Musculoskeletal Pain, Memory, and Aging:
Cross-Sectional and Longitudinal Findings
ABSTRACT


The general aim of this thesis was to investigate potential differences in performance on test for memory functioning between participants with and without self-reported musculoskeletal pain across the adult life span in a population based sample. Chronic musculoskeletal pain is a major health related problem of our western society. A common complaint related to chronic pain is about cognitive difficulties in attention, memory, and decision making. A number of studies have demonstrated that people with pain also perform worse on tasks measuring, for example episodic memory, semantic memory, and working memory. The present thesis aimed at replying these findings, by using a non-clinical population based sample. The potential differences in memory performance between people with and without pain were examined across the adult life span, in order to disentangle potential pain by age interactions. This was made by using both cross-sectional and longitudinal data. Study I aimed at study differences in episodic memory performance, semantic memory performance, and implicit memory performance, between people with and without musculoskeletal pain. Differences were found for all three memory systems, but disappeared after controlling for years of formal education. In Study II an extension of the first study was made, in which performance on a range of cognitive tests were analysed with respect to differences between people with and without pain. General differences were demonstrated, but yet again, years of education together with depression ruled out the effects. The most robust effects were found for word comprehension and construction ability. Finally, Study III used 5- and 10 year follow up studies to examine change over time in cognitive performance as a function of pain. The main finding from this study was that semantic memory for the oldest is impaired over time as a function of pain. An additional analysis showed similar patterns, regardless of age, for construction ability. The general conclusions from the three studies were that participants in a population based, non-clinical sample, that reported widespread musculoskeletal pain perform worse on a range of cognitive tasks as compared to participants that did not report about musculoskeletal pain. This pattern of results is in line with previous research on the topic, but also differ, as most of the differences disappeared when years of education were considered. Controlling for
years of education did not rule out some of the longitudinal effects, that were obtained in study III, suggesting that replications with longitudinal designs are recommended. The mediating role of attention loss in understanding the effects of pain on memory are discussed, and put into some question.

Key words: musculoskeletal pain, cognitive functioning, episodic memory, semantic memory, implicit memory, cross-sectional, longitudinal, age.
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Umeå, September, 2005

Stefan Söderfjell
LIST OF PAPERS


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INTRODUCTION

Most people probably experience pain on some occasion their life. It is almost certainly no enjoyable experience, and it presumably lead to attempts to try to get rid of it. Hopefully the pain won’t last so long, and disappears after resting for a while. In industrialised societies however, the experience of pain is something that a huge number of people suffer from every day, every waking minute for months and years. Long lasting musculoskeletal pain in the back and neck is one of the most, if not the most, common reasons for sick leave and costs the society enormous amounts of money each year. The work loss in British industry attributed to similar disorders were 33 million working days in 1981, 67 million in 1991 and 81 million in 1992 (Symonds, Burton, Tillotson, & Main, 1995). In Sweden the cost of these disorders for the society are calculated to approximately 30 billion Swedish kronor per year (Norlund, & Waddell, 2000). Public statistics demonstrate that the number of people suffering from musculoskeletal pain in the back, neck, shoulders, arms and legs are somewhere around 50 % of the adult population (SCB, 2004).

Besides societal costs, and individual suffering, people with pain also frequently report about cognitive problems related to their pain (Schnurr & MacDonald, 1995; Iezzi, Archibald, Barnett, Klinck, & Duckworth, 1999; McCracken & Iverson, 2001). Keeping track of medications, keeping scheduled appointments, following through on exercise programs, being able to perform previous work tasks, following conversations in interpersonal interactions, and making simple decisions in daily living are all examples of difficulties often reported by people with musculoskeletal pain (Iezzi et al., 1999).

Cognitive dysfunctions have been demonstrated in studies with cognitive testing as well (Landrø, Stiles, & Sletvold, 1997; Grace, Nielson, Hopkins, & Berg, 1999; Kessels, Aleman, Verhagen, & Van Luijtenaar, 2000; Glass & Park, 2001; Grisart & Van der Linden, 2001; Park, Glass, Minear, & Crofford, 2001; Grisart, Van der Linden, & Masquelier, 2002), although the subjective complaints sometimes are greater than what is found when examining the performance on cognitive tasks (Grace et al., 1999). Park et al., (2001) suggested that people with diagnosed fibromyalgia perform like older adults on test for working memory, episodic memory, and semantic memory, and found that patients with fibromyalgia performed similarly to people 20 years older. Besides that not much has been said about the role of age in the relationship between
musculoskeletal pain and memory. The present thesis aims at examining
cognitive performance for people with and without self-reported
musculoskeletal pain over the adult life span, by use of cross-sectional data
as well as by use of longitudinal data. Findings from 6-month follow up
studies (Kessels et al., 2000) for whiplash patients demonstrated a
significant improvement in cognitive functioning as compared to the
period immediately after the accident. As the majority of whiplash
patients are fully recovered within two to three months these data suggest
a casual relationship between musculoskeletal problems and cognitive
functioning that will be further addressed in the longitudinally designed
study in the present thesis.

Further, potential gender differences in the relationship with pain and
memory will also be addressed in the present thesis as women perform
better than men in episodic memory tasks (Herlitz, Airaksinen, &
Nordström, 1999; Herlitz, 2002) and report pain more frequently than
men (Berkley, 1997).

Comparisons will be made for tests for episodic memory (both
aggregated measures and measures of a number of single tests), recall and
recognition subcategories of episodic memory, semantic memory
(aggregated measures and a number of measures of single tests for word
fluency, word comprehension, and general knowledge), implicit memory,
working memory with or without divided attention, general cognitive
functioning, and construction ability. Based on previous research a
difference is expected between groups with and without pain on measures
for episodic memory, semantic memory, working memory, and
construction ability. The most profound differences are expected for
attentional demanding tasks, such as episodic memory, working memory,
and construction ability. The reason for this is that previous studies have
suggested that pain consumes some of the limited capacity one has to
process information, and therefore, processing of information that are
attentional demanding is expected to suffer.

As previous studies of cognitive dysfunctions in people with pain
mainly have examined clinical pain groups (fibromyalgia and whiplash
syndromes) not much has been said about cognitive dysfunctions for
people in the normal population with undiagnosed, self-reported
musculoskeletal pain in back, shoulders, arms and legs. As this group is so
large (the prevalence will be examined), it is of interest to see if pain can
be detrimental to such a group as well. The thesis starts at introducing the
concept of pain more generally, and thereafter gradually approaching the
particular aims just presented.
**Pain and musculoskeletal disorders**

During the last fifty years a number of variants of musculoskeletal syndromes have emerged, with similar symptoms and different names: Work related musculoskeletal disorders, work related myalgia, whiplash injuries, fibromyalgia, neck-shoulder myalgia, and low back pain (Johansson, Windhorst, Djupsjöbacka, & Passatori, 2003). The most common areas of musculoskeletal pain are in the neck and shoulders, and in the back (SCB, 2004). The general symptoms of these related pain syndromes is that pain occurs on a local point, spreads over time, and in the end becomes general (Johansson et al., 2003).

Allan, and Waddell (1989), in a historical overview, reviewed back pain and the consequences of it. They claim that pain in the back has existed in a similar fashion through the history of mankind, but that the interpretation and treatment of it has changed. During this century, and particularly during the latest two decades, all western societies have been struck by an epidemic form of chronic impairment of functioning, sick leave and early retirement with unspecified back pain as the main cause. According to Waddell, & Waddell (2000) this is not only due to changes in the pathology of back pain or due to the fact that back pain, including neurophysiological or psychological findings, has become more common. Rather than that, the heavy increase of back pain incidence, they suggest, seems to be partly socially and culturally conditioned. This is probably true not only for pain in the back, but also for pain in the shoulders, neck, arms, and legs. Because of the societal costs and the suffering for the pain struck individuals, pain and musculoskeletal disorders are concepts that have become familiar in our society. Despite of that, a lot of questions about the phenomenon of musculoskeletal pain still need to be answered in order to be able to help people deal with it more effectively.

**Definition of pain**

Pain is not easily defined. One reason is that it means different things to different people. All kinds of pain have three dimensions of pain, and these dimensions are unique to each person (Wall, 2000). The dimensions are sensory, affective, and evaluative. They were derived from a categorisation of people’s subjective descriptions of their experience. Words that constituted the sensory dimension were, for instance, “hot”, “burning”, “scalding”, and “searing”. They described the pure sensation of the pain. The affective words described what the pure sensation was doing to them. Examples of affective words were “exhausting”, “terrifying”, and “punishing”. Finally, the evaluative words expressed the degree of suffering; for example, “annoying”, “miserable”, and “unbearable”. 
According to the International Association for the Study of Pain (IASP), pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage (Merskey, and Bogduk, 1994). According to Loeser and Melzack (1999) this is the best definition of pain. This definition avoids tying pain to the stimulus, which is necessary since many people report pain without any tissue damage or any likely pathophysiological cause. There is usually no way to distinguish their experience from that due to tissue damage by way of subjective report. If they regard their experience as pain and if they report it in the same ways as pain caused by tissue damage, Merskey and Bogduk (1994) suggest that it should be accepted as pain. Besides the fact that pain can occur without tissue damage, Wall (2000) and Melzack and Wall (1996) exemplifies another problem of the simple injury and pain link by means of people who suffer from analgesia (no ability to feel pain despite serious injury). Until the 1960’s pain was considered an inevitable sensory response to tissue damage. There was little room for the affective and cognitive dimensions of pain (Loeser et al., 1999). The rather mechanistic view of pain, mentioned above, needs to be complemented by models that involve psychological, social, organizational and cultural factors, together with the pure physiological and biological ones, in order to gain more knowledge about the phenomenon (Nachemson, and Jonson, 2000).

A very influential theory that tried to integrate physiological and psychological factors was the gate control theory which suggests that a neural mechanism in the spinal cord acts like a gate that modulates or blocks nociception information to be processed by the central nervous system (Melzack, and Wall, 1965). According to the gate control theory of pain, our thoughts, beliefs, and emotions may affect how much pain we feel from a given physical sensation. The fundamental basis for this theory is the belief that psychological, social and emotional, as well as physical factors guide the brain’s interpretation of painful sensations and the subsequent response.

Pain categorization
According to Turk, and Melzack (1992) pain can be divided into five subcategories. Those are regardless of intensity. The first one, *acute pain*, is the pain associated with tissue damage, inflammation or a disease process that is of relatively brief duration. Examples of things leading to such pain is getting stung by a bee or spraining ones ankle. Another kind of acute pain is called *acute recurrent pain*, and is a pain that comes and goes with fairly regular intervals. Migraine headache and menstruation pain
exemplifies such pain. The duration of acute pain is that it does not stay for longer than three weeks (Nachemson et al., 2000). If the pain persists more than 12 weeks it is said to be chronic. Rheumatoid arthritis, fibromyalgia and musculoskeletal disorders are examples of chronic pain. Sometimes, pain that is referred to as chronic gradually becomes worse over time. For instance cancer pain often shows this pattern. Then the pain is referred to as chronic progressive pain. The final subtype of pain is called laboratory-induced pain and is a pain induced by nociceptive stimulation in a laboratory setting, for example an electric shock. The main societal problem related to pain, derives from chronic pain.

Components of pain
Loeser and Melzack (1999) talk about four different components, or aspects, that constitute the phenomenon of pain. All of these must be emphasised in order to find ways for treatment. The components are nociception, perception of pain, suffering and pain behaviours. Nociception is the detection of tissue damage by specialised transducers attached to A delta and C fibres. In principal nociception is the stimulus that creates the conditions for the pain experience.

Perception of pain is triggered by the noxious stimulus, such as an injury or a disease but can also be generated by lesions in the peripheral or central nervous system, as seen, for instance, in patients with stroke. Acute pain is initially associated with specific autonomic and somatic reflexes, which disappear with chronic pain. The person’s thoughts and emotional status influence the pain experience. Anxiety, stress, depression, and a focus on the pain are associated with increased pain, whereas relaxation, optimism and distraction lead to a reduction of pain (Druckman & Bjork, 1991).

Suffering is the evaluative and affective response of the pain experience. This response can also be induced without pain, as when a loved one dies. Finally, pain behaviour is the observable behaviours that are associated with pain and suffering. Examples of pain behaviours are grimacing, saying “ouch”, crying, lying down, talk about the pain, and refusing to work. The behaviours probably are influenced by real or expected environmental consequences. All these behaviours are observable by others and can be quantified. The behaviours, together with history and physical examination serve as a ground for inferring the existence of nociception, pain and suffering.

One example of pain behaviour, of particular interest for this thesis, is basic cognitive performance, such as memory, attention, and perception. People with musculoskeletal pain often report about difficulties in areas of
memory and concentration, problem solving, abstract thought, and cognitive efficiency (Schnurr et al., 1995; Iezzi et al., 1999; McCracken et al., 2001). These cognitive problems have been empirically documented as well, (see below).

**Pain and gender**

Gender differences have been demonstrated for various forms of clinical pain syndromes (Lundberg, 1996, 1996; Unruh, 1996; Berkley, 1997; Eriksen, Svensrød, Ursin, & Ursin, 1998; Eriksen, Ihlebaek, & Ursin, 1999; Ihlebaek, Eriksen, & Ursin, 2002). Women report pain more frequently, and more symptoms in general, not merely those of a particular kind. Possible explanations have been proposed to be cultural, social role expectations, situational factors, earlier experiences, psychological, and biological (Berkley, 1997). Fillingim and Maixner (1995) also demonstrated, in a review article of gender differences in experimentally induced pain, that females usually are more sensitive, i.e. have lower thresholds, to induced pain, as compared to males. As women perform better than men in episodic memory tasks (Herlitz, Airaksinen, & Nordström, 1999; Herlitz, 2002) and report pain more frequently than men the possible pain by gender interaction will be addressed.

**Cognitive aspects of pain**

Cognitive approaches to pain are concerned with the way person’s perceives, interprets and relates to the pain (Weisenberg, 1999). A number of different cognitive aspects have been found to influence the pain experience. The beliefs that person’s holds about their pain, for instance in terms of cause, explainability, duration, dangerousness and fear-avoidance, is one such factor and have been found to influence pain in a number of studies (Williams, Robinson, and Geisser, 1994; Klenemanet al., 1995; Jensen, Romano, Turner, Good, and Wald, 1999; Linton, Buer, Vlaeyen, and Hellsing, 1999; Strong, Ashton, and Chant, 1992; Vlaeyen, and Linton, 2000; Walsh, and Radcliffe, 2002).

Perceived control is another factor that is important for both acute and chronic pain. An extensive literature documents the impact that appraised control has on emotional and behavioural adjustment to chronic pain. Perceptions of control over pain, among other things, predict lower levels of pain and disability (Jensen, Turner, and Romano, 2001), and fewer pain behaviours (Buescher et al., 1991). On the other end of the continuum, perceptions of helplessness predict depression (Turner and Clancy, 1986; Keefe and Williams, 1990) and psychosocial and physical impairment (Turner and Clancy, 1986).
Related to perception of control is the theory of self-efficacy. Self-efficacy refers to a person’s trust in his or her skills necessary to succeed with an upcoming task (Bandura, 1977). Expectations of personal efficacy are derived from four principal sources of information. These are performance accomplishments, vicarious experience, verbal persuasion, and physiological states. It is hypothesized that expectations of personal efficacy determine whether coping behaviour, which will be discussed below, will be initiated, how much effort will be expended, and how long it will be sustained in the face of obstacles and aversive experiences. This is obviously of great importance for the pain experience. Studies of the relationship between self-efficacy and pain have found that higher self-efficacy are related to higher pain tolerance (Weisenberg et al., 1996; Kashikar-Zuck et al., 1997; Keefe et al., 1997), and successful treatment outcome of chronic pain (Jensen et al., 2001; Strong et al., 2002).

Yet another factor that can affect the perception of pain is the various kinds of cognitive errors, or distortions, that people make. One common error, with respect to pain, is the tendency to make negative self-statements and have overly negative thoughts and ideas about the present and the future. This is referred to as catastrophizing and has been found to greatly influence pain and disability (Keefe et al. 1997; Jensen et al., 2001).

Pain-related beliefs, perception of control, self-efficacy and cognitive distortions influence not only the perception of pain per se, but also the things that people do to minimize their symptoms of pain. This is called coping strategies and has been conceptualized as ‘the person’s cognitive and behavioural efforts to manage (reduce, minimize, master or tolerate) the internal and external demands of the person-environment transaction that is appraised as taxing or exceeding the person’s resources’ (Folkman et al., 1986).

Coping can be classified partly by the mode of action used and partly by the function it serves (Weisenberg, 1999). The actions that can be used are (1) direct action, (2) action inhibition, (3) information search and (4) intrapsychic, or cognitive, processes. The functions of the above actions can be problem focused or emotion focused. Passive coping strategies like depending on others for pain control or avoiding activities, have been found to be associated with greater pain (Lawson, Resor, Keefe, and Turner, 1990; Geisser, Robinson, and Henson, 1994).

All of the above mentioned links between cognitive factors and pain have, in principal, dealt with how our way of thinking affects the way we perceive and experience pain. Another way of looking at the pain-cognition link is by means of how pain is related to and influences our
basic cognitive functions, such as memory, perception and attention. This is a far less studied topic than the influence that beliefs, coping, catastrophizing and self-efficacy have on pain.

As previously mentioned people with pain often complains about cognitive difficulties. There are also a number of studies that have reported an actual cognitive impairment for pain struck individuals compared to those that don’t suffer from pain. Gimse, Bjorgen, Tjell, Tyssedal, and Bo (1997) suggested a causal connection between cognitive malfunctions and whiplash injuries on tests of learning and memory as well as prolonged attention and concentration. This causality has been documented in meta-analyses of longitudinal effects of whiplash injuries on cognitive functioning (Kessels et al., 2000). Whiplash patients showed significantly more problems on tests of working memory, attention, immediate and delayed recall, visuomotor tracking, and cognitive flexibility, compared to healthy controls when measured immediately after the accident. When patients were tested 6-months after the accident significant cognitive improvements were demonstrated. Since most patients diagnosed with whiplash disorder fully recover after 2-3 months this improvement in cognitive functioning after six months were expected, if pain causes cognitive dysfunction.

Grace et al., (1999) found concentration and memory deficits in patients with fibromyalgia. Also Landrø et al., (1997) found that fibromyalgia patients were significantly impaired on long-term memory functioning compared with a control group. This difference disappeared when controlling for depressive status. Moreover, Glass et al., (2001) and Park et al., (2001) found significant performance impairment on test for working memory, free recall and verbal fluency for fibromyalgia patients compared to age matched controls, even after controlling for depression and anxiety. In a meta-analysis Kessels et al., (2000) found that chronic whiplash patients showed significantly more problems on tests of working memory, attention, immediate and delayed recall, visuomotor tracking, and cognitive flexibility, compared to healthy controls. Some other studies (Grisart et al., 2001; 2002) have demonstrated that explicit memory is related to pain while implicit memory remains unaffected.

The above studies all dealt with clinical groups suffering from diagnosed pain syndromes, such as pain from whiplash injuries and fibromyalgia. As the total population includes a lot of people that experience pain in a more regular, everyday fashion, it would be of interest to see if this more regular kind of pain is related to cognitive functioning as well, by use of a population based sample.
Pain, cognitive functioning, and aging
Although previous studies have demonstrated negative relationships between various memory functions and musculoskeletal pain syndromes, not much has been said about age effects of this relationship. One reason for including age in this area of interest is that there is a possibility that pain can interact with age in the decline in cognitive functioning. This hypothesis has gained mixed support in previous studies with some studies emphasizing an impact of self-reported health (Perlmutter & Nyquist, 1990; Hultsch, Hammer, & Small, 1993; Earles, Connor, Smith, & Park, 1997; Wahlin, Maitland, Bäckman, & Dixon, 2003) and others not (Salthouse, Kausler, & Saults, 1990; Earles & Salthouse, 1995).

One reason behind inconsistencies is that different studies have used different designs, cross-sectional or longitudinal, lending to different results (Hultsch, Hertzog, Small, McDonald-Mizczak, & Dixon, 1992; McDonald-Mizczak, Herzog, & Hultsch, 1995). Wahlin et al., (2003) found that, while the cross-sectional relationship between subjective health, memory, and aging was non-significant, longitudinal change in perceptions of subjective health were related to change in episodic memory performance. According to Waddell et al., (2000) pain is influenced by social and cultural factors. Therefore it could be the case that different age cohorts have different views about pain. In order to control for potential age-cultural differences, it is important to examine the effects of pain on memory over the adult life span, by use of cross-sectional as well as longitudinal designed studies.

The relationship between pain and age is somewhat complex. Some studies demonstrate an increase in pain severity and frequency with age (e.g., Crook, Rideout, & Browne, 1984). Frequency of fibromyalgia (Wolfe, Ross, Anderson, Russell, & Hebert, 1995) and frequency of joint pain (Badley & Tennant, 1992) have been found positively related to age. The majority of studies, however, have found that pain is related to age according to an inverted U-function with an increase in the middle age and a decrease thereafter (Waddell, 1998). For example, there are studies demonstrating that overall prevalence of pain complaints (Andersson, Ejlertsson, Leden, & Rosenberg, 1993) and low back pain (Wright, Barrow, Fisher, Horsley, & Jayson, 1995) show this pattern. Yet another study has demonstrated an age-related decrease in the prevalence of pain problems (Sternbach, 1986).

While a lot of previous studies have demonstrated that pain is negatively related to cognitive performance, less have been said about whether the strength and character of this relationship varies as a function of age. As a result, while we know that pain and memory are related, we
have less insight into causal relationships and long-term consequences of pain.

When it comes to the effect of age on the cognitive system, it is well known that cognitive functioning changes as we get older. There is also a vast amount of evidence that some memory functions are more sensitive to aging than others (see Salthouse, 1991; Craik & Jennings, 1992; Light, 1992; Kausler, 1994, for reviews). One distinction is that between declarative and non-declarative memory systems (Ryle, 1949; Cohen & Squire, 1980; Schacter, 1987; Squire, Knowlton, & Musen, 1993). The declarative system is concerned with encoding, storing, and retrieving information that are under conscious control. It is sometimes referred to as a “knowing that” form of knowledge (Ryle, 1949). This system can be further divided into episodic memory and semantic memory (Tulving, 1972; 1983).

Episodic memory deals with personally experienced events or episodes, such as remembering what one had for breakfast, what time one got up yesterday morning, and the colour on the walls at the office. Numerous studies have demonstrated that episodic memory is highly age sensitive (see Craik et al., 1992; Kausler, 1994, for reviews). The episodic memory system could be further divided into the subsystems of recall and recognition (Gregg, 1976; Hirst, Johnson, Kim, Phelps, & Volpe, 1986; Hirst, Johnson, Phelps, & Volpe, 1988; Cabeza et al., 1997). Of these subsystems, recall seems more age sensitive than is the case for recognition (Nyberg et al., 2003).

Semantic memory, the second declarative subsystem, deals with general knowledge of the world. Comprehension and understanding of language and words, as well as knowledge about facts, fall under the semantic memory system. These kinds of memories are less affected by age, than is the case for episodic memory (see Light, 1991; Craik & Jennings, 1992, for reviews).

Yet another way of subdividing the declarative memory system is with regard to the time elapsing from encoding to retrieval. A division has been made between short-term memory stores (working memory) and long-term memory stores (Atkinson & Shiffrin, 1968; Baddeley & Hitch, 1974; Baddeley, 1986). Deficits in working memory as a function of age have been found in a number of studies (Salthouse, 1991; Kausler, 1994 for reviews).

The non-declarative memory system, sometimes called the “knowing how” form of knowledge (Ryle, 1949) deals with processing of information where retention is not accompanied by conscious recollection of the original learning situation. Examples of non-declarative memory use
are in acquisition of motor skills, perceptual priming and classical conditioning (Squire, 1993). Another often used word for non-declarative memory is implicit memory (Schacter, 1987). Age seems to play a less important part when it comes to implicit memory, although previous results yield contradictory results. A number of studies with relatively large samples have addressed this issue. Age effects have been found in some of these studies (Davis et al., 1990; Hultsch et al., 1991; Small et al., 1995) but not in others (Park & Shaw, 1992; Nyberg et al., 1996; Maki et al., 1999). Large-scale meta-analyses have also been conducted. Fleischman and Gabrieli (1998) found that 85% of the studies of age effects of implicit memory reported no such effects. Mitchell (1995) also reported a lack of age effects. Yet, other meta-analyses (Light & La Voie, 1993; La Voie & Light, 1994; Light, Prull, La Voie, & Healy, 2000) have demonstrated age effects on implicit memory.

As age is related to pain and cognitive functioning, and, as we have seen, pain is negatively related to basic cognitive functioning it can be the case that cognitive dysfunctions for people with pain are more or less prominent in different ages. This will be examined in the present thesis, cross-sectionally as well as longitudinally by using data from a project that satisfies both of these methodological interests, namely the Betula project.

The Betula project

For a detailed description of the Betula project, all the data collected, the procedure of collecting them, and overview of Betula research, Nilsson et al., (1997) and Nilsson et al., (2004) is recommended. A brief description will follow below.

The Betula project took place in Umeå in Sweden, a city of, at the time of the project start, somewhere around 100 000 inhabitants. Umeå is sometimes called the city of birch trees. The latin family name of birch tree is betula, and therefore the name of the project. The Betula project is a prospective cohort study with the aim of examining the development of health and memory in adulthood and old age. It started in 1988 and at present, three waves of data collection have been completed (T_1: 1988-1990; T_2: 1993-1995; T_3: 1998-2000). A fourth wave (T_4) started in 2003 and will be completed in 2005. In the first three waves of data collection (T_1-T_3) four different samples of participants have participated (see Table 1 for an overview of the design; T_1-T_3). A new sample (S_4) was also included in T_4. The first sample (S_1) was tested at T_1, T_2, T_3 and T_4. At T_4, two new samples were added (S_2 and S_3; each with 1000 participants), and at T_5, yet another new sample (S_3) was included. A total of 600 persons were included in this sample, with 50 individuals in each
of 12 age cohorts. This makes it possible to control for practice effects in 
S1-S3. At T4, the remaining participants of each sample (S1-S4) were, or 
will be retested.

Participants
The participants were chosen by random selection from a register of the 
population for Umeå. First they were contacted by mail in which they 
were informed about the project, that they had been randomly selected, 
that participation was voluntary, and that their anonymity would be 
guaranteed. Mails were sent to a total of 1,976 persons (first sample, first 
wave of measurement) in order to obtain a total of 100 subjects in each 
age cohort. The time it would take for the health and memory assessment 
would be somewhere around 1.5-2 hours each.

<table>
<thead>
<tr>
<th>Year</th>
<th>Sample</th>
<th>Age at testing</th>
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<tr>
<td>1988-90 (T1)</td>
<td>S1</td>
<td>35 40 45 50 55 60 65 70 75 80</td>
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<tr>
<td>1993-95 (T2)</td>
<td>S1</td>
<td>40 45 50 55 60 65 70 75 80 85</td>
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</tr>
<tr>
<td>1998-00 (T3)</td>
<td>S1</td>
<td>45 50 55 60 65 70 75 80 85 90</td>
</tr>
<tr>
<td></td>
<td>S2</td>
<td>70 75 80 85</td>
</tr>
<tr>
<td></td>
<td>S3</td>
<td>45 50 55 60 65 70 75 80 85 90</td>
</tr>
<tr>
<td></td>
<td>S4</td>
<td>40 45 50 55 60 65 70 75 80 85 90</td>
</tr>
</tbody>
</table>

A few days after the letters were sent, the subjects were contacted by 
phone in order to make appointments for the examinations. In this 
process 976 persons (49 %) from the original sample were excluded for 
various reasons (see Nilsson et al., 1997). The reasons for not participating 
were that they refused, could not be reached via telephone, reported 
themselves to ill to participate, suffered from mental retardation or 
suspected dementia, had a sensory handicap, had another language than 
Swedish as their native, and failed to show up at the memory test session. 
Excluded subjects were replaced until there were a total of 100 individuals 
in each age cohort. The representativeness of the subjects was examined by
using public information from Statistiska Centralbyrån (SCB, 1985) to compare with non participants and the whole of Sweden on several demographic variables. This revealed no differences between the subjects and the non participants. A difference was found consisting of a higher income and level of education for the participants in the study compared with Sweden as a whole (p<.01). This difference is probably not particularly surprising, as a university is located in Umeå. Gender distribution and background characteristics for the first sample at the first wave of measurement are presented in Table 2.

Table 2
Gender distribution and background characteristics for each age cohort for the first sample (S1) at the first wave of measurement (T1)

<table>
<thead>
<tr>
<th>Age</th>
<th>Females/Males</th>
<th>Years of education</th>
<th>Mini-mental state examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>50/50</td>
<td>13.9 (2.6)</td>
<td>28.6 (1.2)</td>
</tr>
<tr>
<td>40</td>
<td>52/48</td>
<td>13.5 (3.5)</td>
<td>28.5 (1.4)</td>
</tr>
<tr>
<td>45</td>
<td>54/46</td>
<td>12.7 (4.2)</td>
<td>28.2 (1.6)</td>
</tr>
<tr>
<td>50</td>
<td>60/40</td>
<td>10.4 (3.7)</td>
<td>28.2 (1.6)</td>
</tr>
<tr>
<td>55</td>
<td>54/46</td>
<td>8.9 (3.3)</td>
<td>28.3 (1.6)</td>
</tr>
<tr>
<td>60</td>
<td>46/54</td>
<td>8.8 (3.2)</td>
<td>28.1 (1.6)</td>
</tr>
<tr>
<td>65</td>
<td>54/46</td>
<td>8.2 (2.9)</td>
<td>27.7 (1.6)</td>
</tr>
<tr>
<td>70</td>
<td>48/52</td>
<td>8.2 (3.3)</td>
<td>27.6 (1.6)</td>
</tr>
<tr>
<td>75</td>
<td>53/47</td>
<td>7.5 (2.8)</td>
<td>26.8 (1.6)</td>
</tr>
<tr>
<td>80</td>
<td>59/41</td>
<td>7.4 (3.1)</td>
<td>26.2 (2.4)</td>
</tr>
</tbody>
</table>

Note. Standard deviations is given in the parentheses

Data collection
One purpose of the health examinations was to uncover some variables that could be related to pain and stress. Both subjective and objective measurements of health were used. The objective measurements consisted of different blood parameters, systolic and diastolic blood pressure, heart rate, use of medications, sensory functioning and previous visits to the doctor.

The subjective health data consisted of ratings on a range of different health variables (See Table 3).
Table 3
Overview of subjective health variables

<table>
<thead>
<tr>
<th>Health in general</th>
<th>Bronchi problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back pain</td>
<td>Breath catching</td>
</tr>
<tr>
<td>Pain in shoulders, arms or legs</td>
<td>Swollen legs</td>
</tr>
<tr>
<td>Pain in joints</td>
<td>Dizziness</td>
</tr>
<tr>
<td>Worry in heart/chest</td>
<td>Loss of appetite</td>
</tr>
<tr>
<td>Pain in stomach</td>
<td>Urinating problems</td>
</tr>
<tr>
<td>Sleeping difficulties</td>
<td>Feelings of loneliness</td>
</tr>
<tr>
<td>Often tired</td>
<td>Seeing problems</td>
</tr>
<tr>
<td>I often feel depressed</td>
<td>Hearing problems</td>
</tr>
<tr>
<td>Anxious, worried</td>
<td>Skin problems, itching, leg wound or similar</td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
</tr>
</tbody>
</table>

The questions could be answered by “yes” or “no” and were in a questionnaire that also contained questions related to socio-economic status, such as years of education and present occupation. The questions of particular interest in the present thesis were the ones concerning pain in the back, and pain in shoulders, arms, or legs. As depressive status is normally controlled for in studies of the relationship between pain and cognitive functioning (e.g. Landrø et al., 1997; Park et al., 2001) the single question about feeling depressed is also of importance in the present thesis.

Of the questions regarding socio-economic factors, years of education is important, as some studies (e.g. Cote & Moldofsky, 1997; Iezzi, Duckworth, Vuong, Archibald, & Klinck, 2004) have found that years of education can moderate the effects of pain on memory functioning.

One of the purposes of the memory examinations was to cover a wide variety of processes and hypothetical memory systems. The test battery was put together so that it would measure different long- and short-term memory processes, semantic and episodic memory systems, retrospective and prospective memory, intentional and incidental memory and the impact of focused or divided attention on memory recall. Thus, the tests were selected with the criteria that they should be rooted in existing theories of memory. A detailed description of the material and the procedures of data collection can be found in Nilsson et al., (1997). An overview of the cognitive tests that were administered in the four waves of data collection can be seen in Table 4.
Table 4
*Overview of the memory tasks and other cognitive tasks used in the Betula study*

**Episodic memory:**
- Free recall of enacted sentences (T1-T4)
- Two cued recall tests of enacted sentences (T1-T4)
- Recognition of nouns presented in enacted sentences (T1-T4)
- Source recall of enacted sentences (T1-T4)
- Free recall of nonenacted sentences (T1-T4)
- Two cued recall tests of nonenacted sentences (T1-T4)
- Recognition of nouns presented in nonenacted sentences (T1-T4)
- Source recall of nonenacted sentences (T1-T4)
- Recognition of faces (T1–T4)
- Recognition of names (T1–T4)
- Free recall of words with or without concurrent card sorting at study or test (T1–T4)
- Cued recall of facts (T1–T2)
- Source recall of facts (T1-T2)
- Prospective memory (T1–T4)
- Free recall of memory for activities (T1–T4)

**Semantic memory:**
- Recall of general knowledge (T1–T2, T4)
- Word fluency, initial letter A (T1–T4)
- Word fluency, initial letter M, five-letter words (T1–T4)
- Word fluency, initial letter B, names of professions (T1–T4)
- Word fluency, initial letter S, five-letter names of animals (T1–T4)
- Word comprehension (T1–T4)

**Priming:**
- Name-stem completion (T1–T4)
- Word fragment completion (T2–T4)

**Other tasks:**
- Block design (T1–T4)
- Tower of Hanoi (T2–T3)
- Mini-Mental State Examination (T1–T4)
- Draw-a-man-test (T1–T2)
- Letter digit substitution (T3–T4)
OVERVIEW OF STUDIES

Brief summaries of each of the three empirical studies are provided below. The first one deals with the relationship between subjectively reported pain and performance on aggregated measures for episodic memory, semantic memory, and implicit memory across the adult life span. In the second study this issue is further examined by looking at the relationship between subjectively reported pain and each of the underlying tasks in the aggregations. Yet again this was examined over the adult life span. In both of these studies a cross-sectional design was used. The third study used a longitudinal design in order to examine potential differences in longitudinal changes in memory performance between participants with and without pain at various age cohorts.

Study 1

The aim of this study was to examine potential differences in performance on test for episodic memory, for semantic memory, and for priming (implicit memory) between participants with and without subjectively reported pain over the adult life span and between females and males. Previous studies (e.g. Landrø et al., 1997; Grace et al., 1999; Glass et al., 2001; Grisart et al., 2001; Park et al., 2001; Grisart et al., 2002) have demonstrated such differences between patients with fibromyalgia and healthy controls, but these studies have not included age as a factor. Data were gathered from 1000 participants from 10 age cohorts (35, 40, 45,......80 years old) with 100 participants in each age cohort. After exclusion of participants with pre-clinical signs of dementia the total number of participants included was 929. The participants answered a number of health related questions and took part in extensive memory testing. Among the health questions, two concerned pain (“Do you have pain in your back?” and “Do you have pain in your arms, legs, or shoulders?”) and could be answered by yes or no. The participants were divided into one of four groups; (1) those with no pain, (2) those with pain in the back but not in the shoulders, arms, or legs, (3) those with pain in shoulders, arms, or legs but not in the back, and (4) those with pain in the back and in the shoulders, arms, or legs. Over the age cohorts somewhere around 50 % of the participants reported one or more pain complaints. The distribution of participants as to pain category in the 10 age cohorts can be seen in Figure 1.
Figure 1. Distribution of participants in the 10 age cohorts divided in categories of no pain complaints (NP); Pain in the back but not in the shoulders, arms or legs (BaP); pain in shoulders, arms or legs but not in the back (ShP); and, both pain in the back and pain in shoulders, arms, or legs (BoP).

The prevalence of pain related complaints is in line with public statistics for the Swedish population (SCB, 2004). These four categories were compared on aggregated measures for episodic memory, semantic memory, and implicit memory. The episodic memory aggregation consisted of test for of free and cued recall of sentences with and without enactment; recognition of enacted sentences; recognition of names and faces; recall of newly acquired facts; source recall; free recall of words with or without concurring task at encoding or retrieval phase; memory for activities during the test session; and a test for prospective memory. The semantic memory category consisted of four different word fluency tasks, a test for word comprehension and a test for general knowledge. Finally, implicit memory was measured by means of a word stem completion task.

The data were analysed by means of a number of 4 (Pain) X 10 (Age) X 2 (Gender) Analyses of variance (ANOVA’s) with the three memory aggregations as dependent factors. The results showed that the group with no pain outperformed the group with both pain complaints on episodic memory and semantic memory (see Figure 2). No Pain by Age, Pain by
Gender, or Pain by Age by Gender interactions were revealed, suggesting similar relationships between pain and memory over the adult life span and across the sexes.

![Figure 2. Episodic and semantic memory performance for participants with no pain complaints (NP), participants with pain in the back (BaP), participants with pain in the shoulders, arms or legs (ShP), and participants with both pain in the back and pain in shoulders, arms, or legs (BoP).](image)

Previous studies have emphasised the importance of controlling for depression and education in studies of the relationship between pain and memory. Depression in this study was measured by a single question (“Do you feel depressed?”). Controlling for this single question did not alter the results, which are in line with Glass et al., (2001) and Park et al., (2001). Controlling for years of education however, eliminated the significant differences between the two extreme groups, suggesting a higher level of education for participants without pain. The conclusions were that participants with musculoskeletal pain in the back, shoulders, arms, and
legs have worse episodic and semantic memory capacity compared to participants without these pain syndromes. The difference is not necessarily explained by means of pain, but should probably be understood as a consequence of an interaction between educational level, occupation and pain.

**Study 2**

This study aimed at comparing participants with and without self-reported musculoskeletal pain in a normal population with regard to performance on a range of tests for episodic memory, semantic memory, and other cognitive functions and to see if expected differences interacted with age. The study was an extension of study 1 in the sense that the underlying tests from the aggregations in study 1 in this study were analysed separately, in order to examine more specific cognitive deficits for the pain struck participants. The participants completed tests for free and cued recall of sentences with and without enactment, recognition test of enacted sentences, names and faces, test for recall of newly acquired facts, test for source recall, test for free recall of words with or without concurring task at encoding or retrieval phase, test of memory for activities during the test session, test for prospective memory, four different word fluency tasks, a test for word comprehension, a test for general knowledge, a WAIS-R Block Design test (Wechsler, 1981), and a Mini-Mental State Examination for general cognitive functioning. The participants also answered a number of questions related to musculoskeletal pain (i.e. “I have pain in my back” and “I have pain in my shoulders, arms, or legs”). In this study two groups of participants were included, (1) those with no pain complaints (“NoP”), and (2) those with both pain in the back and pain in shoulders, arms, or legs (“BoP”). 2 (Pain) X 10 (Age) Analyses of variance (ANOVA’s) showed that participants with pain performed worse on a range of tasks as compared to participants without pain, and that these differences occurred regardless of age as no Pain by Age interactions were obtained. Of 35 dependent cognitive measures, the participants with pain performed worse on 33, compared to the group without pain. Differences were greater for visually presented material compared to enacted material, for recall compared to recognition, and for semantic memory compared to episodic memory. The most robust effects of pain were displayed on tests for vocabulary and
construction ability (Block design) as these were the only effects that remained significant after controlling for years of education and reported depression in separate analyses. When depression and education were controlled for in the same analysis, even these effects were eliminated suggesting interplay between pain, depressive status, and educational level in the negative effects on cognitive functioning. The results in this study differ from previous studies on the effects of pain on cognitive performance (e.g. Grace et al., 1999; Glass et al., 2001; Grisart et al., 2001; Park et al., 2001; Grisart et al., 2002) as education in these studies have not eliminated the effects. One suggested reason is that these studies have dealt with more severe, clinical pain syndromes such as fibromyalgia, while the present study has examined the effects of reported pain in a normal population.

**Study 3**


The present study aimed at investigating effects of self reported musculoskeletal pain and age in a population based sample on test for semantic memory, episodic memory, recall, recognition, working memory, implicit memory, construction ability, and general cognitive functioning. By use of a longitudinal design potential differences in change over time between pain groups were also examined. Data was obtained at three occasions with five years interval and 221 participants, age 35 to 80 years at the first time of measurement, were included. The inclusion of participants was based on their answers on a number of statements related to musculoskeletal pain (i.e. “I have pain in my back” and “I have pain in my shoulders, arms, or legs”). The participants were divided in two groups, those with no self reported musculoskeletal pain at any of the measurement occasions, and those with reported pain in their backs, shoulders, arms and legs at all measurement occasions. The participants were further subdivided into three age cohorts: Middle-age (age 35-50 years of age at the first time of measurement), Young-old (55-65 years of age at the first time of measurement), and Old-old (70-80 years of age at the first time of measurement). Separate analyses were conducted for each age cohort. The data were analysed by means of repeated measures analyses of variance (ANOVA’s) and subsequent repeated measures analyses of covariance (ANCOVA’s) in order to partial
out potential effects of education. Two waves of such analyses were performed, one that included data from the first two times of measurement (T1 and T2), and one that included the data from the first and third times of measurement (T1 and T3). Main effects of pain were found for semantic memory, episodic memory, recall, recognition, working memory, implicit memory, and construction ability, participants with reported musculoskeletal pain performing worse than participants with no reported pain. When education was controlled for no main effects remained statistically significant. However, for the oldest (70-80 years of age at the first time of measurement), a Time of testing by Pain interaction was revealed for semantic memory, suggesting a steeper time-related decline on semantic memory for the participants with pain, as compared with participants without pain (see Figure 3).

![Figure 3. Estimated mean z score semantic memory at T1 and T3 for the oldest age cohort (Old-old) as a function of pain category, adjusted for years of education.](image)

A series of additional analyses were performed in which two sub samples of participants were included and compared with respect to changes in cognitive performance from T1 to T3. These were (1) those that reported pain at T1 but reported no pain at T3, and (2) those that reported no pain at T1 but reported pain at T3. The first sample consisted of 44 participants and the latter consisted of 16 participants. The samples differed in years of education (p<.05) but not in age (p>.05). The first group (Pain at T1, no pain at T3) had more years of education than the latter group. Years of education was used as covariate in a series of
repeated measures ANCOVA’s in which performance on each of the cognitive measures at T₁ and T₂ were examined with respect to differences between the two groups. These analyses revealed a significant Time of testing by Group interaction for construction ability (block design). Group 2 (no pain at T₁, pain at T₂) showed an impairment in performance between T₁ and T₂ while the other group showed a slight improvement (see Figure 4).

![Figure 4](image_url)

*Figure 4.* Estimated mean z score construction ability at T₁ and T₂ for the group with pain at T₁ but not at T₂, and the group with no pain at T₁ but pain at T₂.

The conclusion from the present study are that musculoskeletal pain reports in a normal population are negatively related to cognitive functioning, but that this is a weak relationship, as the majority of effects can be explained by the fact that the groups differ with respect to education. As was the case in study 1 and 2, semantic memory yet again is found negatively related to pain. As semantic memory is more affected by pain than is the case for episodic memory the explanation given in previous studies, that pain is attention consuming, and steals capacity to process other information thereby must be completed with other explanations, or it could be the case that semantic memory is more attentional demanding at retrieval than is the case for episodic memory. A final point made in the present study is that use of longitudinal data can help reveal pain related effects of memory over time, effects that might pass unseen if only cross-sectional data are used. As previous cross-sectional studies have not found any Age by Pain interactions, the use of
longitudinal data can help reveal differences in change over time as a function of pain. Preliminary evidence for these longitudinal effects was demonstrated for semantic memory and construction ability but with the risk of being products of mass significance, this preliminary finding should be treated with great caution though until replications are made.

GENERAL DISCUSSION
The main objective of the thesis was to examine the relationship between musculoskeletal pain and different memory functions and other cognitive functions across the adult life span. While previous studies have demonstrated that pain is negatively related to cognitive functioning, not much has been said about differences in this relationship as a function of age. Another objective was to use a sample with undiagnosed musculoskeletal pain from the normal population, as compared to previous studies that have focused on extreme groups of pain patients from clinical samples. As more than half of the people in the adult population report one or more symptoms of musculoskeletal pain, it is of interest to examine if the pain and memory relationship is valid for this sample as well. A third objective was to examine potential differences in cognitive development for various age cohorts, over 5 and 10 year intervals as a function of musculoskeletal pain. Again, while pain and cognitive functioning have been found negatively related when studied cross-sectionally, not much have been said about possible longitudinal pain related changes in cognitive functioning.

Overall findings
Taken together, the results in the three studies suggest that, if background variables are not considered, participants with self reported, widespread musculoskeletal pain in the shoulders, arms, legs, and back, perform slightly worse on a range of cognitive tasks as compared to participants with no such pain reported. This is in line with previous studies on clinical groups of pain patients (e.g. Landrø et al., 1997; Grace et al., 1999; Glass et al., 2001; Grisart et al., 2001; Park et al., 2001; Grisart et al., 2002), that also have demonstrated general cognitive dysfunctions on behalf of the pain patients, as compared to healthy controls. Theses differences between groups, in the present studies, seem to occur regardless of age, as no pain by age interactions were obtained. However, in study 3, which used a longitudinal design, instead of the cross-sectional approach used in study 2 and 3, the oldest cohorts of participants with musculoskeletal pain, demonstrated significantly greater impairment in
semantic memory than the participants that did not report pain during a 10 year interval. Another similar effect was obtained for construction ability (block design). When it comes to semantic memory, the seemingly most robust pain related effects is found for tasks associated with this memory system. This will be discussed below under the section of potential causes behind pain related cognitive dysfunctions. A number of potential causes and mediators are suggested in explaining the negative effect of pain on cognitive functioning, beginning with the factor that in study 1, 2, and 3 seem to play a major part in the pain and memory relationship, namely years of education.

Education
Controlling for years of education was in the present thesis found to eliminate most of the effects of pain on memory. A recent study by Iezzi et al. (2004) on the relationship of education to cognitive performance with chronic pain patients indicates the importance of education, as does a study by Cote and Moldofsky (1997). The moderating effect of education can be explained in several ways. First, a positive relationship has been demonstrated between educational level and intellectual functioning measured in performance on free-recall tests and working memory tasks (Inouye et al., 1993; Herzog & Wallace, 1997). Education and cognitive ability probably covaries, in the sense that education leads to better cognitive ability, and good cognitive ability lead a person to enjoy studying. Furthermore, as education is likely to lead to better intellectual and cognitive capacity, this can thereby lead to better coping strategies for dealing with pain problems (Lorig et al., 1989; Park & Jones, 1997).

Second, educational level can affect pain experience indirectly via the kind of job the education has led to. High levels of education can increase the opportunity to work in a healthy physical and psychosocial environment (Erikson & Jonsson, 1993). Psychosocial risk factors include time pressure, monotony, uncertainty, lack of support and low satisfaction with the job (Hoogendoorn, van Poppel, Bongers, Koes, and Bouter, 2000; Hoogendoorn, Bongers, de Vet, Houtman, Ariëns, van Mechelen, and Bouter, 2001) while physical risk factors include heavy work and vibrations, sitting too much or too little, lack of breaks, uncomfortable postures and highly repetitive movements (Hoogendoorn, van Poppel, Bongers, Koes, and Bouter, 1999). A recent review by Linton (2001) showed a clear association between psychological variables and future back pain. There was strong evidence that job satisfaction, monotonous tasks, work relations, demands, stress, and perceived ability to work were related to future back pain problems. Further, moderate evidence was established
for work pace, control, emotional effort at work, and the belief that work is dangerous.

Third, it could be the case that people with lower levels of education are more likely to report pain (and due to their working conditions more likely to experience more severe and disabling pain) and that pain (not education) affects memory performance. This has been demonstrated by Park et al. (2001). They used education-matched groups and found that fibromyalgia had a significantly negative effect of memory, while Cote et al., (1997), who also compared fibromyalgic patients with healthy controls, found that controlling for education in an ANCOVA ruled out the many of the effects. In the studies of this thesis ANCOVA’s were also used, with similar effects as in Cote et al., (1997). It is possible that use of ANCOVA and matching can lead to different results. One advantage with using ANCOVA, or say disadvantage of using matching procedures, is that matching groups forces one to exclude participants that might differ in some important aspects from the ones that are included in the matched sample. Anyway, the moderating effect of education on the relationship between pain and memory should be further analyzed.

**Attention**

Maybe the most frequent explanation of the cause of the pain related memory dysfunction is the possibility that pain serve as a distracting factor, and consumes some of the limited attentional capacity to process concurrent tasks, such as encoding of information. Pain has been found to impair performance on attentional tasks in a number of studies (Miron, Duncan & Bushnell, 1989; Ecclestone, 1994; Ecclestone, Crombez, Aldrich, & Stannard, 1997; Grisart & Plaghki, 1999). As attentional processes are involved in memory tasks that require conscious encoding and recollection, this can of course in part explain why memory performance on explicit memory tasks is impaired when one is experiencing pain. This effect, however, should occur regardless of educational level and should be greater for episodic memory tasks as compared to semantic memory. In the present studies, semantic memory was considered more sensitive to pain than was the case for episodic memory, which makes this explanation incomplete, unless it is the case that semantic memory is more attentional demanding at retrieval than is the case for episodic memory.

**Depression**

Nearly 50% of persons with chronic pain suffer from depression (Turk, 1996; Linton, 2000). Also, depression is related to impaired cognitive
performance (Burt et al., 1995; Kindermann & Brown, 1997; Veiel, 1997). This has led previous researchers to include controls for depressive status in the examination of pain and memory relationship. In previous studies the results have been contradictory after controlling for depression. Landrø et al., (1997) found that controlling for depressive status ruled out the relationship between fibromyalgia and cognitive performance. In their study they compared fibromyalgic patients with patients that had major depression, and healthy controls and found that both pain struck fibromyalgic patients and depressed patients were significantly impaired on long-term memory tasks requiring effortful processing, compared to healthy controls. When the fibromyalgic group was decomposed to those with and without depression, only the depressed sample demonstrated memory deficits. However, the group with major depression was not measured for pain, which confounds the results, as Linton (2000b), concludes that there is strong evidence that depression is linked to future back pain. Glass et al., (2001) and Park et al., (2001) found memory impairment for fibromyalgia patients remained even after controlling for depression and anxiety. A limitation of their study is that they did not test the control group for education. They selected fibromyalgia patients who were not clinically depressed, but they could nevertheless be more depressed than the control group. In study 1 and 2, controlling for the single question about depression did not rule out any of the effects, but it is of course possible that use of a more precise measure for depressive status could yield another picture.

**Stress and anxiety**

Another explanation is related to stress. A close relationship between pain and stress has been found in a number of studies (Flor et al., 1985; Johansson et al., 1999; Lundberg, 1999; Tracey, Walker & Carmody, 2000). Furthermore, stress may cause inefficient encoding and retrieving of memory material (McEwen & Sapolsky, 1995; Kirschbaum, Wolf, May, Wippich & Hellhammer, 1996; Newcomer et al., 1999; Neylan et al., 2001; Lupien et al., 2002). Also, low cognitive capacity in itself might be stressful, and as stress is related to pain it is quite possible that basic cognitive functioning can mediate pain experience indirectly, as well as the pain can mediate cognitive functioning. A related concept is anxiety. Grace et al., (1999) found that partialling out anxiety weakened the relationship between pain and memory functioning, and suggested that anxiety together with pain severity can explain the cognitive deficits. In study 1 control was made for cortisol level, pulse rate and blood pressure
but these objective measures of stress did not change any effects of pain on memory.

Limitations/Caveats
Some problems with the studies for the present thesis should be mentioned. By far the most limiting factor in the present studies is the measure of musculoskeletal pain. In these studies the pain variables consisted of dichotomous statements (yes/no) on two pain related questions, and no data on symptom severity, duration or disabling consequences are available. Clearly, in future studies, more appropriate measures of pain has to be included, which measure more dimensions of pain, such as localization, duration, severity, kind of pain, and impact that the pain has on the person. The same should be true for the question about depression that was used for controlling for depression in study 1 and 2. Limited was also the measure for cortisol level that was used in study 1. Level of cortisol varies considerable during the day, and one single measure is hardly optimal.

Despite these limitations the studies indicates that there are differences in memory regarding how participants have answered the pain related statements. A reasonable hypothesis is that better and more precise measures of pain rather would strengthen this effect. The group of participants that reported pain probably consist of a variety of pain ranging from very severe to almost any pain, and the group of participants that did not report pain probably consist of participants with a range from no pain at all to a little pain, but not enough to report about it. In the fourth wave of data collection (T4) the dichotomous questions about back pain and pain in shoulders, arms, or legs were completed by 5-point scales of magnitude for the same statements. A question regarding chronic pain (5-point scale) was included as well in this wave of data collection. A preliminary analysis of these data for another sample supports this hypothesis. Of the participants that answered “no” on the question about pain in the back 26 % rated that they had pain in the back on the 5-point scale. Of the participants that rated “no” on the question regarding pain in the shoulders, arms, or legs 33 % rated that they had pain in the shoulders, arms, or legs on the 5-point scale. In the present studies these participants that answered “no” but still experienced weak or moderate levels of pain were impossible to identify and could therefore not be excluded. However, these participants probably weaken the effects found in the present thesis. Thus, even if this is only hypothetical reasoning, the effects of pain on cognitive functioning that have been demonstrated in these studies should be treated as valid. Preliminary analyses of this sample
also demonstrated that the participants with pain in the back, and in the shoulders, arms, or legs scored significantly higher (ps<.001) on the question regarding chronic pain, as compared to the group without pain, and the group with local pain (back or shoulders, arms, or legs). In the group with both pain complaints 65% reported about chronicity. These results lend preliminary support to the hypothesis suggested in the three studies that the group that answered yes on both questions were chronics.

**Implications**

There are at least two areas of implications that could be drawn from the present thesis. First, as the above studies, together with previous research, show that pain is associated with worse cognitive performance, this can have practical implications for people suffering from pain, such as having hard to remember important things at work or at home, keeping track of medications, understand and remember instructions from physiotherapists and other medical personal, stay focused in conversations, and so on. It can be of importance for physicians to gain a better understanding of the nature and legitimacy of their patients cognitive complaints, in order to take them seriously, treat their complaints respectfully, and hopefully better adjust instructions and demonstration so that the patients more easily can remember and learn. As differences in performance on word comprehension in study 2, and word fluency (Park et al., 2001) have been found, it could be the case that a patient suffers from language understanding problems and language production problems. This could have implications for the possibility to understand the “medical” language used by doctors and physiotherapists.

Finally, as so many people in the population suffer from musculoskeletal pain problems, pain should be controlled for in studies of our cognitive system.

**Future studies**

All of the above mentioned explanations probably have something to say in explaining the cognitive dysfunction in pain participants. What is still needed is to integrate these explanations into one model, in order to have a better understanding of direct and indirect causes of the dysfunction. Future studies should emphasise this, buy using for instance structural equation modelling techniques.

Moreover there is a need of more longitudinal studies to replicate on the findings in study 3. These studies should use better measures of pain in order to examine changes in cognitive functioning over time as a function of changes in pain magnitude and duration.
Then there is a need of experimental designed studies, with randomized groups, and laboratory induced pain, in order to find out more about the true casual relationship between pain and memory and other cognitive functions.
REFERENCES


