

Understanding Comorbid Pain and Emotions

To Del

Örebro Studies in Psychology 40



MATILDA WURM

**Understanding Comorbid Pain and Emotions
A transdiagnostic approach**

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Title: Understanding Comorbid Pain and Emotions:
A transdiagnostic approach.

Publisher: Örebro University 2018
www.oru.se/publikationer-avhandlingar

Print: Örebro University, Repro 08/18

ISSN 1651-1328
ISBN 978-91-7529-250-2

Abstract

Matilda Wurm (2018): Understanding Comorbid Pain and Emotions: A transdiagnostic approach. Örebro Studies in Psychology 40.

Experiencing pain, including an emotional reaction, is part of being human. Emotional comorbidity is common in pain patients, and correlated to higher symptomatology and worse treatment outcome. The shared vulnerability model suggests that many vulnerability and maintaining factors may be involved in both pain and emotional problems. Hence, they may be transdiagnostic. Since our knowledge about these shared factors is lacking, potential targets for risk assessment, prevention, and treatment are likely underutilized. The overarching aim of this dissertation was to further our understanding of comorbid musculoskeletal pain and emotional problems by investigating the role of transdiagnostic factors. Specifically, it was studied if levels of shared vulnerabilities (negative affect and anxiety sensitivity) and symptomatology covary in pain patients depending on the occurrence of comorbid social anxiety symptoms (Study I); if peer-related stress predicts musculoskeletal pain problems over time in adolescents, and if this is mediated by worry and moderated by gender (Study II); and if symptomatology can be decreased in pain patients with comorbid emotional problems by using an internet delivered unified protocol for emotional disorders (Study III). Results show that vulnerabilities covaried with comorbid pain and social anxiety. Also, peer-related stress predicted musculoskeletal pain problems in adolescents and was mediated by worry for girls. However, the internet-delivered unified protocol did not unequivocally decrease symptomatology. In sum, the studies in this dissertation provide partial support for the role of transdiagnostic factors in comorbid musculoskeletal pain and emotional problems. A transdiagnostic approach may offer a parsimonious understanding of the development and maintenance of this comorbid symptomatology.

Keywords: Transdiagnostic approach, musculoskeletal pain, emotions, comorbidity, shared vulnerability model, social factors, gender

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Acknowledgements

These last years have been a learning process on many levels. It has been both better and worse than I expected, and maybe it is simply difficult to prepare for what doing a PhD entails. Nevertheless, I've learned a lot, both expected and unexpected things. Since learning is important to me in life, I cannot be anything but happy with the outcome. Naturally, this project would not have been possible on my own.

First of all, I want to thank all the participants in my studies for filling in questionnaires, and the pain clinics and schools that participated in recruitment and data collection. There are also several people I want to thank:

Katja Boersma, my main supervisor. I was on my way to the States for a few months with a newborn baby and had just decided not to apply for a PhD-position when I found out that you would be the main supervisor for the new position at CHAMP. That made it impossible to resist. You have, not surprisingly, influenced me more than anybody else in my approach to research. For this, I count myself lucky! Now, at the end of my time as a PhD-fellow, I am very grateful that you, of all seniors possible, became my main supervisor. Thank you for your availability, for helping me keep my focus, for all the knowledge you've shared and for your understanding of life's interferences. I hope I'll be like you when I grow up.

Maria Tillfors, my second supervisor. Thank you for providing the overlap between pain and social aspects, which I have enjoyed. I will always be amazed by your dedication, your fast reading skills and your eye for detail. Thank you also for regularly checking in on stress levels, for bus trips to Uppsala, and for your unpretentious companionship. I have enjoyed working with you!

Steven Linton for planting an important seed by urging me to apply for a PhD-position and apparently, to my surprise, noticing me through graduate training.

Annika Norell-Clarke and Rikard Wicksell for encouragement and valuable feedback at my half-time seminar.

Besides teaching me new skills, this PhD journey has also connected me to several people that I have grown to love and rely on. I will be forever grateful that I was not alone on this journey and I hope you will stick around!

Mika, thank you for your friendship and availability in moments of need, for your big heart and intelligence. I fell in love with you during psychology training and I'm happy that research and publishing started with you. The beginning of this journey would not have been the same without you.

Johan, thank you for giving me an excellent start. I enjoy your mind that lets us discuss a large variety of things, not all pain-full (sorry, I had to). I'm hoping for more game-nights, conversations and generally more time spent together (if your kids ever manage to stay snot free long enough)!

Sara for sharing your choir with me, being an excellent room-mate and co-author and always available for questions. Also (probably unbeknownst to you) for teaching me an important lesson about kindness when I needed it. Sofia for being a true friend and savior and providing support in times of need, for shared politics and interests. Having you around means a lot and work would not be the same without you. I hope to be able to spend more time with you at some point! When we retire, perhaps?

Malin, you have an excellent brain for research and often provide answers when I need them, not least about statistical models or (naturally) stress. I'd co-author with you again anytime! You have also provided a shoulder to cry on and an ear when I've needed to vent. Life as a PhD-student would have been harder without you! I am particularly glad to share memories of rainforests, coral reefs, and cable railways with you.

Serena, you are (almost) the odd one out as you are one of the few who had a baby after *finishing* your PhD. That also means that you have pretty much always been around. I enjoy what we share when it comes to environmental issues and the longing for the country-side. One day, it will happen!

There are many more PhD students that have accompanied me on parts of the way. With many of you, I have shared moments and/or see potential for the future, so thank you: Annika, Elin, Linnea, Tor, Farzaneh (we have to meet up in our yards soon), Niloufar, Shane, Nanette, Vivi, Delia, Darun.

Co-authors not mentioned previously:

Lia Ahonen, for being who you are and making our Masters' thesis a great experience.

Malin Olofsson, for whipping up articles and letting me contribute.

Ester Klein Strandberg & Caroline Lorenz for your companionship and hard work with the data-collection for Study III.

Monica Buhrman for all the days crushing numbers in Uppsala, and, together with Fredrik Holländare for assistance and cooperation on the SÅS-project resulting in Study I and III.

Tove Lundberg and Anna Malmquist for the amazing journey we did together. Is it smart to edit a book while doing a PhD, someone might wonder? No, not really, but working with you on the book was a real pleasure and made a project that could have been really hard to pull off doable. I am impressed by your skills and your minds and I'm happy to call you friends!

Ida Flink, for reminding me what I learned during the courses on academic writing and for the help in getting Study II in shape.

I also want to thank everybody at the psychology department, especially Selma, our current head of department. You make a big difference for the work environment, and being a boss really suits you.

Everybody at CHAMP, for creating a welcoming and inspiring research environment that I would be happy to stay in a while longer.

Corona and Katarina for keeping me sane on the way and for giving me the opportunity to regularly do something I truly love.

Peter and Margareta, my parents and first psychologists, even though one of you was never formally trained. For a long time, I would have laughed out loud if anyone would have told me I'd become a psychologist, even though I had, at an early age, worked myself through bookshelves of psychological literature, and (in hindsight) showed many of the signs. Life surely works in surprising and unpredictable ways. Thank you for your contributions to who I am and where I am today. I am content.

Del. I don't even know where to begin. Thank you for keeping life interesting! Thank you for the network you've provided and for teaching me to go out and network myself. Thank you for endless hours of ground service, thousands of cooked meals and for being such a fantastic Mapa to our kids. Without you, and the feeling that Mika and Nico were getting the best care with or without me around, this dissertation would have been hard to pull off. Thank you also for believing in me and for enjoying my successes and giving me the space to travel and work, even if it meant spending vacations alone with the kids (sometimes with my parents!). Thank you for proof-reading texts you had a hard time to follow and that you were not always given a lot of notice to complete. I love and admire you and I'm proud to be with you. I'm very much looking forward to spending some post-PhD time with you.

Mika and Nico. Where do I even find the words to tell you what you mean to me? How I longed for you! This process, like the rest of life, would have been very different without you. Thank you for forcing me to come home, reminding me to stop working and to concentrate on what really matters in life: Playing with you, seeing you develop, and being the best I can for you. You are the best thing that ever happened to me and I am so proud of you both.

List of studies

This dissertation is built upon three studies, which will be referred to by their roman numbers I-III.

- Study I: Wurm, M., Edlund, S., Tillfors, M., & Boersma, K. (2016). Characteristics and consequences of the co-occurrence between social anxiety and pain-related fear in chronic pain patients receiving multimodal pain rehabilitation. *Scandinavian journal of pain*, 12 (2016) 45-52.
- Study II: Wurm, M., Flink, I., Anniko, M., Tillfors, M., & Boersma, K. (submitted). Musculoskeletal pain in adolescents: Prevalence, and the role of peer-related stress, worry, and gender in the development of pain problems over time. *Journal of Psychosomatic Research*. Invited to revise.
- Study III: Wurm, M. Klein Strandberg, E., Lorenz, C., Tillfors, M., Buhrman, M., Holländare, F., & Boersma, K. (2017). Internet delivered transdiagnostic treatment with telephone support for pain patients with emotional comorbidity: a replicated single case study. *Internet Interventions* 10 (2017) 54-64.

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Introduction

Humans are intimately familiar with the experience of pain, which is a complex experience including physical reactions, thoughts, and emotions. In fact, pain is the most common reason for seeking help in primary care and is often accompanied by psychiatric problems (Kallionien, Bernhardsson, Grohp, Lisspers, & Sundin, 2010). Despite the fact that pain is a common human experience, we lack a sufficiently detailed understanding of the multiple factors influencing the development and maintenance of pain problems or how to treat them.

During the last decades, practitioners and researchers have increasingly agreed on a biopsychosocial understanding of pain. In fact, it has been firmly established that psychological factors are central to the understanding of a pain experience (Karos, 2017; Linton, 2013b; Linton & Shaw, 2011). For example, pain related fear and fear avoidance have been shown to influence the development from acute to chronic pain (Crombez, Vlaeyen, Heuts, & Lysens, 1999; Vlaeyen & Linton, 2012; Westman, Boersma, Leppert, & Linton, 2011). However, people in pain have to be understood as a heterogeneous group and several studies have confirmed the existence of subgroups in pain populations (Bergbom, Boersma, Overmeer, & Linton, 2011; Boersma & Linton, 2006; Hirsch et al., 2014). One subgroup of people with pain problems that emerges consists of those with comorbid emotional problems. There is a need to expand our knowledge about factors that can be important in understanding the relationship between pain and emotion and also about how these factors interact within the individual.

Comorbidities between pain problems and emotional problems, such as anxiety and depression, are common. Individuals with these comorbidities generally report additional problems, such as higher disability, worse treatment outcome, and lower return to work (Castro et al., 2009; Demyttenaere et al., 2007; Lerman, Rudich, Brill, Shalev, & Shahar, 2015). One way of understanding the co-occurrence between comorbid pain and emotional problems is to use a theoretical approach applicable across diagnoses. One model with such a transdiagnostic approach is the shared vulnerability model (Asmundson & Katz, 2009). It proposes that shared predisposing and maintaining factors could explain the development and maintenance of comorbid pain and emotional symptoms. The model is appealing in the understanding of comorbid pain and emotional problems

and is valuable for the development of treatments. However, more research is needed to establish its validity.

This dissertation sets out to further our understanding of the underlying factors implicated in the development, maintenance, and treatment of pain problems with a main focus on comorbid pain and emotional problems, using the shared vulnerability model as a framework. The dissertation is based on three studies, which will be presented using the Roman numerals I-III.

The psychological study of pain

History

Historically, Descartes proposed that tissue damage excites pain fibers that lead directly to the brain where a pain sensation is produced (Descartes, 1644). Hence, for a long time, pain was understood as a sensation caused by tissue damage, that is, a simple matter of cause and effect involving specialized nerve fibers and pain areas in the brain.

In the 1960s, Melzack and Wall (1965) presented a new theory that included psychological aspects and challenged theories of specificity (that is, the existence of specific pain receptors). Their gate control theory proposed the involvement and interaction of several neural systems modulating the effect of arriving impulses. Impulses could, but did not have to, be caused by tissue damage. Pain perception was believed to be influenced by numerous feedback loops and dependent on, among others, attentional and emotional as well as cognitive-evaluative processes. These were, in turn, believed to be influenced by genetic predispositions, but also by previous experiences. Thus, the gate control theory highlighted the importance of psychological factors in the experience of pain. It succeeded in explaining how pain can be experienced without the presence of tissue damage (or even without the presence of a hurting limb, such as in phantom pain) as well as how sometimes no pain is experienced despite severe tissue damage. The gate-control theory has since been discussed and confirmed in numerous studies (for a brief summary, see Dickenson, 2002).

Melzack (1999) later expanded on the gate control theory, mainly by proposing the existence of a “body-self neuromatrix”, a complex neural network forming our sense of self. He differentiated this sense of self from our physical body and argued that it could be experienced without actual inputs from the body. This would make it a central agent in the experience of pain since pain perception is dependent on the interpretation of a vast

number of stimuli. He proposed the neuromatrix to be influenced by genetic predispositions and sensory input, but also by cognitive interpretation and emotional inputs. Moreover, he highlighted the important contribution of stress on the development of pain problems. Hence, Melzack presented pain as a multidimensional experience and the perception of pain as dependent on how the neural networks in the brain interpret, and are shaped by, diverse stimuli and experiences.

The last decades have further explored cortical changes in the context of pain, underlining the distinction between nociception and pain. For example, it has been shown that persistent pain leads to a sensitization of specific neural networks involved in the experience of pain (Moseley & Flor, 2012). This central sensitization is adaptive and can assist with tissue healing, but can also lead to prolonged problems, since stimuli reaching the brain may be interpreted as potentially dangerous and can elicit pain, even when no nociception is present. Hence, people may experience pain simply because there is a perceived risk of physical injury, unrelated to the actual risk.

Clearly, pain problems are complex and dependent on more than just biological factors. Simple cause–effect models have also been disconfirmed by showing that the level of disability differs significantly for people with similar levels of pain intensity or physical abnormalities, such as bulging discs (Brinjikji et al., 2015; Crombez et al., 1999). In addition, our knowledge about psychological factors in pain has been expanded (Crombez et al., 1999; Severeijns, Vlaeyen, Van den Hout, & Weber, 2001). Today, a biopsychosocial model is generally agreed upon (Gatchel, Peng, Peters, Fuchs, & Turk, 2007).

Definition of pain terms

Pain is a complex biopsychosocial phenomenon. The International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Merskey & Bogduk, 1994). A cognitive-evaluative component is also included in the definition, since tissue damage may not necessarily be present, but the stimulus may be interpreted as connected to such damage by the person experiencing the pain. For example, pain catastrophizing has been found to be an important determinant of the pain experience, increasing it, even in the absence of tissue damage (Flink, 2011). These emotional and cognitive factors are

involved in both short-term, sudden pain experiences and those that persist over a longer period of time.

Pain experiences are typically specified as being either acute or chronic. Chronic pain is generally defined as pain that persists beyond a certain point in time (usually 3 months), when potential tissue damage should have healed (Turk & Okifuji, 2001). However, the onset of pain problems is often hard to establish and many people experience pain that is not present all the time, but reoccurs regularly over many years (Nicholas, Linton, Watson, & Main, 2011). In these cases, chronic pain may be defined as pain occurring regularly over a period of 6 months (Krismer & Van Tulder, 2007). In this dissertation, chronic pain is defined as lasting longer than 3 months (Merskey & Bogduk, 1994).

The study of pain is often divided up into its purported causes (such as cancer-related pain, or inflammatory diseases) or, when the causes are obscure, by location (headache, abdominal pain, back pain). This dissertation primarily uses location as the commonality and will specifically focus on musculoskeletal pain. Musculoskeletal pain is defined as pain in the muscles, ligaments, tendons, and bones. It is often non-specific, that is, no physical cause for the pain can be established. For example, in low back pain, only about 5–10% of cases can be explained by specific tissue damage or physical changes (Krismer & Van Tulder, 2007). This does not imply that the pain is not real. However, it highlights the complexity of understanding pain and the importance of psychological factors.

The term “pain problem” is used throughout this dissertation, which is defined as pain that leads to suffering and some functional impairment in everyday life. This is in line with the World Health Organization (WHO)’s International Classification of Functioning, Disability and Health (World Health Organization, 2001). The WHO states that functional impairment may include the inability to perform certain movements, as well as avoidance behaviors, and a limitation of activities due to fear of pain. In this dissertation, in contrast to a more biomedical approach, functional impairment is understood as related not only to pain intensity or tissue damage, but also to psychological factors. This is based on, for example, studies showing that pain-related fear is a better predictor of functioning than pain intensity, and that people reporting the same pain intensity may have different levels of pain functioning (Crombez et al., 1999; Krismer & Van Tulder, 2007). Hence, functional impairment is dependent on pain coping. If a person copes with pain adaptively and is able to live life in a,

for the individual, satisfactory and meaningful manner, we may not consider this person to have a pain problem, despite the presence of pain.

In summary, pain is a multifaceted experience, dependent on a variety of emotional and cognitive-evaluative factors. How these factors interact will influence the development and maintenance of pain in an individual. Since experiencing pain is part of being human, a better understanding of pain problems could potentially make a great difference for the lives of individual people in pain and for society as a whole.

Epidemiology

Many people experience chronic pain. For example, chronic low back pain is reported by about half of the population at some point in their lives (for a review, see McBeth & Jones, 2007). A European review estimated a point prevalence of any chronic pain of 17.1% (Reid et al., 2011). This is comparable to a large survey study conducted in 15 European countries and Israel (N = 46,394) with a point prevalence of chronic pain lasting longer than 6 months of 19% (range in the separate countries: 12–30%) (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006). In the case of chronic musculoskeletal pain, prevalence numbers vary, depending on the operationalization of pain and the samples used (Steingrimsdóttir, Landmark, Macfarlane, & Nielsen, 2017). For example, one study in 35,550 European workers found a 1-year prevalence of 46.1% for back pain and 44.6% for pain in the neck/upper extremities, with large variations between countries and professions (Farioli et al., 2014). In adolescents, pain problems are also remarkably prevalent, but, again, vary depending on operationalization. For example, a review reported the prevalence of back pain as being between 8% and 44% (McBeth & Jones, 2007).

For the individual, pain can mean a limitation of activities, such as lower participation in work and social activities. This can have financial consequences, but can also influence feelings of self-worth (Banks & Kerns, 1996; Morley, Davies, & Barton, 2005). Additionally, pain problems are a strain to society in terms of health care costs and benefit payments, which can amount to between €2,000 and almost €10,000 per year and person, according to a European review (Leadley, Armstrong, Lee, Allen, & Kleijnen, 2012).

Generally, prevalence increases with age and is higher in women and girls. Women are overrepresented in clinical settings and report more health problems in the general population, both in adolescent and grown-up populations (King et al., 2011; Tsang et al., 2008). Therefore, it is important

to take gender into account when studying pain problems. This dissertation analyzes the role of gender in Study II, where gender is investigated as a moderator in the development of pain problems.

In sum, pain problems are a strain to the individual and to society as a whole, which stresses the importance to further our knowledge about factors influencing the development and maintenance of pain.

Theoretical framework

Pain psychology

Pain is still understood as a mostly physical phenomenon by most lay people, many patients, and some professionals. When we go beyond physical aspects of pain, we immediately add complexity, but we also access new possibilities of understanding a pain experience. It is apparent from IASP's definition that the experience of pain is closely intertwined with the area of psychology. Important attempts have been made to organize the complexity that ensues when psychological factors are included in the understanding of a pain experience and the development of pain problems. This has led to the formation of a whole area of research: the area of pain psychology.

Today, pain psychology is firmly situated within a biopsychosocial understanding of pain. In a review, a biopsychosocial model of pain is presented as including biological and somatic processes, with feedback loops to and from autonomic, endocrine, and immune systems (Gatchel et al., 2007). Psychological aspects include cognitive and emotional processes that are connected to biological aspects, such as the endocrine system. Both biological and psychological factors are influenced by genetics. Social aspects include, among others, our sociocultural surroundings, family environment, and interpersonal relationships. This dissertation focuses on psychological and social factors, understanding that there is a bidirectional influence between these factors and biological aspects mentioned in the biopsychosocial model of pain.

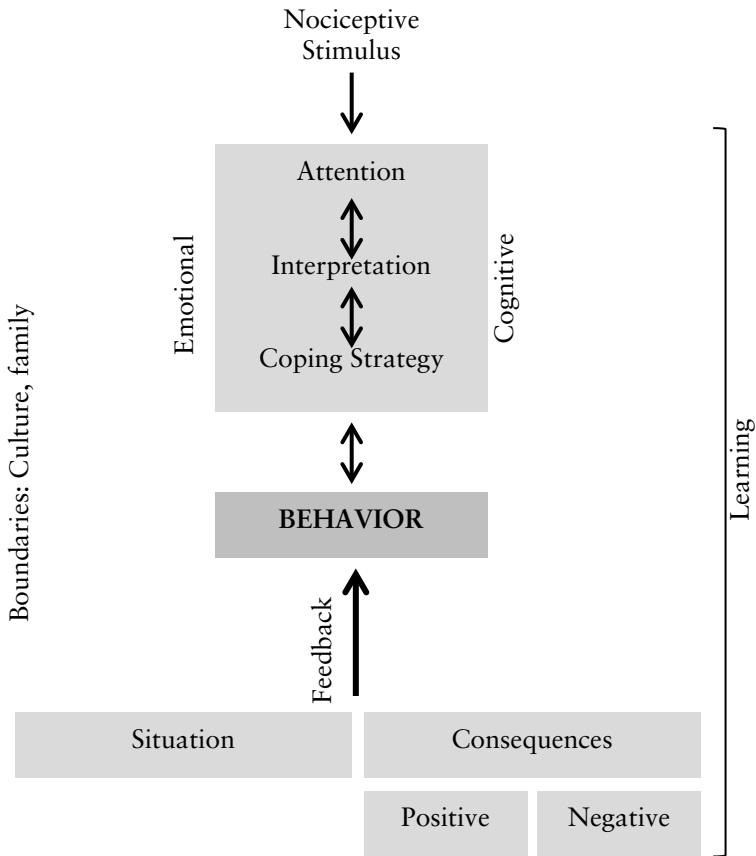


Figure 1. A modern view of pain perception from a psychological perspective. (Linton, 2005, 2013a).

One example of an integrated model of the psychology of pain has been presented by Linton (2005, 2013a). The model is generic and depicts a normal pain process that is applicable to both acute and chronic pain. In the model, shown in Figure 1, the process starts with a nociceptive stimulus, potentially, but not necessarily, dependent on tissue damage. This nociceptive stimulus first has to be noticed in the array of stimuli reaching our brain. Since noticing pain is often crucial for our survival, in most situations attention will be diverted to the pain stimulus if it is novel or strong enough. Next, the stimulus is interpreted, involving both cognitive

and emotional processes, and, taking into consideration available coping strategies, a decision is made on how to react to it. Coping strategies are here understood as a person's efforts to handle the painful experience. Depending on the consequences following the behavior, it will be more or less likely to be repeated in the future: learning occurs. This whole process is framed by cultural or situational conditions, which may influence and limit potential reactions. For example, some pain behaviors, such as collapsing on the floor, may be deemed inappropriate. Also, a person's pain behavior can look very different when surrounded by family, where help may be elicited, compared to when alone. For most people, the experience of pain results in quick recovery, but a minority never completely recover.

This generic model can provide a basis for explaining individual differences. Here, in the normal perception of pain, different outcomes are possible, depending on how a person reacts to nociception. For example, an attentional bias towards potentially painful stimuli can lead to hypervigilance, where a person will start to detect increasingly weaker stimuli and interpret them as dangerous. A negative interpretation of a painful stimulus as dangerous may cause a strong emotional reaction, which can lead to protective and, possibly, maladaptive strategies, such as avoidance. Negative reinforcement may also lead a person with pain to repeat behaviors that result in a decrease in pain intensity in the short term, but have long-term negative consequences. These reactions have been found to be quite characteristic of people with long-term pain problems which has led researchers to develop a more specific application of the generic model of pain psychology: the fear-avoidance model (Lethem, Slade, Troup, & Bentley, 1983; Vlaeyen & Linton, 2000).

The fear-avoidance model, presented in Figure 2, was proposed almost two decades ago and depicts how someone with a catastrophic interpretation of a painful experience can develop pain-related fear, which leads to the avoidance of potentially painful stimuli. Avoidance behaviors may, in turn, lead to the development of chronic pain and disability (Crombez, Eccleston, Van Damme, Vlaeyen, & Karoly, 2012; Vlaeyen & Linton, 2000). The basic tenets of the fear-avoidance model have been firmly established in a large number of empirical studies on the subject. For example, a meta-analysis of 46 independent samples found moderate to large positive correlations between pain-related fear and disability (Zale, Lange, Fields, & Ditre, 2013). Also, the specific construct "pain catastrophizing", a central aspect of the model, has been extensively studied

and confirmed as an important factor in the development of chronic pain and functional impairment (Quartana, Campbell, & Edwards, 2009).

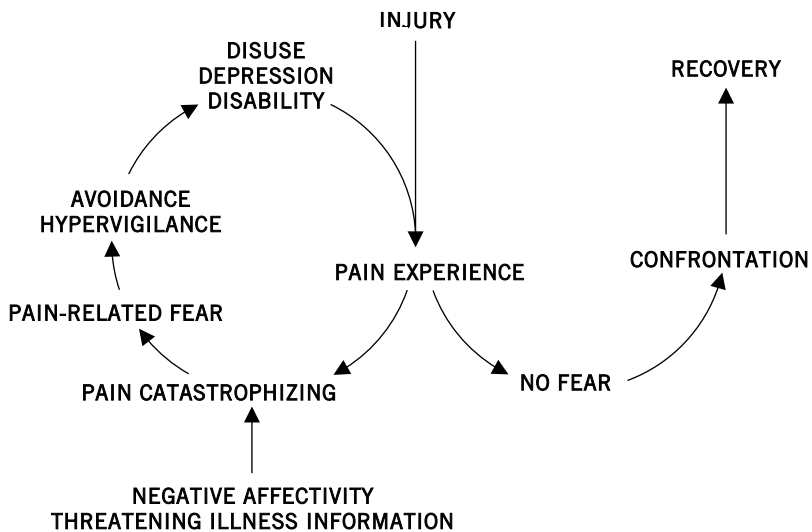


Figure 2. The fear avoidance model of pain (Vlaeyen & Linton, 2000).

Pain catastrophizing is defined as an “exaggerated negative mental set brought to bear during actual or anticipated pain experience” (Sullivan et al., 2001). However, in line with the literature in clinical psychology, pain catastrophizing has recently been argued to show great similarity to worry and rumination (Flink, Boersma, & Linton, 2013). It was proposed that pain catastrophizing overlaps with worry and rumination and that these cognitive processes share the core purpose of being problem solving attempts to downregulate negative affect. As a result, catastrophizing, worry, and rumination can be viewed and studied as transdiagnostic factors, which opens up new perspectives and aligns pain catastrophizing, worry, and rumination as forms of repetitive negative thought (RNT) (Watkins, 2008). Indeed, cognitive processes, like pain catastrophizing, worry, or rumination, can be experienced as helpful and can lower negative emotions short-term. These processes can seem to help a person pay attention to and avoid potentially harmful situations (pain catastrophizing), get a better understanding of their problem (rumination), or prepare them for potential

dangers in the future (worry). Overall, however, studies have shown that these types of thinking lead to lower problem-solving abilities and overall worse problem severity, especially when they are abstract and have negative content (Watkins, 2008).

In summary, emotions (not least fear), and their cognitive behavioral correlates, have a firmly established role in the psychology of pain. Since emotions have an important role in the perception and experience of pain and strongly drive behavior, an area that has garnered attention is comorbidity between emotional and pain problems.

Emotional comorbidity

There is a clear overlap between pain problems and emotional problems. People with chronic or recurring pain are more likely than people without pain to also have emotional disorders, and vice versa (Castro et al., 2009; Demyttenaere et al., 2007; Tegethoff, Belardi, Stalujanis, & Meinschmidt, 2015). This is true in both general population samples (McWilliams, Cox, & Enns, 2003; McWilliams, Goodwin, & Cox, 2004; Von Korff et al., 2005) and pain populations (Bair, Robinson, Katon, & Kroenke, 2003). More specifically, a large European study showed that 20% of people with chronic pain had comorbid depression (Breivik et al., 2006).

The prevalence of anxiety is more varied, depending on the diagnoses included. Nevertheless, anxiety symptoms are clearly elevated in people with chronic pain compared to healthy controls (Burke, Mathias, & Denson, 2015; Demyttenaere et al., 2007). For example, the results from the world mental health survey showed pooled (across countries) odds ratios of 1.9 for the prevalence of social anxiety, 2.1 for panic disorder/agoraphobia, and 2.7 for generalized anxiety disorder when comparing people with and without back/neck pain in 18 countries (Demyttenaere et al., 2007). That is, anxiety disorders are about twice as prevalent in people with back/neck pain compared to healthy controls. For some, the pain experience predates the emotional disorder, whereas for others, the emotional problems came first (Lerman et al., 2015; Tegethoff et al., 2015). Consequently, the relationship between pain and emotional problems may be reciprocal.

People who have both a pain problem and comorbid emotional problems are facing additional challenges. For example, pain patients with emotional comorbidities have been shown to have worse symptomatology, such as higher pain intensity and functional disability compared to pain patients without emotional comorbidity (Bair et al., 2013; Lerman et al., 2015).

Also, they have been shown to have worse outcome after pain treatment, with higher pain intensity and a lower likelihood to return to work (Michaelson, Sjölander, & Johansson, 2004; Vowles, Gross, & Sorrell, 2004). Hence, pain patients with emotional comorbidities seem to have additional needs that may not be met in clinical practice today.

There are still gaps in our understanding about why these comorbidities are so common, how pain and emotional problems interact, and why some people with pain problems present with emotional comorbidity and others do not. One way of developing our understanding is to take a so called transdiagnostic approach and focus on commonalities between pain and emotional problems. This can for example be done by investigating which psychological factors are associated with the development and maintenance of their co-occurrence. Each of the studies in this dissertation aims to contribute to this, but Study I specifically focuses on comorbidity by studying comorbid social anxiety in a sample of pain patients undergoing multimodal pain rehabilitation.

Transdiagnostic approaches

Transdiagnostic approaches were originally developed to explain why comorbidities are so common in psychiatric clinical practice. For example, 55% of people with anxiety diagnoses have more than one diagnosis at the same time, and 76% have more than one diagnosis during their lifetime (Allen, McHugh, & Barlow, 2008). Hence, a patient can present with different complaints over time (Kessler et al., 2007) or simultaneously fulfill diagnostic criteria for more than one diagnosis (Kessler, 1997; Olofsdotter, Vadlin, Sonnby, Furmark, & Nilsson, 2016). Additionally, it has been observed that treating one disorder sometimes leads to improvement in another disorder (Barlow et al., 2010; Mansell, Harvey, Watkins, & Shafran, 2004). This has raised questions about a potential shared etiology and led to the development of transdiagnostic approaches. Successively, transdiagnostic models have also been developed to clarify potential mechanisms in the overlap of pain and emotions. One of these transdiagnostic models, the shared vulnerability model, is at the heart of this dissertation and will be described in more detail below.

A transdiagnostic model of pain and emotions: the shared vulnerability model

This dissertation is based on the shared vulnerability model, which is an example of a transdiagnostic model in the overlap of pain and emotional

problems. This is important, since neither the generic model of pain (Figure 1) nor the fear-avoidance model (Figure 2) fully explains why comorbidities between pain and emotional problems are so common. The shared vulnerability model suggests pathways for the development of comorbid problems and how they may be maintained. It also identifies potential treatment targets. The model fits into a biopsychosocial understanding of pain, with a focus on shared vulnerabilities that, via the influence of biological, emotional, and/or cognitive processes, may lead to problems in one or more areas.

The model depicted in Figure 3 proposes that underlying factors such as biological and psychological vulnerabilities (for example, negative affect, anxiety sensitivity, biological thresholds), in combination with triggering events (for example, traumatic life events, stressors), give rise to emotional responses. These responses in turn are regulated (or dysregulated) by biological and psychological factors, including cognitive factors and behaviors (for example, hypervigilance, catastrophizing, avoidance), potentially giving rise to both pain problems and emotional disorders (Asmundson, Abrams, & Collimore, 2008; Asmundson & Katz, 2009). These shared vulnerability factors, triggers, and potential maintaining mechanisms may therefore explain the high comorbidity between pain and emotions. The model has been developed for co-occurring chronic pain and anxiety and is mainly based on research focusing on comorbid pain and post-traumatic stress disorder (PTSD). As there is a lack of empirical evidence confirming its validity in other emotional problems, it is important to confirm that the model is applicable to other comorbid emotional problems, that is, to establish whether it can be generalized. This is the aim of Study I, which focuses on comorbid social anxiety and pain.

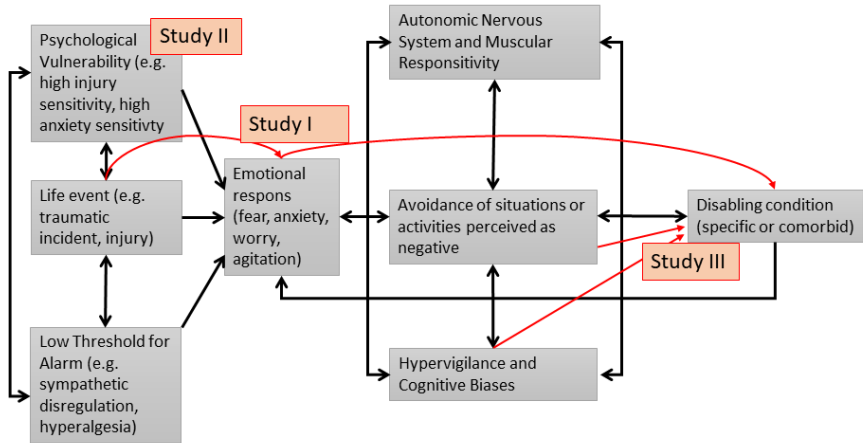


Figure 3. The shared vulnerability model (Asmundson, Abrams, & Collimore, 2008; Asmundson & Katz, 2009). Red boxes indicate the studies included in this dissertation.

A transdiagnostic approach to comorbid pain and emotions

Two vulnerability factors suggested by the shared vulnerability model are anxiety sensitivity and negative affect. Study I focuses on the potential role of these factors. People with high scores on these factors can be more sensitive to experiencing stressors, such as pain and emotional experience, more intensely. Both negative affect and anxiety sensitivity are elevated in pain patients (Asmundson & Katz, 2009; Asmundson, Wright, & Hadjistavropoulos, 2000; O'Brien, Atchison, Gremillion, Waxenberg, & Robinson, 2008). The concept of anxiety sensitivity is especially interesting, since it contains psychological, somatic, and social aspects (Zinbarg, Barlow, & Brown, 1997). It is commonly measured with the Anxiety Sensitivity Index (ASI) (Reiss, Peterson, Gursky, & McNally, 1986), which measures fear of anxiety-related symptoms. It contains items such as: "When I notice that my heart is beating rapidly, I worry that I might have a heart attack" (somatic concern), "When I cannot keep my mind on a task, I worry that I might be going crazy" (psychological concern), and "It is important to me not to appear nervous" (social concern). Anxiety sensitivity therefore has potential for being a central mechanism in the understanding of comorbid emotional and pain problems. Specifically, Study I follows pain patients through a multimodal pain rehabilitation and studies subgroups

with different levels of social anxiety and pain-related fear to compare the associations with anxiety sensitivity and negative affect as well as pain and emotional symptomatology before and after treatment.

Another important and still understudied link in the model is the link from trigger (“life event” in the original model) to mediator (for example “emotional response” in the model) to outcome (“disabling condition”). This is the aim of Study II, a longitudinal study of the development of musculoskeletal pain in a sample of general population adolescents. Specifically, the study investigates whether there is a prospective link between interpersonal, peer-related, stress (as a trigger) and the development of pain, and whether the emotional response worry can act as a mediator between this stressor and the development of pain. Potential gender differences are included in the analyses. Furthermore, the link between cognitive and behavioral maintaining mechanisms and outcome is studied. Study III tests whether a transdiagnostic treatment targeting maintaining factors, such as maladaptive cognitions and avoidance, is a feasible approach to address comorbidity. Specifically, this is tested by offering an internet-delivered unified protocol to former pain rehabilitation patients with residual problems and comorbid emotional problems. An overview of the factors studied in this dissertation is presented in Table 1.

Table 1. Overview of transdiagnostic factors studied in this dissertation.

Study	Transdiagnostic factor	Understood as
I	Anxiety sensitivity	Vulnerability factor
I	Negative affect	Vulnerability factor
II	Peer-related stress	Predictor/vulnerability factor
II	Worry	Mediator/maintaining factor
III	Avoidance	Maintaining factor
III	Maladaptive cognition	Maintaining factor

Social aspects in the context of pain

The biopsychosocial model of pain is, as mentioned previously, well established today and generally agreed on by researchers and practitioners. Pain models therefore generally include biological and psychosocial aspects. Yet, much remains to be understood, not least concerning social aspects. For example, a review attempting to give an overview of the biopsychosocial

model of pain accounts for areas of research in the biological and psychological domains, but fails to account for studies in the social area. (Gatchel, et al., 2007). Indeed, having the biopsychosocial model as a starting point without mentioning social aspects seems common (Andrasik, Flor, & Turk, 2005; Covic, Adamson, Spencer, & Howe, 2003; Koleck, Mazaux, Rasclé, & Bruchon-Schweitzer, 2006; Truchon, 2001). This is unfortunate, since social aspects are clearly important in the context of pain and may have clear transdiagnostic reach.

There are several ways social factors can be considered in the context of pain. For example, social functioning is affected in chronic pain and is closely related to emotions. Studies show that adolescents with pain have fewer friends than their peers without pain and that social withdrawal is common in grown-ups with pain problems (Forgeron et al., 2010; Mitchell & MacDonald, 2009). Also, pain patients have been reported to describe a feeling of lowered self-esteem and shame about not functioning at the same level as before pain onset (Gustafsson, Ekholm, & Ohman, 2004). This has been confirmed in a meta-analysis showing lower self-esteem in people with chronic pain compared to healthy controls (Burke et al., 2015). Signaling transdiagnostic reach, shame and low self-esteem are also common symptoms in social anxiety, and may in turn lead to a higher fear of being judged, more self-criticism, and more avoidance of social situations, all symptoms and behaviors common in social anxiety (Clark & Wells, 1995; Cox, Fleet, & Stein, 2004; Gilbert, 2000; Gilbert & Miles, 2000). Thus, pain problems may lead to or exacerbate social difficulties and interact with social fears. In fact, there is a raised prevalence of social anxiety in pain populations (11–36%) compared to the general population (0.5–15%) (Furmark et al., 1999; Gadermann, Alonso, Vilagut, Zaslavsky, & Kessler, 2012). Since social functioning is understudied in the context of pain, this dissertation sets out to study transdiagnostic risk factors with social content. For example, in Study I individual social functioning in the context of pain is investigated by studying comorbid social anxiety in pain patients.

Likewise, Study II addresses social risk factors, specifically interpersonal stress. Interpersonal stress is a social risk factor that may have an influence on the development of pain problems over time. In adolescents, peer-related stress has mainly been researched in the form of bullying. For example, a meta-analysis shows that adolescents with experience of bully victimization are twice as likely to report psychosomatic symptoms, including musculoskeletal pain, compared to adolescents without this experience in both longitudinal and cross-sectional studies (Gini & Pozzoli, 2013). It is

unclear whether interpersonal stress at a lower level, of a type that may be experienced on a more daily basis, would have similar effects, but there are cross-sectional studies showing that there is a positive correlation between interpersonal stress and somatic problems in adolescents (Murberg & Bru, 2004; Natvig, Albrektsen, Anderssen, & Qvarnstrøm, 1999). Since adolescence is a period where pain problems start to develop and where peer relationships are especially important, this is a key period to study with regard to interpersonal stress and the development of pain over time (Viner et al., 2012). Study II in this dissertation therefore longitudinally analyzes the influence of social risk factors in the environment, in the form of peer-related stress, on the development of pain problems.

The treatment of pain

A lot of effort is invested in the treatment of chronic pain. When available treatments from primary care are insufficient, professionals from various disciplines are involved in secondary care in the form of multimodal pain rehabilitation (SBU, 2010). Not everybody has access to multimodal treatments, however, and for some, even these resource intense treatment options may not be sufficient. In fact, the effects of available treatments on pain functioning and pain intensity are usually small to medium (Guzmán et al., 2001). Despite the common focus on emotional distress and cognitive-behavioral techniques, the needs of pain patients with emotional comorbidities may not be met if more severe emotional problems are not sufficiently dealt with in pain clinics (McCracken & Turk, 2002). In fact, emotional comorbidity in pain patients has been linked to less pain reduction, lower return to work self-efficacy, lower actual return to work, and higher levels of pain-related disability following pain treatment (Michaelson et al., 2004; Vowles et al., 2004). Therefore, there is a need for further development of treatments for chronic pain patients who also suffer from emotional problems.

Psychological treatments of pain are well established today and are usually based on cognitive-behavioral principles (Eccleston, Morley, & Williams, 2013). Here, higher functioning rather than lower pain intensity is commonly the main goal of treatment. Since pain-related fear, avoidance, and maladaptive coping strategies influence the development of a pain problem (Vlaeyen & Linton, 2012), these factors are often targeted during treatment. In line with this, exposure treatment has been shown to be effective for patients who are avoiding activity due to pain or fear of pain (López-de-Uralde-Villanueva et al., 2016). In line with the similarities in

maintaining mechanisms, many of these treatment targets are also part of cognitive behavioral treatments for emotional problems. Hence, one way of achieving better treatment results for people with comorbid pain and emotional problems may be to target these shared transdiagnostic factors, such as avoidance tendencies or maladaptive cognitions, instead of using treatments that target pain and emotional problems separately.

One promising treatment is the Unified Protocol for Emotional Disorders (UP) (Barlow et al., 2010). It is based on the premise that emotional problems, such as depression and anxiety, have a shared etiology and can be treated by targeting the same factors. The UP teaches emotional awareness and targets emotional avoidance and maladaptive cognition. It has been found effective in the treatment of emotional disorders (Bullis, Fortune, Farchione, & Barlow, 2014). Also, it has been suggested to be applicable to other disorders and has shown promising results in the treatment of pain and comorbid emotional problems in a small study with adolescents (Allen, Tsao, Seidman, Ehrenreich-May, & Zeltzer, 2012). Therefore, this treatment was selected as the treatment model in Study III.

When developing a treatment that targets underlying mechanisms in pain patients with emotional comorbidities, the mode of delivery is important to consider. Many pain patients have difficulties with mobility as well as cognitive functioning, such as concentration (Berryman et al., 2013; 2014; Hart, Wade, & Martelli, 2003). This can make it harder to access and utilize treatment. To solve the problem of accessibility, internet-delivered treatment options have been studied (Andersson, 2016). Internet-delivered treatments also have the advantage that the patients can access material at a time and to the extent convenient to them. This may have the great advantage of enabling the patient to take breaks and utilize treatment in smaller instalments, to skip days when concentration is particularly difficult, and to re-read material as many times as necessary. Generally, internet delivered cognitive behavioral therapy (CBT) based treatments have shown effect for both emotional problems and pain problems (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Buhrman, Gordh, & Andersson, 2016). There have also been studies showing positive results for patients with pain problems and comorbid emotional problems (Buhrman et al., 2015; Dear et al., 2015). Therefore, Study III uses internet delivery as the modality for treatment with the aim to test the effects of the transdiagnostic unified treatment protocol for patients with chronic pain and emotional problems.

Aim

The overarching aim of this dissertation is to further our understanding of comorbid musculoskeletal pain and emotional problems by investigating the role of transdiagnostic factors in the context of pain and emotions. Specifically, research questions are:

- Do levels of proposed vulnerability factors (negative affect and anxiety sensitivity) and symptomatology covary in pain patients depending on the occurrence of comorbid social anxiety symptoms (Study I)?
- Does peer-related stress predict musculoskeletal pain problems over time, and is this relationship mediated by worry and moderated by gender (Study II)?
- Can we decrease emotional and pain problems in pain patients with comorbid emotional problems by using an internet-delivered unified protocol for emotional disorders (Study III)?

Empirical studies

This dissertation is based on three studies using mainly two different populations. Study I and III used samples of adult chronic pain patients. Study I was part of a larger study about emotional aspects and pain (social anxiety and pain) collecting pre-, post-, and 1-year follow-up data from patients undergoing multimodal pain rehabilitation at a Swedish pain clinic. It is based on data from patients for whom both pre- and post-data were available. Study III also used patients from secondary care, but up to 3 years after they underwent a multimodal pain rehabilitation. For inclusion, which was self-selected, participants were required to have residual pain problems and comorbid emotional problems. Study II used a sample of general population adolescents. Adolescents were 13 years old at baseline and were followed for 2 years. The study used the first three waves of a larger study (The Three Cities Study) following all adolescents in grades 7–9 in all public schools in three cities in Mid-Sweden. All three studies were approved by the Regional Ethical Board in Uppsala (Study I: No. 2011/10; Study II: No. 2013/384; Study III: No. 2013: 349). The tenets of the World Medical Association’s declaration of Helsinki were followed for all three studies regarding informed consent, confidentiality, and use of collected data for research purposes only (World Medical Association, 2014).

Study I

Characteristics and consequences of the co-occurrence between social anxiety and pain-related fear in chronic pain patients receiving multimodal pain rehabilitation treatment

Introduction

Chronic pain often goes hand in hand with other problems. It is well established that chronic pain problems are related to pain-related fear and maladaptive pain coping, such as avoidance (Vlaeyen & Linton, 2012). Also, pain problems commonly co-occur with emotional problems, such as anxiety disorders (Artner et al., 2012). Several studies have shown that pain patients are a heterogeneous group in whom comorbidities are common and influence treatment outcome negatively (De Rooij, Van der Leeden, Roorda, Steultjens, & Dekker, 2013; Huijnen, Rusu, Scholich, Meloto, & Diatchenko, 2015; Rusu, Boersma, & Turk, 2012; Westman et al., 2011). This raises questions about the causes for this heterogeneity – that is, why many, but not all, pain patients have emotional comorbidities.

Comorbidity may be explained by vulnerability factors, such as anxiety sensitivity and negative affect. These and other vulnerability and maintaining factors are proposed to be shared across diagnostic entities and are therefore defined as transdiagnostic factors. The shared vulnerability model suggests that these factors can lead to pain, anxiety, or comorbidity between pain and anxiety (Asmundson et al., 2008; Asmundson & Katz, 2009). One understudied anxiety disorder co-occurring with pain problems is social anxiety disorder. This could be important, since social anxiety is elevated in pain patients (Gadermann et al., 2012) and studies show a potential negative influence of pain on social factors, and vice versa (Mitchell & MacDonald, 2009; Sutherland & Morley, 2008; Thomtén, Boersma, Flink, & Tillfors, 2016). To test the generalizability of the shared vulnerability model, it is important to study subgroups of pain patients with different levels of emotional comorbidity, such as social anxiety, and to establish whether comorbidity is connected to levels of vulnerability factors, such as anxiety sensitivity and negative affect. Also, it would be important to study if the potential subgroups vary with regard to treatment outcome. Thus, the current study uses person-centered methods and focuses on variation in potential transdiagnostic vulnerability factors (anxiety sensitivity and negative affect) as well as symptomatology before and after treatment in groups with different levels of pain related fear and social anxiety.

Aim

The aim of this study was to investigate the covariation of suggested transdiagnostic vulnerability factors in comorbid pain and anxiety. This was done by investigating the occurrence of subgroups with different patterns of social anxiety and pain-related fear in a chronic pain population receiving multimodal pain rehabilitation. Also, the characteristics of these potential subgroups regarding negative affect, anxiety sensitivity, and treatment outcome were investigated.

Method

Design

This study used a prospective observational design with two measurement points, pre- and post-treatment, in a sample of chronic musculoskeletal pain patients receiving multimodal pain rehabilitation.

Participants and procedure

Participants consisted of 180 chronic pain patients (82% female; 90% born in Sweden; 36% with a university education, 49% with an upper secondary school education, 13% with only compulsory school education) receiving multimodal pain rehabilitation at a Swedish pain clinic. The average duration of pain problems was 13.2 years since first pain episode (range: 2–46 years; standard deviation (SD) = 9.3). Most (77%) had generalized pain, defined as pain in more than six areas (divided up into the left and right side of the body). Age ranged from 21 to 70 (mean age = 45.58 years; SD = 10.81). Of the patients indicating employment status before treatment, 42% reported that they were not working.

Measurements

All measurements had sound psychometric properties. They were based on self-report using pen and paper questionnaires filled in before and after treatment. The Swedish versions of all questionnaires were used.

Measures used for subgrouping

Pain related fear was considered a proxy for maladaptive pain coping, and operationalized and assessed using the Tampa Scale of Kinesiophobia (TSK) (Miller, Kori, & Todd, 1991). *Social anxiety* was assessed with the first part of the Social Phobia Screening Questionnaire (SPSQ) (Furmark et al., 1999).

Measures used to validate subgroups

Functional impairment due to social anxiety was assessed using the impairment scale of the SPSQ (Furmark et al., 1999). *Pain catastrophizing* was assessed using the Pain Catastrophizing Scale (PCS) (Sullivan, Bishop, & Pivik, 1995). *Symptoms of anxiety and depression* were assessed using the Hospital Anxiety and Depression scale (HAD) (Zigmond & Snaith, 1983).

Vulnerability measures

Anxiety sensitivity was assessed using the Anxiety Sensitivity Index (ASI) (Reiss et al., 1986). *Negative affect* was assessed using the negative affect subscale of the short form of the Positive And Negative Affect Schedule (PANAS) (Thompson, 2007).

Outcome measures

Pain severity and interference with daily life were assessed using the first part of the Multidimensional Pain Inventory (MPI) (Kerns, Turk, & Rudy, 1985). *Efficacy to communicate work related needs* was assessed using the Return To Work Self-Efficacy scale (RTWSE) (Shaw, Reme, Linton, Huang, & Pransky, 2011).

Analyses

All analyses were done in SPSS, version 22 (SPSS Inc., Chicago, IL, USA). Standardized scores of pre-treatment social anxiety and pain-related fear were used as variates for a cluster analysis. A cluster analysis is a person centered method grouping participants according to their similarities in two or more variables. The aim is to create groups that are distinct from each other, but where the individual members included in each group are similar to each other. First, a hierarchical cluster analysis was performed, using Ward's method with squared Euclidian distances (Bergman, 1998). This was followed by a K-means cluster analysis using the hierarchical cluster solution center points as the starting point (Bergman, 1998; MacQueen, 1964). Clusters are considered homogenous with explained error sums of squares (EESS) values of around 67% (Bergman & El-Khoury, 2003). Subgroups were validated and described, and finally compared regarding transdiagnostic vulnerability factors and outcome using chi-square test of independence and one-way analysis of variance (ANOVA).

Results

Four distinct clusters with different patterns on social anxiety and pain-related fear emerged. The clusters were named (1) low scores (LS), (2) pain-related fear only (PF), (3) social concern only (SC), and (4) high social anxiety and pain-related fear (PF-SA). The cluster solution is shown in Figure 4. Clusters did not differ from each other regarding most demographic variables. However, the PF cluster contained significantly more men (34%) than the SC or PF-SA clusters (9% respectively). Also, the PF-SA cluster contained significantly more people with a low-level education and less with a university education compared to the LS cluster.

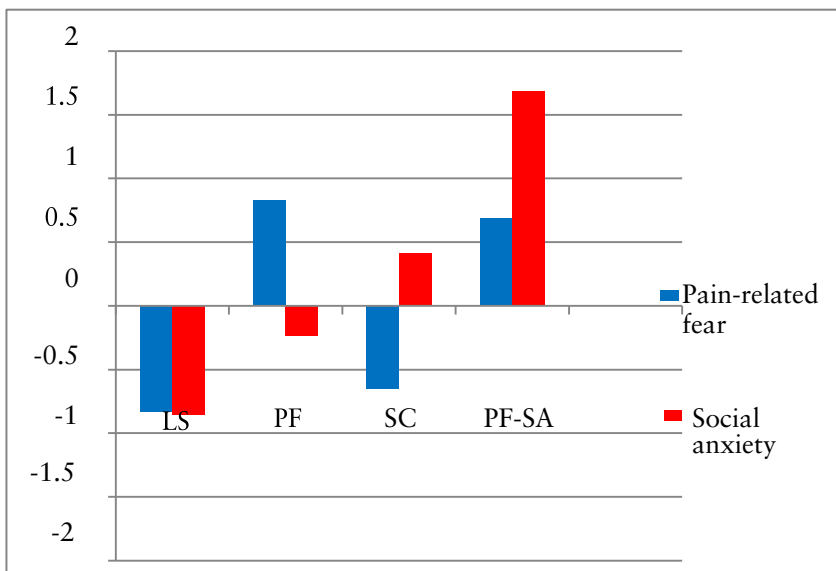


Figure 4. Standardized scores of social anxiety and pain-related fear in the four-cluster solution.

Numbers indicate standard deviations. 0 = mean. LS = low scores cluster (35% of the sample); PF = pain-related fear cluster (29%); SC = social concern cluster (19%); PF-SA = pain-related fear--social anxiety cluster (17%).

The validation of the cluster solution showed that groups with high social anxiety also scored higher on functional impairment due to social anxiety, and that groups with high pain-related fear also scored high on pain catastrophizing. Generally, groups with higher scores on pain-related fear and/or social anxiety also scored higher on depression and anxiety.

An overview giving mean scores on vulnerability factors and outcome is presented in Table 2. Superscripts in Table 2 indicate significant post-hoc test differences between subgroups. Where groups share a superscript, post-hoc tests did not detect a significant difference between these subgroups. Results showed that patients with high social anxiety and pain-related fear had significantly higher scores in vulnerability factors (anxiety sensitivity and negative affect), higher general emotional symptomatology, and lower efficacy to communicate needs compared to the low-scores cluster, both pre- and post-treatment. No differences between groups were found regarding pain intensity or pain interference.

Table 2. Description and comparison of clusters on vulnerability factors and outcome.

Cluster	Low score (LS)	Pain-related fear (PF)	Social concern (SC)	Pain-related fear & social anxiety (PF-SA)	Total
Anxiety sensitivity (ASI (0-64)) M(SD)					
Pre	8.5 (5.8) ^c	16.3 (11.2) ^{a,b}	14.8 (9.7) ^{b,c}	23.8 (9.4) ^a	14.6 (10.4)
Post	9.9 (6.4) ^{cb}	14.7 (11.4) ^{a,b}	13.6 (8.2) ^b	25.7 (10.3) ^a	13.8 (9.9)
Negative affect (PANAS (5-25)) M(SD)					
Pre	8.9 (3.4) ^b	11.9 (4.7) ^{a,b}	10.9 (3.7) ^b	14.9 (5.5) ^a	11.2 (4.7)
Post	9.6 (3.4) ^b	11.4 (4.9) ^{a,b}	10.4 (3.6) ^b	16.5 (6.0) ^a	11.0 (4.7)
Pain intensity (MPI (0-6)) M(SD)					
Pre	4.0 (.9)	4.2 (1.0)	3.9 (1.1)	4.7 (1.1)	4.2 (1.0)
Post	3.8 (1.1)	4.0 (1.2)	3.9 (.9)	4.0 (1.1)	3.9 (1.1)
Pain interference (MPI (0-6)) M(SD)					
Pre	4.2 (1.2)	4.8 (.8)	4.3 (1.1)	4.8 (.8)	4.5 (1.0)
Post	3.9 (1.1)	4.3 (.9)	4.1 (1.0)	4.5 (.8)	4.2 (1.0)
Efficacy to communicate needs (RTWSE (7-70)) M(SD)					
Pre	53.2 (13.8) ^b	40.9 (18.1) ^b	37.2 (17.5) ^b	33.1 (19.4) ^a	43.3 (18.4)
Post	52.5 (12.5) ^b	43.2 (16.1) ^b	40.4 (19.7) ^b	33.1 (21.2) ^a	44.5 (17.7)
Anxiety (HAD (0-21)) M(SD)					
Pre	6.5 (4.2) ^b	9.1 (4.7) ^b	9.4 (4.9) ^{a,b}	12.4 (5.1) ^a	8.8 (5.0)
Post	6.2 (3.8) ^b	7.7 (4.3) ^{a,b}	7.8 (3.4) ^{a,b}	11.2 (4.0) ^a	7.8 (4.2)
Depression (HAD (0-21)) M(SD)					
Pre	6.9 (3.9) ^b	9.4 (4.4) ^{a,b}	9.1 (4.3) ^{a,b}	11.2 (4.7) ^a	8.7 (4.5)
Post	6.2 (4.2) ^b	7.7 (3.6) ^{a,b}	8.4 (4.1) ^{a,b}	9.3 (5.0) ^a	7.6 (4.3)

ASI = Anxiety Sensitivity Index; HAD = Hospital Anxiety and Depression scale; MPI = Multidimensional Pain Inventory; PANAS = Positive And Negative Affect Schedule; RTWSE = Return-To-Work Self-Efficacy questionnaire.

Figure 5 visually displays how the four subgroups relate to one another before and after treatment. Scores further away from the center indicate more problems, reinforcing that the comorbid subgroup had the highest level of difficulties, not least regarding the vulnerability factors.

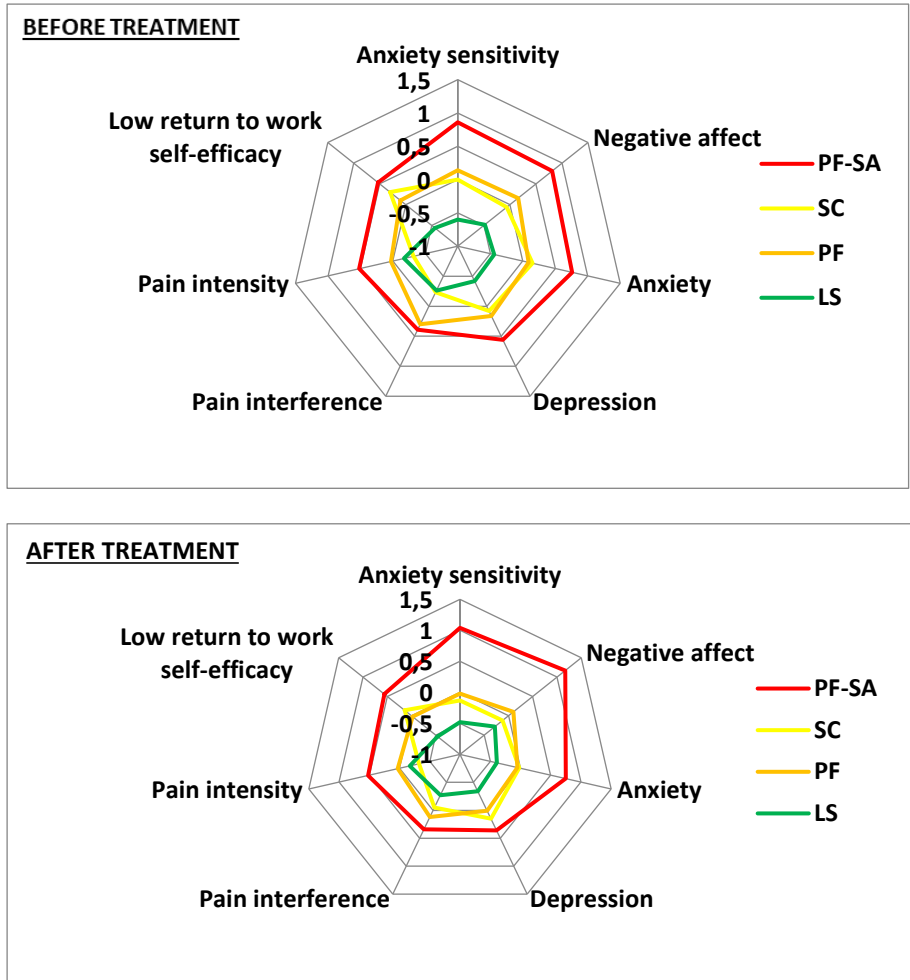


Figure 5. Radar graphs showing the four clusters' z-scores before and after treatment and, hence, the differences in patterns of symptomatology for clusters.

Discussion and Conclusion

The results of this study suggest that comorbidity between pain and emotional problems is related to high scores on proposed transdiagnostic vulnerability factors, high symptomatology, and worse treatment outcome. This highlights the role of shared factors in the development of comorbid pain and emotional problems and confirms the generalizability of the shared vulnerability model to other diagnoses besides PTSD, in this case social anxiety. The subgroup of pain patients with high scores on social anxiety and pain-related fear scored high on anxiety sensitivity and negative affect compared to a subgroup who had low social anxiety and pain-related fear. This comorbid group also showed residual emotional problems post-treatment, such as anxiety scores at clinically significant levels. Overall, rehabilitation results were suboptimal even when compared to problems experienced by the group high on pain-related fear only, which indicates that social anxiety contributes to, or goes hand in hand with, added complexity for pain patients.

One conclusion of this study is that patients with high scores in pain-related fear and social anxiety may benefit from being detected pre-treatment and may have additional treatment needs that are not met in current treatment programs. Additional treatment options for these patients should therefore be developed to better address potential underlying transdiagnostic factors and psychosocial difficulties, such as difficulties communicating needs to others.

Study II

Musculoskeletal pain in adolescents: Prevalence, and the role of peer-related stress, worry, and gender in the development of pain problems over time

Introduction

Many health complaints increase during adolescence (Kessler et al., 2007; King et al., 2011). For example, pain problems are common (Stanford, Chambers, Biesanz, & Chen, 2008; Sundblad, Saartok, & Engström, 2007) and are often related to mental ill health and other negative outcomes, such as school absenteeism (Cohen, Vowles, & Eccleston, 2010; King et al., 2011; Petersen, Bergström, & Brulin, 2003). The reasons for this development are still understudied and possibilities for prevention and treatment are therefore likely underutilized.

Interpersonal stressors have been related to the experience of pain and may therefore be relevant in the development of pain problems. In adolescents, this has mainly been studied in the form of bully-victimization showing that adolescents who experience bully victimization have a higher risk for health problems, such as pain, compared to their peers without this experience (for a meta-analysis, see Gini & Pozzoli, 2013). However, more common, everyday peer-related stressors may also be relevant (Murberg & Bru, 2004; Natvig et al., 1999). For example, in a cross-sectional study Murberg et al. (2004) showed that peer-related stress predicted pain problems in a sample of adolescents. Hence, there is some empirical evidence for the relationship between everyday interpersonal stressors and pain problems, but longitudinal studies are still needed. Additionally, potential mediators and moderators need to be studied further.

Adolescents can differ in how they react to peer-related stressors, which could mediate outcome. For example, worry has been shown to play a role in, among others, the development of pain problems (Brosschot & Van Der Doef, 2006; Ehring & Watkins, 2008; Ottaviani et al., 2016). Worry may therefore mediate the relationship between peer-related stressors and pain problems, but this relationship still needs to be empirically established. Also, girls generally report more pain problems. It has been suggested that peer-related stress is a more potent stressor for girls than for boys, and that girls have a higher tendency to use worry and other forms of RNT in response to stressors (McLean & Anderson, 2009; Nolen-Hoeksema & Jackson, 2001; Rudolph, 2002). Hence, gender might act as a moderator between peer-related stress and worry.

Aim

The first aim of Study II was to analyze the prevalence of pain problems, including potential gender differences, in adolescents followed over 3 years. The second aim was to study if peer-related stress predicted musculoskeletal pain problems over time, whether this relationship was mediated by worry, and whether gender acted as a moderator.

Method

Design

A longitudinal panel design with yearly measurements was used, following adolescents from 7th to 9th grade.

Participants and procedure

This study was based on a sub-sample of participants from the Three Cities Study, a 5 year longitudinal study on the development of mental health problems in a cohort of adolescents (N = 3,336), with a specific focus on comorbidity and transdiagnostic processes. In the current study, adolescents who were in 7th grade at first data collection were followed for 2 additional years. In 7th grade, participants (N = 1,453) were 13.19 years old (SD = 0.42, range 12–15). Of these, 91.1% of the baseline sample filled in questionnaires in 8th grade (N = 1,336) and 81.3% in 9th grade (N = 1,181). This resulted in 1,137 participants filling in questionnaires at all three time-points (78.3% of the baseline sample, 46% girls). Of these, 88.9% were born in Sweden and 71.5% lived with both their parents. A logistic regression showed that the 316 participants lost over time were more likely to have parents who were divorced (B = 0.49, SE = 0.14, OR = 1.62) or born outside of Europe (B = 0.59, SE = 0.22, OR = 1.81) compared to participant filling in measurements at all three time-points. No differences were found regarding gender, being born in Sweden, interpersonal stress, worry, or musculoskeletal pain problems ($p < 0.10$, range 0.42–0.64).

Measurements

All measurements were pen and paper self-report questionnaires with well-established psychometric properties. Swedish versions were used for all questionnaires.

Sociodemographic information was assessed asking participants for their age, gender, and whether they had been born in Sweden. They were also

asked where their parents were born and whether their parents had separated. *Peer-related stress* was assessed using the peer pressure subscale of the short form of the Adolescent Stress Questionnaire (Anniko, Boersma, Van Wijk, Byrne, & Tillfors, accepted; Byrne, Davenport, & Mazanov, 2007). *Trait worry* was assessed using the Penn State Worry Questionnaire for Children (Esbjørn, Reinholdt-Dunne, Caspersen, Christensen, & Chorpita, 2013). *Musculoskeletal pain* was defined as pain in the back, neck, or shoulders. The presence and duration of musculoskeletal pain during the last 6 months was assessed with one item of the Health Behavior in School-Aged Children Symptom Checklist (Haugland & Wold, 2001): “How often during the last 6 months have you suffered from the following symptoms: Pain in the back/neck/shoulder?” The question could be answered with “rarely or never”, “about every month”, “about every week”, “more than once a week”, or “about every day”. *Pain intensity* was assessed by asking how painful the back/neck/shoulder pain had been on average on a scale of 1 “not at all painful” to 10 “very painful”. *Pain interference* was assessed using three items asking if the pain had impaired function during the last 6 months at (a) school, (b) in leisure activities, or (c) in the contact with friends (answerable with 1 (“no”), 2 (“yes, a bit”) or 3 (“yes, definitely”). *Pain problems* were operationalized using the variables pain frequency and duration, pain intensity, and pain interference. Based on these variables, five *pain grades* were created (following Vervoort, Logan, Goubert, De Clercq, & Hublet, 2014; Von Korff, Ormel, Keefe, & Dworkin, 1992). Grade 0 = pain experienced rarely or never; Grade I = Pain experienced at least every month with low pain intensity and no/low impairment; Grade II = pain experienced at least every month with high pain intensity, but no/low impairment; Grade III = pain experienced at least every month with medium impairment; and, Grade IV = pain experienced at least every month with high impairment. Pain grades were validated using scores of *depressive symptoms*, assessed using the Centre for Epidemiology Studies Depression Scale for Children (CES-DC) (Weissman, Orvaschel, & Padian, 1980), *self-esteem* assessed using the Rosenberg’s self-esteem scale (RSE) (Bair et al., 2003), and *anxiety symptoms* assessed using the Overall Anxiety Symptoms and Impairment Scale (OASIS) (Norman, Hami Cissell, Means-Christensen, & Stein, 2006).

Pain grades III and IV were collapsed and labelled as signifying having a pain problem including at least moderate functional impairment. Pain grades 0, I, and II were collapsed and labelled as having no pain problem. Thus, the dichotomous variable “pain problem” was created for analyses,

where 1 = pain problem (pain grades III and IV) and 0 = no pain problem (pain grades 0–II). This dichotomous variable was used as the outcome variable for the main analyses.

Analyses

Pain grades were validated by comparing groups regarding the variables used for grading (pain intensity, frequency, and impairment), as well as regarding peer-related stress, and variables known to correlate with pain problems (anxiety, depression, and self-esteem) (Gustafsson et al., 2004; Vervoort et al., 2014; Wager et al., 2013) using one-way ANOVA. Chi square analysis was used to investigate gender differences in the prevalence of pain grades.

The main analyses consisted of a moderated mediation analysis using model 7 of the PROCESS custom dialog box, version 2.16, for SPSS, developed by Hayes (2017), with 5,000 bootstrap samples and heteroscedacity-consistent standard errors. Interpersonal stress in 7th grade was entered as the predictor, musculoskeletal pain problems in 9th grade as the outcome, worry in 8th grade as a mediator and gender as a moderator between interpersonal stress and worry. Also, musculoskeletal pain problems and worry in 7th grade were entered as covariates.

Results

Validation of pain grades

The validation of pain grades showed mean score differences in the expected direction, with pain grades III and IV generally reporting worse scores. Adolescents with pain problems also reported more anxiety and depression, and lower self-esteem compared to their peers without a pain problem. An overview is presented in Table 3.

Table 3. Validation of pain grades.

Pain Grades	Function 3-9	Intensity 1-10	Frequency 1-5	Depression 0-60	Anxiety 0-20	Self esteem 10-40	Interpersonal stress 4-20
0	8.71 ^a	1.36 ^a	1 ^a	8.53 ^a	2.00 ^a	32.59 ^a	5.18 ^a
I	8.42 ^b	2.82 ^b	2.34 ^b	13.76 ^{bc}	3.42 ^{bc}	30.37 ^b	5.91 ^b
II	7.84 ^c	7.26 ^c	3.46 ^c	17.00 ^{bc}	3.74 ^{bc}	29.26 ^{bc}	6.21 ^{bc}
III	5.84 ^d	5.88 ^d	3.49 ^c	20.17 ^{cd}	5.11 ^{cd}	27.72 ^{cd}	7.21 ^c
IV	3.40 ^e	6.88 ^{cd}	3.95 ^c	23.94 ^d	6.90 ^d	26.43 ^d	7.08 ^{bc}
Total	8.25	2.68	1.81	11.83	2.87	31.23	5.64
F	644.81*	870.05*	1053.64*	61.89*	44.50*	30.90*	18.23*
df	4	4	4	4	4	4	4

* $p < 0.001$. Superscripts indicate significant post-hoc test differences between subgroups. Where groups share a superscript, post-hoc tests did not detect a significant difference between these subgroups.

Prevalence of musculoskeletal pain problems over time

Table 4 shows an overview of pain grades over time, both for the group as a whole and separately for girls and boys. The prevalence of pain problems (pain grades III and IV) was 8.4% in 7th grade, 10.5% in 8th grade, and 9.9% in 9th grade. No gender differences were detected regarding prevalence in 7th grade ($\chi^2 (1, N = 1,453) = 3.06, p = 0.08$), even though there was a trend towards gender differences (9.7% for girls vs. 7.2% for boys). In contrast, in 8th grade ($\chi^2 (1, N = 1,336) = 18.75, p < 0.001$) significantly more girls than boys reported pain problems (14.3% vs. 7.1%). A similar pattern was seen in 9th grade ($\chi^2 (1, N = 1,181) = 13.94, p < 0.001$; 13.4% vs. 6.9%). In short, the prevalence of pain problems over time increased in girls, but not in boys.

Table 4. Prevalence of pain grades over time (%).

Pain Grades	7 th grade			8 th grade			9 th grade		
	Boys	Girls	Total	Boys	Girls	Total	Boys	Girls	Total
0	58.2	50.3	54.4	52.8	42.0	47.8	54.5	39.7	47.7
I	28.4	29.4	28.8	31.1	32.3	31.7	29.8	33.1	31.3
II	6.3	10.6	8.3	9.0	11.3	10.1	8.8	13.8	11.1
III	5.0	6.4	5.6	4.7	10.8	7.6	4.4	9.0	6.5
IV	2.2	3.3	2.8	2.4	3.5	2.9	2.5	4.4	3.4
Total N	765	688	1,453	708	628	1,336	637	544	1,181

Peer-related stress, worry, and gender in the development of musculoskeletal pain

The moderated mediation model explained a small, but significant ($p < 0.001$) part of the variance (between 7% (CoxSnell) and 14% (Nagelkerke)). An overview is given in Figure 6 and Table 5.

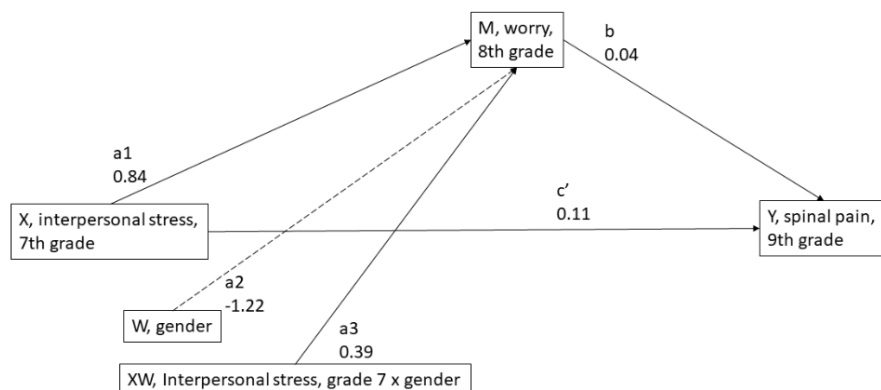


Figure 6. Results of the moderated mediation ($N = 1,137$). Unstandardized regression coefficients (B) are presented. Pain problems 7th grade and worry 7th grade were entered as covariates. X = predictor; Y = outcome; M = mediator; W = moderator. Solid lines indicate statistical significance ($p < 0.05$).

As can be seen, interpersonal stress in 7th grade significantly predicted musculoskeletal pain 2 years later with a direct effect of $B = 0.11$ ($SE = 0.03$, $p < 0.001$, 95% bootstrap confidence interval (BootCI) (0.05, 0.18)). Furthermore, worry mediated this relationship. Also, there was an interaction effect between gender and interpersonal stress. The conditional indirect effect was significant for girls ($B = 0.016$; 95% BootCI (0.004, 0.036); $SE = 0.008$), but not for boys ($B = 0.002$; 95% BootCI (-0.005, 0.03); $SE = 0.004$). This suggests that worry mediates the relationship between interpersonal stress and the development of pain problems in girls, but not in boys.

Table 5. Results of the moderated mediation (N = 1,137).

Predictor	Outcome					
	M (Worry 8 th grade)			Y (Musculoskeletal pain problems 9 th grade)		
	Coeff.	SE	p	Coeff.	SE	p
X, Interpersonal stress, 7 th grade	a ¹ 0.84	0.31	< 0.01	c'	0.11	< 0.001
M, Worry, 8 th grade				b	0.04	< 0.01
W, Interpersonal stress, 7 th grade x gender	a ³ -0.39	0.18	< 0.05			
Covariates						
Musculoskeletal pain problems, 7 th grade	0.46	0.88	0.60		1.55	< 0.001
Worry, 7 th grade	0.56	0.04	< 0.001		0.01	0.47
Constant	15.03	2.00	< 0.001		-4.58	< 0.001

Unstandardized regression coefficients are presented. SE = standard error.

Discussion and Conclusion

The results of this study show that a subgroup of adolescents in the sample suffered from musculoskeletal pain that negatively affected their lives in school, during leisure activities, and/or in their contact with friends. Hence, our results show that musculoskeletal pain is a problem for adolescents, especially for girls. Also, results show that peer-related stress and worry may be important mechanisms in the development of adolescents' musculoskeletal pain problems.

In line with earlier studies (for a review, see King et al., 2011), more girls than boys reported pain problems, and girls seemed to be more vulnerable when experiencing interpersonal stress (Rudolph, 2002). Girls scored higher on worry compared to boys, although levels of peer-related stress were generally low for the whole group. This also is in line with studies showing that girls show a higher tendency to use repetitive negative thought (McLean & Anderson, 2009; Nolen-Hoeksema & Jackson, 2001). Importantly, these studies are contrasted by others showing that girls do not use repetitive negative thought more than boys when stressor load is taken into account (Hamilton, Stange, Abramson, & Alloy, 2015; Stange, Hamilton, Abramson, & Alloy, 2014; Østerås, Sigmundsson, & Haga, 2016). In the current study, only peer-related stress was studied. Hence, the tendency to worry in girls may have been higher simply because they had an overall higher stressor load in other areas compared to boys.

All in all, this study highlights avenues of prevention and treatment, since school-based programs could be used to work more effectively on levels of peer-related stress. Also, the tendency to worry could be assessed to detect adolescents at risk. Worry could also be used as a potential treatment target. Clearly, it would be important to further investigate peer-related stress and worry in adolescents to influence the health of the emerging grown-up population.

Study III

Internet delivered transdiagnostic treatment with telephone support for pain patients with emotional comorbidity: a replicated single case study

Introduction

Pain patients commonly have emotional comorbidities (Castro et al., 2009). These comorbidities correlate with worse treatment outcome, such as lower return to work and higher pain-related disability (Michaelson et al., 2004; Vowles et al., 2004). Consequently, it is important to find ways to improve treatment outcome for this group of pain patients.

One way of improving treatment outcome may be to focus on underlying transdiagnostic factors. As suggested by the shared vulnerability model (Asmundson & Katz, 2009), chronic pain problems and emotional problems share several underlying factors, such as anxiety sensitivity, threat focused cognitions, and avoidance. A focus on these transdiagnostic factors allows researchers and practitioners to simultaneously target pain and emotional problems in the same individual as well as treating pain patients with different emotional comorbidities with the same treatment protocol. This may be a way forward in improving treatment outcome for pain patients with emotional comorbidity.

One prominent transdiagnostic treatment protocol is the Unified Protocol for Emotional Disorders (UP, Barlow et al., 2010). The UP has been shown to be effective for patients with anxiety and depression by successfully targeting underlying transdiagnostic factors, such as emotional reactions, avoidance, and repetitive negative thinking, and has also shown promising results in a small single case study with two adolescents suffering from comorbid pain and emotional problems (Allen et al., 2012; Bullis et al., 2014; Sauer-Zavala et al., 2012). However, the UP has not yet been tested in an adult sample with comorbid pain and emotional problems.

Patients with comorbid pain and emotional problems may need additional help to enable them to utilize treatment, which makes it important to consider different modes of treatment delivery. For example, both mobility and concentration can be impaired (Berryman et al., 2013; 2014). To increase the accessibility of treatments, internet-delivered treatments have been developed (Andersson, 2016). Internet delivered treatments enable patients to work on material from their home and to choose when, and for how long, to work on it, which may be a great advantage when concentration varies. Internet-delivered treatments work well for patients with emotional problems as well as patients with pain

problems (Andrews et al., 2010; Buhrman et al., 2016), especially when including therapist guidance (Baumeister, Reichler, Munzinger, & Lin, 2014; Dear et al., 2015). Therefore, an internet-delivered, therapist-guided treatment using the UP may provide a step forward for patients with pain problems and a variation of comorbid emotional problems.

Aim

The aim of this study was to test if the Unified Protocol of Emotional Disorders can be used to influence emotional and pain symptomatology in people with comorbid pain and emotional problems. Specifically, the aim was to test the feasibility and effects of a telephone and e-mail guided internet-delivered version of the Unified Protocol of Emotional Disorders as a secondary intervention for former pain rehabilitation patients with residual pain problems and comorbid emotional problems.

Method

Design

A replicated single case experimental design (SCED) was used (N = 5). A flow-chart of the treatment design is shown in Figure 7.

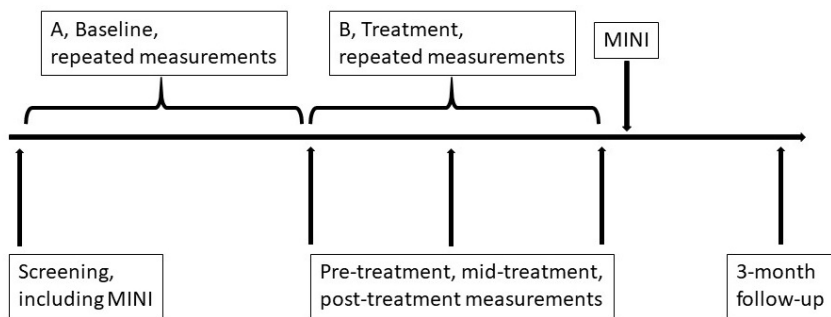


Figure 7. Flowchart of measurements. MINI = Mini International Neuropsychiatric Interview.

Table 6. Characteristics of participants at screening.

	Age	Gender	Diagnoses	Pain localization	Pain, years	Education	Employment status
1	45	F	GAD	Generalized ¹	4	University	Working
2	57	M	-	Neck, arms, hands, head	17	University	80% sick leave
3	34	F	SAD, GAD, Dysthymia	Neck, shoulders, head, other	7	University	100% sick leave
4	54	M	Agoraphobia, GAD	Neck, shoulders, hands, lower abdomen	7	High school	100% sick leave
5	42	F	GAD	Generalized ¹	11	University	50% sick leave

¹Generalized pain = pain in more than 6 areas. GAD = generalized anxiety disorder; SAD = social anxiety disorder.

Participants

Participants consisted of five former pain rehabilitation patients (three females), aged 34– 57. Participants responded to an advertisement sent to them via mail from the pain clinic or primary care center where they had undergone their pain rehabilitation. Hence, the sample was self-selected. More information about the participants is presented in Table 6.

Inclusion criteria were: (a) chronic pain problems (≥ 3 months duration and an average score of ≥ 5 on the Örebro Musculoskeletal Pain Screening Questionnaire (ÖMSPQ–sv) (Linton, Nicholas, & MacDonald, 2011), (b) depressive symptoms (≥ 15 on the Montgomery Åsberg Depression Rating Scale (MADRS-S, Svanborg & Åsberg, 2001) and/or anxiety symptoms (≥ 7 on the Overall Anxiety Symptoms and Impairment Scale (OASIS, Norman, Hami Cissell, Means-Christensen, & Stein, 2006), (c) having received multimodal rehabilitation within the last three years, (d) age ≥ 18 years, (e) fluency in reading and writing Swedish, and (f) internet access. Exclusion criteria were: (a) ongoing or planned psychological treatment delivered by a psychologist or a psychotherapist, (b) planned surgery, (c) severe depression (> 36 on the MADRS-S), and d) suicidal ideations, ongoing alcohol or substance abuse, and/or ongoing psychosis (assessed using the Mini International Neuropsychiatric Interview (MINI, Sheehan et al., 1998). After the recruitment process the protocol was tested in a pilot trial (Lorenz & Klein Strandberg, 2016). Participants lived up to 194 km from the study location ($M = 61$ km). They were randomly assigned to one of three therapists: a clinical psychology student in the last year of training, a postgraduate clinical psychology fellow and a certified clinical psychologist.

Measurements

All measurements were self-report questionnaires. Most were filled in on a secure platform online. Exceptions were self-reported improvement and patient satisfaction, which were administered as paper and pen questionnaires via mail.

Screening measures

Pain coping problems were assessed using six out of ten items from the short version of the Örebro Musculoskeletal Screening Questionnaire (ÖMSPQ) (Linton, Nicholas, & MacDonald, 2011). *Depressive symptoms* were assessed with the Montgomery Åsberg Depression Rating Scale (MADRS) (Svanborg & Åsberg, 2001). *Anxiety symptoms* were assessed with the

Overall Anxiety Symptoms and Impairment Scale (OASIS) (Norman et al., 2006). *Psychopathology* (suicidality, alcohol and drug use, psychotic symptoms) was assessed using parts of the MINI (Sheehan et al., 1998).

Outcome measures

General anxiety and depressive symptoms were assessed weekly with the OASIS and the Overall Depressive Symptoms and Impairment Scale (ODSIS) (Bentley, Gallagher, Carl, & Barlow, 2014). *Pain and pain coping problems* were assessed by asking participants on a weekly basis how much pain on a scale of 1–10 they had experienced during the last week and, further, by using the short version of the ÖMSPQ (Linton, Nicholas, & MacDonald, 2011) pretreatment, mid-treatment, post-treatment and at follow-up. *Diagnostic status* was assessed pre- and post-treatment using the MINI (Sheehan et al., 1998).

Feasibility measures

Completion and compliance were assessed by examining the number of participants who completed the whole treatment within the given time frame as well as the number of homework exercises registered on the platform. Patient satisfaction was assessed by asking participants to rate their overall satisfaction with the treatment, and whether they would recommend it to a friend. Self-reported improvement on UP targets was assessed by asking participants whether they were experiencing considerable improvement in emotional avoidance, unhelpful emotion-driven behavior, the ability to observe emotion-driven behavior without judgement, overestimation of probabilities and catastrophizing, and emotional discomfort caused by physical sensations.

Treatment

The treatment consisted of an adapted telephone and e-mail guided internet-delivered version of the patient workbook of the UP (Barlow et al., 2010). The treatment is transdiagnostic and targets underlying mechanisms relevant in both pain and emotional problems, such as avoidance and catastrophizing. Modules contained the following topics: motivation and goals, understanding emotions, mapping emotions, non-judgmental awareness, understanding thoughts, emotional avoidance, emotion-driven behavior, emotional experiences and physical sensations, emotional exposure, and making a plan for maintenance.

The treatment was administered via a secure platform, which included an email function for participants' questions. Therapists gave feedback within 24 hours (during workdays). Telephone support was provided contingent on starting a new module. The phone calls were standardized.

Analyses

Graphs of the repeated ratings were analysed by visual inspection to identify trends, that is, the general direction in which data were changing (Kazdin, 2011). The percentage of scores above the clinical cut off (≥ 8) in the OASIS and ODSIS during baseline and treatment were compared and changes in participants' mean levels on OASIS, ODSIS, and pain intensity from baseline to treatment phase were calculated. Also, Nonoverlap of All Pairs (NAP) and Tau-U scores were calculated. NAP, is a nonparametric quantitative approach comparing every measurement during baseline with every measurement during treatment to determine overlap, non-overlap, or tie (Parker & Vannest, 2009). Scores between 0 and 0.65 are defined as small effects, 0.66–0.92 as medium, and > 0.92 as large (Parker & Vannest, 2009). Tau-U is calculated by dividing the net improvement sum, S , by the number of pairs in the data and expresses the trend in data as the percentage of data points that have improved over phases (Parker, Vannest, Davis, & Sauber, 2011). Scores below 75% are considered questionable, whereas scores of 75–90% are considered to indicate an effective treatment, and above 90% a highly effective treatment (Parker et al., 2011).

Results

Anxiety, depression, and pain measurements

The graphs for visual inspection are shown in Figure 8. Generally, there was no clear trend during baseline, except for participant 4 regarding anxiety and participant 5 regarding depression where a downward trend was seen. During treatment, only participant 4 showed a clear downward trend on depression and anxiety. Scores at the 3-month follow-up were either stable or further decreased for all participants.

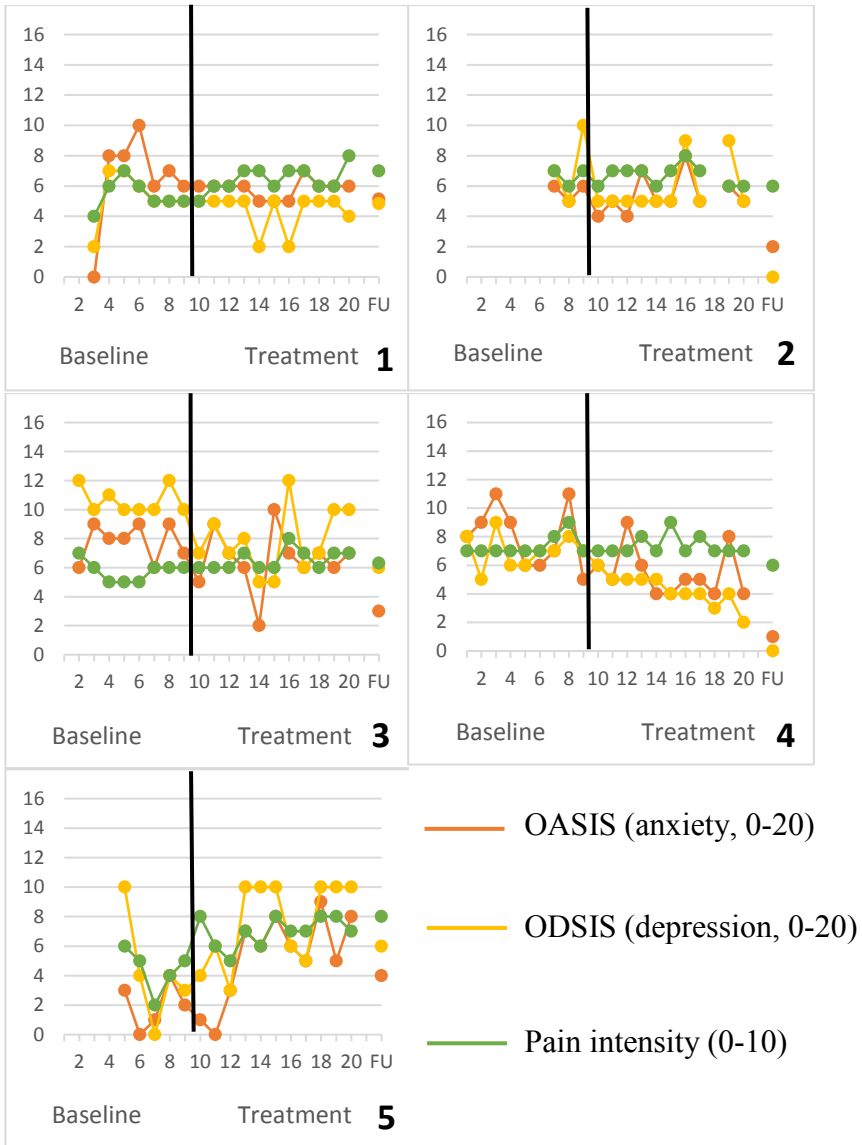


Figure 8. Individual graphs visualizing repeated measurements. FU = 3-month follow-up. Numbers on the x-axis indicate number of measurements. The vertical line indicates treatment start.

Regarding OASIS, two (1, 4) participants showed decreases on the percentage of clinical scores during treatment, whereas two (3, 5) showed an increase. Four (1–4) showed slight decreases in mean scores from baseline to treatment phase, whereas one (5) showed an increase. Three participants (1, 3, 4) showed changes in the medium range on NAP scores, but scores were only significant for participant 4. Tau-U scores were questionable for all participants.

Regarding ODSIS, two participants (3, 4) showed a decrease in scores above the clinical cut-off during treatment. Two (1, 2) showed no changes and one (5) showed an increase. When comparing mean scores between baseline and treatment, four participants (1–4) showed a decrease whereas one (5) showed an increase. NAP scores were in the medium to large range for four participants (1–4), but were significant for only two (3, 4). Tau-U scores showed questionable results for all participants except for participant 4 whose scores indicated a highly effective treatment. With regard to pain intensity and pain coping problems, neither mean changes, NAP, nor Tau-U scores showed an effect, except in participant 5 for whom an increase in pain intensity was detected.

Diagnostic status

Four out of five participants (1, 3, 4, 5) fulfilled diagnostic criteria for one or more DSM-diagnoses before treatment. Post-treatment, two of these (1, 4) were no longer diagnosed with any emotional disorder.

Feasibility and patient satisfaction

All participants completed the full program, including the 3-month follow-up, in the given time frame of 10 weeks, except for one participant (3) who needed 14 weeks due to a 3 week vacation. Participants were active on the platform where they filled in 44–54 individual exercise reports. Participants reported satisfaction with the treatment (two were very, three mainly satisfied) and responded that they would recommend it to a friend.

Self-reported improvement on UP targets

Four participants reported improvement in the ability to observe emotions without judgment and in emotional discomfort due to bodily sensation. Three participants reported improvement in emotional avoidance, unhelpful emotion-driven behavior, and overestimation of probabilities and catastrophizing. Participants 1 and 2 reported improvement on all five

areas, participant 4 in four areas, participant 2 in two areas, and participant 5 in one area.

Discussion and Conclusion

In this study, participants generally reported improvement in the targeted transdiagnostic factors, but this did not translate into reliable changes in emotional or pain problems. Hence, the treatment did not manage to achieve improvements in outcomes for pain patients with emotional comorbidities. In fact, changes on symptomatology were smaller than what was reported in other studies using the UP for other target groups (Farchione et al., 2012) or a different treatment approach for a similar target group (Dear et al., 2015).

Considering satisfaction and compliance, the participants reported that they were highly or mainly satisfied with the treatment and would recommend it to a friend. They worked through all ten modules and were active on the platform.

Participants also reported improvements in transdiagnostic factors directly targeted by the UP, such as emotion-driven behavior. The lack of change in outcome variables may indicate that the treatment manual may have to be further refined to better meet participants' needs. For example, in the current study, participants decided on the content of exposure hierarchies themselves and mainly focused on emotional difficulties and social situations. Also, participants may have needed more time, such as when working with the module containing exposure exercises. This is indicated by the fact that the two participants who still reached diagnostic criteria-post treatment (3, 5) reported that they did not feel they had improved in catastrophizing and avoidance, two treatment targets that are believed to be central mechanisms in both emotional disorders and pain problems.

Overall, the study shows that pain patients with comorbid emotional problems find an internet-delivered version of the UP satisfactory and beneficial, even though treatment effects on pain problems and emotional problems are at best small and heterogeneous. Future research should continue to develop treatment content and delivery to optimize treatment results.

General discussion

This dissertation set out to further our understanding of the role of transdiagnostic factors in the context of comorbid pain and emotional problems. Specifically, it was investigated whether the proposed vulnerability factors negative affect and anxiety sensitivity, and symptomatology covaried in pain patients dependent on the occurrence of comorbid social anxiety symptoms (Study I); whether peer-related stress predicted musculoskeletal pain problems over time in adolescents, and whether this relationship was mediated by worry and moderated by gender (Study II); and, finally, whether emotional and pain problems could be decreased in pain patients with comorbid emotional problems by using an internet-delivered unified protocol for emotional disorders (Study III).

Results show that anxiety sensitivity and negative affect covary with comorbid pain and emotional problems (Study I). Results also show that peer-related stress predicts the development of pain over time, and that, in girls, this relationship is mediated by worry (Study II). The possibility of decreasing emotional and pain symptoms by using the transdiagnostic unified protocol treatment was not confirmed (Study III). Nevertheless, the results in several ways confirm the validity of the shared vulnerability model, which was the theoretical framework for this dissertation. Also, the results highlight the importance of factors that have been suggested as transdiagnostic factors for understanding pain and emotional comorbidity. This may have implications for assessment and treatment as well as prevention. In this general discussion, these issues will be addressed, starting with an in-depth discussion of the findings in relation to the research questions.

Answers to research questions

Study I aimed to investigate the covariation of suggested vulnerability factors with comorbid pain and anxiety and to study if the shared vulnerability model could be generalized to comorbid pain and social anxiety. This was done by investigating the occurrence of subgroups with different patterns of social anxiety and pain-related fear in a chronic pain population receiving multimodal pain rehabilitation, and by comparing these subgroups with regard to levels of transdiagnostic vulnerability factors (anxiety sensitivity and negative affect) as well as treatment outcome. Results show that pain patients could be meaningfully divided into subgroups and that the subgroup with high pain-related fear and social

anxiety also had significantly higher scores on anxiety sensitivity and negative affect when compared to the group with low scores on pain related fear and social anxiety. Thus, comorbid pain and emotional problems covaried with high scores on factors that have been understood as transdiagnostic vulnerability factors (Asmundson & Katz, 2009). This is in line with earlier studies. For example, two cross-sectional studies using structural equation modelling showed the importance of anxiety sensitivity and negative affect in the development of pain problems (Wong et al., 2014; 2015). The subgroups in Study I also varied regarding treatment outcome, since the comorbid subgroup had residual problems post-treatment. This confirms that there are subgroups of pain patients for whom existing treatments may not be sufficient. It also connects worse outcome to comorbidity and to the covariation with high scores on suggested vulnerability factors.

Results from Study I suggest that it may be important to assess potential transdiagnostic vulnerability factors pre-treatment and to tailor treatments to individuals to ensure that the needs of patients with comorbidities are met. Specifically, treatments need to have a more holistic focus and also include a focus on, for example, interpersonal functioning and general emotion regulation skills. This could potentially result in better overall functioning that includes lowering levels of emotional symptomatology to subclinical levels. Clearly, more research is needed to find out how to provide pain patients with emotional comorbidities with a treatment that better meets their needs. For example, treatments that have been successful in lowering levels of anxiety sensitivity (Smits, Berry, Tart, & Powers, 2008), treatments focusing emotional awareness and expression (Lumley et al., 2017), or other treatments targeting shared factors should be tested in samples of pain patients with comorbidities.

Study II investigated the prevalence of musculoskeletal pain problems in adolescents, as well as the predictive and mediating role of transdiagnostic factors in the development of musculoskeletal pain problems over time. Also, the moderating role of gender was studied. Specifically, it was studied whether peer-related stress predicted the development of musculoskeletal pain problems in adolescents, whether this development was mediated by worry, and whether the mediation was moderated by gender. The results showed that 8.4% of adolescents suffered from musculoskeletal pain that influenced their everyday life to some extent (pain grades III and IV) at age 14, compared to 10.5% at age 15, and 9.9% at age 16. Other studies using pain grades have studied clinical samples of adolescents (Wager et al., 2013)

or different age groups, which makes a direct comparison difficult. For example, a large study (N = 10,650) in a general population sample of 10–21-year-olds (mean age = 14.33 years) classified 14% of the sample as having pain problems (pain grades III or IV) in any area. Earlier studies generally show a higher prevalence of pain problems in girls (King et al., 2011), which was confirmed in the present study. Indeed, whereas the prevalence for boys was more or less stable across the three measurement points (7.2%, 7.1%, and 6.9%), girls in the sample reported a higher prevalence of musculoskeletal pain problems over time (9.7%, 13.4%, and 14.3%).

The development of musculoskeletal pain problems was predicted by peer-related stress and, for girls, mediated by worry. Thus, it was confirmed that interpersonal stressors, even at more normative levels, are important in the context of pain, something that longitudinally has been studied only in the bullying literature (Gini & Pozzoli, 2013). Likewise, the importance of worry, a form of repetitive negative thought (RNT), was confirmed. This is in line with previous research showing that RNT is involved in both somatic and emotional problems (for a review, see Watkins, 2008). For example, RNT has been linked to prolonged physical activation, which has been suggested to explain the relationship between RNT and physical complaints (Brosschot, Gerin, & Thayer, 2006; Ottaviani et al., 2016). In pain, RNT has been shown to correlate with worse pain complaints and has been implicated in the development of chronic pain problems (Flink, 2011; Quartana et al., 2009; Severeijns et al., 2001). In this study, it was shown that worry, a form of RNT, may be an important link between stressors and musculoskeletal pain problems for girls, since the relationship between peer-related stress and worry was moderated by gender. In summary, the results of Study II confirm that peer-related stress and worry are important transdiagnostic factors involved in the development of pain problems over time.

Study III aimed to test if levels of emotional and pain problems could be influenced positively by using a transdiagnostic unified treatment. This was tested by recruiting former pain rehabilitation patients with residual pain problems and emotional comorbidity and treating them using an internet-delivered, therapist-guided unified treatment approach. According to participants' self-report, transdiagnostic factors were successfully targeted. Opposite to expectations, this did not translate into reliable changes on outcome measurements. Overall, the study is in line with other studies showing that pain patients with emotional comorbidities are a group with

complex problems who may generally have worse treatment outcomes (McCracken & Turk, 2002). This is also in line with the results of Study I, in which pain patients with comorbidity still scored high on anxiety sensitivity and negative affect, as well as on emotional symptomatology post-treatment. It should be noted that the particular target group had already received multimodal rehabilitation with a suboptimal outcome and may have had especially challenging difficulties that were hard to treat.

While development is needed to improve treatment effects, it is encouraging that the treatment was feasible and patient satisfaction was high. In fact, written feedback given by participants online, or when sending back the pen and paper questionnaire, was formulated in an overwhelmingly positive fashion. This encourages further studies using modified transdiagnostic treatment protocols, rather than discarding the treatment altogether because of poor effects on outcome. In addition, a transdiagnostic treatment approach has a sound theoretical and empirical base. Many of the factors suggested as transdiagnostic treatment targets, such as avoidance and the regulation of emotional reactions, have been successfully treated in numerous studies, leading to positive changes for patients with emotional problems as well as pain patients (for meta-analyses, see Aldao, Nolen-Hoeksema, & Schweizer, 2010; López-de-Uralde-Villanueva et al., 2016). In line with suggestions in Study I, transdiagnostic treatments focusing on emotion regulation difficulties (Linton & Fruzzetti, 2014; Lumley et al., 2017) or treatments focusing on maladaptive cognitions, such as thought suppression (Hasenbring & Verbunt, 2010; Hülsebusch, Hasenbring, & Rusu, 2016), show promise for the future of clinical treatments for pain and emotional comorbidity.

Findings in relation to the theoretical framework

This dissertation used the shared vulnerability model as a theoretical framework. The shared vulnerability model is a transdiagnostic model developed to understand the high comorbidity between pain and emotional problems (Asmundson et al., 2008; Asmundson & Katz, 2009). It proposes that underlying factors in the form of biological and psychological vulnerabilities (such as negative affect, anxiety sensitivity, or biological thresholds), in combination with triggering events (traumatic life events, stressors), give rise to emotional responses that are in turn regulated or dysregulated by biological and psychological factors, including cognitive factors and behaviors (such as hypervigilance, catastrophizing, or avoidance), potentially giving rise to both pain problems and emotional

disorders (Asmundson & Katz, 2009). These shared vulnerability factors, triggers, and potential maintaining mechanisms may therefore explain the high comorbidity between pain and emotional problems. An overview of the studies in relation to the shared vulnerability model is shown in Figure 9.

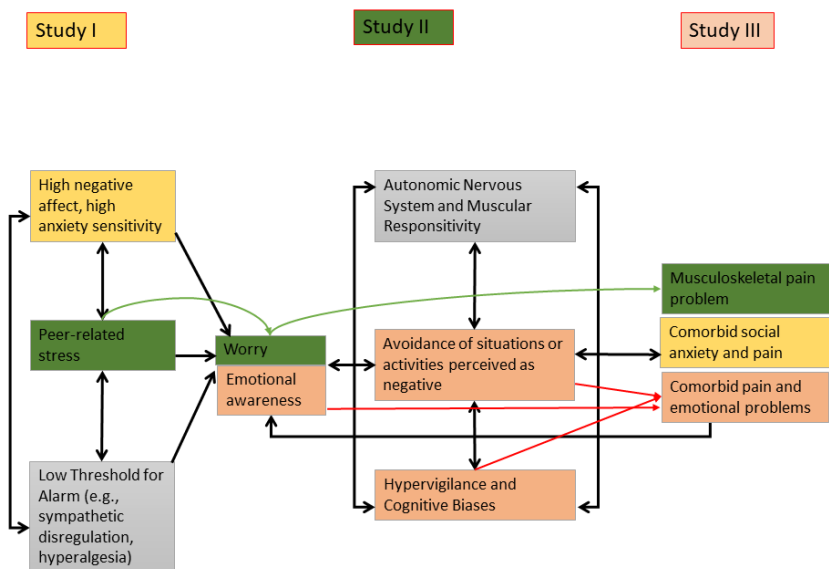


Figure 9. The three studies in the dissertation in relation to the shared vulnerability model. Variables in the grey boxes were not studied in this dissertation.

In relation to the shared vulnerability model, Study I (visualized by yellow boxes in Figure 9) set out to test whether psychological vulnerability (anxiety sensitivity, trait negative affect) covaried with comorbid social anxiety and pain problems to test the generalizability of the shared vulnerability model. The shared vulnerability model is largely based on studies in samples of pain patients with comorbid PTSD, but has been suggested to also be applicable to pain and other emotional comorbidities. Since the model proposes anxiety sensitivity and negative affect as vulnerability factors involved in the development of both emotional and pain problems, it was expected that pain patients with emotional comorbidities would score higher on anxiety sensitivity and negative affect

compared to those without emotional comorbidity. This was confirmed by Study I. Hence, it can be concluded that the model seems to be applicable to social anxiety. However, since all variables in Study I were measured concurrently, the results cannot establish causality or the direction of the relationship. Thus, it cannot confirm whether anxiety sensitivity and negative affect function as vulnerability factors preceding the development of pain and social anxiety. Nevertheless, the results confirm the covariation of the proposed vulnerability factors with comorbid problems and higher symptomatology in the expected direction. Since the subgroups also scored high on pain-related fear and catastrophizing, the propositions of the fear-avoidance model (Figure 2) are strengthened considering the relationship between high catastrophizing, high fear avoidance, and symptomatology. Also, the paths suggested by the shared vulnerability model (Figure 3) are confirmed as likely. Specifically, high vulnerability covaried with high fear and catastrophizing, which has been shown to lead to avoidance and disability (Crombez et al., 2012). Here, again, measurements were taken concurrently and cause cannot be established. In sum, Study I highlights the potential of applying the propositions of the shared vulnerability model in the context of comorbid pain and emotions.

Study II, in turn, analyzed if the path from triggers (in this case, peer-related stress) via worry to pain problems suggested by the shared vulnerability model can be confirmed (visualized by green boxes and arrows in Figure 9). Results from Study II partly support the theoretical model. Peer-related stress predicted pain problems and worry was shown to act as a mediator between stressors and pain problems for girls. Since no longitudinal data was previously available, Study II contributes uniquely to our understanding of how stressors and worry may interact and lead to the development of pain problems over time. The lack of a mediation effect in boys could possibly be explained by the comparable stability of pain problems over time in boys. Also, even though the study had a large sample, there may not have been enough boys reporting a pain problem to determine the influence of worry on the development of pain problems in boys. Peer-related stress predicted pain problems for both girls and boys, but the mechanisms involved in the development of pain problems for adolescents who experience peer-related stress may differ depending on gender. Alternative mechanisms involved in the development of pain should therefore be investigated further, including potential gender differences.

The adolescents with pain problems also scored higher on depression and anxiety compared to their peers without pain problems. Even though

comorbidity was not specifically investigated in this sample, this confirms that pain problems were indeed accompanied by higher levels of emotional problems. Since the shared vulnerability model suggests that shared vulnerability and maintaining factors may lead to the development of both pain and emotional problems, the results further strengthen the propositions of the shared vulnerability model.

Study III, in turn, tested an internet-delivered unified protocol for emotional disorders on pain patients with emotional comorbidity. This treatment aimed to target transdiagnostic factors suggested to maintain problems to investigate if this would result in changes in comorbid pain and emotional problems (visualized by red boxes and arrows in Figure 9). The shared vulnerability model suggests that stressors lead to the development of problems via emotional, cognitive, and behavioral factors, such as fear, worry, maladaptive cognitions, or avoidance. Consequently, targeting these factors by raising emotional awareness, working on maladaptive cognitions, and lowering avoidance (all targets of the UP) should lead to less symptomatology. The results of Study III are conflicting. The study confirmed that several factors could be successfully targeted in treatment (that is, patients reported change on these factors), but this did not lead to changes in pain or emotional problems. Hence, the results of Study III cannot be said to support the model.

There may be several reasons for the results in Study III. Patients' self-reports of changes in the targeted mechanisms may not be reliable, since the measurements used to assess change were not psychometrically validated. Hence, there may have been no changes in symptomatology, because the underlying mechanisms were not successfully targeted. This is possible, but rather unlikely, since participants' feedback was in line with reported exercises, such as exposure training, where they showed clear improvement. Nevertheless, it would be important, in future studies, to use reliable measures of improvement in mechanisms to improve the ability to draw valid and reliable conclusions. Alternatively, the participants' problems may not have been severe enough to detect a clear change. Pain problems are often cyclical and it is likely that participants applied to participate in the study when their problems were more severe. There was a fairly long waiting period between screening and treatment, which may have led to a regression to the mean. In fact, at screening, all participants had depression scores on clinical levels, and three out of five had scores on clinical levels on anxiety. At baseline, means were at subclinical levels for depression and

anxiety for all but one participant. Considering this, it was positive that follow-up scores remained low or decreased further.

Alternatively, it is possible that participants needed a longer treatment and more time for central homework exercises, such as exposure, to take effect. This would be in line with previous studies showing better effects with longer treatment protocols (Farchione et al., 2012). Clearly, more research is needed to further develop treatments for pain patients with emotional comorbidities. Specifically, it would be valuable if a longer treatment protocol was tested and more reliable process measurements were added.

In sum, the studies in this dissertation confirm the overlap between pain and emotional problems as well as the importance of several of the transdiagnostic factors suggested by the shared vulnerability model, such as anxiety sensitivity, negative affect, peer-related stress (trigger), and worry. This highlights the importance of transdiagnostic factors in the development of pain problems, emotional problems, or comorbid pain and emotional problems. At the same time, transdiagnostic approaches are still new and being developed.

Transdiagnostic approaches

Since transdiagnostic approaches are still being developed, there are some concerns that need to be discussed. Firstly, transdiagnostic factors are not well defined, beyond being shared across diagnoses. The fact that they are shared across diagnoses implicates them as risk- or maintaining factors of symptomatology, but this nevertheless leaves practitioners and researchers with a large number of potential transdiagnostic factors (as suggested by Mansell, Harvey, Watkins, & Shafran, 2009). Therefore, questions regarding the usefulness of transdiagnostic approaches have been raised, since having to attend to many different transdiagnostic factors does not streamline clinical practice or theoretical understanding, compared to having to attend to many different diagnostic areas (Mansell et al., 2009). Also, the factors suggested are on multiple levels. For example, anxiety sensitivity is seen as a trait, whereas avoidance is closer in time to the development of problems and potentially more mutable. On top of that, some transdiagnostic factors may simultaneously function as a vulnerability factor, a maintaining factor, and an outcome. For example, social anxiety is a diagnosis and, hence, an outcome influenced by transdiagnostic vulnerability factors. At the same time, existing social anxiety can be a vulnerability factor for other problems. Social anxiety may, for instance,

lead to social withdrawal and in this way increase the risk for depression. Hence, there is a built-in risk for circular reasoning. Secondly, it is still empirically unexplained why people with high scores in the same transdiagnostic factor can develop different symptoms (multifinality), and why people with high scores in different transdiagnostic factors can develop the same diagnosis (divergent trajectories). Even though we still largely lack empirical studies and there are knowledge gaps, attempts have been made to propose explanations based on the existing literature. To strengthen the general applicability of transdiagnostic approaches in the overlap of pain and emotions, these attempts are presented below.

Current concerns, such as those raised by the social environment, and other moderators have been suggested to explain the problems of multifinality and divergent trajectories. Mansell et al. (2004) originally suggested the existence of current concerns mainly to explain multifinality (Mansell et al., 2004; Nolen-Hoeksema & Watkins, 2011). A current concern would explain the diverse outcome for people who share a vulnerability factor, but have different experiences and contexts influencing how this vulnerability is expressed. Thus, peer-related stress may be especially threatening during a period of time where peer relationships become increasingly important, such as during adolescence. This may be especially true for girls, considering the results in Study II, which indicated that there may be potential gender differences in the threat value of peer-related stressors.

Explanations for multifinality and divergent trajectories have been further developed by Nolen-Hoeksema and Watkins (2011) in an article presenting a heuristic for the development of transdiagnostic models. They distinguished between distal and proximal transdiagnostic risk factors, that is, those that are temporally further away (and often, but not always, harder to change) and those that are closer in time to the onset of symptoms (and often, but not always, easier to change). They proposed that distal risk factors influence proximal risk factors, which in turn are moderated by three types of conditions that influence outcome: conditions that raise concerns or themes (current concerns, such as a threatening social context leading to a diagnostic criteria where fear is prevalent), conditions that shape responses (such as observing certain behaviors in others), and conditions that change the reward value of a stimuli (generally biological, such as how rewarding food is to the individual). As there may be an overlap between the definition of a transdiagnostic risk factor and a moderator, Nolen-Hoeksema and Watkins (2011) presented an important distinction:

moderators are identified by their temporal position between risk factors and disorder and, in contrast to the transdiagnostic risk factors, do not themselves lead to psychopathology. Also, moderators are limited to biological and contextual factors. This presents important distinctions and goes a long way towards understanding the different factors involved. For example, factors proposed by the shared vulnerability model can be divided into more distal vulnerability factors (negative affect, anxiety sensitivity, certain triggers), more proximal maintaining factors (avoidance, maladaptive cognitions), and moderators (such as the strength of a person's physical reaction to potential stressors or emotion). If a smaller number of central transdiagnostic factors can be identified, transdiagnostic approaches may be advantageous in simplifying both assessment and treatment for people with comorbid pain and emotional problems. This would enable clinicians to treat diverse symptomatology in a parsimonious way in the same clinical setting.

Social factors

This dissertation proposes that social factors may play an important role in comorbid pain and emotions. As mentioned previously, social functioning is affected in chronic pain (Forgeron et al., 2010; Mitchell & MacDonald, 2009). Also, pain patients describe a feeling of lowered self-esteem and shame, which may in turn lead to a higher fear of being judged, more self-criticism, and more avoidance of social situations, all symptoms and behaviors that are common in social anxiety (Burke et al., 2015; Clark & Wells, 1995; Cox et al., 2004; Gilbert, 2000; Gilbert & Miles, 2000; Gustafsson et al., 2004). Thus, pain problems may lead to, or exacerbate, social difficulties and interact with social fears, which is confirmed by the fact that there is a raised prevalence of social anxiety in pain populations (11-36%) compared to the general population (0.5-15%) (Furmark et al., 1999; Gadermann et al., 2012). This was confirmed by the results reported in this dissertation. For example, in Study I it was shown that social anxiety is prevalent in pain samples. The subgroup of pain patients with comorbid pain-related fear and social anxiety comprised 17% of the whole sample. The subgroup had mean social anxiety scores (32.5, SD 8.2 on the SPSQ) comparable to scores of a clinical sample with social anxiety (Furmark, personal communication, February 19th, 2014).

The studies in this dissertation approach social factors in several different ways. Social factors may be both internal (individual differences in social functioning) and external (involving the social network, and how somebody

is treated by their social environment). It can be argued that social aspects can be positioned in different parts of the shared vulnerability model. In the studies in this dissertation, social anxiety was, amongst others, used as a proxy for an anxiety disorder to investigate whether the shared vulnerability model could be generalized (Study I). Social anxiety can also be understood as a proxy for individual social functioning, which may play a role in the context of pain, for example when communicating needs (Study I). To be able to effectively and appropriately communicate needs may be important in the contact with health care services, when communicating adaptation needs at work, and when talking to friends and family.

Since people with pain problems commonly describe a loss of social networks, someone with previously existing social anxiety may face additional problems, since many pain-related situations are also social in nature and involve talking to authorities, such as doctors and bosses. Hence, people with both social anxiety and pain problems may have a higher tendency to use maladaptive coping strategies, such as avoidance, which in turn has been linked to worse outcome. The link between avoidance and outcome is, for example, proposed by the fear-avoidance model shown in Figure 2 (Vlaeyen & Linton, 2012). Thus, social anxiety may be understood as both an outcome and a vulnerability factor, and may be closely linked to maintaining factors, such as avoidance. This is in line with Nolen-Hoeksema and Watkins (2011) who suggest that the same factor may have several functions.

Additionally, it has also been suggested that catastrophizing and fear reactions after an acute pain episode can lead to avoidance of social interactions, which in turn would lead to more depression (due to fewer positive experiences), fewer endorphins, and, finally, a higher risk of developing chronic pain problems (Hasenbring, Hallner, & Klasen, 2001). This highlights the potentially bidirectional nature of social functioning in pain problems.

In Study II, peer-related stress was shown to function as a contextual social trigger leading to the development of pain problems over time. This highlights the role of individuals' social contexts in the development of problems and is in line with studies showing that positive peer relationships are a protective factor in the context of pain (Fleischman, Hains, & Davies, 2011). At the same time, adolescents with pain have been shown to have fewer friends compared to those without pain (Forgeron et al., 2010). Hence, the results of this dissertation highlight the importance of social networks. This has previously been highlighted in the context of couples,

where interactions with a validating and emotional disclosure content have been shown to have the potential for positive pain-related outcomes, such as more adaptive emotion regulation strategies and lower pain-related distress (Cano & Williams, 2010).

In Study III, social functioning was not specifically assessed, except in the diagnostic interview, which diagnosed one of the five participants with social anxiety disorder. Nevertheless, several participants developed exposure hierarchies including social situations, such as talking to former colleagues, saying no to family members, or contacting insurance companies or employers. This is in line with previous studies connecting pain problems to lower self-efficacy in communicating adaptation needs at work (Thomtén et al., 2016). In sum, results underline that pain-related situations often are social in nature and that there is an overlap between pain and social difficulties.

In conclusion, even though the main focus of this dissertation was on transdiagnostic factors in the overlap between pain and emotional problems, many of these factors have a clear connection to the social context that patients with pain live in. How social networks can be utilized in the context of pain and emotions may be important to consider, and future studies should focus more on social aspects in the context of pain.

Gender

The studies in this dissertation had some interesting results with regard to gender that need to be discussed further. For example, Study II showed gender differences in pain prevalence, and also indicated gender differences in the tendency to worry. These differences in the tendency to worry may subsequently have influenced the development of pain problems over time. The study showed no gender differences in 7th grade. In 8th and 9th grade (from age 14), the prevalence of girls' musculoskeletal pain problems increased, whereas prevalence among boys stayed on the same level. This could potentially be explained by the start of puberty and menarche for girls, which would be in line with studies showing an influence of hormonal factors on pain in women (Wijnhoven, de Vet, Smit, & Picavet, 2006). For example, a Norwegian study showed a higher risk for chronic pain in girls with early menarche (< 12 years) in a cross-sectional sample of adolescents aged 12–18 (Kløven, Hoftun, Romundstad, & Rygg, 2017). These studies give one possible explanation for the gender differences found in this dissertation, but the exact applicability to understanding the gender differences in Study II remains unclear. Moreover, psychosocial factors

associated with early menarche may confound results. Girls with early pubertal timing may be exposed to psychosocial stressors to a higher degree compared to girls with later pubertal timing (Skoog, 2013). Since gender was also shown to be a moderator in the relationship between peer-related stress and worry, the relationship between these factors needs to be explored further.

Girls in Study II seemed to be more vulnerable to reacting with worry when experiencing interpersonal stress. Looking at average scores, they reported the same amount of peer-related stress in 7th grade compared to boys, but did score higher on worry. This is in line with studies showing that girls from a certain age generally show a higher tendency to use RNT (McLean & Anderson, 2009; Nolen-Hoeksema & Jackson, 2001). This suggests that differences in pain prevalence may be linked to differences in the experience of emotions and, further, differences in the use of emotion regulation strategies (such as worry and other RNTs). In contrast, there have also been studies showing that girls do *not* use RNT more than boys when stressor load is taken into account (Hamilton et al., 2015; Stange et al., 2014; Østerås et al., 2016). Rather, these studies have shown a higher stressor load in girls compared to boys. In line with this, higher prevalence of RNT in grown-up women has been linked to a higher life-time prevalence of sexual assault in women compared to men and to a higher experience of uncontrollable negative events in the life of women (Nolen-Hoeksema, Larson, & Grayson, 1999; Nolen-Hoeksema & Jackson, 2001), all factors that indicate a higher stressor load.

Study II looked only at peer-related stress and did not include other stressors. Hence, the tendency to worry in girls may have been higher simply because they had an overall higher perceived stressor load compared to boys. Alternatively, there may be gender differences in the type of situations that are considered stressful. Possibly, girls are more sensitive to interpersonal stressors and the interpersonal context therefore becomes more of a current concern to them. This is confirmed by earlier studies indicating that social stressors may be more potent for girls than for boys (Rudolph, 2002). Therefore, gender differences in stressor loads or in the salience of interpersonal situations, with a resulting higher tendency for girls to use RNT, could explain the higher prevalence of pain problems in girls shown in Study II and in other studies in the field (King et al., 2011; Petersen et al., 2003; Stanford et al., 2008; Sundblad et al., 2007).

Clinical implications

The results in this dissertation have clear clinical implications. As has been mentioned previously, transdiagnostic approaches have the potential advantage to simultaneously prevent and treat several disorders in the same person, as well as offering group treatments to people with different disorders or a combination of different disorders (Mansell et al., 2004). This has immense clinical appeal.

The effectiveness of transdiagnostic treatments is unclear when looking at the results of Study III. Clearly, the internet-delivered, adapted version of the UP used in the study did not have the expected effects on symptomatology. Nevertheless, the results from this dissertation support that a clinical approach looking at several comorbid disorders simultaneously and actively relating them to each other could be important and parsimonious. The results of the studies in this dissertation confirm that comorbidity between pain and emotional problems exists and is accompanied by higher scores on proposed vulnerability and maintaining factors. The results do not confirm that comorbid pain and emotional problems can be successfully treated simultaneously using the UP. Nevertheless, results highlighted other factors relevant for prevention and treatment, such as anxiety sensitivity, peer-related stressors, and RNT.

In Study I, data was collected in a clinical setting showing that pain patients with comorbid social anxiety scored high on trait negative affect and anxiety sensitivity. These are understood as vulnerability factors in the shared vulnerability model and could therefore be used at assessment to find patients at risk of prolonged and more severe problems, including comorbidities. By definition, traits are seen as unchangeable, but some studies have shown that anxiety sensitivity can be influenced. For example, a review showed the efficacy of CBT in reducing anxiety sensitivity (Smits et al., 2008). Also, anxiety sensitivity is commonly measured with the Anxiety Sensitivity Index, which contains items with somatic, psychological, and social content. The inclusion of these three areas makes anxiety sensitivity an especially useful concept in the overlap between pain and emotions. Since people with high anxiety sensitivity are more likely to experience emotions more frequently and more strongly compared to those with low anxiety sensitivity, treatments targeting anxiety sensitivity can provide tools to handle these emotions, including emotional reactions due to social interactions or the experience of pain. Hence, anxiety sensitivity could also be targeted in treatment and used as an outcome for measuring effects of transdiagnostic treatments.

In Study II, peer-related stress was shown to be a predictor of musculoskeletal pain problems in a general population of adolescents. Results therefore indicate that peer-related stress can be an important target for school-based prevention of pain problems. The potential for school-based programs targeting peer-related stress should therefore be investigated further.

Study II showed that worry mediated the relationship between peer-related stress and musculoskeletal pain problems in girls. This highlights worry as a potential mechanism in the development of musculoskeletal pain problems in the general population. Additionally, worry has been implicated in the development of anxiety and depressive disorders, reinforcing its importance as a central mechanism in mental health. Worry could be assessed at screening to detect adolescents at risk, but could also be a target in prevention and treatment. Since worry will likely be a factor for *some* boys, even though the conditional effect did not reach statistical significance for boys in Study II, this should be assessed for all adolescents. Recently, worry and other forms of RNT have been suggested as meaningful targets in the prevention of emotional problems (for a review, see Topper, Emmelkamp, & Ehring, 2010). This has led to the development of treatments specifically targeting RNT (Topper, Emmelkamp, Watkins, & Ehring, 2017; Watkins, 2009). For example, one study showed good results in a sample of adolescents and young adults, reporting considerably lower levels of RNT, anxiety, and depression 12 months after treatment when compared to a waiting list control (Topper et al., 2017). Considering the results of Study II, these treatments could potentially also lower the risk of the development of pain problems and may be especially useful for individuals with comorbid emotional problems.

Methodological considerations

There are methodological considerations regarding the studies in this dissertation. For example, all studies relied on self-report measurements, which can be influenced by social desirability, participants' memory, and other factors (Kazdin, 2010). Nevertheless, with only few exceptions, established measurements with sound validity and reliability were used. Also, self-report measurements allowed for efficient data collection, making it possible to include a large number of participants. Nonetheless, the studies could have benefited from alternative sources of information, such as health care visits, or information on return to work or use of medication.

Some methodological considerations are specific to the separate studies and will be discussed below.

Study I used a self-selected sample of patients undergoing multimodal pain rehabilitation. Only about a third of the patients starting treatment during the relevant time period chose to fill in measurements both before and after treatment and could be included in the analyses. This raises questions about the external validity and generalizability of the study, especially since no data was available to compare those who chose to participate with those who did not. There is a risk that some subgroups, such as patients with worse problem profiles or those with lower Swedish language skills, had a lower participation rate. To strengthen external validity, participants' demographic data (gender, age, pain area, employment, pain duration) was compared to other studies with similar samples, which was possible since Study I used data from a clinic connected to the Swedish Quality Registry for Pain Rehabilitation. Comparisons showed differences only in the higher ratio of women to men in Study I and a longer pain duration (an average of 14 compared to 8 years) (Milton et al., 2013). Thus, it was confirmed that participants in Study I generally overlapped well with pain patients in other pain rehabilitation clinics, which increases the external validity.

The clusters in Study I, shown in Figure 4, also differed from each other on demographic data. For example, there were significantly more men in the pain-related fear (PF) cluster than in the social concern (SC) or pain-related fear-social anxiety (PF-SA) clusters. This may be explained by gender differences in scores on pain-related fear, since a previous study showed higher scores for men (Bränström, & Fahlström, 2008). A recent study using cluster analysis indicated that patients high on pain-related fear were less likely to receive multimodal pain rehabilitation after assessment, which may influence the gender ratio of clinical samples (Svanberg, Stålnacke, Enthoven, Brodda-Jansen, Gerdle, & Boersma, 2017). This study also found a cluster high on pain-related fear and distress, with worse treatment outcome, but, in contrast to our study, the comorbid cluster contained more men than the other clusters. In sum, this indicates that our results may be influenced by the gender distribution between our clusters. Clearly, it is important to further study the influence of gender on pain variables.

The PF-SA cluster in Study I had significantly lower education levels than the LS cluster. This is in line with earlier studies showing that education level, or other indicators commonly used to assess socioeconomic status, influences levels of pain problems and treatment outcome (Brekke,

Hjortdahl, & Kvien, 2002; Haase, Kuhnt, & Klimczyk 2012; Poleshuck, & Green, 2008). The differences between clusters in gender and levels of education should be kept in mind when interpreting the results and when planning studies in the future.

Anxiety sensitivity and negative affect were theoretically understood as vulnerability factors in Study I, but assessed concurrently with pain-related fear and social anxiety symptoms. This is a limitation, since concurrent measurement does not permit any conclusions on direction of relationships to confirm the function of anxiety sensitivity and negative affect as vulnerability factors. Timing has therefore mainly been theoretically inferred and the term “vulnerability factor” is used based on previous studies and existing theory. Nevertheless, the methodology does allow for the analysis of covariation, which was clearly demonstrated.

Study I used data from before and just after treatment. A longer follow-up period would have allowed several additional analyses and would therefore have been preferable. For example, it would have been important to explore whether treatment gains were retained over time. Also, it could have been investigated whether developmental paths differed for the subgroups detected in Study I and whether differences between subgroups of pain patients persisted over time.

In Study II, pain was operationalized by using pain duration, frequency, and intensity, as well as functional impairment, to create pain grades. This was based on earlier studies making an effort to describe the multidimensionality of pain problems, although the exact questions used varied slightly (Vervoort et al., 2014; Von Korff et al., 1992). For example, Study II used items on functional impairment in three areas, whereas Vervoort and colleagues (2014) only used one item asking adolescents if their pain influenced their daily/usual activities. This variation, as well as the fact that pain grades were not reported for specific areas of pain in Vervoort et al. (2014), makes it hard to compare prevalence numbers. Unfortunately, this is a common problem in pain research. In fact, a recent review of epidemiological studies showed that no two studies from independent research groups used the same operationalization of chronic pain (Steingrimsdóttir et al., 2017). This problem is also relevant to Study II. Nevertheless, using pain grades has the advantage of including several pain characteristics, which captures the multidimensional nature of a pain problem. It also makes the distinction between experiencing pain and having a pain problem, which includes functional impairment. This can be argued to increase the ecological validity. Also, the basic operationalization

of the separate pain grades in terms of pain intensity and level of functional impairment was in line with previous studies (Vervoort et al., 2014; Von Korff et al., 1992), so variation should, at worst, be small.

In Study III, a Single Case Experimental Design was used, which has the great advantage of enabling the researcher to study individual development. In this design, baseline and treatment scores are compared and participants are used as their own controls. This emphasizes control of internal over external validity. One specific threat to the external validity in a single case design is the small sample size, which makes generalizability unclear. It could be that, by chance, participants in Study III differed significantly from the average pain patient with comorbidity, especially since only a small percentage of the invited patients chose to participate. However, participants were all former pain rehabilitation patients with a clinically meaningful problem profile (longstanding pain duration, sick leave, comorbid emotional disorders), which raises the likelihood of external validity. In sum, there is no direct data suggesting that the patients in Study III would not be representative. Nevertheless, the fact that this is a type of design with unclear generalizability of results should be kept in mind.

Participants in Study III were asked yes/no questions on improvement in five factors targeted by the UP. The answer to these questions may have been influenced by the participants' investment in the study (for example a strong wish to gain something from their hard work) or not wanting to disappoint their therapist, which would be a threat to internal validity. Therefore, results should be considered with caution. Nevertheless, questionnaires were completed in the participants' home, without a therapist present. Scores and feedback should therefore be comparable to other treatment studies with therapist support.

In addition, outcome measures used in Study III may not have been sensitive enough to pick up changes, especially considering that, for some participants, baseline levels of anxiety and depressive symptoms were already relatively low, leaving less room for improvement. Alternative measurements, as well as more stringent inclusion criteria, such as emotional problems on clinical levels at treatment start, may have changed results, but this remains unclear.

Two of the studies in this dissertation (Studies I and III) used methods that enabled person-centered analyses. This is most evident in Study III where individual development was plotted throughout a ten-module treatment using a Single Case Experimental Design. This is a great advantage when trying to establish whether individuals with different sets

of symptoms or levels of transdiagnostic factors differ regarding their path through treatment. Finding this out is crucial, since individual development may get lost in group-based statistical approaches. For the same reason, Study I used a cluster analysis, which is a person-centered method grouping individuals according to their scores on two or more variables. This made it possible to study group differences arising due to these different patterns on the variables used for grouping. This is important, since pain patients have been shown to be a heterogeneous group (see for example Bergbom, Boersma, Overmeer, & Linton, 2011) in which certain subgroups, such as those with emotional comorbidities, seem to have higher symptomatology and specific treatment needs that are not properly met in current treatments. Using person-centered methods highlights the existence of these subgroups and can therefore be seen as one of the strengths of this dissertation.

Future directions

This dissertation has raised some questions that should be considered for future studies.

Firstly, future studies should further develop transdiagnostic approaches and study factors with potential as central transdiagnostic factors. This dissertation confirms some of the factors suggested by earlier studies, such as RNT and anxiety sensitivity, but it needs to be investigated further how vulnerabilities interact with stressors and lead to the development and maintenance of symptomatology. This is particularly urgent in the overlap of pain problems and emotional problems. Pain complaints and emotional problems are the most common reasons for seeking primary care (Kallionen et al., 2010). Also, pain problems seem to be increasing in the general population (McBeth & Jones, 2007) and emotional problems seem to be increasing in adolescents (Collishaw, 2015), which indicates that pain and emotions will need increasing attention in the future. Hence, a better understanding of the factors influencing this development is needed. For this, it is important to develop high quality longitudinal studies that enable researchers to study processes involved in the development of pain and emotional problems over time. More advanced statistics, such as structural equation modeling should be considered to enable the study of more advanced models, simultaneously including several factors.

Secondly, Study II highlighted peer-related stress and worry as important factors influencing the development of pain problems in adolescents. These results need to be replicated and it should be studied further how peer-related stressors influence the development of pain problems, and in whom.

It is likely that some subgroups of adolescents experience peer-related stress to a higher degree than others. Also, studies that can map subgroups with different trajectories of development using more advanced statistics, such as growth curve modeling, would be advantageous. It would further be important to test the preventive effect of targeting worry and peer-related stress in a community sample. This is important because pain problems and emotional problems, as well as comorbidity of pain and emotional problems, cause considerable cost for society and the individual.

Thirdly, treatment effects need to be improved for patients with comorbid pain and emotional problems. The development of treatments that resonate with patients' experiences and are perceived as credible and helpful, but that also are successful in changing symptomatology, needs to be continued. Pain patients are a heterogeneous group in which emotional comorbidity is common. Also, pain rehabilitation is often delivered in group settings. Therefore, it may be unhelpful and inefficient to treat pain problems separately from emotional problems, which makes transdiagnostic approaches appealing. Also, as briefly mentioned previously, some studies point to the usefulness of treatments with an emotional focus for pain patients. For example, a single case experimental design study using a hybrid treatment combining more traditional pain exposure with emotion regulation-focused additions from dialectical behavior therapy showed promising results in pain patients with high levels of catastrophizing (Linton & Fruzzetti, 2014). Another study compared emotional awareness and expression therapy (EAET) to CBT and education about fibromyalgia in a sample of fibromyalgia patients (Lumley et al., 2017). The authors found that EAET was better than education and as good as CBT on most counts. In fact, EAET had better results compared to CBT on fibromyalgia symptoms and widespread pain, and a higher percentage of patients reaching at least 50% pain reduction. This highlights the importance of considering emotion-focused interventions for pain patients. Also, treatment approaches based on acceptance and commitment therapy (ACT), targeting cognitions and emotions that impact behavior, have shown promising results for both adults and adolescents (Wetherell et al., 2011; Wicksell, Melin, Lekander, & Olsson, 2009). However, contrary to these promising results, Study III did not support the potential of the transdiagnostic unified protocol treatment tested for pain patients with comorbidity, even though one of the main focuses of the UP also is emotional awareness and emotional experiencing. Given the questions

remaining, for example whether the poor results relate to the suitability of the mode of delivery, this should be studied further.

One way to establish the effectiveness of this existing protocol would be to study it in a face-to-face intervention, to make sure that it was not the mode of delivery via the internet that led to lack of effects. This would also make it possible for the therapist to assist more hands-on in exposure sessions, potentially leading to better outcome. Nevertheless, internet-delivered treatments should be explored further for this group, given the generally positive empirical results in pain patients, including pain patients with comorbidities (Buhrman et al., 2015). Also, there are clear advantages of internet-delivered treatments for groups with mobility problems and concentration issues, which is relevant for many pain patients.

Pilot work before conducting Study III reinforced the importance of the form of delivery and the content of the material for pain patients with comorbid problems. In the pilot study, only two out of twelve participants completed the whole treatment in roughly the given time frame. In contrast, in Study III, all patients completed the treatment, which can be seen as an improvement. This could be due to a further shortening and simplification of the texts, but also to the telephone support that was added in Study III. Even though telephone support has elsewhere been reported not to improve results significantly (Melville, Casey, & Kavanagh, 2010), other studies with telephone support have shown good results regarding both attrition and outcome (Buhrman et al., 2004; Dear et al., 2015). Also, the fact that the phone call was made contingent on continuing to the next module, may have helped participants to keep to the schedule.

Different protocol lengths should be tested to see if more time spent on important parts of the treatment, such as exposure, would lead to clearer changes in symptomatology. This is important, since studies using the UP in other samples used longer protocols with better results (Farchione et al., 2012). At the same time, studies with emotional content for pain patients showed better results with treatment lengths comparable to Study III (Linton & Fruzzetti, 2014; Lumley et al., 2017). Hence, the influence of treatment length remains unclear and needs to be studied further.

Summary and concluding remarks

In sum, the results of this dissertation confirm that a transdiagnostic approach, specifically the shared vulnerability model, can be utilized in the understanding of the overlap between pain and emotional problems. It was shown that vulnerabilities, such as anxiety sensitivity and negative affect, covary with comorbid pain and social anxiety, confirming that the shared vulnerability model can be generalized to other emotional problems besides PTSD. It was shown that interpersonal stressors in the form of peer-related stress predict musculoskeletal pain problems in adolescents, and it also confirmed the important role of worry in the development of musculoskeletal pain problems, at least for girls. Thus, important gender differences were highlighted. However, the clinical applicability of the shared vulnerability model was not confirmed, since the treatment that attempted to change factors believed to maintain problems did not lead to changes in symptomatology.

The results of this dissertation highlight the importance of several factors in the development of pain problems that are also involved in emotional problems. Not least, social factors are stressed as important. In sum, it is crucial not to view pain and emotional problems as two distinct entities. Considering where their aetiology and maintenance overlap will open up new avenues of prevention and treatment. This is an important area, since both pain and emotional problems are very common and cause great suffering for the individual and large costs for society.

Conclusions

- ❖ In clinical pain populations, there is a subgroup with social anxiety.
 - The group with comorbid social anxiety and pain has worse symptomatology and worse treatment outcome than groups of pain patients without comorbid social anxiety.
 - In pain rehabilitation settings, it is therefore important to take social functioning into consideration.
 - Pain patients with comorbid social anxiety report high levels of transdiagnostic vulnerability factors (negative affect, anxiety sensitivity) both before and after treatment.
- ❖ Interpersonal stress in the form of peer-related stress affects the development of pain problems over time in adolescents.
 - Worry is a driving force in this development, mediating the relationship between peer-related stress and musculoskeletal pain problems for girls. Hence, worry may explain the gender differences commonly found in pain research.
- ❖ It may be possible to influence transdiagnostic factors in pain patients with comorbid emotional problems and these changes are considered relevant by participants. Nevertheless, it remains unclear whether it is possible to influence levels of emotional and pain problems.
 - Specifically, a transdiagnostic, internet-delivered treatment seemed feasible and patients reported changes in the transdiagnostic factors targeted, but changes in anxiety, depression, and pain characteristics were small or unclear.
- ❖ Transdiagnostic approaches seem to offer a parsimonious understanding of the development and maintenance of symptomatology in the overlap between pain and emotional problems.

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