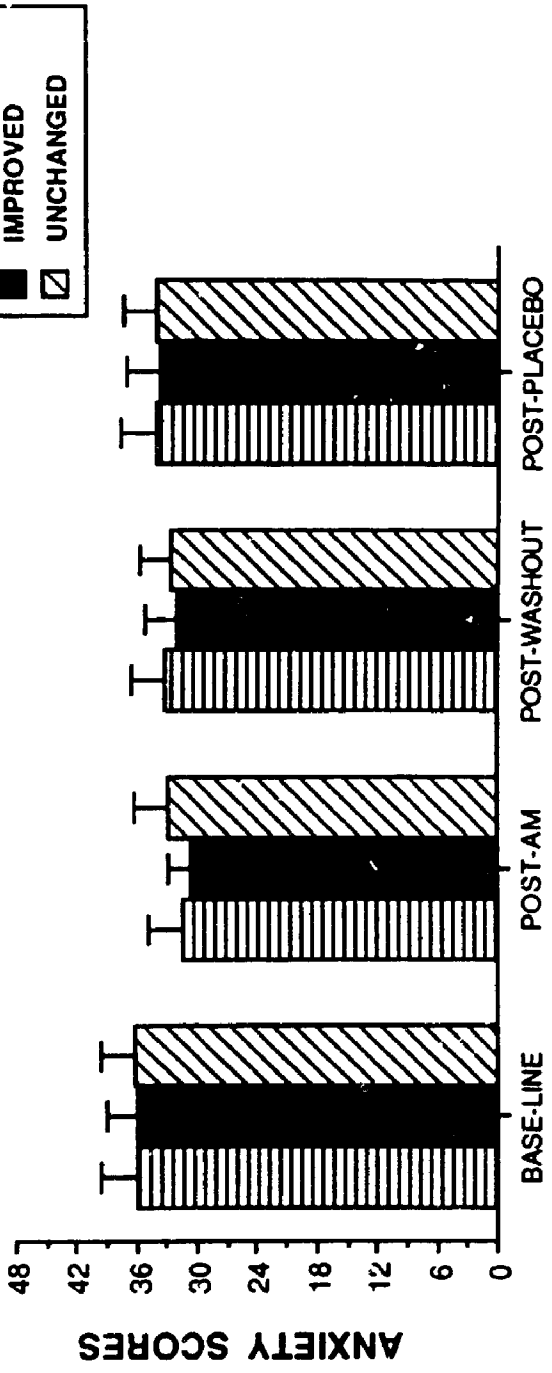
Legend: Error bars represent 1 standard error of the mean

Figure 9
Hypochondriasis Scores Over Time



Legend: Error bars represent 1 standard error of the mean

Figure 10
Spielberger State Anxiety Inventory Scores Over Time



Legend: Error bars represent 1 standard error of the mean

For pain threshold, the effects for time approached statistical significance ($F = 2.26$, $P < .055$) (Figure 3). For pain tolerance, a significant interaction was found for group by time (Figures 4 and 11). It can be seen that the group which received Am first showed an increase in pain tolerance after the Am period, while the Pl first group showed a decrease at the same time. As well the Pl first group had a higher score post-placebo than the Am first group. However, only after the Am period was there a significant difference between the groups, with the Am first group showing a higher pain tolerance than the Pl first group ($t(34) = 2.23$, $p < .05$).

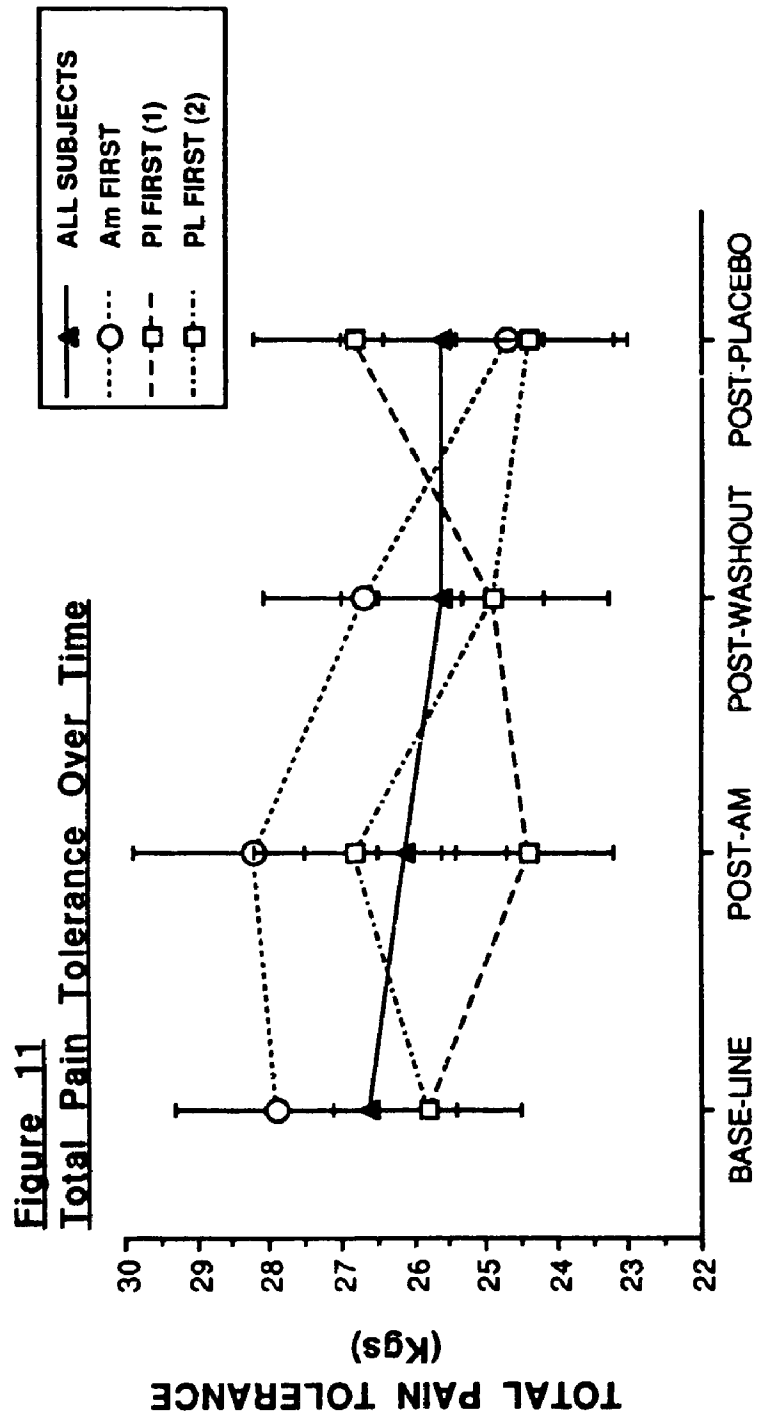
Tukey's HSD test was selected for all pairwise post-hoc comparisons. This test sets the experimentwise error rate for all pairs of comparisons (Kirk, 1982). Alpha was set at the .05 level. The results from the significant overall tests for time are listed below:-

a. For the McGill pain scores, the values were significantly lower at the post-Am period than at baseline. No other comparisons were significant (error term=27.9) (Figure 5).

b. For the total myalgic score, the values were significantly higher at the post-Am period than at any other time. No other comparisons were significant (error term = 31.83) (Figure 6).

c. For the Sickness Impact Profile, the scores at baseline were significantly higher than at all other times (error

Figure 11
Total Pain Tolerance Over Time



Legend: Error bars represent 1 standard error of the mean

term = 15.55). No other comparisons were significant. (Figures 7 and 12).

d. For depression, the value at baseline was significantly higher than all other times (error term = 15.26). No other comparisons were significant. (Figure 8).

e. For hypochondriasis, the value at baseline was significantly higher than that of the post-Am period (error term = 3.52). No other comparisons were significant. (Figure 9).

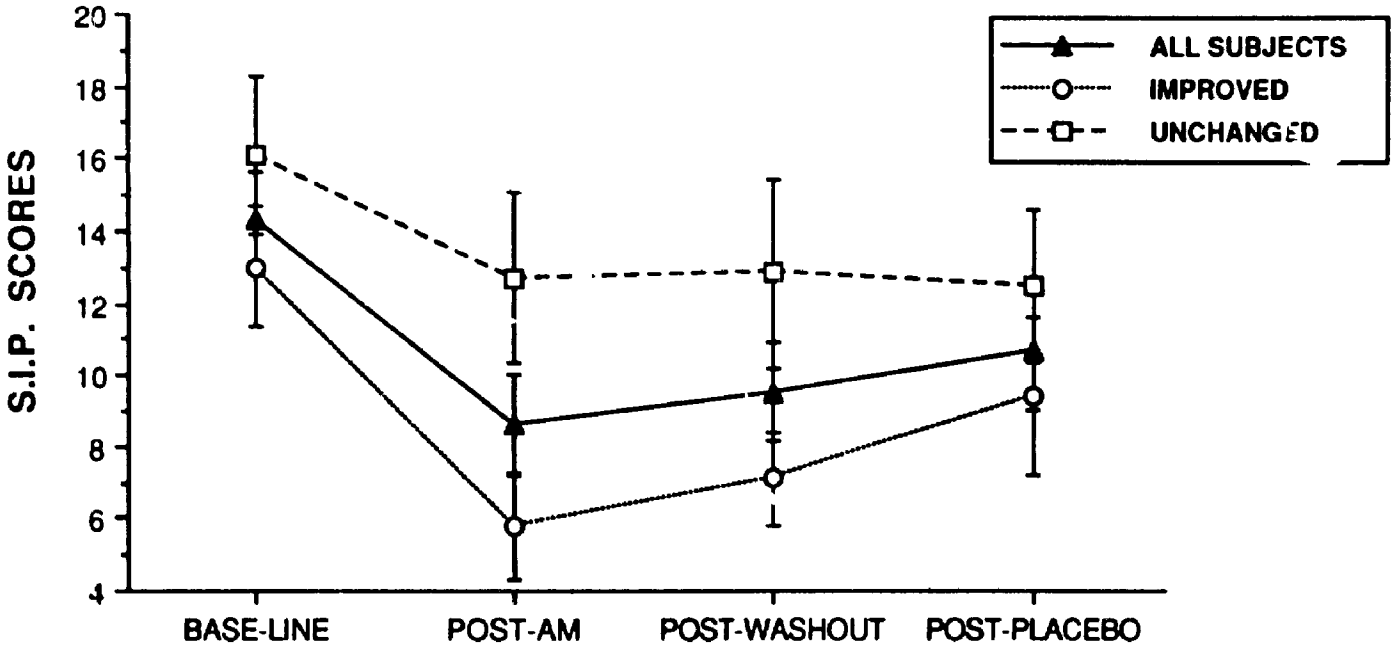
f. For anxiety, the value at baseline was significantly higher than that of the post-Am period (error term = 27.79). No other comparisons were significant. (Figure 10).

Second Set of Analyses.

What is the pattern of association among the main study variables?

Pearson product moment correlations of the main study variables are displayed in Tables 4a for the baseline measures and 4b for the post-Am measures. At baseline, the measures of pain responsiveness: pain threshold, tolerance and total myalgic score show highly significant positive correlations with each other. Levels of pain, as measured by the MPQ, were negatively correlated with the previous 3 variables, but only the correlation between pain and pain tolerance reached statistical significance. Hypochondriasis was also significantly positively correlated with pain and

Figure 12
Sickness Impact Profile - Demonstrating Interactive Effects



Legend: Error bars represent 1 standard error of the mean

Table 4a.

Correlations between the main study variables at baseline.

	AGE	LEN	TMS	PTH	TOL	SIP	HYP	DEP	ANX
AGE	-								
LEN	.37*	-							
TMS	.02	.02	-						
PTH	-.00	-.08	.70+	-					
TOL	-.03	.19	.61+	.66+	-				
SIP	.09	.37*	-.21	-.13	-.24	-			
HYP	-.02	.07	-.25	-.43**	-.29*	.31*	-		
DEP	-.15	.04	-.29*	-.16	-.13	.60+	.40**	-	
ANX	-.19	-.16	-.13	.00	-.15	.35*	-.00	.26	-
PAIN	-.19	-.17	-.23	-.23	-.44**	.21	.34*	.26	.27

Table 4b.

Correlations between the main study variables after amitriptyline.

	AGE	LEN	TMS	PTH	TOL	SIP	HYP	DEP	ANX
AGE	-								
LEN	.37*	-							
TMS	.06	-.14	-						
PTH	-.09	-.13	.81+	-					
TOL	-.06	-.04	.45**	.51+	-				
SIP	.12	.22	-.31*	-.31*	-.09	-			
HYP	-.05	.17	-.35*	-.38*	-.18	.46**	-		
DEP	-.10	.13	-.25	-.23	-.09	.76+	.30*	-	
ANX	-.20	-.21	-.12	-.24	-.04	.34*	-.25	.64+	-
PAIN	-.05	.34*	.00	-.15	-.22	.52**	.22	.61+	.48**

* = p < .05
** = p < .01
+ = p < .001

Legend: LEN = Length of symptoms; TMS = Total myalgic score; PTH = Pain threshold; TOL = Pain Tolerance; SIP = Sickness impact profile; HYP = Hypochondriasis; DEP = Depression; ANX = Anxiety; PAIN = MPQ score

significantly negatively correlated with pain threshold and tolerance levels.

Sickness impact shows the highest number of significant correlations of all the variables, being positively correlated with the length of symptoms, anxiety, depression and hypochondriasis. Depression is also significantly negatively correlated with the total myalgic score.

After the amitriptyline period, the pattern of correlations is similar to those at baseline. Sickness impact shows the same significant correlat. ; as at baseline with the addition of significant negative correlations with total myalgic score and pain threshold and a positive correlation with pain levels. Pain tolerance is only positively correlated with pain threshold and the total myalgic score, but the total myalgic score and pain threshold are also significantly correlated with sickness impact and hypochondriasis.

The pattern and strength of positive associations between the measures of sickness impact, anxiety, depression and hypochondriasis increases after the Am period. As well, pain is positively correlated with sickness impact, anxiety and depression, but not with hypochondriasis as it was at baseline. Further, anxiety shows a highly significant positive correlation with depression which was not present at baseline. Lastly, length of symptoms becomes positively correlated with pain

levels post-Am, but is no longer significantly correlated with sickness impact.

Correlations within the individual variables across the different testing sessions show a strongly significant positive pattern (Table 5). With two exceptions, all are significant at the $p < .001$ level. The exceptions are the correlations between anxiety at baseline and after the placebo period, and the correlation of pain scores between the baseline measure and after the amitriptyline period. Both of these are significant at the $p < .01$ level.

For the measures of pain responsiveness, pain threshold shows the strongest pattern of correlations and the total myalgic score the weakest. Most of the other variables show strong patterns of correlations across testing times. However, overall, both the pain scores and the anxiety ratings show only moderate to strong patterns.

Estimates of well-being after the treatment periods.

A comparison of subjective global estimates of well-being between the post-Am and post-Pl revealed that patients rated themselves as significantly improved after the amitriptyline period ($X^2 = 21.6$, $p < .001$). Eight patients (22%) showed some placebo response. (Table 6). However, most of the patients rated themselves as unchanged after the placebo period. In contrast, after the amitriptyline treatment period, the majority of the patients rated themselves as being either moderately or markedly improved.

Table 5

Correlations within the main study variables across time

5a. Total Myalgic Score

	B.L.	P-AM.	P-WO.
B.L.	-		
P-AM	.74	-	
P-WO	.70	.87	-
P-PL	.60	.82	.86

5b. Sickness Impact Profile

	B.L.	P-AM.	P.WO.
B.L.	-		
P-AM	.76	-	
P-WO	.79	.86	-
P-PL	.67	.77	.71

5c. Total Pain Threshold

	B.L.	P-AM.	P-WO.
B.L.	-		
P-AM	.83	-	
P-WO	.90	.89	-
P-PL	.88	.85	.88

5d. Hypochondriasis

	B.L.	P-AM.	P.WO.
B.L.	-		
P-AM	.70	-	
P-WO	.72	.74	-
P-PL	.69	.79	.82

5e. Total Pain Tolerance

	B.L.	P-AM.	P-WO.
B.L.	-		
P-AM	.72	-	
P-WO	.93	.75	-
P-PL	.85	.92	.82

5f. Anxiety

	B.L.	P-AM.	P.WO.
B.L.	-		
P-AM	.64	-	
P-WO	.67	.74	-
P-PL	.44	.59	.73

5i. McGill Pain Scores

	B.L.	P-AM.	P-WO.
B.L.	-		
P-AM	.50	-	
P-WO	.62	.70	-
P-PL	.67	.60	.68

5j. Depression

	B.L.	P-AM.	P.WO.
B.L.	-		
P-AM	.76	-	
P-WO	.79	.86	-
P-PL	.67	.77	.71

Legend: B.L. = Baseline; P-AM = Post Amitriptyline; P-WO = Post-Washout; P-PL = Post-Placebo.

Table 6.

Patient global treatment efficacy ratings after amitriptyline and after placebo.

	POST-AM	POST-PLACEBO
RATING	N	N
1. WORSE	3	8
2. UNCHANGED	6	20
3. MINIMALLY IMPROVED	7	5
4. MODERATELY IMPROVED	12	2
5. MARKEDLY IMPROVED	8	1

Chi^2 (4df) = 21.6, $p < .001$

On the basis of the estimates at the post-Am period, the subjects were divided into two approximately equal groups for further data analysis. One group, who rated themselves as either worse, unchanged, or minimally improved was classed as "unchanged" (n = 16). Those patients who rated themselves as either moderately or markedly improved were classed as "improved" (n = 20). No significant differences were found between the two groups on sex ratio, age, or duration of pain (Table 7).

However, of the main study variables at baseline, one variable showed a statistically significant difference between the groups, and another approached statistical significance. The McGill pain questionnaire (PRI) scores for the improved group were significantly lower than the unchanged group ($t(34) = 2.7$, $p < .01$) (Figure 5). For pain tolerance, the improved group had higher tolerance levels than the unchanged group ($t(34) = 1.82$, $p < .077$) (Figures 4 and 11).

Third Set of Analyses

With the subjects divided into improved and unchanged groups, is there a significant change in the dependent measures across time in response to treatment?

A between groups Manova with repeated measures was performed for the effects of group, group by time and time

Table 7.

Descriptive data of the improved and unchanged groups

		Improved	Unchanged
Female:Male ratio		18:2	14:2
N of subjects		20	16
Age (yrs)	$\bar{X}$	40.6	39.4
	SD	10.5	10.1
Duration of pain (yrs)	$\bar{X}$	5.6	4.7
	SD	5.5	3.8

(Table 8). Significant effects were found for group ($p < .05$) and time ($p < .0001$) but not group by time. (Tables 8a and 8b). As with the initial Manova (Table 2c), univariate F tests for time were significant for all the main variables except pain threshold and tolerance (Table 8c).

The data were next analyzed in 3 steps. Firstly, individual variables were separately analyzed for time and group (improved or unchanged) by time effects. Next, the group data were examined separately to further explore the group effect reported in table 8a. Then, post-hoc Tukey HSD tests were calculated for the variables that demonstrated statistically significant effects. Lastly, a priori planned contrasts were carried out for each variable in turn, comparing the values at the post-Am and the post-Pl periods.

Taking the individual variables separately, the repeated measures Anovas (Table 9) confirm the results of the univariate F tests (Table 8c), with all the variables except pain threshold and tolerance levels showing significant effects for time. However, unlike the results of the data for the Am-first and Pl-first groups (Table 3), no significant interaction was found for group by time for pain tolerance. But, a significant interaction was found for group by time in the data for the sickness impact profile (Table 9f, Figure 7 and Figure 12). The significant difference was between the groups at 2 testing periods,

Table 8.

Multivariate analysis of variance for group effects in the improved and unchanged groups.

8a. Multivaraiate analysis for group effects.

	Value	Exact F	Hypoth df	Error df	Sig of F
(a) Pillais	.4668	2.41	8.00	22.00	0.049

8b. Multivariate analysis of variance for (a) group by time, and (b) time.

	Value	Approx F	Hypoth df	Error df	Sig of F
(a) Pillais	.2588	0.97	24.00	246.00	0.509
(b) ''	.6998	2.94	24.00	246.00	0.0001

8c. Univariate F tests for time for main study variables.

Variable	Hypoth SS	Error SS	Hypoth MS	Error df	F	Sig of F
TMS	866.00	2769.05	288.67	31.83	9.06	0.0001
PTH	129.72	2370.23	43.24	27.24	1.59	0.198
PTOL	312.85	8152.65	104.28	93.71	1.12	0.348
PAIN	348.08	2507.70	116.02	28.82	4.03	0.010
HYP	40.45	306.79	13.48	3.52	3.38	0.013
SIP	442.25	1353.41	147.51	15.55	9.48	0.0001
ANX	442.55	2467.59	111.39	28.36	3.93	0.013
DEP	543.41	1328.03	181.13	15.26	11.86	0.0001

Legend: TMS = total myalgic score; PTH = pain threshold; PTOL =Pain tolerance; HYP = hypochondriasis; SIP = sickness impact; ANX = anxiety; DEP = depression.

Table 9.

Multivariate analyses by time for the individual variables.

9a. Averaged multivariate test for total myalgic score

	SS	DF	MS	F	SIG
Within cells	2957.59	102	29.87		
Time	936.77	3	312.26	10.45	0.0001
Group by Time	192.09	3	64.03	2.14	0.100

9b. Averaged multivariate test for pain threshold

	SS	DF	MS	F	SIG
Within cells	2719.42	102	27.47		
Time	171.80	3	57.27	2.08	0.107
Group by Time	129.25	3	43.08	1.57	0.202

9c. Averaged multivariate test for pain tolerance.

	SS	DF	MS	F	SIG
Within cells	8861.60	102	89.51		
Time	200.55	3	66.85	0.75	0.527
Group by Time	45.35	3	15.12	0.17	0.917

9d. Averaged multivariate test for pain

	SS	DF	MS	F	SIG
Within cells	2511.03	102	27.90		
Time	354.06	3	118.02	4.23	0.008
Group by Time	109.03	3	36.34	1.30	0.279

9e. Averaged multivariate test for hypochondriasis

	SS	DF	MS	F	SIG
Within cells	351.87	102	3.91		
Time	46.41	3	15.47	3.96	0.011
Group by Time	19.35	3	6.45	1.65	0.184

9f. Averaged multivariate test for sickness impact

	SS	DF	MS	F	SIG
Within cells	1353.42	102	15.56		
Time	442.55	3	147.52	9.48	0.0001
Group by Time	129.49	3	43.16	2.77	0.046

9g. Averaged multivariate test for anxiety

	SS	DF	MS	F	SIG
Within cells	2501.02	102	27.79		
Time	324.17	3	108.06	3.89	0.012
Group by Time	23.61	3	7.87	0.28	0.837

9h. Averaged multivariate test for depression

	SS	DF	MS	F	SIG
Within cells	1563.68	102	17.73		
Time	625.53	3	208.51	12.00	0.0001
Group by Time	86.16	3	28.72	1.65	0.183

post-Am and post-placebo ($t(34) = 2.64$, $p < .01$, and $t = 2.14$, $p < .04$ respectively).

As the Manova for group (unchanged or improved) by time reached statistical significance, the effect of the order of treatment with group over time was explored. It was found that there was not a significant interaction for order by group by time (Table 10a).

For the individual groups, including the main study variables, no significant effect was found for time in the unchanged group (Table 10b). However, for the improved group, a highly significant ($p < .0001$) effect was found for time with repeated measures Manova. Univariate F tests showed that all but pain tolerance had significant effects for time (Table 11).

Tukey's HSD test was selected for all pairwise post-hoc comparisons in the improved group. As with the first set of analyses, alpha was set at the .05 level. The results from the significant overall tests for time are listed below:-

a. For the McGill pain scores the values were significantly lower at the post-Am period than at any other time. No other comparisons were significant (error term = 24.4) (Figure 5).

b. For the total myalgic score the values were significantly higher at the post-Am period than at any other time. No other comparisons were significant (error term = 33.62). (Figure 6).

c. For pain threshold the value post-Am was significantly

Table 10.

Averaged multivariate analysis of variance group (amitriptyline or placebo first) by group (unchanged or improved) by time.

10a. Group by group by time.

	Value	Approx F	Hypoth df	Error df	Sig of F
Pillais	0.251	0.868	24.00	228.00	0.645

10b. Multivariate analysis of variance for time in the unchanged group.

	Value	Approx F	Hypoth df	Error df	Sig of F
Pillais	0.751	1.16	24.00	84.00	0.293

10c. Multivariate analysis of variance for time in the improved group.

	Value	Approx F	Hypoth df	Error df	Sig of F
Pillais	0.950	2.83	24.00	147.00	0.0001

Table 11.

Univariate analysis of variance for the main study variables, in the improved group.

Variable	Hypoth SS	Error SS	Hypoth MS	Error df	F	Sig of F
TMS	1111.44	1815.71	370.48	33.62	11.10	0.0001
PTH	269.54	1388.43	89.84	25.71	3.49	0.022
PTOL	52.09	4767.38	17.36	88.28	0.19	0.898
PAIN	476.56	1317.18	158.85	24.39	6.51	0.001
HYP	60.14	193.10	20.05	3.57	5.61	0.002
SIP	564.35	695.39	188.11	12.87	14.61	0.0001
ANX	282.67	1623.07	94.22	30.05	3.13	0.033
DEP	481.31	703.18	160.43	13.02	12.32	0.0001

Legend: TMS = total myalgic score; PTH = pain threshold; PTOL =Pain tolerance; HYP = hypochondriasis; SIP = sickness impact; ANX = anxiety; DEP = depression.

higher than at baseline. No other comparisons were significant (error term = 25.71). (Figure 3).

d. For the Sickness Impact Profile, the scores at baseline were significantly higher than at all other times (error term = 12.87). As well the score post-Am was significantly lower than at the post-Pl period (Figure 7).

e. For depression, the value at baseline was significantly higher than at the post-Am and post-washout periods (error term = 13.02). As well the score at the post-Am period was significantly lower than the score the post-Pl period (Figure 8).

f. For hypochondriasis, the value at the post-Am period was significantly lower than those of either the baseline or the post-washout periods (error term = 3.57). No other comparisons were significant. (Figure 9).

g. For anxiety, the value at baseline was significantly higher than that of the post-Am period (error term = 30.05). No other comparisons were significant. (Figure 10).

The values of the a priori planned contrasts within measures across the post-Am and post-Pl periods were calculated using paired, one-tailed t-tests (Table 12). For these data, the alpha level is not controlled for in the number of contrasts. For the total myalgic score and pain threshold, scores were significantly higher post-Am compared with the post-Pl period. For the McGill pain scores, depression, hypochondriasis and sickness impact, scores were significantly lower post-Am than post-placebo.

Table 12.

Planned contrasts of the main study variables in the improved group at the post-amitriptyline and post-placebo periods

VARIABLE	t-test	df	Sig. level	
McGill pain score	-3.56	19	p < .0001	**
Total Myalgic Score	7.27	19	p < .0001	**
Pain threshold	2.15	19	p < .025	
Pain tolerance	0.53	19	p > .05	
Sickness Impact Profile	-2.79	19	p < .01	*
Hypochondriasis	-2.17	19	p < .025	
Anxiety	-1.83	19	p > .05	
Depression	-2.99	19	p < .005	*

Legend: * = p < .05, ** = p < .01 when controlling for alpha level in the number of contrasts

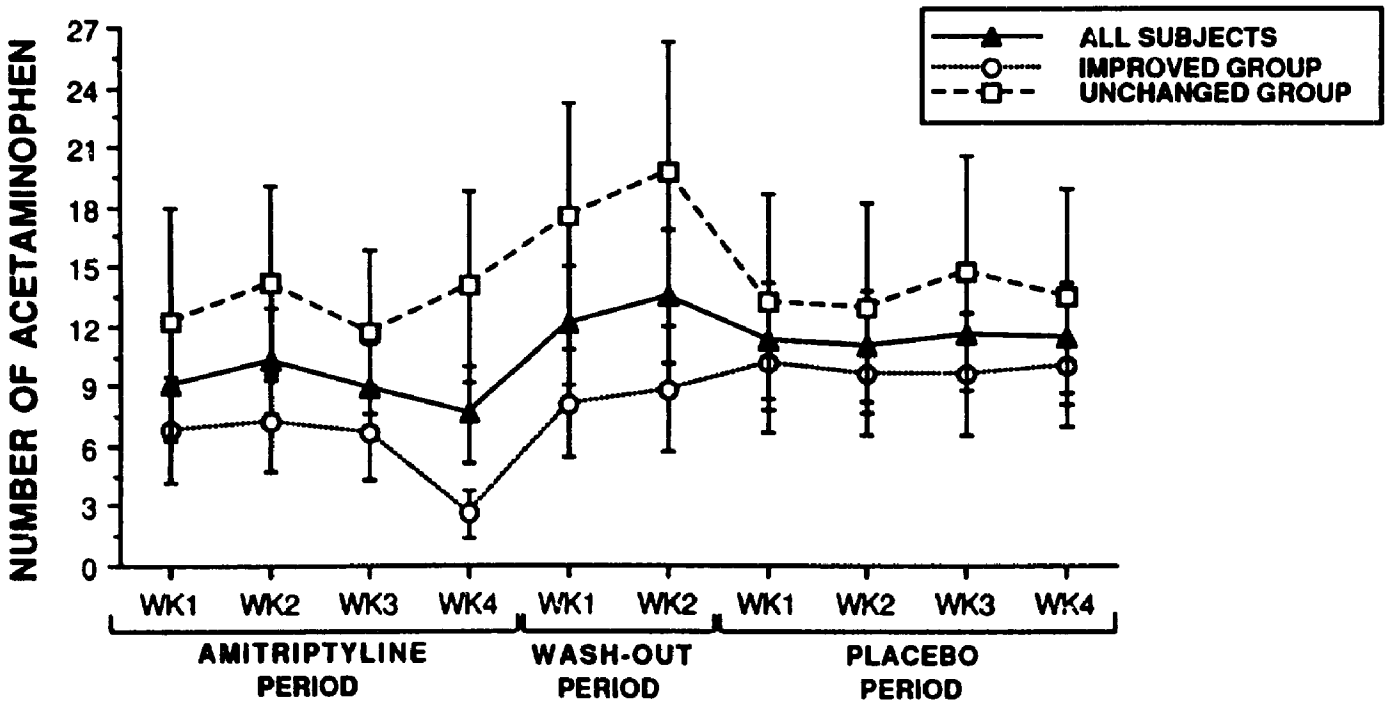
However, the significance of these data alters appreciably when the type 1 error is controlled for in the 8 possible pl anned contrasts in the manner of Dunn-Bonferonni (Dayton and Schafer, 1973). Thus, a value of greater than 2.76 would be needed for the t-test to be significant at the $p < .05$ level, and a value of greater than 3.49 would be needed for significance beyond the .01 level. Therefore, a further inspection of table 12 shows that, controlling for the number of contrasts, only four variables would achieve statistical significance, that is sickness impact and depression at the $p < .05$ level, and pain and the total myalgic score at the $p < .01$ level.

Number of analgesics taken, by group, over time.

Some interesting, and confirmatory, data on pain levels between the groups emerges when the data of the number of analgesic pills taken by the subjects over the different treatment periods is examined (Figure 13). Taking the data for all the subjects, the number of pills taken was significantly less at the fourth week of the amitriptyline period than either of week 1 or week 2 of the washout period ($t(35) = 2.05$ and 2.16 respectively, both $p < .05$). It also approached statistical significance with values lower than all the placebo period values ($p > .05 < .01$).

Within the unchanged group, there were no statistically significant differences across time. However, within the improved group, the number of pills taken in week 4 of the

Figure 13
Number of Acetaminophen Taken Over Time



Legend: Error bars represent 1 standard error of the mean

amitriptyline period was significantly lower than the values at all other times (p values varied between $p < .05$ to $p < .005$). No other comparisons were significantly different.

Comparing the values of the two groups across time, the improved group has lower mean values than the unchanged group at each period. However, because of the wide range of variability in the unchanged group, only 3 comparisons reached statistical significance. These were at the fourth week of the Am period and in the first and second weeks of the washout period (all less than $p < .01$).

Fourth Set of Analyses

With the subjects divided into improved and unchanged groups, which variables at baseline, and post- amitriptyline, best predict group membership after the amitriptyline treatment period?

The first discriminant function analysis was developed using the main study variables at baseline, plus age, and the length of time of symptoms. A stepwise discriminant function, using Wilks' method, was used because the purpose of the discriminant function was two-fold: firstly, in a manner analogous to multiple regression, the intention was to find how much each variable contributed to the anticipated significant discriminant function; secondly, the purpose was to examine the accuracy of the classification to group

membership by the function (Marascuilo and Levin, 1983).

Due to the fact that there were only 2 groups, only one function was developed. Cut off levels for the function were specified a priori and set at an overall function significance level of $p \leq .05$. Four variables contributed to this significant function (Table 13a). Of these, pain was responsible for most of the variance accounted for by the equation (64.8%), followed by the length of symptoms (24.4%). Pain tolerance (7.8%) and hypochondriasis (3%) contributed to a much lesser extent. The total variance accounted for by the discriminant function was 29.5%.

Of the 4 variables, pain and length of symptoms contributed in a positive direction, and pain tolerance in a negative direction (Table 13b). Large differences in pain scores, and to a lesser extent, differences in the length of time of symptoms, were the most important discriminating variables.

Seventy-two percent of all cases were correctly classified to their respective groups on the basis of the linear combination of these 4 variables. The improved group was the easier to classify, with 80% correctly allocated to the proper group, compared to an only 62.5% correct classification in the unchanged group.

The same 10 variables, this time taken at the post-Am period, were entered into another stepwise discriminant function analysis with the unchanged and improved groups. The limits of the analysis were set to exclude those

Table 13.

Discriminant function on improved and unchanged groups using the main variables at baseline.

13a. Summary Table.

Step	Variable	Wilks' Lambda	Sig	% Var
1.	Pain	0.8099	.011	19.1
2.	Length of pain	0.7378	.010	7.2
3.	Pain tolerance	0.7147	.019	2.3
4.	Hypochondriasis	0.7056	.038	0.9

X^2 of discriminant function (4 df) = 10.51, $p < .038$

13b. Standardized function coefficients

1.	Pain	0.904
2.	Length of pain	0.659
3.	Pain tolerance	-0.413
4.	Hypochondriasis	-0.243

13c. Predicted group membership by classification.

Actual Group	N	Predicated group membership	
		Group 1 (%)	Group 2 (%)
1. Unchanged	16	10 (62.5)	6 (37.5)
2. Improved	20	4 (20.0)	16 (80.0)

72.22% overall correctly classified

variables that did not contribute to more than 1% of the variance.

This function accounted for a much larger percentage of the variance between the 2 groups - 57.2% - and was significant at the $p < .0001$ level. Three variables contributed to the function (Table 14a). Again, pain contributed most to the variance that was accounted for (64.3%). This was followed by the total myalgic score (31%) and anxiety (4%). Like the first discriminant function, therefore, pain was the most important variable in discriminating between the 2 groups. However, in the second equation, the total myalgic score was also an important discriminating variable. Pain was loaded in a negative direction with the other 2 variables being loaded in a positive direction (Table 14b).

Overall, 91.66% of subjects were correctly allocated to their respective groups with 95% correctly classified in the improved group, and 87.5% in the unchanged group.

Table 14.

Discriminant function on improved and unchanged groups using the main variables after the amitriptyline period.

14a. Summary Table.

Step	Variable	Wilks' Lambda	Sig	% Var
1.	Pain	0.6292	.0002	37.0
2.	Total Myalgic Score	0.4514	.0000	17.8
3.	Anxiety	0.4283	.0000	2.3

X^2 of discriminant function (4 df) = 23.93, $p < .0001$

14b. Standardized function coefficients.

1.	Pain	-1.142
2.	Total Myalgic Score	0.852
3.	Anxiety	0.330

14c. Predicted group membership by classification.

Actual Group	N	Predicated group membership	
		Group 1 (%)	Group 2 (%)
1. Unchanged	16	14 (87.5)	2 (12.5)
2. Improved	20	1 (5.0)	19 (95.0)

91.66% overall correctly classified.

Discussion

The major aim of the present study was to investigate the effects of low-dose amitriptyline on pain responsiveness in fibrositis patients. Taking all the subjects as a group, it was found that the total myalgic score increased significantly after the period when the subjects were taking amitriptyline (Am) as compared to all the other testing periods. Pain, anxiety, depression, hypochondriasis and sickness impact, also changed significantly over the study period. As well, improvements which approached statistically significant levels, were found in pain threshold.

The most important finding of this study emerged after the results of all the subjects were re-analyzed into 2 groups, on the basis of those subjects who responded to Am and those who did not respond. For the subjects who responded to Am, it was found that highly significant improvements were found in pain, local pain sensitivity, sickness impact and depression, when comparing the results after the Am period with the results after the placebo period. Statistically significant improvements were also found in the generalized pain threshold levels and hypochondriasis. No statistically significant improvements were found in the subjects who did not respond to Am.

Finally, it was found that levels of pain at the inception of the study were significantly lower in those

subjects who eventually responded to Am, as compared to those who did not respond.

Based on the baseline values of the main study variables, a statistically significant discriminant function was developed which predicted response the to Am with a 72% accuracy. Pain levels and the length of time that the patients had been experiencing their condition were the most important variables in the discriminant function equation.

The main emphasis throughout the discussion of the results will be placed on the pain and pain responsiveness data. However, the clinical and psychological implications of the results will also be discussed.

The demographic composition of the study population agrees with previously published studies on fibrositis patients; that is, there was a high ratio of females to males (Carette et al, 1986; Wolfe et al, 1985), the mean age of the subjects was close to forty (Felson and Goldenberg, 1986; Scudds et al, 1987; McCain and Scudds, 1988), and they had been experiencing their condition for a mean of approximately 5 years (Felson and Goldenberg, 1986). It should be emphasized at the outset of this chapter that fibrositis is a troubling and difficult condition to treat. The length of time that the patients in this study had been experiencing their condition attests to that. Further, as the results indicated, the level of dysfunction that they were experiencing had wide-ranging

effects on their lives. Thus, the clinical efficacy of amitriptyline in this group of patients is an important finding.

Overall Treatment Effects

The results of the overall multivariate analysis of variance showed that there was a highly significant effect for time ($p < .0001$) over the study period. Multivariate analysis was chosen for the primary analysis because, clinically, the purpose of the study was to assess the overall effect of Am on a series of variables (Tabachnick and Fidell, 1983). Thus, Am had an overall effect on the general symptoms of fibrositis. The initial analysis considered the data of the two groups based on those who took placebo first or Am first. No significant effect was found for group. This indicates that the effects were present regardless of the order in which the patients took the active medication.

When the main variables were considered separately, it was found that each of pain, the total myalgic score, hypochondriasis, depression, anxiety, and sickness impact had highly significant changes over the study period (each beyond the $p < .01$ level). None of these variables had interaction effects for group (Am or placebo first) by time.

Pain threshold changed over time, and this effect approached statistical significance ($p < .055$). It reached

its highest level after the Am period as compared to the three other testing sessions.

For pain tolerance, no significant effect was found for time, but a significant interaction was present for group by time. It is difficult to account for this last finding. The results show that a statistically significant difference existed between the groups only after the Am period. Subjects who received Am first were higher on pain tolerance than the placebo-first group. However, if the data are viewed from a different perspective (see Figure 11), it can be seen that the group which received placebo first had their highest score after the placebo period. This would correspond to the second visit of the Am group. All subjects would then have their highest score on the second visit, with gradually decreasing scores after that visit. Therefore, the changes in tolerance may not reflect a difference due to Am, but merely the effects of a gradual reduction in pain tolerance over time.

There were different patterns of change in the individual variables. For the McGill pain scores, pain was at its lowest at the post-Am period. Using Tukey's test, a statistically significant difference was found only between the score at base-line and the post-Am score. The decrease in pain could reflect a strong placebo effect of being in a study. This is unlikely because Carette and co-workers (1986) and Goldenberg et al (1986) have also found statistically significant decreases in pain levels in

fibrositis patients after treatment with Am. As well, the present data that resulted from dividing the groups into responders and non-responders, more clearly demonstrates the effects of the active treatment.

The baseline value of the McGill PRI, 13, was lower in this study than in a recent study with fibrositis patients, which found a PRI score of 25.5 (Perry et al, 1988). Part of the difference between the studies may be because the 4 "miscellaneous" sub-scales of the MPQ were not included in this study. However, it is unlikely that the inclusion of these scales would have almost doubled the scores. It is therefore possible that the sample of patients in this study were suffering from less pain than in the report of Perry et al (1988).

The effects of Am on the total myalgic score are clearer than its effects on pain levels. As compared to the other three testing sessions, the TMS was found to be significantly altered only after the Am period. This improvement in TMS agrees with the findings of Goldenberg et al (1986) who found a significant increase in tender point scores in fibrositis after a 4-week period of Am when compared to placebo. It is also in partial agreement with the findings of Carette et al (1986) who found that low-dose Am caused significant improvements after a 5-week period, although it did not do so after nine weeks.

The other important finding about the TMS data is that, not only does tender point sensitivity improve after

treatment with Am, but it does so quite rapidly. As well, values returned within the 2-week wash-out period to pre-treatment levels. Its effects, therefore, are quite rapid in onset and are short-lived. No previous study has demonstrated this point. The other two studies using Am, which were mentioned above, did not use cross-over designs and did not report any follow-up data. The present study, using a placebo-controlled cross-over design, was thus able to demonstrate changes after the withdrawal of Am.

The data obtained with the dolorimeter are all the more impressive because, the value is not just a self-report measure. Most fibrositis patients are not aware that they are particularly sensitive over the points that were measured with the dolorimeter. They either "ache all over" or ache in a p rticular area of the body. They may become aware of generalized tenderness and hypersensitivity, but rarely do they complain of pain at the specific fibrositis tender points.

These observations are well exemplified by the reports of two subjects. At the beginning of the study, one subject, who had a pain threshold value of less than 1 kg, would flinch at the slightest touch in any part of her body. Another subject, who responded very well to the medication, said that "I had forgotten what it is like to put on my overcoat without it hurting my shoulders". These comments would indicate changes in general sensitivity. That the TMS changes without the patient being aware of it,

not only shows alterations in local sensitivity but also that it may be regarded as an objective, and relatively bias-free, measure.

Each of the other variables of hypochondriasis, depression, anxiety, and sickness impact, all showed significantly higher scores at base-line than at any other time (by Tukey's test). No other comparisons were significant. The statistically significant effects for time in these variables may therefore have been due to the placebo response of being in a study. However, it is unlikely that this explanation is responsible for all the effects found in these variables. For each variable the lowest score was found after the Am period. After the wash-out period, the scores had risen higher than the after post-Am levels and raised further after the placebo period.

The score of 10.6 on the Hypochondriasis scale of the BPI indicates that the patients had mildly raised scores when compared to the normative values (see Figure 2). This is in agreement with Scudds et al (1987) who found that fibrositis patients had significantly higher levels of hypochondriasis as compared to normal subjects and to patients with R.A.. Also, in comparison with the women of study 1 and study 2, the predominantly female sample of this study show higher values on hypochondriasis. This is also in agreement with the results of other studies who used different instruments, but also found that fibrositis patients had higher levels of hypochondriasis than normal,

and clinical, control groups (Payne et al, 1982; Wolfe et al (1984); Ahles et al (1986).

As was mentioned in the previous chapters, caution must be taken in the interpretation of the hypochondriasis data. In the present study, these results will be put into the context of the overall pattern of results from the pain, depression and anxiety scores.

The Beck Depression Inventory scores were reduced after the amitriptyline period as compared to base-line. However, the base-line group score of 12.3 indicates that they did not display high levels of depression at the start of the study. Beck and Beamesderfer (1974) recommend a high cut-off score of 21 and a low cut-off score of 14, or greater, when screening for depression in psychiatric patients. In another report, Beck et al (1961) found a mean score of 18.1 in what they classed as "mildly depressed" psychiatric patients. In a large group of medical patients with mixed diagnoses, it was found that 64% had scores of 10 or less, on the BDI, and a further 20% had scores between 11 and 20. On the basis of this, they proposed that a score between 11 and 20 be classed as mildly depressed.

Within the context of these data, then, the present sample may have had mild elevations on the BDI. Previous studies have also examined levels of depression in fibrositis. One of these studies used the BDI and found that a group of 22 fibrositis patients had a mean score of 10.7 (standard deviation = 7.3) on the BDI (Clark et al,

1985). These scores did not differ significantly from a group of matched muscle-pain control subjects. The authors concluded that the fibrositis patients were not suffering from clinical depression.

Other data on depression in fibrositis is available using different instruments, such the MMPI, the BPI, and the depression scale of the AIMS (Payne et al, 1982; Ahles et al, 1984; Scudds et al, 1987; Hawley et al, 1988). In general, their results indicate that fibrositis patients do not experience high levels of depression, but show significant elevations when comparing the data to normal, healthy control groups.

For state anxiety, the mean score for the group at base-line was 36.0 (standard deviation = 9.0) which compares favorably with the published values of 41.3 (standard deviation = 12.5) for a group of general medical and surgical patients (GMS) without psychiatric complications (Spielberger et al, 1970). A raw score of 36 would lie on the thirty-sixth percentile of the GMS patients. As well, mean values of 36.1 (standard deviation = 7.7) have been reported in a study with normal, healthy adults (Morgan and Horstman, 1978).

The present results are also in accord with the findings of Clark et al (1985) who found a state anxiety score of 41.9 (standard deviation = 13.0) in a group of fibrositis patients. Therefore, compared to previous data, the present sample of fibrositics was not experiencing

significantly elevated levels of state anxiety.

Due to the fact that only 7 of the 12 scales of the Sickness Impact Profile were used in this study (mean score at baseline of 14.2, S.D. = 4.7), it is difficult to compare the overall scores on the SIP with previously published literature. However, one report published data from each of the SIP scales in a study which compared a large sample (n = 107) of chronic low-back pain patients with the control data of R.A. patients (n = 79) (Follick et al, 1985). Extrapolating from their data on the 7 scales that were used in this study, a mean overall score of 23 was found for the back-pain patients, and 13 for the R.A. patients. Some confirmation of the present results comes from a recent study which compared R.A. and fibrositis patients for functional ability using work assessment methods (Cathey et al, 1988). They report that fibrositis subjects performed 58.6%, and the R.A. group 62.1%, of the work done by normal subjects.

Therefore, in comparing the data from the present study with previous studies, it would seem that the fibrositis patients had levels of functional interference that were similar to R.A. patients, but lower than chronic back pain sufferers. This is interesting because R.A. patients, with their obvious physical limitations, could well be expected to score relatively high on measures of sickness impact. That the fibrositis patients of this study were approximately equal to the R.A. group score indicates that,

even in the absence of obvious physical pathology, their symptoms have a broad effect on their lives.

The relationship between the main study variables.

More insight is gained into the relationship between the measures of pain responsiveness from the simple correlations between them. Although all the correlations between pain threshold, pain tolerance and the TMS were significant beyond the $p < .01$ level, TMS and pain threshold were more highly correlated with each other than with pain tolerance. Therefore, they may be measuring a similar dimension. However, the correlation of .70 at baseline between TMS and pain threshold means that 51% of the variance is not accounted for by the other variable. These data may be interpreted to mean that pain threshold and TMS are related, but are not measuring exactly the same dimension. A similar relationship is found between the pain threshold and pain tolerance measures (Rollman, 1983).

At base-line, the level of pain was negatively correlated with each of the measures of pain responsiveness, but only with pain tolerance did this reach statistically significant levels ($p < .01$). However, at the post-Am period, no significant correlations were found between pain and any of the responsiveness measures.

It is interesting that neither pain nor TMS had many significant correlations at baseline with the other main study variables. Pain was positively correlated with

hypochondriasis, and depression was negatively correlated with the TMS. At the post-Am period, however, pain was significantly positively correlated with the length of time in pain, the SIP, depression and anxiety, but not hypochondriasis. As well, depression was then significantly correlated with the SIP, anxiety, hypochondriasis and pain, but not the TMS. The pattern of correlations was stronger, and more logical, after the amitriptyline period, than at baseline. This change in pattern is reflected in the strength of the intercorrelations between the measures of anxiety, depression, SIP, and hypochondriasis. It is not particularly surprising that there are changes in individual correlations over time. However, the changes in the pattern of correlations may reflect some underlying differences in the subjects between the two testing sessions. Possibly, after the amitriptyline period, an increase in the homogeneity within the group's scores on each of measures have may lead to higher intercorrelations. However, as reflected by the error bars, there does not seem to be much change in the variability of the scores.

It is possible that the scores, particularly among measures of pain, anxiety, depression, hypochondriasis, and the SIP, were more random at baseline because the subjects were unfamiliar with the inventories. After the first testing session, their answers became more consistent. An examination of the means of the various self-report inventories over time shows that, for each measure, scores

were higher on the initial visit that at any other time. This may have been an indication of a response style effect at that period which was less pronounced at the other times.

An examination of the intercorrelations within each variable over time gives some support to this explanation. Overall, highly significant correlations were found within variables across time. However, for the more objective measures of pain responsiveness, the correlations were as high with the baseline scores as at any other time. Generally, for the self-report measures, correlations with the baseline scores were slightly lower than at any other time.

The positive correlations that were found in this study between pain levels and depression have been reported by numerous authors and have led others to question whether chronic pain is possibly a variant of depression (for example Sternbach, 1978; Ward et al, 1984; France, 1987). In fact, the finding that the administration of anti-depressants to depressed chronic pain patients had positive effects on both symptoms, gave support to this idea.

However, it is now widely accepted that anti-depressants can act as analgesics in many different types of chronic pain patients who are not experiencing clinically high levels of depression (see France, 1987; and Feinmann (1985) for excellent reviews of the topic). As well, a normally therapeutic anti-depressant dose with one

of the tricyclic anti-depressants is within the region of 150 to 300 mg per day and it takes up to 3 weeks to reach therapeutic levels. This compares to an analgesic dose of around 50 mg per day, with an onset of action within a week to 2 weeks for pain relief.

At the start of the present study, the subjects as a whole were possibly experiencing mild levels of depression and low-to-moderate levels of pain. Both of these decreased significantly after the amitriptyline period. Levels of depression dropped below the "mildly depressed" cut-off point (from a BDI score of 12.3 to 6.4). However, the analysis of the present data, first controlling for pain levels in depression and then depression levels in pain, show that the decreases in pain and depression were independent of each other.

The mode of action of the tricyclic anti-depressants on depression is not yet fully known, and their effects on the psycho-pharmacology of chronic pain is even less clear. Amitriptyline is a tricyclic anti-depressant which is a potent and relatively specific serotonin (5-HT) reuptake inhibitor. Pain, depression, and sleep, are three of the main central neurochemical processes in which 5-HT plays a significant role (Feinmann, 1985). As well, these three are often disturbed in fibrositis.

The importance of serotonin in pain transmission was most clearly demonstrated in an excellent series of studies by Basbaum and Fields (1978, 1984). They showed that 5-HT

rich neurons act presynaptically to potentiate the release of enkephalins and endorphins, which in turn have been repeatedly shown to reduce endogenous pain levels. By implication, and through subsequent experimental evidence, an increase in the synaptic availability of 5-HT would raise the levels of endogenous opiates and lead to a reduction in pain.

It is interesting that the effects of the manipulation of brain serotonin levels on experimentally induced pain have produced conflicting results. For example, Ward et al (1984) did not find significant reductions in pain tolerance levels to the cold-pressor test after either doxepin or desipramine. However, neither of these drugs have a high specificity for serotonin. In contrast to this, the injection of the tryptophan hydroxylase inhibitor p-chlorophenylalanine reduced pain shock thresholds in rats (Harvey and Lints, 1971). As well, Dennis and Melzack (1980) clearly demonstrated that 5-HT potentiated the response of morphine in rats, but did so in different ways to different pain threshold measures. They showed that there was no increase in pain threshold in the tail-flick test (a phasic stressor) but there was a highly significant increase in threshold to the formalin test (a tonic stressor). It is possible that the effects of an increased availability of serotonin are most effective in tonic stressors, which are taken to be more mimetic of clinical pain.

The importance of sleep disturbance on the symptoms of fibrositis patients has been elegantly demonstrated in a series of studies by Moldofsky and co-workers (Moldofsky, 1982, 1986; Moldofsky and Scarisbrick, 1976; Moldofsky and Warsh, 1978; Moldofsky et al, 1984). A summary of their results reveals that selective deprivation of level 4 (non-REM) sleep may lead to the onset of fibrositis-related symptoms in otherwise normal, healthy subjects. Serotonin is important in the initiation of the onset of non-rapid eye movement sleep. Non-REM sleep abnormalities were also found in fibrositis patients, and in post-traumatic muscle-pain patients. As well, the symptoms of fibrositis patients are inversely related to plasma-free levels of tryptophan. Lastly, the authors associate nocturnal myoclonus, which is present in many other painful syndromes, with sleep abnormalities.

Taken together, the implications of the findings above are that sleep disturbances may be intimately connected with the symptoms of fibrositis and other chronic pain syndromes. Both of the previous studies which used amitriptyline in the treatment of fibrositis report improvements in the quality of sleep after Am (Carette et al, 1986; Goldenberg et al, 1986).

It is one of the limitations of the present study that no measure of sleep quality was used. However, some evidence is available from the "sleep sub-scale" of the SIP. A post-facto analysis of this scale (which consists of

7 items) shows a significant difference over time by repeated measures analysis of variance ($F = 2.98$, $p < .05$). Post-hoc Tukey's test showed that the significant difference ($p < .05$) lay between the baseline period and the post-Am period. No other contrasts were significant. Therefore, the present data are in agreement with previous findings, and show that the present sample of patients also improved in sleep-related areas after taking amitriptyline.

Responders and non-responders to amitriptyline with group effects on the main study variables.

At each testing session, after baseline, the subjects were asked to rate their overall feelings of well-being on a five point categorical scale. A comparison of the ratings between the post-amitriptyline and post-placebo periods showed highly significant differences between the rating periods. Overall, patients gave significantly higher ratings of well-being after the Am period compared with after the placebo period. Thus, from the patients viewpoint, they felt subjectively better.

However, not all patients rated themselves as being improved after amitriptyline. A total of 20 patients, or 55% of the study population, rated themselves as being either moderately or markedly improved. This is in exact agreement with the data from Carette and co-workers (1986). In that study, 55% of patients also reported that they felt either moderately or markedly improved after taking Am. The

authors considered that the classifications of "moderately or markedly improved" constituted a clinically meaningful improvement.

On the basis of the classification from Carette et al (1986), the subjects of the present study were divided into responders (those who improved) and non-responders (those who were unchanged) after the Am period. Thus, 20 patients were classed as improved, and 16 were unchanged (non-responders).

The data of the main study variables were then re-analyzed in the light of the new groups - improved and unchanged. No significant differences were found between the groups on any of the demographic variables of age, sex-ratio, or duration of pain. However, the improved group had been experiencing their condition for slightly less time than the unchanged group.

Of the main study variables - TMS, pain, pain threshold, pain tolerance, hypochondriasis, depression, anxiety and sickness impact - only one variable showed statistically significant differences between the groups at baseline. It was found that pain levels were significantly lower at baseline in the group that improved compared to those who did not improve after amitriptyline. This is an important and surprising finding because pain is the most salient complaint in fibrositis. It means that those who are less affected by their condition are more likely to improve after treatment. This point will be explored

further at the end of the chapter.

The initial series of analyses were next repeated in the same order to explore the effects of the new groupings over time. First, a significant effect was found for group which means that the groups responded differently when all the variables were analyzed together by Manova. Next, no significant effect was found for time. This indicates that, although the groups responded differently, the difference was more likely to be one of magnitude rather than direction. That is, the "unchanged" group's scores changed in the same direction, and at the same testing period as the "improved" group. However, the amount of change in the unchanged group was much less. Lastly, a highly significant effect was found for time (period of testing), which is the same as in the initial analyses, and was to be expected.

The analysis of the results of the individual variables with the two groups demonstrated similar results to those found in the initial series. That is, significant effects were found for time in each of pain, TMS, hypochondriasis, depression, anxiety, and the SIP. No significant effects were found for either pain threshold or tolerance levels.

Two differences in the results were found between the initial and second sets of analyses. These were for interaction effects of group by time. Unlike the initial analysis, no significant interaction was present for pain tolerance. This is not surprising as the grouping variable had changed. However, a significant interaction was found

for group by time in the Sickness Impact Profile. It can be seen that the pattern of change across testing periods is different between the groups (Figure 11). For the unchanged group, the scores were highest at baseline and then remained constant across each of the other testing sessions. For the improved group, the scores were lowest at the post-Am period than at any other period. The only statistically significant difference between the groups was at the post-Am period.

The data were next analyzed according to the responses of the individual groups on the overall series of variables. However, it should be remembered when considering these analyses that the sample sizes in the sub-groupings was small. When using multivariate analysis of variance, it is recommended that there should be 10 subjects per variable but 5 subjects per variable can be considered adequate (Tabachnick and Fidell, 1983). The projected sample size at the inception of the study, before drop-outs, was 40 subjects. This was an adequate size for the overall group analyses. The creation of small sub-groups would reduce the power of the tests and might possibly lead to a type 2 error. However, as the original intention of the study was to analyze the data primarily as a series of related variables, the analyses proceeded in a manner similar to the initial analyses.

For the "unchanged" group, no significant overall effect was found for time. If no significant overall effect

is found in multivariate analyses, it is recommended that the analysis should not proceed any further (Kirk, 1982). That recommendation was followed in the present study.

Because the unchanged group did not change significantly over time, the change over time that was found in the whole group must have come largely from those subjects who improved. This is quite understandable. What is somewhat surprising is the magnitude of the change. The overall effect for time in the improved group was beyond the $p < .0001$ level, which is impressive, given the small sample size.

The magnitude of the change over time in the individual variables is equally impressive. As well, the analyses produced valuable insight into the actual time-period of the changes in the variables, particularly the psychological measures. For the post-hoc analyses, both Tukey's HSD and paired t-tests were presented because it was felt that both types of analyses gave insight into the trends in the data over the study period. However, although both analyses are presented and discussed in the following pages, greater credence must be given to those values that were found to be statistically significant after the Bonferroni adjustments, i.e. pain, the total myalgic score, depression, and sickness impact.

Analysis of variance with repeated measures demonstrated that all the variables, except pain tolerance, altered significantly over time. Pain tolerance did not

nearly approach statistically significant levels (F = .19). This lack of change may be reflective of previous findings that an increased availability of serotonin did not have an effect on pain perception. But, this is unlikely to be the case, as pain threshold values altered appreciably after Am. Pain tolerance levels have been shown to be lower in fibrositis subjects than normal healthy controls (Scudds et al, 1987). It was expected that pain tolerance would improve after successful treatment with Am, but they did not. In fact, the pain tolerance data were remarkably constant across time. Pain tolerance levels are taken to be more reflective of cognitive, rather than peripheral sensory, processes (Merskey and Spear, 1967). It is possible that the stability in pain tolerance levels may have resulted from a lack of overall change in cognitive processing due to the short length of time that the subjects were taking Am. A more concrete change in perceptual style might take a longer time to emerge. Therefore, it would be interesting to examine fibrositis patients again with the same medication, but over a much longer time period.

The clearest data of the other study variables comes from the MPQ and the TMS. The values of each of these were improved significantly after the amitriptyline period compared to any other time. Therefore, for each of these variables, the effect was rapid in onset and cessation. Paired t-tests confirmed this and showed highly significant

differences between the post-Am and post-placebo periods. These data are both statistically and clinically significant. Levels of pain at baseline decreased from 10.21 to 3.42 after amitriptyline. As well, TMS increased from 21.1 to 27.3 over the same period. Recently Simms et al (1988) recommended that an improvement of 25% in tender point score should be taken as being clinically significant. The TMS data of this study would fall into that category.

The number of analgesics that the subjects took over the study period offer further insight into the nature of the change in pain. Due to the large range of difference in pill-taking behaviors, few comparisons reached statistically significant levels. However, an examination of the mean scores exposes some interesting trends. Firstly, in support of the MPQ results, the unchanged group were taking almost twice as many pills as the improved group after the first week of the amitriptyline period. By the end of that period, they were taking approximately 4 times the number of analgesics as the improved group. This comparison was statistically significant.

Secondly, the number of analgesics taken by the improved group over the Am period decreased steadily over the 4 week period. The unchanged group did not change over the same period. The only time that the pill-taking behavior was markedly increased in the unchanged group was in the wash-out period. These are interesting findings. For

the improved group, it might well mean that the number of analgesics taken was a genuine indicator of reductions in pain levels. However, for the unchanged group, the number of pills seems to be, at least in part, indicative of pill taking behavior. The number of pills that they took was approximately the same in the amitriptyline and the placebo periods. However, when they were not taking the study medication (either active or placebo) their pill-taking behavior increased. These results are further indications of the complex nature of the experience of pain. A seemingly simple indicator of pain can produce complex results because of the wide range of the individual expression of pain at the sensory and behavioral levels.

For each of sickness impact, hypochondriasis, and anxiety, the values at baseline were generally higher than those after the amitriptyline period. However, the data from the t-tests indicates that the difference may not solely reflect a change due to the active medication.

For anxiety, by Tukey's HSD, the only significant difference was found between the baseline measure and post-Am. Statistically, this would indicate that amitriptyline was effective in reducing anxiety. However, both the t-test and the HSD do not indicate that significant differences existed when comparing Am with placebo. Therefore, the reductions in anxiety cannot be presumed to be as a result of amitriptyline, but may simply be an indication of reductions in anxiety levels due to the subjects'

expectations of symptom relief.

The results on the hypochondriasis scale stand in contrast to those for anxiety. Tukey's test showed that the values at the post-Am period were lower than those at base-line and at the post-washout period. However, the t-test did show significantly lower levels of hypochondriasis at the post-Am period when compared with the post-placebo period. The effect was small, however, and did not reach statistically significant levels when Bonferroni adjustments were made to the significance level.

The depression scores are similar to those of anxiety, sickness impact, and hypochondriasis, in that the base-line values were higher than other time periods. Taken together, these data may be indicative of a different response style at baseline which was not present at the other testing periods, and was less present for the directly pain-related variables.

Within depression, however, it was also found that the post-washout period was also significantly lower than at baseline. This may well be an indication that the two-week wash-out period was not long enough for all of the effects of amitriptyline to be completely removed. In comparison with the post-placebo period, the levels of depression were much lower after Am by Tukey's HSD and paired t-test. The values of the SIP were also significantly lower post-Am as compared with post-placebo by Tukey's HSD and paired t-test.

Lastly, using Tukey's test, the values for pain threshold improved after Am as compared to baseline. The paired t-test data show that there was also a significant improvement in threshold values after Am when compared to placebo. Thus, pain threshold, which was taken as a general measure of pain responsiveness, improved after successful treatment. Previous findings have shown that fibrositis patients have lower generalized pain thresholds than normal controls, and have been classified as being hypervigilant to painful stimulation. The present data indicate that these low values may return towards normal levels after successful treatment. A full discussion of the implications of these results on the hypervigilance and adaptation-level paradigms will be presented in the general discussion section.

Predictors of responding and non-responding group membership.

The purpose of the final series of analyses was to see which variables best predicted membership of the improved and unchanged groups, and to assess the accuracy of that prediction. First, taking the variables at baseline, a discriminant function resulted in an overall 72% accuracy of prediction to groups. The responders were the easiest to identify, with 80% being classified into the correct group.

Overall, four variables accounted for 29.5% of the variance between the groups. However, two variables alone

accounted for most of the variance (26.3%). Of these, pain was the most important predictor of group membership, followed by the length of time in pain. Therefore, the main discriminators between the groups were high pain levels, longer pain experience and, to a lesser extent, low pain tolerance levels and low levels of hypochondriasis. In summary, people with a more recent onset of fibrositis that also had lower levels of pain, were more likely to improve after taking amitriptyline.

The variables that most clearly separated the groups after the amitriptyline period were similar to those that predicted group membership. The discriminating variables of pain, TMS, and anxiety together were responsible for 57% of the variance between the groups. The function was characterized by low levels of pain, and a high total myalgic score. Together, these variables accounted for almost 55% of the variance between the groups. Anxiety also contributed significantly to the equation but its effects were small. On the basis of the 3 variables, almost 92% of the subjects were correctly classified to groups with a 95% correct allocation in the improved group.

Limitations of the study.

The most important limitation of the present study is the short length of time that the patients were taking the active medication. A longer period of time, with frequent follow-up periods, would give a greater understanding of the change in the variables used in this study.

Another limitation is that, although experimenter and patient were both blind to group membership, each had his(her) own perceptions of group membership in response to treatment. This may have biased the results. In future, data collection would be better performed by a study rater who was blind to any of the other conditions and had no experimental bias for either positive or negative results.

The results of this study may also be limited in their generalizability only to those patients who are experiencing mild to moderate symptoms from fibrositis.

Finally, a larger sample size is recommended for future studies, especially if there is an intention that sub-groups will be formed in some way. The relatively small sample size in the present study led to difficulties in the interpretation of the sub-groups' results because of the diminished power of the analysis. The number of subjects available for fibrositis studies is not, however, large. Therefore, clinical realities and statistical desires sometimes clash.

Summary statement

Clearly, pain was the most important predictor of treatment success, as well as being the most important discriminator between the groups after treatment. Therefore, a general conclusion that can be drawn from this study is the importance of accurate pain measurement. Several different measures were used in the present

research to assess change in a group of patients with no "obvious" physical signs of disease. Many of these measures were related to each other and some of these changed in response to treatment. But, it was pain, as measured by the McGill Pain Questionnaire PRI, that provided the most pertinent information. To a certain extent, this validates the fibrositis patients' own symptomatic complaints, because both objective and subjective measures changed in the responders. In the non-responders, no measures changed. Fibrositis patients are difficult to treat, and in some medical circles even the diagnosis of fibrositis is still not accepted. If the results of this study can lend some support to the legitimacy of the patients' complaints in some way, then this research will have been of use.

Chapter 6

"What we observe is not nature itself, but nature exposed to our method of questioning."

Heisenberg

General Discussion

The present research examined the question "Is there a relationship between disease state and pain responsiveness?". For both the patient populations who took part, the answer is "Yes", a significant positive relationship exists between disease state and pain responsiveness.

The first 2 studies, with rheumatoid arthritis subjects, found that the standardized pain threshold and tolerance levels of three stressors were inversely correlated with disease activity. Therefore, as disease activity increases, pain threshold and tolerance levels decrease. Conversely, as disease activity decreases, pain threshold and tolerance levels increase. Over all the analyses with all the variables, disease activity was the most frequent single predictor of pain responsiveness.

In the third study, with fibrositis subjects, changes in pain responsiveness and other related variables were examined in relationship to treatment with amitriptyline. Pain threshold and the total myalgic score, measured with the dolorimeter, improved after treatment when compared

with placebo. Pain tolerance levels did not change. However, three important pieces of information emerged. First, the magnitude of the change was much larger for TMS than for pain threshold. Second, significant changes in pain responsiveness occurred only in those patients who responded to treatment. Third, the improvements in TMS and pain threshold were transitory and quickly returned to their previous values after the active treatment was withdrawn.

Hypervigilance and adaptation-level effects.

Within the fibrositis subjects, an overall measure of well-being was used in the place of the more "objective" measures of disease activity that were employed with the R.A. subjects. However, in both studies it was shown that pain responsiveness was not static but varied predictably in a positive relationship with disease activity.

Previous studies, with other chronic pain populations, have demonstrated similar effects. For example, Malow and co-workers (Malow et al, 1980; Malow and Olson, 1981) showed that generalized pain thresholds were reduced in patients with myofascial pain dysfunction syndrome. These diminished pain thresholds returned towards normal values, i.e. they increased after successful treatment. Similar findings have been reported for headache sufferers and patients with diabetes (Philips and Hunter, 1982; Morley et al, 1984). As well, it has been shown that myofascial pain syndrome patients have areas of heightened local tenderness

which improve after treatment (Graff-Radford et al, 1989). Each of these diagnostic groups could be classified as being "hypervigilant" to painful stimuli. This implies that their style of perceptual processing is such that they are predisposed to attend to certain classes of events, in this case pain (Chapman, 1978; 1986). Therefore, they would perceive a particular painful event as being more than normally painful.

For each of these groups, an improvement in disease state was accompanied by a raising of pain threshold. The implication from these data is that an increase in pain threshold towards normal levels is desirable. The fibrositis patients' results would certainly support that position. They previously have been shown to have lower pain threshold and tolerance levels when compared to normal controls (Scudds et al, 1987). In the present research, both generalized pain thresholds and local tenderness improved after treatment.

However, other studies have shown an opposite response which Rollman (1979) named the "adaptation-level effect". This means that a potentially noxious event is perceived with reference to endogenous pain levels. Thus, the patient would be more likely to rate the novel noxious stimulus as less painful than would other, pain-free subjects. There is also evidence that these higher-than-normal pain threshold values return towards normal after successful treatment (Callaghan et al, 1978; Nyquist and Eriksson, 1981). For

these patients a "good" result produced a reduction in pain threshold.

The apparent conflict between the adaptation-level and hypervigilance theories is problematic. Part of the difficulty is the inherent problem of defining a "normal" range of values in response to painful stimuli. Perceptual systems allow a wide variation of response to change within the environment. Any alteration of that normal range would imply that the limits are reduced, leading to some level of disability. For vision and audition, the results of a permanent alteration of perceptual range are relatively easy to assess and to understand. For several reasons, such is not the case with pain.

Firstly, wide ranges of individual differences exist within normal individuals to different painful stimuli. Secondly, in the absence of any profound central nervous system damage, it would seem that alterations in perceptual response-styles are only temporary, because values return quickly towards normal after successful treatment. Third, pain responsiveness may either increase or decrease about some "normal" value for that individual.

Some insights into the prediction of "hypervigilance" or "adaptation-level" effects can be gained from the present research, as well as an examination of other patient populations.

The positive relationship between responsiveness and disease activity in the R.A.'s is more in accord with

hypervigilance theory than adaptation-level theory. The most consistent single predictor of pain responsiveness was disease activity which is reflective of physiological change. The psychological variables were less important as predictors of responsiveness than disease activity. By implication, it was the underlying patho-physiology and not the perceptual style, that changed.

For the fibrositis patients, the total myalgic score improved much more percentage-wise than the pain threshold. It is likely that TMS is an indicator of some, as yet unidentified, underlying pathophysiological process. If this is so, then alterations in pain thresholds may be secondary to an improvement in distal physiological processes, not central perceptual mechanisms. As well, the rapid onset and disappearance of the changes in responsiveness after successful treatment with amitriptyline indicates that the changes may be more neurochemical than perceptual. An increase in the synaptic availability of serotonin is much more likely to lead to alterations in other physiological processes than to changes of perceptual style.

Therefore, increased sensitivity to painful stimuli may not be as a result of hypervigilance, because that implies a central perceptual change. A more likely explanation is that these changes are secondary to peripheral or central physiological processes.

Support for this position comes from a recent study which examined pain responsiveness in matched groups of fibrositis and MPS patients (Scudds et al, 1989). It was found that the MPS subjects had higher dolorimeter pain threshold levels than fibrositis patients, except in the particular area in which the MPS subjects complained of symptoms. The authors concluded that the altered pain thresholds in both groups of patients were indicative of some underlying painful pathology and postulated that the generalized reductions in pain threshold in the fibrositis patients were indicative of some wide-spread, but currently unknown, pathology.

Therefore, the "hypervigilance" findings may be reflections of underlying painful symptoms of pathological processes which, in turn, produce hyperalgesia in the affected area. Thus, migraineurs show the greatest increases in sensitivity on the same side as their headache (Nattero et al, 1987). MPS, and myofascial pain dysfunction syndrome patients also show the greatest changes in sensitivity in the areas which are local to their symptomatology (Fricton and Schiffman, 1987; Scudds et al, 1989).

In contrast to these reports, adaptation-level effects have been found with normal subjects in the laboratory, and in chronic low-back pain patients. Rollman (1979) and Chen and Treede (1985), have elegantly demonstrated that normal subjects make reference to the magnitude, or quality, of

one painful stimulus when they are required to make judgments of the magnitude of another painful stimulus.

It is very interesting that, clinically, adaptation-level effects have only been demonstrated in one chronic pain syndrome - chronic low back pain (Callaghan et al, 1978; Naliboff et al, 1981; Yang et al, 1985). These patients may be viewed as tne "classic" chronic pain syndrome patients, in as much as the length of their painful condition far outlasts the expected resolution of any underlying pathology. Behavioral and psychological changes often ensue with resultant life-style alterations which are often accompanied by depression and learned helplessness (Bradley et al, 1981; Deyo et al, 1982; Skevington, 1983).

Adaptation-level effects may be typical of this type of chronic pain syndrome. These effects may be viewed in the context of the overall psychological adaptations that result from the chronic pain experience. Therefore, a lessening of sensitivity to pain would be both biologically and perceptually beneficial and adaptive.

However, the same argument must also hold true for patients with increased sensitivity to painful stimuli. What is the biological and psychological significance of hypervigilance? If, there is an underlying, on-going and acutely painful pathophysiological process, then the significance would be the same as with any other acute pain. That is, it would lead to a reduction in mobility and

to the avoidance of further harm until the pathology is alleviated. Other, psycho-social, changes would also occur as a result of prolonged pain. However, these changes would reduce quickly, as with the fibrositis patients in the present research, after successful treatment. Such rapidity of improvement is uncommon in chronic low-back pain after treatment interventions.

It is worthy of note that pain tolerance levels, more indicative of psychological processes, did not change over the short length of the study with amitriptyline. But, they did change, over a much longer time period, in the R.A. patients. It would be interesting to investigate any alterations in pain tolerance levels over a long period of time in those fibrositis patients who respond well to treatment and to compare them with non-responders. Tolerance levels should raise, but more slowly than pain thresholds as cognitive and perceptual adjustments are made by the patient to his or her improved bio-psycho-social state.

Summary

Therefore, a resolution to the apparently contradictory hypervigilance and adaptation-level theories is that both are correct. However, each theory reflects the nature of the underlying pain syndrome in which it occurs. Adaptation-level effects may well be perceptual adaptations, but hypervigilance effects are more likely to be as a result of local physiological changes.

Accounting for the variance in pain responsiveness.

Throughout this dissertation, numerous references have been made to the wide range of individual differences in pain threshold and tolerance levels which are found within and between subjects. Statistically significant regression analyses could only predict a small amount of the variance in pain responsiveness. Anxiety, depression, age, and hypochondriasis, all of which have some bearing on pain, added little to the analyses. What accounts for the rest of the variance?

Biological influences, such as disease activity, obviously play a part. The endorphins, and other neurochemicals, such as 5-HT, are also relevant. Serotonin is involved in pain, sleep disturbance and depression, and sometimes these three symptoms are present in one patient at the one time. In other patients, only one, or two of them are found. Therefore, it is not possible to infer that these three symptoms always have the same neurochemical substrate. There are many types of pain, as well as different causes for depression, and for sleep disturbances. To identify the neurochemical communalities amongst syndromes which have different types of pain, depression and sleep disorders would lead to major advances in the treatment of pain.

It was interesting that the rheumatoid factor titre in the first two studies also accounted for a small part of

the variance. Whether this was as a result of differences in personality style, or to some disease process, is not known. However, this serendipitous result illustrates how little is known about the factors that contribute to overall pain threshold and tolerance levels. Does gender contribute on the basis of biological or social modeling differences? Similarly, does sleep disturbance increase pain sensitivity through bio-chemical or psychological means? Chance findings may answer some of the questions, but future research should address the problem of pain responsiveness in a multi-dimensional manner which was the approach of the present research.

These are not purely hypothetical questions. The factors that influence pain threshold and tolerance levels are very important to at least 10% of the population at any one time - the people in pain (Crook et al, 1984). A greater understanding of these factors may lead to novel, and more effective treatments for pain.

The investigation of individual variables may produce individual results. But, pain is a multi-dimensional experience. Therefore, future research in the area should concentrate on its multi-factorial nature. Cognitive style, response bias, expectations, and other psychological factors should be investigated at the same time as the underlying physiological mechanisms that mediate the physiological substrate of pain responsiveness.

Conclusions

Chronic pain syndromes pose many problems for researchers, clinicians and particularly, for the pain patient. Many factors influence the pain experience and the present research addressed several of these. The length of this dissertation attests to the complexity of the inter-relationship that is found in any study that deals with the nature of pain.

By attempting to investigate, and measure, a single aspect of pain, one is continually struck by the fact that knowing only one facet is not enough. Many disciplines, each with its own viewpoint and methods of investigation, need to ask the same research question, at the same time. Only through inter-disciplinary pain assessment, treatment and research will the mosaic of pain be clearly understood.

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Appendix A

Diagnostic Criteria for Rheumatoid Arthritis

DIAGNOSTIC CRITERIA FOR CLASSICAL OR DEFINITE RHEUMATOID ARTHRITIS

1. Morning stiffness.

2. Pain on motion or tenderness in at least one joint.

3. Swelling due to soft tissue thickening or fluid in at least one joint.

4. Swelling of at least one other joint within three months previously.

5. Symmetrical joint swelling.

6. Subcutaneous nodules over bony prominences.

7. X-ray changes typical of rheumatoid arthritis.

8. Positive agglutination test.

9. Poor mucin precipitate from synovial fluid.

10. Characteristic histologic changes in the synovial membrane.

11. Characteristic changes in nodules.

For the diagnosis of "classical" rheumatoid arthritis, seven of the above criteria must be satisfied. In criteria 1 through 5 the symptoms must be continuous for at least six weeks.

For the diagnosis of "definite" rheumatoid arthritis, five of the above criteria must be satisfied. Criteria 1 through 5 also must be fulfilled in the above manner.

(From: Ropes et al, 1958)

Appendix B

Consent Form for Study 1

CONSENT FORM

I, ..., understand that this experiment involves three procedures that will induce pain. I will be asked to put my forearm in a pressure algometer which consists of a weight resting on top of my arm. I will attempt to keep the pressure on as long as possible although I understand that I may freely remove my arm at any time. In a similar manner, on the other arm, I will have a pressure device which applies a steadily increasing pressure applied. Again, though I agree to keep my arm under the weight as long as possible, I may withdraw it at any time. Finally, I understand that I will have two small electrodes attached to the back of one hand through which I will feel electrical pulses ranging from a faint touch to a sharp pricking. Stimulation will be terminated promptly when I indicate that I do not wish to proceed further. I understand that I will also be asked to complete a questionnaire.

I understand that my participation in this experiment is voluntary and that I may leave at any time, if I do not wish to continue, without my status being prejudiced in any way.

DO YOU HAVE ANY QUESTIONS?

I have been given the opportunity to ask questions and have had them answered to my satisfaction. I understand that I have any further questions I may telephone Roger Scudds, psychology student, at 679-2612 or 433-8921.

I understand the data I will provide will be used anonymously and that I will not be identified by name as having taken part in this study.

Before we being could you please answer the following question: Have you taken any pain killing medication in the last 12 hours?

If yes, please specify .....

Having read the above, I agree to participate in this research project.

Signature _____

Address _____

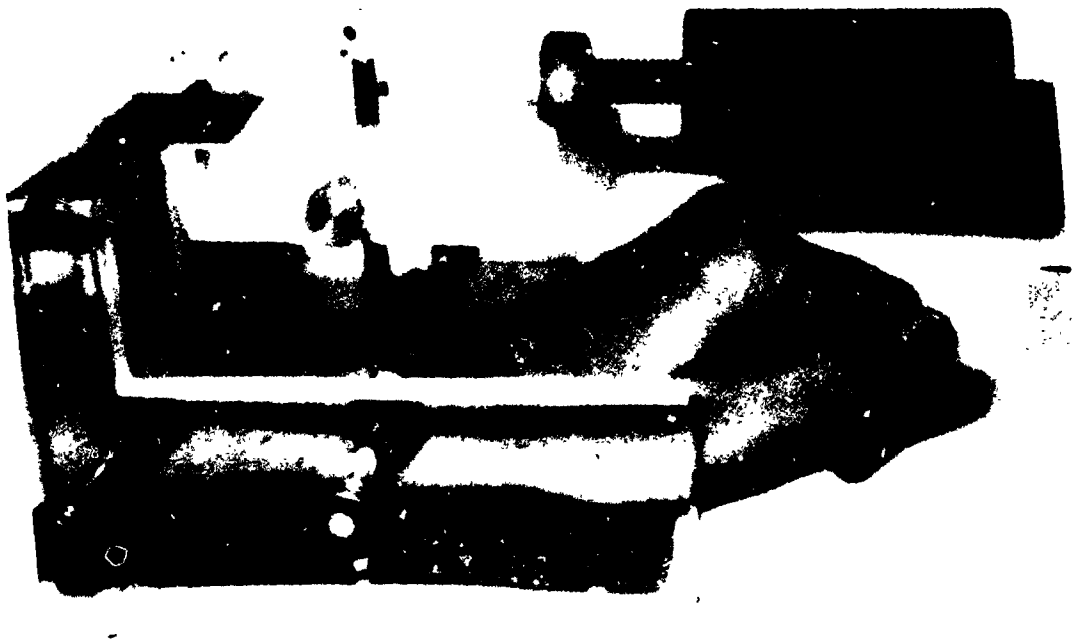
_____

_____

Date _____

Appendix C

Forgione-Barber Pressure Algometer



Appendix D

The Dolorimeter

Appendix E

Basic Personality Inventory

BASIC PERSONALITY INVENTORY

DIRECTIONS

On the following pages you will find a series of statements which a person might use to describe himself. Read each statement and decide whether or not it describes you. Then indicate your answer on the separate answer sheet. If you agree with a statement or decide that it does describe you, answer TRUE. If you disagree with a statement or feel that it is not descriptive of you, answer FALSE. In marking your answers on the answer sheet, be sure that the number of the statement you have just read is the same as the number on the answer sheet.

Answer every statement either true or false, even if you are not completely sure of your answer.

		TRUE	FALSE
1.	It's easy for me to keep fit and healthy.	____	____
2.	My present situation is hopeless.	____	____
3.	I care about what other people think of me.	____	____
4.	Sometimes I feel like smashing things.	____	____
5.	I would enjoy betting on horses.	____	____
6.	No one is making things work out badly for me.	____	____
7.	I feel frightened when I have to go out alone.	____	____
8.	I never see faces of old friends appear before me out of nowhere.	____	____
9.	Many times I act on impulse.	____	____
10.	I enjoy being with people.		
11.	I have given up hope of every amounting to anything.	____	____
12.	I frequently think of the same silly thing over and over for hours.	____	____
13.	Sometimes my legs lose their strength so that I can't walk.	____	____
14.	I rarely feel disappointed.	____	____
15.	Very few things excite me.	____	____
16.	I would never intentionally hurt someone's feelings.	____	____
17.	For the most part people are honest.	____	____
18.	Someone has stolen my free will.	____	____
19.	Even at the end of a hard day, I remain relaxed and at ease.	____	____
20.	I seem to hear an unknown voice wherever I go.	____	____
21.	I would not do something foolhardy just for the fun of it.	____	____
22.	I keep my distance from other people.	____	____
23.	I deserve my share of good luck.	____	____

24.	There have been days when I have done things without being able to recall anything at all about them.	____	____
25.	I am free of aches and pains.	____	____
26.	There is not much to be interested in any more.	____	____
27.	Some movies make me quite happy or sad.	____	____
28.	No one gets away with insulting me.	____	____
29.	I have been in trouble with the law more than once.	____	____
30.	I rarely feel that someone is trying to get the best of me.	____	____
31.	Although I really try, I cannot stop feeling tense.	____	____
32.	I do not experience peculiar voices warning me of danger.	____	____
33.	I often behave in a reckless manner.	____	____
34.	I like to speak to strangers.	____	____
35.	I am only suited for the lowest and most simple sort of work.	____	____
36.	I sometimes have convulsions and seizures that I cannot control.	____	____
37.	My stomach is easily upset.	____	____
38.	My future is cheery.	____	____
39.	I would not be tempted by a promise of getting something for nothing.	____	____
40.	I can get along quite well with irritable people.	____	____
41.	No matter how easy or safe it was, I would never steal money.	____	____
42.	I can tell that someone has searched through my possessions a number of times.	____	____
43.	I remain quite cool when things go badly.	____	____
44.	Fancy colored lights sometimes float through my brain.	____	____

45.	Ideas do not race through my head faster than I can speak them.	____	____
46.	Most of the time I prefer to be alone.	____	____
47.	I am the type of person who can be relied upon.	____	____
48.	I don't think my life is worth living.	____	____
49.	I seldom have any bodily discomfort.	____	____
50.	I live a gloomy and boring life.	____	____
51.	At times I say things about my friends that aren't nice.	____	____
52.	If someone does something I dislike, I usually tell that person about it.	____	____
53.	I would enjoy cheating certain people.	____	____
54.	I never have the feeling that someone is out to do away with me.	____	____
55.	It frightens me to think about things that bother me.	____	____
56.	Ordinary things never appear "foggy" or far away to me.	____	____
57.	Sometimes I suddenly get up and act without warning or reason.	____	____
58.	I would rather work with a group of people than by myself.	____	____
59.	I am no good to anyone.	____	____
60.	I have nightmares almost every night.	____	____
61.	My skin is often red and inflamed.	____	____
62.	I enjoy just about everything I do.	____	____
63.	I never weep or feel like weeping.	____	____
64.	I don't mind having someone tell me what to do.	____	____
65.	I know of no excuse for taking advantage of someone of the opposite sex.	____	____
66.	I feel that I am in great danger from those who wish to harm me.	____	____

67. Other peoples' actions rarely make me anxious. _____ _____

68. I sometimes hear voices which no one else understands. _____ _____

69. I am careful in almost everything I do. _____ _____

70. I try not to get involved in conversations with others. _____ _____

71. I think my parents would have reason to be proud of me. _____ _____

72. I have strange fears of places and things. _____ _____

73. My back does not bother me. _____ _____

74. Others seem to lead happier lives than I do. _____ _____

75. I can remember a few unpleasant things about my childhood. _____ _____

76. Slow people make me angry. _____ _____

77. I think that I could commit a crime and get away with it. _____ _____

78. I rarely feel that people look for my weaknesses. _____ _____

79. I worry when a train or bus is late. _____ _____

80. I never confuse my own thoughts with a real person talking to me. _____ _____

81. I'll try almost anything regardless of the consequences. _____ _____

82. I have a number of close friends. _____ _____

83. My whole life is one big mistake. _____ _____

84. I have periods when my mind races ahead so fast that I cannot think clearly. _____ _____

85. Whenever I am worried about something I get cramps. _____ _____

86. I live a very satisfying and rewarding life. _____ _____

87. I am careful not to have any bad thoughts. _____ _____

88. My family life has been happy and free of arguments. _____ _____

89. Most salespeople would not cheat a customer. _____ _____

90. When people whisper, I feel they might be talking about me. _____ _____

91. I have the ability to concentrate without my mind wandering. _____ _____

92. I see bright pictures in my head when I don't want to. _____ _____

93. I can work for a reasonable length of time without becoming bored. _____ _____

94. I avoid speaking with people as much as I can. _____ _____

95. I usually do most of my daily tasks quite well. _____ _____

96. I have no interest at all in the opposite sex. _____ _____

97. I seldom have a cough or sore throat. _____ _____

98. Life is extremely dull for me. _____ _____

99. I try to avoid jobs I dislike. _____ _____

100. Bossy people can expect an argument from me. _____ _____

101. No one does things for nothing. _____ _____

102. Most people treat me openly without having concealed motives _____ _____

103. Sometimes my own thoughts scare me so much that I think I'm going to pass out. _____ _____

104. My memory is as good as it ever was. _____ _____

105. I often take risks without stopping to think about the results. _____ _____

106. I dislike going out alone. _____ _____

107. People are better off without me. _____ _____

108. I frequently experience terrible headaches. _____ _____

109. I often have pains in odd parts of my body. _____ _____

110. Something interesting happens to me almost every day. _____ _____

111. I am never cross with a loved one. _____ _____

112. I avoid quarrelling with others.	____	____
113. Gambling has no appeal to me.	____	____
114. I often have the feeling that I am not liked.	____	____
115. I generally feel quite comfortable when being introduced to strangers.	____	____
116. I can't always decide whether a minute or an hour has passed.	____	____
117. I am not the type to be bored one minute and excited about something the next.	____	____
118. I am happier alone than when with others.	____	____
119. Most people find me an interesting person to talk with.	____	____
120. If things don't improve for me, I may have to do something violent or dangerous.	____	____
121. I hardly ever have "splitting" headaches.	____	____
122. I often have trouble sleeping because I feel so sad.	____	____
123. On some days I am more easily annoyed than on others.	____	____
124. I like to run my own life without interference from anyone.	____	____
125. I admire a successful professional thief.	____	____
126. I never feel like a machine that someone else plugs in and uses.	____	____
127. When I am startled my heart seems to skip a beat and stop.	____	____
128. Things don't appear unusually different to me right now.	____	____
129. I am usually somewhat restless.	____	____
130. I like talking to just about anyone I meet.	____	____
131. I do not consider myself worthy of other people's kindness.	____	____
132. There have been periods of time when I have used alcohol to excess.	____	____

133. Sometimes I get so dizzy I can hardly stand up. _____ _____

134. I always look forward to a new day. _____ _____

135. I have never lied to anyone. _____ _____

136. I believe in obeying those in authority. _____ _____

137. I was not regarded as a discipline problem by my school teachers. _____ _____

138. I am greatly concerned with what people think about me. _____ _____

139. Emergencies seldom make me nervous. _____ _____

140. I often see shadows and think they are people or animals. _____ _____

141. My feelings about people do not change much from day to day. _____ _____

142. I don't care whether or not the people around me are my friends. _____ _____

143. I enjoy the respect of most people who know me. _____ _____

144. I have often used dangerous drugs and chemicals. _____ _____

145. I generally feel warm enough. _____ _____

146. I don't think things will ever get any better for me. _____ _____

147. Occasionally I use my friends to my own advantage. _____ _____

148. I dislike working for a person who is too strict. _____ _____

149. Someone is always trying to trick you. _____ _____

150. I am sure that there is no gossiping about me. _____ _____

151. Little things often upset me. _____ _____

152. I usually know about what time it is. _____ _____

153. I often leave jobs unfinished. _____ _____

154. When I am not feeling well, I like to have someone around to comfort me. _____ _____

155. I am not a particularly kind person. _____ _____

156. I would enjoy watching someone suffer great pain. _____ _____

157. I often have eye strain upon completing a day's work. ____ ____

158. I believe that life is worth living. ____ ____

159. I don't like thinking about personal problems. ____ ____

160. I take great pains to be tactful with other people ____ ____

161. There are many things I consider wrong and wouldn't do. ____ ____

162. I often feel that others are trying to keep me out of their group. ____ ____

163. I remain calm even in the most trying situations. ____ ____

164. I often have the feeling that imaginary things are happening to me. ____ ____

165. I enjoy planning things. ____ ____

166. I am not considered sociable. ____ ____

167. I think I would make a very good leader. ____ ____

168. I do not care what happens to me. ____ ____

169. My joints give me no trouble. ____ ____

170. I feel depressed most of the time. ____ ____

171. As a child I sometimes felt that my parents acted unfairly. ____ ____

172. If someone hurts me, I remember it until I can get even. ____ ____

173. People are always trying to get away with something. ____ ____

174. No one has a magical power to control me. ____ ____

175. I am sometimes disturbed by things that I know can't hurt me. ____ ____

176. Even when left alone, I can find my way around easily. ____ ____

177. At times I am rather careless. ____ ____

178. I enjoy being neighborly. ____ ____

179. I often show poor judgement about things. _____ _____

180. I am very much attracted to members of my own sex. _____ _____

181. I have poor blood circulation. _____ _____

182. I am quite content with my life as it is now. _____ _____

183. I admit my mistakes without ever trying to hide anything. _____ _____

184. I seldom feel like hitting anyone. _____ _____

185. I would feel very guilty if I were caught doing something wrong. _____ _____

186. I never feel comfortable eating food prepared by others. _____ _____

187. I don't worry over what might happen to me. _____ _____

188. At times my surroundings change so much that I think I'm somewhere else. _____ _____

189. I never take unnecessary chances. _____ _____

190. I don't feel I need other people. _____ _____

191. I feel capable of handling many difficult jobs. _____ _____

192. I have been in serious trouble with the law. _____ _____

193. I have a good deal of energy. _____ _____

194. I dislike doing anything new. _____ _____

195. My feelings are sometimes hurt by loved ones. _____ _____

196. I dislike being ordered around by anyone. _____ _____

197. I would do just about anything for money. _____ _____

198. If I fail at something I can only blame myself. _____ _____

199. I am usually too afraid to try anything new. _____ _____

200. I never see things that other people cannot see. _____ _____

201. I usually say the first thing that comes into my mind. _____ _____

202. I truly enjoy myself at social events. _____ _____

203. People don't like me because I have so many faults.	____	____
204. I spend a great deal of time daydreaming about things that only I know.	____	____
205. I lose my breath easily.	____	____
206. I am usually a happy person.	____	____
207. I've never let down a friend in any way.	____	____
208. I do not easily lose patience with others.	____	____
209. Most people do what they can to help others.	____	____
210. I'm usually the first to be blamed if something goes wrong.	____	____
211. Things that upset other people usually do not bother me.	____	____
212. I cannot separate my daydreams from the real world.	____	____
213. I have a well thought out reason for almost everything I undertake.	____	____
214. I like to keep my ideas to myself.	____	____
215. I consider myself to be a generous and pleasant person.	____	____
216. I have been planning to do away with myself.	____	____
217. I never feel faint.	____	____
218. Recent events have made me feel downhearted and miserable.	____	____
219. Sometimes I deliberately avoid a person I dislike.	____	____
220. I get very irritated when someone disagrees with me.	____	____
221. I sometimes have fun teasing animals.	____	____
222. No one is trying to ruin my life.	____	____
223. When I visit a strange place I become very upset.	____	____
224. I can easily understand simple directions	____	____
225. I find it exciting to drive in a fast car.	____	____

226. I enjoy doing things with friends whenever I am able. _____ _____

227. I am not the type of person one remembers after one meeting. _____ _____

228. I do not care for anyone very much. _____ _____

229. I get a lot of headaches. _____ _____

230. I believe that I shall have my share of good luck. _____ _____

231. I always meet my responsibilities. _____ _____

232. No one could ever say that I am hot-tempered. _____ _____

233. Sooner or later people who break the law get caught. _____ _____

234. If certain individuals had not interfered, I would be more successful today. _____ _____

235. I do not panic more quickly than the average person. _____ _____

236. Many times I can hear mysterious voices all around me. _____ _____

237. I seldom do silly things without thinking. _____ _____

238. I make little effort to meet new people. _____ _____

239. Much of what I say is worth paying attention to. _____ _____

240. I always have difficulty sleeping. _____ _____

SCALE	LOWER SCORER	HIGH SCORER
Hypochondriasis	Is without excessive bodily concern or preoccupation with physical complaints. Absenteeism due to ill health likely to be below average.	Frequently thinks he is sick. Complains regularly of peculiar pains or bodily dysfunctions. Discusses such topics, frequently revealing a preoccupation with his complaints
Depression	Reports a usual feeling of confidence, cheerfulness, and persistence, even when experiencing disappointment. Has an optimistic attitude about his future.	Inclines to be down-hearted and show extreme despondency; considers himself to be inadequate; may be listless, remote and pre-occupied; looks at his future pessimistically.
Denial	Accepts his feelings as part of himself; not afraid to discuss unpleasant topics. Can answer questions about himself frankly; avoids impression management. Shows normal affect.	Lacks insight into his feelings and the causes of his behavior. Avoids unpleasant, exciting or violet topics. Relatively unresponsive emotionally.
Interpersonal Problems	Experiences less than average irritation from noise, changes in routine, disappointment and mistakes of others; respects authority and prefers clearly defined rules and regulations; cooperates fully with leadership and readily accepts criticism from others.	If often extremely annoyed by little inconveniences, frustrations or disappointments; will frequently be uncooperative, disobedient, and resistant when faced with rules and regulations; reacts against discipline and criticism.
Alienation	Ordinarily displays ethical and socially responsible attitudes and behavior; reports a sense of obligation toward society and its laws. feels little or no	Expresses attitudes markedly different from common social codes; is prone to depart from the truth and behave in an unethical and untrustworthy manner; feels no guilt.

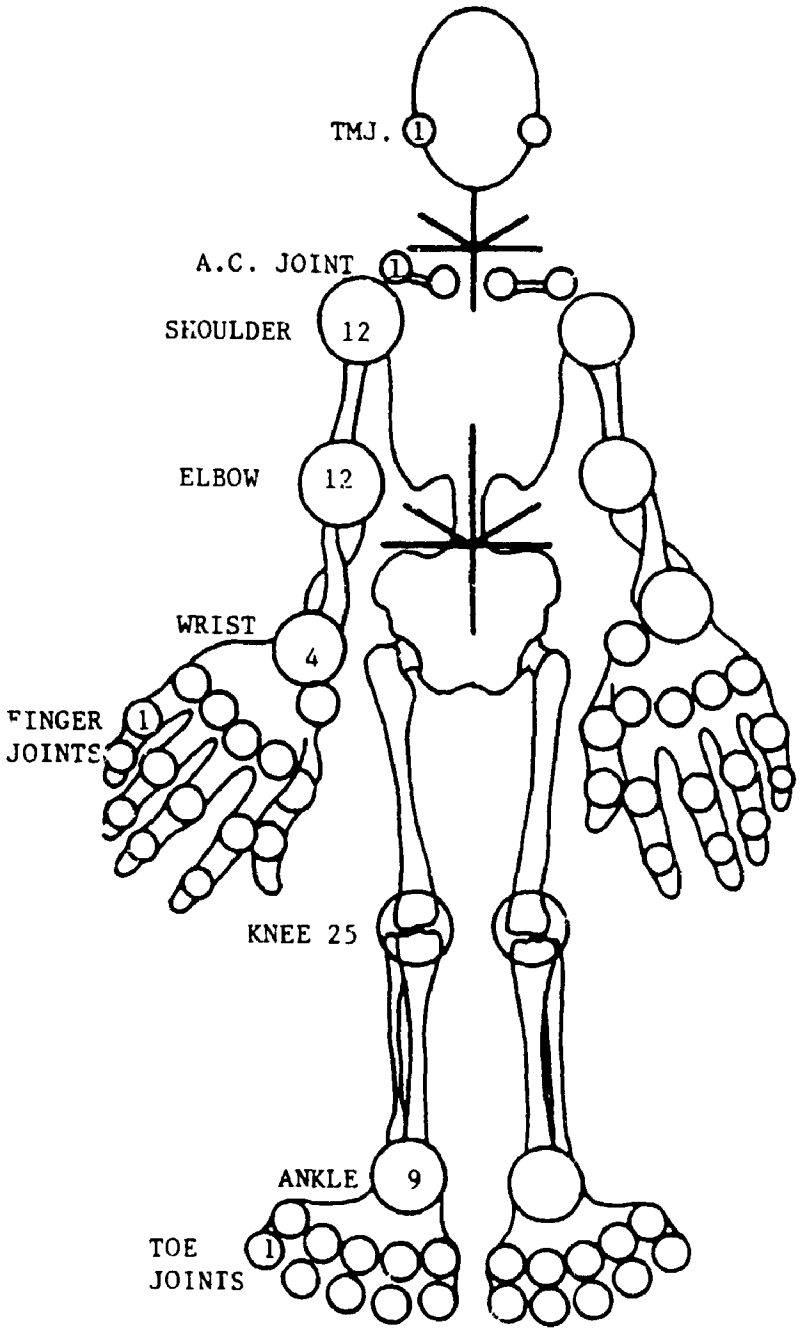
Persecutory Ideas	Trusts others and doesn't feel threatened. Accepts responsibility for the events in his life and doesn't attribute maliciousness to others.	Believes that certain people are against him and are trying to make his life difficult and unpleasant. Inclined to brood.
Anxiety	Remains calm and unruffled even when confronted by unexpected occurrences. Takes things as they come without fear or apprehension. Maintains self control even in a crisis situation.	Easily scared. Little things, even an idea, can throw him into a frenzy of anxiety. Afraid of novelty and of the possibility of physical or interpersonal danger.
Thinking Disorder	Has no difficulty distinguishing his daydreams from reality. Is able to concentrate normally and to maintain sensible conversations.	Is markedly confused, distractable and disorganized. Cannot remember even simple things from day to day. Reports that he feels he is living in a dreamlike world, that people appear different to him and that he feels different from them.
Impulse Expression	Appears to be even-tempered and level-headed; carefully considers the future before acting; generally has the patience to cope with a lengthy and tedious task.	Lacks ability to think beyond the present and to consider the consequences of his actions; is prone to undertake risky and reckless actions; inclined to behave irresponsibly; finds routine tasks boring.
Social Introversion	Enjoys company. Likes to talk and knows many people. Spends much of his time with others.	Avoids people generally. Has few friends and doesn't say much to those he has. Seems to be uncomfortable when around others. Prefers asocial activities.

Self Depreciation	Manifests a high degree of self-assurance in dealing with others. Not afraid to meet strangers; speaks with confidence about a variety of topics; believes in his own ability to accomplish things.	Degrades himself as being worthless, unpleasant, and undeserving. Generally expresses a low opinion of himself and refuses credit for any accomplishment.
Deviation	Generally shows behavior patterns similar to those of a majority of people. Tends to be free from unusual symptoms and modes of thought.	Displays behavior patterns very different from most people's. Admits to unusual and pathological characteristics.

Appendix F

Lansbury Index Weighting

Lansbury Articular Index Weighting



ACTIVE JOINT COUNT: TOTAL

Appendix G

R.A. Functional Classification

A.R.A. FUNCTIONAL CLASSIFICATION

CLASS

1. COMPLETE ability to carry on all usual duties without handicaps.

2. ADEQUATE FOR NORMAL ACTIVITIES despite handicap or discomfort or limited motion at one or more points.

3. LIMITED only to little or none of duties of usual occupation or self-care.

4. INCAPACITATED, LARGELY OR WHOLLY bedridden or confined to a wheelchair; little or no self-care.

Appendix H

Consent From for Study 2

CONSENT FORM

I, ..., understand that this experiment involves three procedures that will induce pain. I will be asked to put my forearm in a pressure algometer which consists of a weight resting on top of my arm. I will attempt to keep the pressure on as long as possible although i understand that I may freely remove my arm at any time. In a similar manner, on the other arm, I will have a pressure device which applies a steadily increasing pressure applied. Again, though I agree to keep my arm under the weight as long as possible, I may withdraw it at any time. Finally, I understand that I will have two small electrodes attached to the back of one hand through which I will feel electrical pulses ranging from a faint touch to a sharp pricking. Stimulation will be terminated promptly when I indicate that I do not wish to proceed further. I understand that I will also be asked to complete a questionnaire. I understand that the testing performed will be exactly identical to the testing on my previous visit.

I understand that my participation in this experiment is voluntary and that I may leave at any time, if I do not wish to continue, without my status being prejudiced in any way.

DO YOU HAVE ANY QUESTIONS?

I have been given the opportunity to ask questions and have had them answered to my satisfaction. I understand that I have any further questions I may telephone Roger Scudds, psychology student, at 679-2612 or 433-8921.

I understand the data I will provide will be used anonymously and that i will not be identified by name as having taken part in this study.

Before we being could you please answer the following question: Have you taken any pain killing medication in the last 12 hours?

If yes, please specify .....

Having read the above, I agree to participate in this research project.

Signature _____

Address _____

_____

_____

Date _____

Appendix I

Diagnostic Criteria for Fibrositis

DIAGNOSTIC CRITERIA FOR FIBROSITIS

1. Chronic widespread muscular aching of at least three months' duration.

2. Non-restorative sleep pattern.

3. Morning stiffness and fatigue.

4. Localised tenderness at 12 or more of 14 specific sites.

5. Skinfold tenderness over the upper scapular region.

6. Normal X-ray and blood tests.

(Smythe and Moldofsky, 1977)

Appendix J

Consent Form for Study 3

LETTER OF INFORMATION

The aim of this study is to examine the effects of a medication, Elavil (amitriptyline), on the symptoms of Fibrositis. This medication has been used for many years, but it is only recently that it has been employed with success to treat pain in various chronic pain syndromes.

The study will last for ten weeks. During that time you will be taking the active medication for four weeks, for two weeks you will receive no medication, and for a further four weeks you will receive a placebo. By comparing the effects of Elavil with those of placebo, we can find the true usefulness of the medication. During the study, you will be examined with a dolorimeter to measure the sensitivity of various points in your body. You will also be asked to complete questionnaires that relate to your pain, your activities and your state of mind. These will be examined four times during the study period.

For the duration of the study, you will be asked to take only ordinary Tylenol and to keep a record of the number of these that you take. You will be asked to stop taking all other non-essential medication. Elavil has some possible side-effects, such as drowsiness, dryness of mouth, constipation and, occasionally raising of blood pressure. If any of these occur, please inform us.

You are free to withdraw from the study at any time without prejudice to your normal care. If you have any questions now, or at any other time please ask them or contact Roger Scudds at 679-2612.

CONSENT FORM

I agree to participate in the research project entitled "The effects of Amitriptyline on pain perception and personality in fibrositis".

I have read and understand the information contained in the accompanying Letter of Information. I understand that confidentiality of information given by me as part of this study will be maintained and that I am free to withdraw from the study at any time without prejudice to my future care and treatment.

Patient's name

_____

Date

_____

Appendix K

McGill Pain Questionnaire

McGILL PAIN QUESTIONNAIRE

Subject # _____

Please circle the words that best describe your pain at this moment. Do not circle more than one word in each group. You may omit any group that does not apply.

1	2	3	4	5
Flickering	Jumping	Pricking	Sharp	Pinching
Quivering	Flashing	Boring	Cutting	Pressing
Pulsing	Shooting	Drilling	Lacerating	Gnawing
Throbbing		Stabbing		Cramping
Beating		Lancinating		Crushing
Pounding				

6	7	8	9	10
Tugging	Hot	Tingling	Dull	Tender
Pulling	Burning	Itchy	Sore	Taut
Wrenching	Scalding	Smarting	Hurting	Rasping
	Searing	Stinging	Aching	Splitting
			Heavy	

11	12	13	14	15
Tiring	Sickening	Fearful	Punishing	Wretched
Exhausting	Suffocating	Frightful	Gruelling	Blinding
		Terrifying	Cruel	
			Vicious	
			Killing	

16
Annoying
Troublesome
Miserable
Intense
Unbearable

Appendix L

Sickness Impact Profile

S I C K N E S S I M P A C T P R O F I L E

THE FOLLOWING INSTRUCTIONS ARE FOR THE SELF-ADMINISTERED QUESTIONNAIRE

PLEASE READ THE ENTIRE INTRODUCTION BEFORE YOU READ THE QUESTIONNAIRE. IT IS VERY IMPORTANT THAT EVERYONE TAKING THE QUESTIONNAIRE FOLLOWS THE SAME INSTRUCTIONS.

INTRODUCTION TO RESPONDENT

You have certain activities that you do in carrying on your life. Sometimes you do all of these activities. Other times, because of your state of health, you don't do these activities in the usual way: you may cut some out; you may do some for shorter lengths of time; you may do some in different ways. These changes in your activities might be recent or longstanding. We are interested in learning about any changes that describe you today and are related to your state of health.

The questionnaire booklet lists statements that people have told us describe them when they are not completely well. Whether or not you consider yourself sick, there may be some statements that will stand out because they describe you today and are related to your state of health. As you read the questionnaire, think of yourself today. When you read a statement that you are sure describes you and is related to your health, place a check on the line to the right of the statement. For example:

I am not driving my car _x_

If you have not been driving for some time because of your health, and are still not driving today, you should respond to this statement.

On the other hand, if you never drive or are not driving today because your car is being repaired, the statement, "I am not driving my car" is not related to your health and you should not check it. If you simply are driving less, or are driving shorter distances, and feel that the statement only partially describes you, do not check it. In all these cases you would leave the line to the right of the statement blank. For example:

I am not driving my car _____

Remember that we want you to check this statement only if you are sure it describes you today and is related to your state of health.

Read the introduction to each group of statements and then consider the statements in the order listed. While some of the statements may not apply to you, we ask that you please read all of them. Check these that describe you as you go along. Some of the statements will differ only in a few words, so please read each one carefully. While you may go back and change a response, your first answer is usually the best. Please do not read ahead in the booklet.

PLEASE RESPOND TO (CHECK) ONLY THOSE STATEMENTS THAT YOU ARE SURE DESCRIBE YOU TODAY AND ARE RELATED TO YOUR STATE OF HEALTH.

---

1. I spend much of the day lying down in order to rest _____
2. I sit during much of the day _____
3. I am sleeping or dozing most of the time - day or night _____
4. I lie down more often during the day in order to rest _____
5. I sit around half-asleep _____
6. I sleep less at night, for example, wake up too early, don't fall asleep for a long time, awaken frequently _____
7. I sleep or nap more during the day _____

_____

CHECK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE _____

PLEASE RESPOND TO (CHECK) ONLY THOSE STATEMENTS THAT YOU ARE SURE DESCRIBE YOU TODAY AND ARE RELATED TO YOUR STATE OF HEALTH.

---

1. I say how bad or useless I am, for example, that I am a burden on others _____

2. I laugh or cry suddenly _____

3. I often moan and groan in pain or discomfort _____

4. I have attempted suicide _____

5. I act nervous or restless _____

6. I keep rubbing or holding areas of my body that hurt or are uncomfortable _____

7. I act irritable and impatient with myself, for example, talk badly about myself, swear at myself, blame myself for things that happen _____

8. I talk about the future in a hopeless way _____

9. I get sudden frights _____

_____

CHECK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE _____

THIS GROUP OF STATEMENTS HAS TO DO WITH ANY WORK YOU USUALLY DO IN CARING FOR YOUR HOME OR YARD. CONSIDERING JUST THOSE THINGS THAT YOU DO, PLEASE RESPOND TO (CHECK) ONLY THOSE STATEMENTS THAT YOU ARE SURE DESCRIBE YOU TODAY AND ARE RELATED TO YOUR STATE OF HEALTH

---

1. I do work around the house only for short periods of time or rest often _____

2. I am doing less of the regular daily work around the house than I would usually do (_____) _____

3. I am not doing any of the regular daily work around the house that I would usually do (_____) _____

4. I am not doing any of the maintenance or repair work that I would usually do in my home or yard (_____) _____

5. I am not doing any of the shopping that I would usually do (_____) _____

6. I am not doing any of the house cleaning that I would usually do (_____) _____

7. I have difficulty doing handwork, for example, turning faucets, using kitchen gadgets, sewing, carpentry _____

8. I am not doing any of the clothes washing that I would usually do (_____) _____

9. I am not doing heavy work around the house (_____) _____

10. I have given up taking care of personal or household business affairs, for example, paying bills, banking, working on budget (_____) _____

_____

CHECK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE _____

A number of the questions in this category involve household chores which you might do less frequently or no longer attempt because of your pain. If you checked any of these, indicate who now does these chores by writing in the blank space (_____) following each question.

PLEASE RESPOND TO (CHECK) ONLY THOSE STATEMENTS THAT YOU ARE SURE DESCRIBE YOU TODAY AND ARE RELATED TO YOUR STATE OF HEALTH.

---

1. I am getting around only within one building _____
2. I stay within one room _____
3. I am staying in bed more _____
4. I am staying in bed most of the time _____
5. I am not now using public transportation _____
6. I stay home most of the time _____
7. I am only going to places with restrooms nearby _____
8. I am not going into town _____
9. I stay away from home only for brief periods of time _____
10. I do not get around in the dark or in unlit places without someone's help _____

_____

CHECK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE _____

PLEASE RESPOND TO (CHECK) ONLY THOSE STATEMENTS THAT YOU ARE SURE DESCRIBE YOU TODAY AND ARE RELATED TO YOUR STATE OF HEALTH

---

1. I am going out less to visit people _____
2. I am not going out to visit people at all _____
3. I show less interest in other people's problems, for example, don't listen when they tell me about their problems, don't offer to help _____
4. I often act irritable toward those around me, for example, snap at people, give sharp answers, criticize easily _____
5. I show less affection _____
6. I am doing fewer social activities with groups of people _____
7. I am cutting down the length of visits with friends _____
8. I am avoiding social visits from others _____
9. My sexual activity is decreased _____
10. I often express concern over what might be happening to my health _____
11. I talk less with those around me _____
12. I make many demands, for example, insist that people do thing for me, tell them how to do things _____
13. I stay alone much of the time _____
14. I act disagreeable to family members, for example, I act spiteful, I am stubborn _____
15. I have frequent outbursts of anger at family members, for example, strike at them, scream, throw thing at them _____
16. I isolate myself as much as I can from the rest of the family _____
17. I am paying less attention to the children _____
18. I refuse contact with family members, for example, turn away from them _____
19. I am not doing the things I usually do to take care of my children or family _____

20. I am not joking with family members as I usually do _____

_____

CHECK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE _____

PLEASE RESPOND TO (CHECK) ONLY THOSE STATEMENTS THAT YOU ARE SURE DESCRIBE YOU TODAY AND ARE RELATED TO YOUR SATE OF HEALTH

---

1. I am confused and start several actions at a time _____

2. I have more minor accidents, for example, drop things, trip and fall, bump into things _____

3. I react slowly to things that are said or done _____

4. I do not finish things I start _____

5. I have difficulty reasoning and solving problems, for example, making plans, making decisions, learning new things _____

6. I sometimes behave as if I were confused or disoriented in place or time, for example, where I am, who is around, directions, what day it is _____

7. I forget a lot, for example, things that happened recently, where I put things, appointments _____

8. I do not keep my attention on any activity for long _____

9. I make more mistakes than usual _____

10. I have difficulty doing activities involving concentration and thinking _____

_____

CHECK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE _____

THE NEXT GROUP OF STATEMENTS HAS TO DO WITH ANY WORK YOU USUALLY DO OTHER THAN MANAGING YOUR HOME. BY THIS WE MEAN ANYTHING THAT YOU REGARD AS WORK THAT YOU DO ON A REGULAR BASIS.

DO YOU USUALLY DO WORK OTHER THAN MANAGING YOUR HOME?

_____ YES _____ NO

IF YOU ANSWERED YES, GO ON TO THE NEXT PAGE.

IF YOU ANSWERED NO:

ARE YOU RETIRED?

_____ YES _____ NO

IF YOU ARE RETIRED, WAS YOUR RETIREMENT RELATED TO YOUR HEALTH?

_____ YES _____ NO

IF YOU ARE NOT RETIRED, BUT ARE NOT WORKING, IS THIS RELATED TO YOUR HEALTH?

_____ YES _____ NO

NOW SKIP THE NEXT PAGE.

IF YOU ARE NOT WORKING AND IT IS NOT BECAUSE OF YOUR HEALTH, PLEASE SKIP THIS PAGE.

NOW CONSIDER THE WORK YOU DO AND RESPOND TO (CHECK) ONLY THOSE STATEMENTS THAT YOU ARE SURE DESCRIBE YOU TODAY AND ARE RELATED TO YOUR STATE OF HEALTH. (IF TODAY IS A SATURDAY OR SUNDAY OR SOME OTHER DAY THAT YOU WOULD USUALLY HAVE OFF, PLEASE RESPOND AS IF TODAY WERE A WORKING DAY.)

1. I am not working at all _____

   (IF YOU CHECKED THIS STATEMENT, SKIP TO THE NEXT PAGE.)

2. I am doing part of my job at home _____

3. I am not accomplishing as much as usual at work _____

4. I often act irritable toward my work associates, for example, snap at them, give sharp answers, criticize easily _____

5. I am working shorter hours _____

6. I am doing only light work _____

7. I work only for short periods of time or take frequent rests _____

8. I am working at my usual job but with some changes, for example, using different tools or special aids, trading some tasks with other workers _____

9. I do not do my job as carefully and accurately as usual _____

_____

CHECK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE _____

THIS GROUP OF STATEMENTS HAS TO DO WITH ACTIVITIES YOU USUALLY DO IN YOUR FREE TIME. THESE ACTIVITIES ARE THINGS THAT YOU MIGHT DO FOR RELAXATION, TO PASS THE TIME, OR FOR ENTERTAINMENT. PLEASE RESPOND TO (CHECK) ONLY THOSE STATEMENTS THAT YOU ARE SURE DESCRIBE YOU TODAY AND ARE RELATED TO YOUR STATE OF HEALTH.

---

1. I do my hobbies and recreation for shorter periods of time _____

2. I am going out for entertainment less often _____

3. I am cutting down on some of my usual inactive recreation and pastimes, for example, watching TV, playing cards, reading _____

4. I am not doing any of my usual inactive recreation and pastimes, for example, watching TV, playing cards, reading _____

5. I am doing more inactive pastimes in place of my other usual activities _____

6. I am doing fewer community activities _____

7. I am cutting down on some of my usual physical recreation or activities _____

8. I am not doing any of my usual physical recreation or activities _____

_____

CHECK HERE WHEN YOU HAVE READ ALL STATEMENTS ON THIS PAGE _____

Appendix M

Spielberger State Anxiety Inventory

SELF-EVALUATION QUESTIONNAIRE

Developed by C. D. Spielberger, R. L. Gorsuch and R. Lushene

STAI FORM X-1

NAME _____ DATE _____

DIRECTIONS: A number of statements which people have used to describe themselves are given below. Read each statement and then blacken in the appropriate circle to the right of the statement to indicate how you *feel* right now, that is, *at this moment*. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

	NOT AT ALL	SOMEWHAT	MODERATELY SO	VERY MUCH SO
1. I feel calm	①	②	③	④
2. I feel secure	①	②	③	④
3. I am tense	①	②	③	④
4. I am regretful	①	②	③	④
5. I feel at ease	①	②	③	④
6. I feel upset	①	②	③	④
7. I am presently worrying over possible misfortunes	①	②	③	④
8. I feel rested	①	②	③	④
9. I feel anxious	①	②	③	④
10. I feel comfortable	①	②	③	④
11. I feel self-confident	①	②	③	④
12. I feel nervous	①	②	③	④
13. I am jittery	①	②	③	④
14. I feel "high strung"	①	②	③	④
15. I am relaxed	①	②	③	④
16. I feel content	①	②	③	④
17. I am worried	①	②	③	④
18. I feel over-excited and "rattled"	①	②	③	④
19. I feel joyful	①	②	③	④
20. I feel pleasant	①	②	③	④

Appendix N

Beck Depression Inventory

BECK INVENTORY

Name: _____ Date: _____

On this questionnaire are groups of statements. Please read each group of statements carefully. Then pick out the one statement in each group which describes the way you have been feeling the PAST WEEK, INCLUDING TODAY. Circle the number beside the statement you picked. If several statements in the group seem to apply equally well, circle each one. Be sure to read all the statements in each group before making your choice.

1. 0 I do not feel sad.
   1 I feel sad.
   2 I am sad all the time and I can't snap out of it.
   3 I am so sad or unhappy that I can't stand it.

2. 0 I am not particularly discouraged about the future.
   1 I feel discouraged about the future.
   2 I feel I have nothing to look forward to.
   3 I feel that the future is hopeless and that things cannot improve.

3. 0 I do not feel like a failure.
   1 I feel I have failed more than the average person.
   2 As I look back on my life, all I can see is a lot of failures.
   3 I feel I am a complete failure as a person.

4. 0 I get as much satisfaction out of things as I used to.
   1 I don't enjoy things the way I used to.
   2 I don't get real satisfaction out of anything anymore.
   3 I am dissatisfied or bored with everything.

5. 0 I don't feel particularly guilty.
   1 I feel guilty a good part of the time.
   2 I feel quite guilty most of the time.
   3 I feel guilty all of the time.

6. 0 I don't feel I am being punished.
   1 I feel I may be punished.
   2 I expect to be punished.
   3 I feel I am being punished.

7. 0 I don't feel disappointed in myself.
   1 I am disappointed in myself.
   2 I am disgusted with myself.
   3 I hate myself.

8. 0 I don't feel I am any worse than anybody else.
   1 I am critical of myself for my weaknesses or mistakes.
   2 I blame myself all the time for my faults.
   3 I blame myself for everything bad that happens.

BECK INVENTORY Page 2

9. 0 I don't have any thoughts of killing myself.
   1 I have thoughts of killing myself, but I would not carry them out.
   2 I would like to kill myself.
   3 I would kill myself if I had the chance.

10. 0 I don't cry anymore than usual.
    1 I cry more now than I used to.
    2 I cry all the time now.
    3 I used to be able to cry, but now I can't cry even though I want to.

11. 0 I am no more irritated now than I ever am.
    1 I get annoyed or irritated more easily than I used to.
    2 I feel irritated all the time now.
    3 I don't get irritated at all by the things that used to irritate me.

12. 0 I have not lost interest in other people.
    1 I am less interested in other people than I used to be.
    2 I have lost most of my interest in other people.
    3 I have lost all of my interest in other people.

13. 0 I make decisions about as well as I ever could.
    1 I put off making decisions more than I used to.
    2 I have greater difficulty in making decisions than before.
    3 I can't make decisions at all anymore.

14. 0 I don't feel I look any worse than I used to.
    1 I am worried that I am looking old or unattractive.
    2 I feel that there are permanent changes in my appearance that make me look unattractive.
    3 I believe that I look ugly.

15. 0 I can work about as well as before.
    1 It takes an extra effort to get started at doing something.
    2 I have to push myself very hard to do anything.
    3 I can't do any work at all.

16. 0 I can sleep as well as usual.
    1 I don't sleep as well as I used to.
    2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
    3 I wake up several hours earlier than I used to and cannot get back to sleep.

17. 0 I don't get more tired than usual.
    1 I get tired more easily than I used to.
    2 I get tired from doing almost anything.
    3 I am too tired to do anything.

18. 0 My appetite is no worse than usual.
    1 My appetite is not as good as it used to be.
    2 My appetite is much worse now.
    3 I have no appetite at all anymore.

19. 0 I haven't lost much weight, if any lately.
    1 I have lost more than 5 pounds. I am purposely trying to
    2 I have lost more than 10 pounds. lose weight by eating less.
    3 I have lost more than 15 pounds. Yes _____ No _____

20. 0 I am no more worried about my health than usual.
    1 I am worried about physical problems such as aches and pains, or upset stomach, or constipation.
    2 I am very worried about physical problems and it's hard to think of much else.
    3 I am so worried about my physical problems, that I cannot think about anything else.

21. 0 I have not noticed any recent change in my interest in sex.
    1 I am less interested in sex than I used to be.
    2 I am much less interested in sex now.
    3 I have lost interest in sex completely.