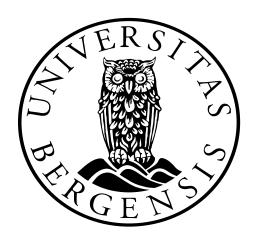
Common Complaints – Common Cure?

Psychiatric comorbidity and predictors of treatment outcome in low back pain and irritable bowel syndrome

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Dissertation for the degree philosophiae doctor (PhD) at the University of Bergen

Scientific environment

The work presented herein was financed through a three year PhD-grant from the Western Norway Regional Health Authority (Helse Vest), and was carried out within the institutional framework of the doctorate program at the Faculty of Psychology, University of Bergen. The thesis is presented through Department of Health Promotion and Development (HEMIL), with supervision from the Stress, Health and Rehabilitation group and Uni Health, Uni Research Bergen.

The first study of the thesis was financed by the Research Council of Norway, the second study was financed with the aid of EXTRA funds from the Norwegian Foundation for Health and Rehabilitation, and the third and final study was financed by the Health Technology Assessment program of the National Institute for Health Research, United Kingdom.

Abstract

The basic hypothesis of the thesis is that the variance in individuals' tolerance and acceptance of subjective health complaints is explained by CATS, the Cognitive Activation Theory of Stress. Sustained activation and rumination in cognitive loops elicit a psychobiological sensitisation in these loops. This is the theoretical foundation for the thesis. The thesis aims at investigating whether there is support for this position by three separate experiments. More specifically, the aims are to investigate the prevalence of psychiatric comorbidity in chronic low back pain (CLBP), predictors of treatment outcome after a brief cognitive intervention for CLBP, and predictors of treatment outcome after a cognitive behavioural therapy for irritable bowel syndrome (IBS).

"Subjective health complaints" are complaints without known pathology or where the complaints exceed objective findings of pathology. Subjective health complaints are experienced by most people but endure and disables in some. In those who suffer from substantial subjective health complaints such as CLBP and IBS, additional somatic and psychological symptoms and complaints are frequent. Previous findings show a high degree of comorbid psychopathology in CLBP, but less is known about the broad range of psychiatric disorders. In paper I the prevalence of psychiatric comorbidity was investigated through structured diagnostic interviews of a large group of sick listed CLBP patients. The results showed a point prevalence of 30% for at least one psychiatric disorder. The diagnoses included a whole range of psychiatric disorders, with the most common being somatoform disorders and anxiety disorders. Besides psychiatric disorders, there were also a high degree of comorbid health complaints. This may support the hypothesis of a generalized sensitization where some individuals get more sensitive than others to a wide range of stimuli, resulting in high comorbidity.

In paper II predictors of treatment outcome were investigated in CLBP patients after a brief cognitive intervention which has been found clinically and cost efficient in terms of return to work. Despite promising results, 30% did not profit from the treatment, and the aim of the paper was therefore to identify the patients who did not return to work. Psychological, cognitive, social and demographic variables were tested in order to see which variables that predicted non-return to work. Subjective and cognitive factors such as perceptions of disability and expectations of return to work were the strongest predictors of a poor treatment outcome (non-return to work). This is in line with the theoretical framework of the thesis, and confirms the importance of acquired expectations of own abilities to cope, as described by CATS. A surprising finding was that previous treatment by physiotherapists predicted prolonged sick leave.

In paper III predictors of treatment outcome were investigated in an effective treatment for another group of patients with substantial subjective health complaints, namely IBS. It was hypothesized that cognitive behavioural treatments (CBT) aiming at changing cognitive and behavioural factors would be successful in treating IBS, and that these factors would predict treatment outcome. This was supported in the paper, where behavioural factors were found to predict treatment success in a tailored CBT treatment for IBS patients. CBT resulted in significantly reduced symptoms and increased function for the IBS patients compared to an antispasmodic treatment. IBS patients that were engaging in unhelpful behaviour at baseline, such as avoidance and control behaviour, were most likely to profit from the CBT treatment. The results thus indicate that CBT should be recommended to these patients.

In conclusion, the thesis supports the theoretical position of CATS (Cognitive Activation Theory of Stress) in the understanding of CLBP and IBS, which is in line with the CBT model for treating CLBP and IBS. More specifically, psychological, cognitive and behavioural factors all appeared to be vital parts of the disorders, while cognitive and behavioural factors were crucial for treatment outcome.

List of publications

- Paper 1 Reme S.E., Tangen, T., Moe, T., Eriksen, H.R. (2010): "Prevalence of psychiatric disorders in chronic low back pain patients" *Submitted*
- Paper 2 Reme S.E., Hagen E.M., Eriksen H.R. (2009): Expectations, perceptions, and physiotherapy predict prolonged sick leave in subacute low back pain. *BMC Musculoskelet Disord*, 10(1), 139.
- Paper 3 Reme S.E., Kennedy T., Jones R., Darnley S., Chalder T. (2010): Predictors of treatment outcome after cognitive behaviour therapy and antispasmodic treatment for patients with irritable bowel syndrome in primary care. *J Psychosom Res*, 68(4), 385-388.

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1. Introduction and theoretical framework

1.1 Subjective health complaints

Subjective health complaints are general health problems that most people experience from time to time, with few or no objective findings to fully explain the complaints (Eriksen, Ihlebaek, & Ursin, 1999). The complaints include musculoskeletal complaints, pseudoneurological complaints (i.e. tiredness, light mood changes, dizziness), gastrointestinal complaints, allergy and "flu". Subjective health complaints are highly prevalent in the general population in Norway (Ihlebaek, Eriksen, & Ursin, 2002), in other Nordic countries (Eriksen, Svendsrød, Ursin, & Ursin, 1998) and cultures (Eriksen, Hellesnes, Staff, & Ursin, 2004; Wilhelmsen et al., 2007). Some seem to be more sensitive to these phenomena, with the result being disabling conditions (Ursin, 1997). Several alternative terms are widely used for these conditions, such as "medically unexplained symptoms", "functional disorders" or "somatisation" (Creed et al., 2010). However, in this thesis "subjective health complaints" will be used throughout when referring to these conditions. As opposed to the other terms, "subjective health complaints" do not make any causal attributions but merely describe the complaints as they are experienced by the individual, thereby offering an advantage over the other terms. Further, unlike the previous mentioned terms, "subjective health complaints" has a core theoretical concept and defies dualistic simplicity of psychological versus organic disorders (Ursin, 1997).

Most of us experience subjective health complaints from time to time, but for some people these health complaints become so persistent and disabling that they impair daily functioning such as ability to work (Ihlebaek, Brage, & Eriksen, 2007). The majority of long term sick leaves in Norway are due to subjective health complaints, with nearly half due to musculoskeletal complaints (Brage & Laerum, 1999; Reiso, Nygard, Brage, Gulbrandsen, & Tellnes, 2001). There is high degree of overlap between different patient groups, and high degree of comorbidity (e.g. Carnes et al.,

2007; Aaron & Buchwald, 2001). The compensational system still demands a clearly defined diagnosis on the sickness certificate, through the International Classification of Primary Care (WHO, 2003). The compensational system thereby forces the general practitioner to choose one of the patients' diagnoses on the sickness certificate, even though the patients often qualify for several diagnoses. This could result in a misleading picture of the patients' spectre of complaints.

In this thesis the basic hypothesis is that the variance in individual understanding and interpretation of pain and discomfort may be explained by CATS, the Cognitive Activation Theory of Stress (Ursin & Eriksen, 2004). The thesis will focus on two patient groups with subjective health complaints, namely chronic low back pain (CLBP) and irritable bowel syndrome (IBS). They both represent examples of subjective health complaints that may become disabling, and both are chronic conditions with high comorbidity and reduced function.

1.2 Low back pain & Irritable bowel syndrome

Despite high degree of overlap between different groups of subjective health complaints, LBP and IBS each have certain characteristics that constitute the disorder.

Low back pain (LBP)

LBP is defined as pain and discomfort localised below the costal margin and above the inferior gluteal folds, with or without referred leg pain (Burton et al., 2006). Most back pain is non-specific, defined as LBP not attributed to recognisable, known specific pathology. Serious spinal pathology is often referred to as "red flags" and includes diseases such as spinal tumor and infection, and inflammatory disease such as ankylosing spondylitis. Spinal infections are rare. Less than 1% is due to inflammatory disease that needs rheumatologic investigation and treatment.

There are still controversies on how specific LBP really is. For most patients with LBP a precise pathoanatomical diagnosis is often impossible due to poor associations between symptoms and anatomical findings (Deyo & Weinstein, 2001).

LBP is very common in the general population, with 40% reporting of some degree of LBP during the last month (Ihlebaek, et al., 2002). Lifetime prevalence of LBP is up to 84%, while 11-12% of the population is disabled by LBP (Airaksinen et al., 2006). The scientific evidence for prevalence of chronic LBP is more unclear, but estimates suggest approximately 23% (Airaksinen, et al., 2006).

Three stages have been identified in the development of chronic disability (Airaksinen, et al., 2006):

- The acute stage (< 4 weeks). The prognosis here is good, 90% settle within 6 weeks, at least sufficient to return to work.
- The subacute stage (4-12 weeks). This is the critical stage for intervention. Psychosocial issues now become more important.
- The chronic stage (> 12 weeks). The psychosocial issues are here very important, with major impact on every aspect of the individual's life, family, and work. The prognosis is poor. Likelihood of return to work diminishes with time. Medical treatment, rehabilitation, and vocational rehabilitation are difficult and the success rate is low.

A sick leave episode due to LBP of 8-12 weeks duration is often referred to as subacute LBP (e.g. Hagen, Eriksen, & Ursin, 2000). In this thesis, however, sick leave episodes of more than 8 weeks duration will be referred to as CLBP since the majority of these patients have a long history of previous sick leave episodes due to LBP (Hagen, et al., 2000).

The transition from acute to chronic LBP is commonly understood as a biopsychosocial process, where biological, psychological, social and behavioural factors interact and contribute to the disability (Turk & Gatchel, 2002; Waddell,

2004a). It is an individual-centred perspective that takes the person, the health problems and the social context in to consideration (Waddell, 2006). More specifically, *biological* refers to the physical or mental health condition, *psychological* refers to the influence psychological factors have on functioning, while *social* recognizes the importance of the social context, pressures and constraints on functioning (Waddell, 2006).

Irritable bowel syndrome (IBS)

IBS is part of the larger group of functional gastrointestinal disorders, and is characterized by symptoms of abdominal pain or discomfort that is associated with disturbed defecation (Drossman, Camilleri, Mayer, & Whitehead, 2002). Diagnoses are usually made based on the Rome II diagnostic criteria (Drossman, Corazziari, Talley, Thompson, & Whitehead, 2000) which includes at least 3 months with abdominal pain or discomfort relieved with defecation; and/or onset associated with a change in frequency of stool; and/or onset associated with a change in form (appearance) of stool. In order to be diagnosed 2 or more of these symptoms have to be present for at least 25% of occasions (Drossman, et al., 2000).

There are controversies regarding the aetiology of IBS, but generally an agreement that there are alterations in the brain-gut-axis (Naliboff, 2007). IBS is a common syndrome with a prevalence of 13% in women and 5% in men (Heaton et al., 1992). However, only about half the people with diagnosable IBS seek medical advice for their symptoms (Heaton, et al., 1992). Those who consult a physician are usually more disabled and likely to present with multiple symptoms (Heaton, et al., 1992).

The biopsychosocial model of understanding functional disorders has been well described and applied to GI-disorders during the last decades (e.g. Drossman, 1996; Naliboff, 2007; Wilhelmsen, 2000). The model implies multicausality where biological and psychosocial factors interact to determine disease and illness. The strong association often seen between IBS and affective disorders suggest common

pathophysiological mechanisms underlying both gastrointestinal dysfunction and certain affective disorders (Mayer, Craske, & Naliboff, 2001). Drossman exemplifies the model of interacting subsystems in IBS by suggesting a possible dysregulation of the central and enteric nervous system linkages, enhanced visceral sensitivity, cortical processes regulating symptom perception, and psychosocial factors uniquely influencing illness experience and behaviour (Drossman, 1996). Naliboff (2007) further suggests that what determines illness behaviour is how the individual perceives, evaluates and acts in response to the symptoms.

1.3 Comorbidity in CLBP and IBS

Comorbid psychopathology in CLBP is a well established finding (Turk & Gatchel, 2002). Reports of additional somatic and psychological complaints are frequent, leaving hardly anyone with LBP as the only complaint (Carnes, et al., 2007; Hagen, Svensen, Eriksen, Ihlebaek, & Ursin, 2006; Von Korff, Crane, et al., 2005). In a survey of 457 patients referred to a spine clinic, less than 2% of the patient population reported LBP as their only complaint (Hagen, et al., 2006). The majority of the patients had widespread musculoskeletal pain, and a substantial proportion reported a significant number of other subjective health complaints as well. This is consistent with previous Norwegian data (Natvig, Eriksen, & Bruusgaard, 2002) and recent findings in the US (Von Korff, Crane, et al., 2005) and UK (Carnes, et al., 2007). Number of pain complaints further increases the likelihood of psychopathology (Katon & Sullivan, 1990), and more widespread pain has been associated with more disability (Kamaleri, Natvig, Ihlebaek, & Bruusgaard, 2008). The association between pain and psychopathology is further strengthened as severity of either condition increases (Carroll, Cassidy, & Cote, 2000). Concurrent psychopathology in CLBP implies poor prognosis (Linton, 2000a; Von Korff, Balderson, et al., 2005), poor outcome (Dersh et al., 2007) and high health care utilization (Engel, von Korff, & Katon, 1996).

Comorbidity is also frequent in IBS (North, Hong, & Alpers, 2007; Orchard, 2003; Vandvik, Lydersen, & Farup, 2006). IBS patients are characterized by both somatic and psychiatric comorbidity (Riedl et al., 2008), and their reduced health, working ability, and use of health resources are largely explained by the comorbid symptoms and disorders (Vandvik, et al., 2006). IBS is particularly strongly associated with anxiety disorders (Lee et al., 2009). Recent findings further suggest that IBS patients have a greater comorbidity across all categories of diagnoses than both the general population and irritable bowel disease patients, and that this is explained by a small percentage (16%) of IBS patients having abnormally high numbers of comorbid diagnoses (Whitehead et al., 2007). Finally, up to 70% of IBS patients report of comorbid LBP compared to only 40% in the general population (Vandvik, et al., 2006). This further illustrates the degree of comorbidity and overlap between disorders, including the two disorders under scrutiny in this thesis.

1.4 Theoretical framework

Several theories have been proposed in order to explain differences in individual health, with essentially two overlapping traditions. The majority of long-term sick leave is caused by subjective health complaints, and one tradition therefore emphasizes formal or "objective" work conditions as responsible for the individual's health complaints, while the other focuses more on the stress management potential of each employee. The recent Cognitive Activation Theory of Stress (CATS) combines physiological and cognitive explanations, and hence represent the extreme end of the continuum with its emphasis on individual factors (Ursin & Eriksen, 2004). The crucial concept in CATS is "expectancy" and is based on previous learning. When the brain has established that one event precedes another, the brain "expects" the second event after the first event or response has been performed. Similarly the brain learns that one type of action (response) leads to a consequence, referred to as response outcome expectancies. The stress stimulus is thus filtered through the brain to answer the crucial questions: what does the stimulus mean and

what can I do about it? According to CATS, the acquired expectations regarding own abilities to cope are crucial for health outcomes. If the individual has learned that no matter what he or she does, there will be no change in the condition (helplessness), or all attempts lead to even worse outcomes (hopelessness), the patient has a negative response outcome expectancy. The negative response outcome expectancy may cause sustained arousal leading to negative health consequences through for example sensitization (Eriksen & Ursin, 2004; Ursin & Eriksen, 2001).

The best known and most influential "objective" model is the demand-control model of Karasek & Theorell that posits an interaction between job demands and job control in predicting psychological strain (Karasek & Theorell, 1990). Jobs with high demands, low control, and low social support carry the highest risk of illness and disease, while jobs with low psychological demands and high levels of control carry the lowest risk. In later developments, Theorell places much more emphasis on individual stress management, coping abilities, and subjective feelings of being in control or being able to cope (Theorell & Karasek, 1996; Theorell, Westerlund, Alfredsson, & Oxenstierna, 2005). This emphasis is more in line with the theoretical and empirical background for CATS and other positions emphasizing the individual variance in responses to "stress".

Another model that has received much attention is the effort-reward imbalance model where the focus is on reward and contractual fairness in employment (Siegrist, 1996). This model builds on the assumption of contractual reciprocity in terms of which accomplished tasks are reciprocated by adequate rewards (e.g. money, esteem, career opportunities). The model assumes that lack of reciprocity in terms of "high cost" and "low gain" elicits strong negative emotions and sustained stress reactions. Similar to the demand-control model, the effort-reward model also deals mostly with cardiovascular disease, and not with subjective health complaints, even though the latter account for most long-term sickness compensation and permanent disability (Reme, Eriksen, & Ursin, 2008).

The contribution from CATS is to offer a pathophysiological model for the relationship between subjective health complaints and long-term sickness compensation. Within CATS, effort-reward imbalance is a discrepancy between set values and actual values, resulting in sustained activation that again may result in pathophysiological consequences. A short term imbalance will not have pathophysiological consequences; it is the long-lasting imbalance that matters according to CATS.

1.5 Cognitive behavioural treatments for LBP and IBS

Cognitive behavioural treatments emphasize the importance of the individuals' understanding of their condition and interpretation of pain and discomfort, which is consistent with the theoretical foundation of the thesis.

Acquired expectations of own abilities to cope are crucial for health outcomes, according to CATS (Eriksen, Murison, Pensgaard, & Ursin, 2005). In line with this position, CBT treatments aim to change the negative response outcome expectancies to positive expectancies, i.e. coping, by challenging and changing dysfunctional cognitions and behaviour. Two such treatments have shown significant effects for LBP and IBS, namely the brief cognitive intervention for CLBP (Hagen, et al., 2000; Indahl, Haldorsen, Holm, Reikeras, & Ursin, 1998), and tailored cognitive behaviour therapy for IBS (Kennedy et al., 2005).

Brief Intervention (BI) for LBP

BI is a brief cognitive intervention where return to normal activity and work is the main goal (Indahl, et al., 1998). Previous studies of BI for LBP have shown significant reduction of sick leave compared to treatment as usual (Brox et al., 2008; Hagen, et al., 2000; Indahl, et al., 1998). The essential feature of the intervention is the use of a cognitive approach through the medical examination and education

conducted by a specialist in physical medicine and rehabilitation (Indahl, et al., 1998). The intervention includes diagnostic clarification, reassurance of normal findings, and encouragement to engage in physical activity as normal as possible. Patients are provided a new understanding of the back pain, and given practical advice about how their back function can be improved. The examination is thorough with detailed feedback on findings and normal functions, and clear and consistent explanations on pain and defence mechanisms. If any "red flags" are identified indicating serious pathology, the patients are referred appropriately. Neurological tests are conducted, and information regarding importance of findings is given (e.g. positive comments about normal findings such as normal nerve function in legs). Painful muscles are identified and if the patient moves in tense ways attention are given to make the patient aware of how muscles become involved and tense, and that maintained tension may worsen the condition. Radiographs are shown and explained, and patients are told that looking for the source of pain on radiographs has limited importance; degenerative changes in the spine are most often normal aging processes and not necessarily painful. Unless symptoms and clinical findings indicate serious spinal disease, the patients are informed about the good prognosis, and the importance of staying active to avoid development of muscle dysfunction. The patients are given assurance that light activity will not do any harm, but, on the contrary, is more likely to reduce their complaints. The main purpose of the intervention is to provide the patients with coping skills to manage their back pain through information, practical advice and reassurance, and to motivate and encourage them to stay active despite the pain. It is important that all personnel involved with the patients give the same message ("all players on the same side"). After the medical examination the patients receive a follow-up session with a physiotherapist, involving an educational and a behavioural part. The purpose of the education is to strengthen the message given in the medical examination, while the purpose of the behavioural component is to help the patient turn the new insight into practical action.

CBT treatments have been applied to IBS patients with successful outcomes (Kearney & Brown-Chang, 2008; Kennedy, et al., 2005; Lackner, Mesmer, Morley, Dowzer, & Hamilton, 2004). The CBT tailored for IBS patients, focuses on the behaviour, thoughts and feelings surrounding IBS. The aim is to improve the way the IBS patients cope with day-to-day life as well as improve their perception of the physical symptoms, both assumed to be partially responsible for perpetuating the complaints and disability (Darnley, Kennedy, Chalder, & Jones, 2006). The way a patient thinks, acts and feels can hence maintain the symptoms of IBS.

The symptoms might be triggered by specific or unspecific factors such as a severe bout of diarrhoea or stress, but maintained and intensified by cognitive, behavioural and emotional responses. Interpretation of abdominal discomfort as threatening (e.g., "this stomach pain means I may have something seriously wrong with my bowel", or "this symptom is abnormal and I must control it") is likely to lead to actions such as frequent visits to the doctor, and increased attention to bodily sensations. In addition, other unhelpful behavioural coping strategies may be engaged in as well as increased by physiological arousal and anxiety. This further leads to the experience of symptoms as more intense and noxious which is again interpreted as threatening, resulting in a vicious circle of fear and avoidant coping in the long term (Kennedy, et al., 2005), similar to the fear-avoidance seen in CLBP patients (Waddell, 2004a). Many patients who suffer from IBS are severely restricted in their activities, not uncommon to that seen in agoraphobia (Salkovskis, 1989). It is often based on the fear of unexpected incontinence, particularly when this would be socially embarrassing (Salkovskis, 1989). This is not to say that IBS is all in the mind. Rather, even though IBS may have physical causes that we do not fully understand, a CBT approach assumes that what a person does, thinks, and feels will aggravate and maintain many of the IBS symptoms.

The first session of CBT will usually focus on a cognitive behavioural assessment, defining problems, and setting goals for the treatment. The remaining sessions include feedback from previous session, homework review, homework discussion, goal setting and recap of key issues. Other important treatment components are

identification of maintaining factors, introduction of IBS specific behavioural and cognitive strategies, and a continuing check of the patient's understanding and acceptance of the treatment rationale (Darnley, et al., 2006).

CBT is now considered to be a well established treatment for anxiety and depression (Feldman, 2007; Hofmann & Smits, 2008), and recent findings suggest its effectiveness on CLBP (Ostelo et al., 2005), somatisation disorder (Allen, Woolfolk, Escobar, Gara, & Hamer, 2006), and fibromyalgia as well (Williams, 2003). The effects of CBT in patient groups with subjective health complaints such as IBS, CLBP and chronic fatigue syndrome (Deale, Chalder, Marks, & Wessely, 1997; Kennedy, et al., 2005; Linton & Nordin, 2006), suggest common psychobiological elements and less specificity than the diagnostic labels suggest.

1.6 Historical perspectives

Conditions of nonverifiable illness, here called subjective health complaints, are not a new phenomenon but were seen and described several centuries ago (Johannisson, 2010; Shorter, 1992). In 1869 Beard described a syndrome of tiredness and multiple complaints that he suggested was caused by emotions leading to exhaustion of the nervous system (Chatel & Peele, 1970). The other tradition was "hysteria", also a widely used concept for conditions without an organic basis to explain the complaints. The condition was originally believed to be present in women only, but was later discovered to strike men as well. Briquet defined hysteria as "a neurosis of the brain in which the observed phenomena consist chiefly of a perturbation of vital activities that serve as the manifestations of affective feelings and passions" (Guze, 1975). In 1850 Briquet outlined the etiological factors of hysteria which highly resembles today's risk factors for subjective health complaints or somatisation disorders (e.g. female gender, "affective" and "impressionable" temperament, low social class, situational difficulties, and family history of the disorder) (Guze, 1975). Neurasthenia and psychastenia were other common terms, and were used by Pavlov on his dogs. Asthenia, neurasthenia and psychasthenia are no longer used in DSM IV

but neurasthenia is still used within the ICD-10 classification system (World Health Organization, 1993) and is still being used in some countries. It has also been suggested as a term for extreme cases of subjective illness (Wessely, 1990).

Various names and labels have been used for the same conditions of subjective health complaints throughout history, and it has therefore been argued that a dimensional classification is more productive than a classification of specific syndromes (Wessely, Nimnuan, & Sharpe, 1999). In the same review, Wessely and colleagues present substantial support for one versus many syndromes (Wessely, et al., 1999). They point at the substantial overlap in case definitions between what they call functional somatic syndromes, the overlap of complaints, non-symptom characteristics and response to same therapies. The substantial overlap between conditions has also been reported by others (Creed, et al., 2010; Aaron & Buchwald, 2001).

1.7 The sensitive personality

Neuroticism is one of the dominant personality factors within the Big Five personality traits. Costa and McCrae defined neuroticism as: "a broad dimension of individual differences in the tendency to experience negative, distressing emotions and to possess associated behavioural and cognitive traits" (Costa & McCrae, 1987, p. 301). Neuroticism has been associated with a heightened experience of bodily sensations (Watson & Pennebaker, 1989), and has later been suggested to be a vulnerability factor which lowers the threshold for pain perception (Goubert, Crombez, & Van Damme, 2004). With a lower threshold for noticing and attending to internal physical sensations, the attentional scanning of both the external and internal environment is fraught with anxiety and uncertainty. The concept of neuroticism closely resembles negative affectivity, defined as a mood-dispositional dimension that reflects pervasive individual differences in negative emotionality and self-concept (Watson & Clark, 1984). Individuals who score high on negative affectivity seem to be hypervigilant for all forms of (external and internal) threat. Negative

affectivity correlates significantly with a range of measures of symptom reporting, but not with objective measures of health (Watson & Pennebaker, 1989). One might therefore assume that negative affectivity causes an increase in the reporting of physical symptoms. However, some have suggested that negative affectivity rather plays a role in the process of misattributing common symptoms to illness-related causes (Petrie, Moss-Morris, Grey, & Shaw, 2004). Watson and Pennebaker suggested the following three explanations for the strong link between negative affectivity and health complaints: 1) high negative affectivity causes health problems (a variant of the classic psychosomatic hypothesis), 2) health problems cause high negative affectivity (the disability hypothesis), 3) individuals differ in how they perceive and respond to bodily sensations (the symptom perception hypothesis) (Watson & Pennebaker, 1989).

1.8 Sensitization

Individuals differ widely in their tolerance and acceptance of subjective health complaints, and consistent with the third hypothesis of Watson and Pennebaker, this could be related to how the individual perceives and responds to bodily sensations (Watson & Pennebaker, 1989). In this thesis sensitization is assumed to be the psychobiological mechanism explaining the differences in individual health. It is suggested to be a multilevel phenomenon occurring in both lower (neural) and higher (cognitive) levels (Eriksen & Ursin, 2004). The neurobiological sensitization is what happens in the neuronal synapses when there is an increased reaction to stimuli (Ursin, 1997). Repeated firing of synapses may result in changed synaptic efficiency, either as sensitization or habituation. The latter involves a decreased reaction due to repeated firing in the synapses, but for pain stimuli there is no habituation (Ursin, 1997). A particular form of sensitization, namely kindling of limbic structures, may further explain why some individuals get more sensitive than others to a wide variety of stimuli. This generalised sensitization would explain the high comorbidity in these conditions, and would offer a model for cross-sensitization from one source of stimuli

to another (Bell, 1994; Bell, Miller, & Schwartz, 1992). Increased pain sensitivity has been demonstrated in patients with LBP (Clauw et al., 1999), fibromyalgia (Vaeroy, Helle, Forre, Kass, & Terenius, 1988), and functional gastrointestinal complaints (Mearin et al., 1995). There seems to be a general agreement that patients with IBS have an increased visceral sensitivity (Mearin, et al., 1995; Naliboff et al., 1997), and the mechanisms suggested seem to be the same as those suggested for sensitization to muscle pain (Ursin, Endresen, Håland, & Mjellem, 1993).

Higher levels of sensitization is suggested to include phenomena such as cognitive or attentional bias (Brosschot, 2002). Brosschot refers to this as cognitive emotional sensitization (Brosschot, 2002). This is believed to cause long-lasting activation and continuing reactivation of specific pain-and illness-related cognitive networks, similar to an attentional bias where too much attention is focused on the back pain or stomach discomfort. The enhanced focus on one or several dominant complaints may be driven by the suggestibility of somatising patients or the clinician and researchers' preoccupation with physical symptoms (Fink, 1996). Cognitive emotional sensitization is further proposed to explain why psychiatric patients are more frequently admitted to medical facilities, and stay longer in hospitals with medical admissions, than patients treated for the same disorder, but with psychiatric illness (Fink, 1990).

Conditions likely to lead to sensitization are when the stimulus is irregular, strong or extreme, the stimulus is relatively unpredictable, or the background level of arousal is high (Overmier, 2002). High levels of background arousal, or sustained activation, may lead to vigilance, and this vigilance may be directed towards the bodily sensations the individual experiences (e.g. low back pain or stomach discomfort). The selective attention to an increased threat appraisal of visceral sensations, together with symptom-related fear, may maintain symptoms in the absence of actual stressors in IBS patients (Naliboff, Frese, & Rapgay, 2008). The sensitized persons are in a state of vigilance, constantly scanning the environment for information related to the pain or illness. The rumination and worrying of the patient after a stressful event and in anticipation of another, is of far more long-standing character than the temporal

effect of the actual stressor, and may be more important for the development of pain or illness than the stressful event itself (Brosschot, Gerin, & Thayer, 2006). For IBS patients, hyper-responsiveness of the enteric nervous system to actual stressors, conditioned fear responses, and cognitive factors, are all suggested to play important roles in the chronicity of complaints (Mayer, 1999; Naliboff, et al., 2008). This is also in line with a cognitive-behavioural perspective; pain-related fear will interfere with cognitive functioning, leaving the fearful patient more attentive to possible signals of threat (hypervigilance), and less able to shift attention away from pain-related information (Vlaeyen & Linton, 2000).

1.9 CATS and CBT

CATS offers a theoretical framework consistent with cognitive behavioural treatments for unspecific disorders such as CLBP (Reme, et al., 2008). Similar to the CATS theory, the CBT model emphasises the importance of the individuals' understanding of their condition and their interpretation of pain. Previous findings demonstrate that CLBP patients have established a negative expectation of personal abilities to gain control of the condition, which is a significant predictor of a poor prognosis (Cole, Mondloch, & Hogg-Johnson, 2002; Haldorsen et al., 2002; Haldorsen, Indahl, & Ursin, 1998; Hildebrandt, Pfingsten, Saur, & Jansen, 1997; Sandstrom & Esbjornsson, 1986). Patients that have acquired negative outcome expectancies often struggle with fear of pain and catastrophic consequences of activity and movement (Vlaeyen & Linton, 2000). The expectancies may involve both stimulus expectancies (e.g. "pain equals injury") and response outcome expectancies (e.g. "work will make my pain worse"). The aim of CBT treatments is to change the negative stimulus and response outcome expectancies into coping, by challenging and changing dysfunctional cognitions and behaviour. A further focus in CBT treatments is to increase the awareness of reinforcing and perpetuating factors. If the individual is in a state of helplessness or hopelessness characterized by negative beliefs, avoidance, passivity, worries, sensitization and more pain, the symptoms that

originally was a response to a stressor (e.g. muscle cramp or diarrhoea) now becomes the main problem. For the individual this might result in a vicious circle where disability is maintained, and where sensitization in pain pathways and higher-level cognitive sensitization might be contributing factors in maintaining the vicious circle (Brosschot, 2002).

1.10 Predictors of treatment outcome – what works for whom?

If the CATS position is right in the emphasis on stimulus and response outcome expectancies for the development of chronic and debilitating subjective health complaints, one would expect a wide range of psychological, cognitive and social predictors of treatment outcome based on the effect of these factors for the learning of coping, helplessness and hopelessness. According to CATS, the essential determinant for stress responses and consequences is the *perceived* relationship between stimulus or response and outcome, not the objectively true contingencies (Ursin & Eriksen, 2004). Previous findings are in agreement with this position in that the most important factors for treatment outcome in LBP are subjective ratings of pain intensity and disability, affective parameters, pain related cognitions, health control beliefs, and coping strategies (Hasenbring, 1998; McCracken & Turk, 2002; van der Hulst, Vollenbroek-Hutten, & Ijzerman, 2005). More objective parameters, like medical data and objective work-related factors, appear less important in predicting treatment outcome (Hasenbring, 1998; Steenstra et al., 2005). Furthermore, one of the strongest predictors of return to work is actually the patients' own belief in being able to return to work (Cole, et al., 2002; Fishbain, Cutler, Rosomoff, & Rosomoff, 1997; Haldorsen, Kronholm, Skouen, & Ursin, 1998; Hildebrandt, et al., 1997; Sandstrom & Esbjornsson, 1986), which could be considered equivalent to coping as defined by CATS, where coping is defined as a positive response outcome expectancy (Ursin & Eriksen, 2004).

Few studies have looked specifically at predictors of treatment outcome after CBT treatments for IBS. Those who have find psychological disturbance to be an

important predictor of a poor outcome. Less baseline anxiety has been found to predict good results by some (Blanchard, Schwarz, Neff, & Gerardi, 1988), whereas others have found a lower likelihood of success with the presence of one or more psychiatric disorders (Blanchard et al., 2006; Blanchard et al., 1992) and baseline depression (Drossman et al., 2003). Although psychological distress overall seems to predict a poor outcome in CBT treatments, studies from other psychological treatments reveal results that point in the opposite direction (Creed et al., 2005; Guthrie, Creed, Dawson, & Tomenson, 1991). Symptom characteristics also show some inconsistencies in the literature, in that severity of gastrointestinal symptoms predicted a poor outcome in one study (Blanchard, et al., 1988) and a good outcome in another (Lackner et al., 2007). The deviant findings indicate that a wide range of psychological and cognitive factors are important for treatment outcome, but they also confirm the importance of subjective factors as previously outlined.

2. Aims of the thesis

Individuals differ widely in their tolerance and acceptance of subjective health complaints. In this thesis the basic hypothesis is that the variance in individual understanding and interpretation of pain and discomfort may be explained by CATS, the Cognitive Activation Theory of Stress. Sustained activation and rumination in cognitive loops elicit a psychobiological sensitisation in these loops. This is the theoretical foundation for the thesis.

The thesis aims at investigating whether there is support for this position by three separate experiments. If sensitisation is as general as suggested by previous literature and the CATS position, one would expect a high degree of psychiatric comorbidity in patients with chronic low back pain. If the CATS position is right in the emphasis on stimulus and response outcome expectancies for the development of chronic and debilitating subjective health complaints, one would expect a wide range of psychological, cognitive, behavioural and social predictors for outcome based on the effect of these factors for the learning of coping, helplessness and hopelessness. If these positions are right, one would also expect that systematic cognitive behavioural treatments directed at cognitive and behavioural factors may be beneficial for patients with irritable bowel syndrome, another condition with strong subjective health complaints and a high degree of comorbidity, and that these factors would predict treatment outcome.

Based on this, the following research questions were formulated for the thesis:

- 1. What is the prevalence of psychiatric comorbidity in chronic low back pain patients?
- 2. What factors predict treatment outcome in chronic low back pain after a brief cognitive intervention?
- 3. What factors predict treatment outcome in irritable bowel syndrome after cognitive behavioural therapy?

3. Summary of papers

3.1. Prevalence of psychiatric comorbidity in chronic low back pain patients

Research question 1: What is the prevalence of psychiatric comorbidity in chronic low back pain patients?

Chronic low back pain (CLBP) patients suffer from a high degree of comorbidity, with a prevalence of comorbid psychiatric disorders ranging from 40%-100%. Psychopathology is most often assessed through questionnaires unsuited for diagnosing, and diagnostic studies show inconsistencies in prevalence numbers. Inconsistencies may be due to setting, methodology or selection. The aim of this study was to assess the prevalence of psychiatric comorbidity in a population of CLBP patients through a psychiatric diagnostic interview.

427 patients sick listed between 2 and 10 months for unspecific LBP were included in the study. All were recruited as part of an ongoing trial in secondary care, and were assessed with the Mini-International Neuropsychiatric Interview (MINI), which is a short structured diagnostic interview for DSM-IV and ICD-10 psychiatric disorders.

Point prevalence of psychiatric disorders was 30%. The diagnoses included 19 Axis I disorders, with the most common being somatoform disorders (17%) and anxiety disorders (11%). Major depressive disorders were reported in 4%. There were no gender differences in prevalence of psychiatric disorders.

A point prevalence of 30% is less than reported from previous studies of psychiatric comorbidity in CLBP (Atkinson, Slater, Patterson, Grant, & Garfin, 1991; Dersh, Gatchel, Mayer, Polatin, & Temple, 2006; Kinney, Gatchel, Polatin, Fogarty, & Mayer, 1993; Polatin, Kinney, Gatchel, Lillo, & Mayer, 1993; Reich, Tupin, & Abramowitz, 1983). The difference could be a result of different compensational systems, different settings were the interviews were conducted, or different characteristics of the populations in the comparative studies. Despite lower prevalence than similar studies, our findings still show that CLBP patients present

with more psychiatric disorders than the general population (Alonso et al., 2004; Bijl, Ravelli, & van Zessen, 1998; Regier et al., 1988). The results further demonstrated that the diagnoses included a wide range of psychiatric disorders. Screening LBP patients for psychiatric disorders in secondary care is therefore important since psychopathology may have serious consequences for prognosis and treatment outcome in CLBP (Airaksinen, et al., 2006; Dersh, et al., 2007; Linton, 2000b).

3.2. Expectations, perceptions and physiotherapy predict prolonged sick leave in chronic low back pain

Research question 2: What factors predict treatment outcome in chronic low back pain (CLBP) after a brief cognitive intervention?

Brief intervention programs for subacute/chronic LBP result in significant reduction of sick leave compared to treatment as usual (Hagen, Grasdal, & Eriksen, 2003; Indahl, et al., 1998). Although effective, a substantial proportion of the patients do not return to work. This study investigates predictors of return to work in CLBP patients participating in a randomized controlled trial comparing a brief cognitive intervention (BI) with BI and physical exercise.

Predictors for not returning to work were examined in 246 patients sick listed 8–12 weeks for LBP. The patients had participated in a randomized controlled trial, with BI (n=122) and BI + physical exercise (n=124). There were no significant differences between the two intervention groups on return to work. The groups were therefore merged in the analyses of predictors. Multiple logistic regression analysis was used to identify predictors for non return to work at 3, 12, and 24 months of follow-up.

At 3 months of follow-up, the strongest predictors for not returning to work were pain intensity while resting (OR=5.6; CI=1.7-19), the perception of constant back strain when working (OR = 4.1; CI=1.5-12), negative expectations for return to work (OR=4.2; CI=1.7-10), and having been to a physiotherapist prior to participation in the trial (OR=3.3; CI=1.3-8.3). At 12 months, perceived reduced ability to walk far

due to the complaints (OR=2.6; CI=1.3-5.4), pain during activities (OR=2.4; CI=1.1-5.1), and having been to a physiotherapist prior to participation in the trial (OR=2.1; CI=1.1-4.3) were the strongest predictors for non return to work. Age below 41 years (OR=2.9; CI=1.4-6.0) was the only significant predictor for non return to work at 24 months.

It appears that return to work is highly dependant on individual and cognitive factors. Patients with a poor treatment outcome were characterized by negative expectations, perceptions about pain and disability, and previous physiotherapy treatment.

3.3. Predictors of treatment outcome in patients with irritable bowel syndrome; a randomized controlled trial from primary care

Research question 3: What factors predict treatment outcome in IBS after a cognitive behavioural therapy?

Few studies have looked specifically at predictors of treatment outcome after cognitive behavioural treatments for IBS. Predictors of treatment outcome were therefore investigated in IBS-patients who participated in a randomized controlled trial in primary care. 149 IBS-patients were randomised to mebeverine hydrochloride (n=77) or mebeverine + cognitive behaviour therapy (CBT) (n=72). CBT offered additional benefit over mebeverine alone (Kennedy, et al., 2005).

Regression analyses were used to identify predictors of work and social adjustment (WASA) 12 months after treatment ended. The intervention groups were analysed separately in order to look at the separate effects in each group. Lower levels of psychological distress (anxiety and depression) at baseline predicted a good outcome in the mebeverine group (β =0.388 (95%CI: 0.07-0.94), p-value=0.03) but not in the mebeverine+CBT group. In the adjusted model for the mebeverine+CBT group less adaptive IBS related behavioural coping predicted a good outcome (β =0.285 (95%CI: 0.01-0.21), p-value=<0.05).

The clinical implications of the results could involve recommending CBT to those patients with IBS in primary care who are engaging in unhelpful coping behaviour.

4. Discussion

4.1. Paper 1

Research question: What is the prevalence of psychiatric comorbidity in chronic low back pain patients?

In this thesis sensitization was suggested to be the psychobiological mechanism explaining differences in individual health (Ursin, 1997). It was hypothesized that given the general nature of sensitization proposed by previous literature (e.g. Bell, 1994; Bell, et al., 1992) and the CATS position (Ursin & Eriksen, 2004), the prevalence of psychiatric comorbidity would be high in chronic low back pain (CLBP) patients. The aim of paper 1 was to investigate the full spectre of psychiatric disorders (Axis I disorders) in CLBP patients on long term sick leave due to LBP.

Previous findings have shown a high degree of comorbid psychopathology in CLBP, but less is known about the broad range of comorbid psychiatric disorders. Measurement methods used in previous studies vary in terms of quality, and the current study therefore included both questionnaire data and a diagnostic interview considered to be the gold standard for assessing psychiatric disorders (Sheehan et al., 1998). Results from the questionnaire data showed that a large proportion of the CLBP patients reported symptoms of depression and anxiety, while diagnostic interview data showed that almost a third qualified for at least one ongoing psychiatric disorder with a whole range of psychiatric disorders present. Besides psychiatric disorders, there were also a high degree of comorbid health complaints. With only a few exceptions, all patients presented additional health complaints beside LBP, and over a third reported that pain was not currently their main problem. This strengthens the previously proposed hypothesis of generalised sensitization where some individuals get more sensitive than others to a wide variety of stimuli, resulting in the high comorbidity seen in our results. It further implies the usefulness of CBT treatments where cognitive and behavioural factors are changed and strategies are

developed for dealing with other factors (e.g. physical, emotional, social or financial) impacting on the condition as well.

The CBT model distinguishes between predisposing, precipitating and perpetuating factors (Beck, 1976). For the CLBP patient predisposing factors might involve an anxious personality or a genetic disposition for back pain, precipitating factors might be a heavy lift or a muscle cramp, while perpetuating factors might be fear-related cognitions and avoidance. The model assumes that physiological (pain), cognitive (fear of engaging in activity) and behavioural responses (avoidance of activity), are linked. Therefore, by modifying one response it is anticipated that changes occur in the other responses. For example, increasing activity (behaviour) may gradually reduce the fear (cognitions) that activity leads to worsening of pain, or challenging and changing dysfunctional beliefs about pain and disability (cognitions) may lead to less anxiety (emotions) and less disability (physiology). The results from paper 1 showed that anxiety disorders were twice as prevalent than depressive disorders, confirming the importance of fear and pain in CLBP, also proposed by others (Vlaeyen, Kole-Snijders, Boeren, & van Eek, 1995). This could result in vicious circles of fear, avoidance, and pain, where low coping and sensitization capture the patients and make them unable to break out of the debilitating circles. The high comorbidity seen in paper I supports the hypothesis of a generalized sensitization where some individuals get more sensitive than others to a wide range of stimuli (Bell, 1994; Bell, et al., 1992; Ursin, 1997). The results further indicate the need for treatments such as CBT in order to break the vicious circles.

4.2. Paper 2

Research question: What factors predict treatment outcome in CLBP after a brief cognitive intervention?

The aim of CBT treatments is to change the behavioural and cognitive factors which are assumed to be partially responsible for perpetuating the participant's complaints

and disability. This is also the aim of the Brief cognitive Intervention (BI) for CLBP, where unhelpful and catastrophic cognitions about the meaning of pain and complaints are challenged and tried changed into more helpful cognitions (Indahl, et al., 1998). In support of the CBT-model, such treatments have proven to be successful in contributing to returning sick listed CLBP patients back to work (Brox et al., 2006; Hagen, et al., 2000; Hagen, et al., 2003; Indahl, et al., 1998; Indahl, Velund, & Reikeraas, 1995). Despite the good results, a substantial proportion of the patients do not return to work. In paper 2 we investigated predictors of not returning to work in order to gain further insight into risk factors for prolongation of sick leave due to LBP. CATS emphasizes the importance of stimulus and response outcome expectancies for the development of chronic and debilitating subjective health complaints (Ursin & Eriksen, 2004). It was therefore hypothesized that a wide range of psychological, cognitive and social factors would predict treatment outcome based on the effect of these factors for the learning of coping, helplessness and hopelessness (Ursin & Eriksen, 2004). The results confirmed the significance of cognitive factors such as expectations and perceptions as predictors for treatment outcome. The cognitive factors were stronger predictors than psychological, social and demographic factors. In line with the CBT-model the cognitive factors could be understood in terms of dysfunctional beliefs which again might have been strengthened by previous physiotherapists.

The patients' expectation of return to work is particularly interesting. Recovery expectations and intentions have previously been found to be highly associated with RTW and reductions in pain and disability (Cole, et al., 2002; Fishbain, et al., 1997; Haldorsen, Kronholm, et al., 1998; Hildebrandt, et al., 1997; Sandstrom & Esbjornsson, 1986). This is in line with the theoretical framework of the thesis. According to CATS, acquired expectations of own abilities to cope are crucial for health outcomes (Ursin & Eriksen, 2004). More specifically, if the LBP patient has learned that no matter what he or she does, there will be no change in the condition, or all attempts lead to even worse outcomes, the patient has a negative response outcome expectancy (Reme, Hagen, & Eriksen, 2009). The negative response

outcome expectancy may cause sustained arousal which could lead to negative health consequences through for example sensitization (Eriksen & Ursin, 2004; Ursin & Eriksen, 2001). The result of this for the patient might be a vicious circle, with negative expectations, sensitization, more pain, and no return to work (Reme, et al., 2009). The BI might have been too brief and insufficient to be able to challenge and change the negative expectations and thereby breaking the vicious circle in all the CLBP patients. A more extensive CBT tailored for CLBP (e.g. Reme & Chalder, 2007) could be effective for those not returning to work after BI, with its focus on interpretation of pain and associated fear, symptom focusing and avoidance. This is currently being followed up in a multicenter RCT where CBT is given in addition to BI and compared to BI only and nutritional supplement in a double blind design.

4.3. Paper 3

Research question: What factors predict treatment outcome in IBS after a cognitive behavioural therapy?

CBT is now a well established treatment for another patient group that shares many similarities with LBP, namely irritable bowel syndrome (IBS). In the third and final paper of the thesis, a similar methodology as applied in study 2 was applied on a group of IBS patients. Predictors of treatment outcome were investigated after a RCT where CBT showed additional effects to antispasmodic treatment for IBS patients in primary care. As with LBP, IBS might be triggered by specific or unspecific factors such as a severe bout of diarrhoea or stress, but maintained and intensified by cognitive, behavioural and emotional responses. Interpretation of abdominal discomfort as threatening is likely to lead to actions such as frequent visits to the doctor, and increased attention to bodily sensations. In addition, other unhelpful behavioural coping strategies may be initiated and increased by physiological arousal and anxiety. This further leads to the experience of symptoms as more intense and noxious which is again interpreted as threatening, resulting in a vicious circle of fear and avoidant coping in the long term. The CBT treatment,

therefore, was aiming at changing the unhelpful avoidance and control behaviour, as well as changing the unhelpful cognitions in the IBS patients (Kennedy, et al., 2005). According to CATS, an individual trapped in a vicious circle of helplessness or hopelessness needs to change the negative response outcome expectancies in order to break out of the circle and experience coping (Ursin & Eriksen, 2004). Response outcome expectancies are changed through new learning experiences. The behavioural part of the CBT is therefore crucial in that it exposes the individual to feared situations and actions where new learning can happen. When the IBS patient, for instance, stops avoiding a social situation and experience that no IBS-related embarrassing accidents occur, the individual will probably experience coping which most likely leads to changed cognitions about social situations and IBS-related accidents. In agreement with the theory, the results from study 3 showed that poor behavioural coping was a significant predictor of a good outcome in the CBT group. IBS patients that were engaging in unhelpful behaviour at baseline, such as avoidance and control behaviour, were most likely to profit from the CBT treatment. The results from paper 3 thus indicates that IBS patients presenting with poor behavioural coping in primary care should be recommended CBT. Behavioural coping was measured through a newly developed scale which could be used in future research trials and clinical settings, for instance by general practitioners when deciding which IBS patients that should be recommended CBT (Reme, Darnley, Kennedy, & Chalder, 2010a).

Another study from the same trial provides further confirmation of the theoretical framework, where behaviour and cognitions were found to mediate the change in the CBT treatment (Reme et al., 2010b). The mediational path for all three outcomes went through change in behaviour, then change in cognitions, before the change in the outcomes. As outlined above, this indicates that when the IBS patient experiences a change in behaviour (e.g. stop avoiding and controlling), the change is followed by a change in cognitions (e.g. less catastrophic beliefs) which again results in reduced symptoms, reduced anxiety and improved function.

5. Conclusions

It was hypothesized that a generalized sensitization in chronic low back paint patients (CLBP) would imply high comorbidity, including psychiatric comorbidity. Paper 1 found support for this hypothesis by showing more psychiatric disorders than in the general population, with a broad range of psychiatric disorders detected in the CLBP patients. It was further hypothesized that the generalized sensitization with the corresponding high comorbidity would result in vicious circles. In paper 2, the significance of cognitive factors was emphasized for treatment outcome in CLBP, indicating that changed cognitions is crucial in order to break out of the vicious circles. Finally, it was hypothesized that cognitive behavioural treatments aiming at changing cognitive and behavioural factors would be successful, and that these factors would predict treatment outcome. This was supported in paper 3 where behavioural factors were found to predict treatment success in a tailored cognitive behavioural therapy for IBS patients.

In conclusion, the thesis supports the theoretical position of CATS (Cognitive Activation Theory of Stress) in the understanding of CLBP and IBS, which is in line with the CBT model for treating CLBP and IBS. More specifically, psychological, cognitive and behavioural factors all appeared to be vital parts of the disorders, while cognitive and behavioural factors were crucial for treatment outcome.

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