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Doctoral Thesis

Exposure and Acceptance in Patients with Chronic Debilitating Pain - A Behavior Therapy Model to Improve Functioning and Quality of Life

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work is easy, life is hard



ABSTRACT

A large number of patients suffer from reduced functioning and quality of life due to longstanding pain. The importance of psychological factors is undisputable and there is today substantial empirical support for treatments based on cognitive behavior therapy (CBT). Nevertheless, previous research also illustrates a clear need for improvements. For example, there is a lack of studies with children and adolescents that are severely disabled by longstanding pain other than headache. Also, the process by which CBT is effective is still rather unclear. Recently, developments within CBT, such as Acceptance and Commitment Therapy (ACT), suggest an approach that, in contrast to reduction or control of symptoms, promotes acceptance of negative private experiences like chronic pain and distress. This type of intervention is aimed at improving functioning and quality of life by increasing psychological flexibility, i.e. the ability to act in alignment with personal values also in the presence of e.g. pain, fear, and negative thoughts. Although studies exist, there is an urgent need for randomized controlled trials with chronic pain patients, especially children and adolescents.

The presented studies were conducted within the development of a clinical model to improve functioning and quality of life in children, adolescents, and adults with chronic debilitating pain. The thesis had two general aims. One, to investigate the effectiveness of an intervention based on values-oriented exposure and acceptance (studies 1, 2, and 4 in the present thesis). Two, to develop and psychometrically evaluate a self-report instrument designed to assess psychological flexibility in people with chronic pain (studies 2 and 5).

Initially, an uncontrolled pilot study (study 1) was conducted with adolescents suffering from chronic idiopathic pain (n=16). Following treatment, large and stable reductions were seen in e.g. functional disability, pain intensity, and catastrophizing, with generally large effect sizes.

Study 3 included people with chronic pain and whiplash associated disorders (WAD) (n=22). Exposure and acceptance delivered in addition to treatment as usual (TAU) was compared with a control group receiving only TAU. Following the exposure and acceptance intervention, improvements were seen in all measures but pain intensity, and these effects were retained seven months following the end of treatment. Furthermore, significant differences following treatment, in favor of the exposure and acceptance group, were seen in e.g. pain disability, life satisfaction, fear of movement, and psychological inflexibility, with moderate to large effect sizes.

In study 4, participants were children and adolescents with chronic idiopathic pain (n=32). The effectiveness of exposure and acceptance was evaluated by comparing it with a multidisciplinary treatment approach including amitriptyline (MDT). The exposure and acceptance group showed large and sustained improvements in all measures, including functioning, quality of life, and pain intensity, with mostly large effects sizes. The exposure and acceptance group performed significantly better than the MDT on e.g. perceived functional ability in relation to pain, kinesiophobia, pain intensity and pain related discomfort, with moderate to large effect sizes.

Parallel to the treatment evaluations, two studies were conducted to develop and evaluate an instrument to assess central and discernible components of psychological flexibility, referred to as the Psychological Inflexibility in Pain Scale (PIPS). In the development study (study 2), data was collected from pain clinics and patient organizations (n=203). Based on an original set of 38 items, principal component

analyses suggested a two-factor solution with 16 items, showing adequate internal consistency and concurrent criterion validity.

In study 5, participants were recruited from a patient organization for people with WAD (n=611). Exploratory and confirmatory factor analyses resulted in a two-factor solution with 12 items, illustrating good reliability and validity. Only items that were retained in both studies 2 and 5 were included in the final version of the instrument. Furthermore, hierarchical regression analyses illustrated that PIPS explained a significant amount of variance in e.g. pain, work absence, life satisfaction, disability, depression, and kinesiophobia.

In conclusion, despite some methodological limitations, the treatment evaluations indicate the effectiveness of the exposure and acceptance intervention, and suggest that it may be superior to TAU only, as well as to a multidisciplinary program including amitriptyline. Furthermore, data from two measurement development studies suggest that PIPS can be used as a reliable and valid measure to assess key components in psychological inflexibility in people with chronic pain. More studies are needed to confirm these findings; especially larger scale randomized controlled trials.

SUMMARY IN SWEDISH/SAMMANFATTNING PÅ SVENSKA

Trots ökad kunskap om smärta och behandling utgör patienter med långvarig handikappande smärta fortfarande en betydande del av sjukvården. Läkemedel och andra symptomreducerande åtgärder har ofta ingen, eller mycket kortvarig, effekt. Patientens egna strategier innefattar vanligtvis att undvika situationer som associeras med en risk för ökad smärta, vilket på sikt tenderar att medföra betydande begränsningar utan någon egentlig förbättring av smärttillståndet. Kognitiv beteendeterapi (KBT) har successivt kommit att framstå som en verksam behandlingsmodell, men metoden behöver vidareutvecklas och det empiriska underlaget förstärkas. Behandlingsstudier med barn och ungdomar efterfrågas, och dessutom behövs studier som tydliggör vilken eller vilka som är de verksamma komponenterna i framgångsrika behandlingar baserade på KBT. På senare tid har förmågan att acceptera smärta och obehag lyfts fram som en betydelsefull komponent i hanteringen av smärta och relaterat obehag. Studier har exempelvis visat att acceptans bidrar till mindre smärtrelaterad oro, nedstämdhet, fysiska och sociala begränsningar och lägre smärta. Inom Acceptance and Commitment Therapy (ACT), en utvecklad variant av KBT, förespråkas acceptans som en del av arbetet med att öka aktiviteter som upplevs värdefulla men som har undvikits därför att de medfört smärta eller annat obehag. En ACT-orienterad intervention bygger på exponering och acceptansstrategier, i syfte att förbättra funktionsförmåga och livskvalitet genom att öka patientens psykologiska flexibilitet (definierat som förmågan att agera konstruktivt i linje med personliga värden och långsiktiga mål, även i närvaro av distraherande smärta eller obehag). Ett begränsat antal ACT-studier med smärtpatienter har tidigare genomförts, men det finns ett stort behov av randomiserade kontrollerade studier (RCT). Dessutom saknas studier som utvärderat effekten av ACT som behandling för barn och ungdomar, särskilt med långvarig smärta.

Avhandlingen innefattar fem olika delarbeten vilka genomfördes inom ramen för utvecklandet av en klinisk behandlingsmodell för patienter med långvarig handikappande smärta. De ingående studierna hade två övergripande syften, att utvärdera effekten av en intervention baserad på exponering och acceptansstrategier (studie 1, 3 och 4) samt att utveckla och utvärdera ett nytt frågeformulär för att mäta psykologisk flexibilitet (studie 2 och 5).

Den första behandlingsutvärderingen (studie 1 i avhandlingen) var en pilotstudie med ungdomar som remitterats till Smärtbehandlingsenheten vid Astrid Lindgrens Barnsjukhus på grund av långvarig, svårbehandlad och handikappande smärta (n=16). Betydande och bestående förbättringar i funktionsförmåga, smärtintensitet, skolnärvaro och katastrofiering uppnåddes efter behandlingen. Resultaten bestod 6 månader efter avslutade behandling och effektstorlekarna var överlag stora.

I studie 3 rekryterades deltagarna från en patientförening för personer med whiplashassocierade besvär (WAD) (n=22). Alla deltagarna i studien fortsatte med pågående sedvanliga sjukvårdskontakter (TAU), och randomiserades till en av två grupper: exponering och acceptansintervention som ett tillägg till TAU eller enbart TAU. Deltagarna i den grupp som fick exponering och acceptansinterventionen förbättrades i alla utfallsmått utom smärtintensitet. Efter avslutad behandling fanns signifikanta skillnader mellan grupperna till exponering och acceptansgruppens fördel, bland annat avseende funktionsförmåga, livskvalitet, rörelserädsla och psykologisk flexibilitet (i huvudsak medelstora till stora effektstorlekar).

I studie 4 inkluderades barn och ungdomar med långvarig handikappande smärta vid Smärtbehandlingsenheten, Astrid Lindgrens Barnsjukhus (n=32). I denna studie randomiserades patienterna till en exponering och acceptansintervention eller till en individualiserad multidisciplinär insats inkluderandes amitriptylin (MDT). Exponering och acceptansgruppen förbättrades signifikant till följd av behandlingen (mestadels stora effektstorlekar), och denna effekt bestod 6 månader efter avslutad behandling. Jämförelsen mellan grupperna visade att exponering och acceptansgruppen förbättrats signifikant mer än MDT-gruppen i flera variabler (med medelstora till stora effektstorlekar), bland annat upplevd funktionsförmåga relaterat till smärta, rörelserädsla, smärtrelaterad oro och smärtintensitet.

Parallellt med behandlingsstudierna genomfördes två olika mätinstrumentstudier för att utveckla och utvärdera ett frågeformulär avsett att mäta psykologisk flexibilitet, kallat Psychological Inflexibility in Pain Scale (PIPS). I den första studien (studie 2 i avhandlingen) konstruerades 38 påståenden (items) med teoretisk anknytning till psykologisk flexibilitet. Data samlades in från smärtkliniker och patientföreningar (n=203). Materialet analyserades med bland annat principalkomponentanalyser, vilka indikerade att en tvåfaktor lösning med 16 items var mest lämplig. Denna version av instrumentet uppvisade tillfredställande reliabilitet och validitet.

I studie 5 genomfördes ytterligare analyser för att utvärdera instrumentets psykometriska egenskaper. Data samlades denna gång in från personer tillhörandes en patientförening för personer WAD (n=611). Både explorativa och konfirmatoriska faktoranalyser genomfördes. Faktoranalyserna resulterade även denna gång i en tvåfaktorlösning. I den slutliga versionen av PIPS behölls bara items som kvarstod efter de statistiska analyserna i både studie 2 och 5. Antalet items i den sista versionen av instrumentet uppgick till 12. Reliabiliteten och validiteten för de båda delskalorna var tillfredsställande. Hierarkiska regressionsanalyser visade även att PIPS förklarade en betydande del av variansen i de olika kriterievariablerna, exempelvis smärta, livskvalitet, funktionsförmåga, ångest och depression.

Sammantaget visar behandlingsstudierna, trots vissa metodologiska brister, att exponering och acceptansinterventionen kan leda till en påtaglig och bestående ökning av funktionsförmåga och livskvalitet. Resultaten indikerar dessutom att exponering och acceptans är bättre än såväl sedvanlig behandling (vuxna med WAD), som multidisciplinärt omhändertagande inkluderande amitriptylin (barn och ungdomar). Resultaten från mätinstrumentstudierna indikerar att PIPS har tillfredsställande psykometriska egenskaper och är ett användbart instrument för att mäta psykologisk flexibilitet hos personer med långvarig smärta. Fler studier behövs för att bekräfta resultaten från dessa studier, särskilt större randomiserade kontrollerade studier.

LIST OF PUBLICATIONS

The thesis consists of the following original papers.

- 1. Wicksell RK, Melin L, Olsson GL. Exposure and acceptance in the rehabilitation of adolescents with idiopathic chronic pain a pilot study. Eur J Pain 2007;11(3):267-274.
- Wicksell RK, Renofalt J, Olsson GL, Bond FW, Melin L. Avoidance and cognitive fusion - central components in pain related disability? Development and preliminary validation of the Psychological Inflexibility in Pain Scale (PIPS). Eur J Pain 2008;12(4):491-500.
- 3. Wicksell RK, Ahlqvist J, Bring A, Melin L, Olsson GL. Can exposure and acceptance strategies improve functioning and life satisfaction in people with chronic pain and whiplash-associated disorders (WAD)? A randomized controlled trial. Cogn Behav Ther 2008;37(3):169-182.
- 4. Wicksell RK, Melin L, Lekander M, Olsson GL. Evaluating the effectiveness of exposure and acceptance strategies to improve functioning and quality of life in longstanding pediatric pain A randomized controlled trial. Pain. In press.
- 5. Wicksell RK, Lekander M, Sorjonen K, Olsson GL. The Psychological Inflexibility in Pain Scale (PIPS) validation and confirmatory factor analysis of an instrument to assess avoidance and cognitive fusion in longstanding pain. Under review.

TABLE OF CONTENTS

ABSTRACT	5
SUMMARY IN SWEDISH/SAMMANFATTNING PÅ SVENSKA	7
LIST OF PUBLICATIONS	9
TABLE OF CONTENTS	10
LIST OF ABBREVIATIONS	12
LIST OF DEFINITIONS	13
1. INTRODUCTION	15
2. BACKGROUND	16
2.1. PAIN – A COMPLEX PSYCHOLOGICAL EXPERIENCE	16
2.2. PREVALENCE AND ECONOMIC ASPECTS OF CHRONIC PAIN	17
2.3. THE IMPORTANCE OF PSYCHOLOGICAL FACTORS IN THE TREATMENT OF CHRONIC PAIN	18
2.4. CBT IN CHRONIC PAIN – EMPIRICAL SUPPORT AND TREATMENT OBJECTIVE	18
2.5. LIMITATIONS OF THE CBT APPROACH IN CHRONIC PAIN MANAGEMENT	19
2.6. LEARNING THEORY APPLIED TO CHRONIC PAIN	20
2.6.1. Respondent conditioning	20
2.6.2. Operant conditioning	
2.6.3. Pain as an interoceptive stimulus	
2.7. THE FEAR-AVOIDANCE MODEL	
2.8. FROM LEARNING THEORY TO RELATIONAL FRAME THEORY	22
2.8.1. Beyond direct learning experiences	
2.8.2. External and internal stimuli	
2.8.3. Refining the learning theory model	23
2.8.4. Our cognitive ability - a blessing and a curse	
2.8.5. Stimulus equivalence	
2.9. RELATIONAL FRAME THEORY (RFT)	
2.9.1. Basic theory and applications to pain	
2.9.2. Clinical implications of RFT	
2.10. ACCEPTANCE AND COMMITMENT THERAPY (ACT)	
2.10.1. Developments within CBT	
2.10.2. The philosophical foundation: functional contextualism	
2.10.3. An ACT-oriented analysis	
2.10.4. An ACT-oriented intervention.	
2.11. Empirical status of ACT	
2.12. ACCEPTANCE AND PAIN	
2.12.1 Correlational studies	
2.12.2. Laboratory studies	
2.12.3. Treatment evaluation studies	
2.13. MEASURING ACCEPTANCE IN CHRONIC PAIN	
3. ASSUMPTIONS AND AIMS	43
3.1. Assumptions	12
3.2. GENERAL AND SPECIFIC AIMS	
J. Z. GENERAL AND SECUTIC AIMS	43

4. METHOD	••••••
4.1. GENERAL OUTLINE OF THE PROJECT	
4.2. Treatment outcome studies - papers 1, 3, and 4	
4.2.1. Participants	
4.2.2. Procedure	
4.2.3. Eligibility and inclusion/exclusion criteria	
4.2.4. Assessment	
4.2.5. Randomization	
4.2.6. Dependent variables	
4.2.7. Intervention – the experimental condition	
4.2.8. Control conditions in studies 3 and 4	
4.2.9. Data analyses	
4.3. MEASUREMENT DEVELOPMENT STUDIES – PAPERS 2 AND 5	
4.3.1. Participants and data collection	
4.3.2. Statistical analyses/analytic approach	
4.4. Measures	
4.5. ETHICS	
5. EMPIRICAL STUDIES WITHIN THE RESEARCH PROJECT	
5.1. Treatment outcome studies	
5.1.1. Study 1: Exposure and acceptance with adolescents - a pilot study	
5.1.2. Study 3: Exposure and acceptance with WAD – an RCT.	
5.1.3. Study 4: Exposure and acceptance with children and adolescents – an RCT	
5.2. MEASUREMENT DEVELOPMENT STUDIES	
5.2.1. Study 2: Preliminary validation of the PIPS	
5.2.2. Study 5: Evaluation of psychometric properties and model fit of the PIPS	
6. GENERAL DISCUSSION	
6.1 Treatment evaluations	
6.1.1. Summary of the treatment outcome studies	
6.1.2. Clinical implications	
6.2. MEASUREMENT DEVELOPMENT	
6.2.1. Summary of the measurement development studies	
6.2.1. Clinical implications	
6.3. Future directions	
6.3.1. Treatment evaluations	
6.3.2. Measurement development	
6.4. Conclusions	
APPENDIX	••••••
ACKNOWLEDGEMENTS	•••••

PAPERS 1 - 5

LIST OF ABBREVIATIONS

ANCOVA Analysis of Covariance ANOVA Analysis of Variance

ACT Acceptance and Commitment Therapy

CBT Cognitive Behavior Therapy **CFA** Confirmatory Factor Analysis

Chronic Pain Acceptance Questionnaire **CPAQ**

EM Expectation-Maximization-Likelihood Method

ITT Intent-to-treat

MDT Multidisciplinary Treatment (including amitriptyline)

PCA Principal Component Analysis

PIPS Psychological Inflexibility in Pain Scale

Pain Treatment Service, Astrid Lindgren Children's Hospital PTS

PTSD Post-Traumatic Stress Disorder

Quality of Life QoL

RCT Randomized Controlled Trial RFT Relational Frame Theory TAU Treatment as Usual VAS

Visual Analogue Scale

WAD Whiplash Associated Disorders

LIST OF DEFINITIONS

Pain

Nociceptive pain Pain resulting from a clearly defined noxious

stimulation (tissue damage) that causes activity in the

nociceptive pathways.

Idiopathic pain Pain in the absence of demonstrable disease and

without evidence of primary metabolic, biochemical, or structural abnormalities underlying the reported

symptoms.

Learning theory

Respondent conditioning When a previously neutral stimulus elicit similar

responses as a significant stimulus after repeated

pairings.

Operant conditioning When consequences following a behavior

(reinforcing or punishing) increase or decrease the probability that this behavior will be repeated in a

similar situation.

Positive reinforcement An increase of desired consequences.

Negative reinforcement A decrease of aversive consequences.

Antecedents Factors occurring before the behavioral response.

Exposure A gradual increase of behaviors previously avoided

(due to negative experiences such as pain and

distress).

Acceptance and Commitment Therapy (ACT)

Acceptance/willingness To notice and acknowledge unpleasant inner

experiences without attempts to change, reduce, or control them, in order to engage in values-oriented

behaviors.

Fusion When negative thoughts and emotions have

excessive or inappropriate impact on behavior, and behaviors are more guided by inflexible verbal networks (rules) than actual environmental

contingencies.

Defusion To recognize and acknowledge a private experience

for what it is (e.g. a thought is a verbal stimuli elicited in a certain context, rather than an exact and fully reliable prediction of the future), without acting

on its content.

Psychological inflexibility The inability to act effectively in accordance with

personal values in the presence of interfering negative private experiences, such as pain and

distress.

Values An important direction in life (e.g. "being a

supportive friend") that cannot be obtained (in contrast to a concrete goal such as "calling my

friends once a week").

Workability How well a particular strategy works, with regards to

a specified goal such as "no pain" or "valued living".

Relational Frame Theory (RFT)

Relational responding Discriminating (or detecting) relationships between

stimuli.

Direct learning Learning that occurs following respondent or operant

conditioning (i.e. pairing of stimuli in temporal proximity, or reinforcement/punishment of a specific

behavior).

Derived learning A generative process in which abilities to relate

stimuli are obtained without direct training (also

derived relational responding).

Mutual entailment Derived learning. The bidirectionality of stimulus

relations. After being directly taught that A is related to B, it is derived that B is correspondingly related to A. For example if A is bigger than B, then B is

smaller than A (see Figure 2.1.).

Combinatorial entailment Derived learning. The relationship that exists

between two stimuli (following multiple exemplar training) based on how they are related to another, intermediary, stimuli. If A is similar to B, and A is similar to C, it is derived that B and C are similar

(see Figure 2.1.).

Multiple exemplar training Repeated presentations of the stimuli, with corrective

feedback following the behavioral response (e.g.

reinforcement following a correct response).

Transf. of stim. functions When two stimuli are related (e.g. A and B), the

function of one stimuli (A) is based on the other stimuli (B), and depends upon how A is related to B

(e.g. same as, opposite, larger than).

Frame of coordination When two or more stimuli are related with

"sameness", and they will elicit similar responses (through transformation of stimulus functions).

Frame of opposition When two or more stimuli are distinguished as

"opposite" (e.g. hot - cold).

Frame of causation Events that are framed based on ideas of cause and

effect. Can be thought of as "if – then" relations. For example "If I drop the glass, then it will break", or "If I go to the party, then I will embarrass myself."

1. Introduction

Despite important advances in research and development of chronic pain treatments, a large number of patients remain debilitated by their condition. Chronic pain is prevalent and brings about extensive costs due to e.g. increased health care utilization and productivity loss. For the individual, costs include a significantly reduced quality of life. Pain can be a repulsive personal experience and the definition of pain as "unpleasant" may well be seen as an understatement for many patients. Chronic pain is also a frequently reported problem among children and adolescents. Importantly, longitudinal studies indicate that this problem may compromise future functioning and life quality for a portion of these individuals, if not effectively addressed. Thus, in adults as well as young patients, the high prevalence, economic burden, and personal suffering associated with chronic pain syndromes are incentives for developing more effective treatments to improve functioning. Unfortunately, pharmacological as well as other medical interventions remain to be insufficient or even useless to many patients in decreasing pain or improving functioning. Thus, given the lack of effective treatments as well as the chronic character of the symptoms and the disabilities they result in, interventions aimed at improving self-management appear sound. Previous research illustrate that interventions based on cognitive behavior therapy (CBT) are particularly promising for people with disabilities resulting from chronic pain. However, data also suggest room for improvements.

Traditionally, a main objective in CBT-oriented chronic pain management has been to reduce or control pain and distress in order to increase physical and social functioning. Recently, acceptance-based approaches within the CBT paradigm have received increasing attention as well as empirical support for a variety of different symptoms, including chronic pain. However, with regards to pain, randomized controlled trials (RCT) using acceptance-oriented interventions are scarce. In addition, the vast majority of CBT-studies have been performed with adult patients. This implies an urgent need to conduct clinical trials based on exposure and acceptance strategies with patients suffering from chronic debilitating pain, especially children and adolescents.

The purpose of the present research project was to develop a clinical model for patients suffering from chronic debilitating pain. More specifically, the initial aim was to improve the treatment approach for pediatric patients presenting with longstanding pain without any clear organic etiology. However, due to promising outcome data and clinical findings, the usefulness of this approach was also investigated with adults. The thesis contains five different studies. An uncontrolled pilot study was followed by two RCT's, one with adults and the other with pediatric patients. Parallel to these treatment evaluations, an instrument was developed to assess psychological flexibility, the central construct and hypothesized mechanism of action in this clinical model. Data from two different samples were collected to investigate the psychometric properties of the instrument. In the first part of the thesis, background, aims, and methods are presented. This is followed by summaries of results, methodological limitations and conclusions for each of the five different studies. In the general discussion, clinical implications of the studies will be described, as well as some suggestions for future research and development.

2. BACKGROUND

2.1. Pain - a complex psychological experience

Pain has been defined by the International Association for the Study of Pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [113]. As indicated by the definition, pain is more than a specific sensation. Since the revolutionary work by Melzack and Wall, it is generally understood as a complex experience which includes both a sensory-discriminatory aspect as well as affective-motivational and cognitive-evaluative dimensions [112]. More recent research supports this notion of pain as a particularly complex phenomenon. Increasingly sophisticated methods such as imaging have facilitated studies that further emphasize the emotional and motivational dimension of pain [19].

There are several types of pain, which need to be properly differentiated. Nociceptive pain is the product of a clearly defined noxious stimulation (tissue damage) that causes activity in the nociceptive pathways. Thus, a distinction is made between nociception and pain which, by definition, is a psychological state [113]. Nociceptive pain can result from various types of traumatic events, such as an injury (acute pain), surgery (post-operative pain), or a painful medical procedure. Also, nociceptive pain may be due to an inflammatory process. Neuropathic/neurogenic pain refers to pain initiated or caused by a lesion or dysfunction in the nervous system [113]. Pain sometimes persists for longer periods, and may be continuous or recurrent in nature. Normally, pain is referred to as longstanding or chronic (used interchangeably throughout the text) when lasting longer than six months [15]. However, a pain duration of three months is sometimes considered a more adequate cut-off, because pain persisting beyond this point may signal a poorer prognosis [89,168].

A large proportion of patients with chronic pain experience persistent or recurrent episodes of pain in the absence of demonstrable disease and without evidence of primary metabolic, biochemical, or structural abnormalities underlying the reported symptoms. This is often referred to as "pain syndrome", "idiopathic pain", "non-malignant", "functional" or "medically unexplained" pain. Despite lack of medical findings, the patient commonly experiences his or her pain as resulting from tissue damage (i.e. nociceptive input).

Psychiatric comorbidity is common among people with chronic pain, especially depression. Studies have indicated that about 20% of people with chronic pain are depressed [15,88]. Comorbid depression may, in turn, contribute to other problems (e.g. insomnia) both in adult and young patients [70,168]. Also, substantially higher prevalence rates of anxiety disorders (e.g. panic disorder, social phobia, PTSD) have been reported [168].

Whiplash associated disorders (WAD) exemplifies complex chronic pain syndromes. WAD commonly results from a motor vehicle accident. The term "whiplash" refers to the back- and forward head movement seen in rear-end collisions (resembling the crack of a whip) [185], and the term "WAD" emerged to recognize the variety of problems reported by individuals with persisting symptoms following a whiplash injury [36]. Although most patients recover from whiplash injuries within eight weeks [155], 14-42% experience symptoms after the acute phase and develop WAD [7]. Recent studies indicate that as many as 50% are not fully recovered after 2 years [137]. WAD includes chronic symptoms of neck pain and stiffness, headache, arm

pain and paresthesias, memory and concentration difficulties, fatigue and sleep problems [155]. Also, a substantial number of patients with persistent symptoms following a whiplash injury suffer from posttraumatic stress disorder (PTSD) [158,159]. There are few variables that can reliably predict which patients are at risk for developing WAD [158]. Both causes and consequences of this condition are frequently debated [143] and the general understanding is that WAD is complex in nature [157,159] and that a multimodal treatment approach should be recommended [143,190]. However, although WAD is a considerable health problem, the number of empirically supported treatments for this group remains limited [143]. Neither is there sufficient knowledge available regarding mechanism(s) of change in successful multimodal interventions for WAD [190].

2.2. Prevalence and economic aspects of chronic pain

There are numerous studies describing the prevalence and incidence of chronic pain in adults, and although differences exist it appears as if chronic pain affects 20% to 30% of the adult population in Western countries [191]. In Sweden, studies with adults have shown prevalence rates between 40 and 65% [14,44]. Recently, in an extensive study by Breivik and colleagues, information regarding chronic pain was collected from several European countries [15]. The prevalence rates ranged from 12% to 30% (18% in Sweden). Participants with pain persisting more than six months were interviewed to further assess severity and impact on daily living. Results showed that, among 4839 participants with chronic pain, 34% described pain as severe, 46% suffered from constant pain, 61% were less able or unable to work, and 21% were diagnosed with depression due to pain. Furthermore, two-thirds were taking prescribed medication and 40% said that they were not satisfied with the effects of treatment.

Pediatric pain has gained increasing attention in recent years. Epidemiological studies have shown frequent occurrence of pain among youths [132]. Of particular concern is the high prevalence of pediatric longstanding pain [31,133-135], and several studies have illustrated the functional disabilities seen in a subgroup of children and adolescents [65,71,128]. Furthermore, despite recommendations from healthcare providers to resume normal activities, a number of these adolescents enter adulthood with severely debilitating pain syndromes, entailing a substantial risk for chronicity [13,181,183].

Debilitating chronic pain results in large financial costs. Variables such as health care utilization (direct costs) and work absence (indirect costs) can be combined to calculate the economic burden of this problem. For example, the European survey revealed that 60% had visited their doctor for pain problems between two and nine times within the last six months [15]. Recently, the Swedish Council on Technology Assessment in Health Care (SBU) estimated that chronic pain results in costs of SEK 7.5 billion/year for direct care, and SEK 80 billion/year for indirect repercussions, primarily related to sick leave and loss of production [147]. There are few studies conducted to calculate the costs involved in pediatric chronic pain. However, a recent study illustrated that the mean cost per adolescent experiencing chronic pain is approximately £8000/year (SEK 98500) in the United Kingdom [152]. The economic implications of effectively addressing pain related disabilities have been highlighted in a Swedish study, in which the preventive effects of productivity loss was clearly shown [81]. Five years following end of treatment, a group receiving CBT had cut costs due to disability to a third as compared with a group receiving usual care plus information (SEK 12.268 as compared with SEK 41.733).

2.3. The importance of psychological factors in the treatment of chronic pain

Pain has been extensively investigated during the last decades and significant biological advances have been made in our understanding of pain and chronic pain syndromes. Nevertheless, a substantial number of patients continue to suffer from detrimental effects due to longstanding pain syndromes. Unfortunately, pharmacological and surgical strategies are often insufficient in alleviating pain and increasing functioning [102]. For example, a review study that evaluated the clinical effectiveness of pharmacological treatments showed that only 30% to 40% of patients reported at least 50% reductions in pain when using the most potent drugs [170].

A large number of studies support the idea that biological factors do not fully account for the pain experience, and that pain in itself does not adequately explain disability [2,79,168,169]. This inconsistency goes both ways; in addition to people reporting pain in the absence of corresponding organic findings, it has been shown that people with clearly identified "abnormalities" did not report pain [68]. Nor do medical variables, obtained through physical testing or imaging, seem to reliably predict reported symptoms or functioning [20,102]. Today, the importance of psychological factors in chronic pain is undisputable [79,172]. Due to the complexity of chronic pain and the lack of effective medical treatments, multidisciplinary approaches combining psychological strategies and physical therapy is normally recommended [49,67,102]. The multidimensional character of chronic pain is also reflected in biopsychosocial models, where contextual factors are incorporated in the conceptualization of pain and disability [187].

When cure or complete symptom alleviation is not readily attainable, treatment strategies may target different goals, such as improved functioning and quality of life or decreases in the use of medication and health care services. In this type of treatment, the patients' ability to cope with pain becomes central and has been the target in a large number of studies [69]. From this perspective, the patient is seen as actively engaged in self-management to lessen pain and improve functioning. Although various definitions may exist, the term "coping strategies" usually refers to behavioral and cognitive efforts to manage pain or stressful situations [2]. In pain management, the objective in coping oriented interventions has traditionally been to increase the patient's techniques of self-control over maladaptive thoughts, emotions, and overt behaviors [171].

2.4. CBT in chronic pain - empirical support and treatment objective

As summarized in several systematic reviews and meta-analyses, there is substantial empirical support for interventions based on CBT for adults with chronic non-malignant pain of various types [38,49,61,78,102,118]. The importance of using psychological therapies in pediatric chronic pain management has also been emphasized, for example in a series of review articles on headache [63], recurrent abdominal pain [66], and disease-related pain [178]. A relatively recent systematic review of 18 RCT's, provided further support for the effectiveness of psychological strategies, especially relaxation and CBT, in reducing the severity of longstanding pain in children and adolescents [30].

Lately, a number of clinical studies have evaluated treatments based on CBT with various types of longstanding pediatric pain conditions. For example, an RCT with recurrent abdominal pain patients evaluated CBT as an addition to standard medical care. For patients receiving a combination of standard care and CBT, pain intensity and school absence dropped after treatment, although no difference between the groups was seen with regards to self-rated disability [141]. In two other studies, patients with juvenile fibromyalgia received CBT-oriented treatments with favorable outcomes

[23,72]. However, no follow-up assessment was performed to confirm the stability of these improvements. Yet another study has reported promising results following a residential program based on CBT for adolescents with various forms of longstanding pain [29].

Although the empirical support for CBT in chronic pain treatment appears strong, especially for adults, there are limitations. Few studies have been conducted with people disabled by WAD, indicating the usefulness of early interventions, a multidisciplinary treatment, and a cognitive behavioral approach [153,160,190]. Thus, although promising, there is a need to evaluate CBT-oriented interventions for this group.

RCT's with pediatric patients disabled by longstanding pain are still scarce [30], and the mentioned systematic review on pediatric chronic pain treatment also revealed that several studies were carried out in non-clinical settings, included only participants with headache, or had very short treatment durations [30]. Moreover, concerns were raised regarding poorly described methodology, especially the content of treatment. Importantly, existing research on pediatric chronic pain illustrates an urgent need to conduct studies with children and adolescents suffering from debilitating chronic pain other than headache, for which pain relief is not the only or the most important outcome [30,129]. Thus, there is still limited empirical evidence regarding the effectiveness of CBT for chronic idiopathic pain in youths. Apart from the studies in the present thesis, there are no studies available that have investigated the effects of an intervention emphasizing exposure and acceptance for this group.

CBT in the context of chronic pain has come to represent a wide variety of interventions (e.g. stress management, problem solving, goal setting, pacing of activities, assertiveness and communication training, meditation, guided imagery, hypnosis, education, cognitive restructuring, distraction methods), aimed at improving patients' self-management skills [171,174]. Notably, to a large extent CBT-oriented pain management has focused on reducing pain and distress. This objective has been targeted by both behavioral and cognitive interventions. The former is illustrated by the use of e.g. relaxation/biofeedback techniques and stress management strategies [78,89,174,175]. In addition to direct symptom alleviation, such interventions are also aimed at increasing the patient's perception of self-control [174]. Cognitive interventions (e.g. decatastrophizing, behavioral experiments, challenging dysfunctional thoughts) have commonly been used to change inaccurate predictions about avoided situations (by changing the content of thoughts), and to reduce the associated fear and anxiety [22,116,175]. Also, interventions specifically aimed at increases in adaptive behaviors using operant treatments have led to improvements in patient activity and medication use [78].

2.5. Limitations of the CBT approach in chronic pain management

Following the increase of studies during the last two decades, the empirical support for CBT with chronic pain is relatively strong [30,118]. Nevertheless, there is substantial room for improvements [206].

First, results from CBT programs have shown superior results compared to both waiting list control groups and active treatment conditions [38,118], but the average effect size is still modest, and a substantial number of patients do not benefit from these treatments due to various reasons [124,173,206].

Second, many of the studies providing the empirical base for CBT in pain management have utilized extensive multimodal treatment programs [38], and a systematic review have provided support for an intensive multidisciplinary

biopsychosocial rehabilitation compared to less intensive interventions [49]. However, such treatments may not be available to a large group of patients, which implies a need to develop interventions that are effective although less extensive.

Third, as described, even if the empirical support is accumulating there are still few studies with children and adolescents disabled by chronic pain other than headache [30].

Fourth, although CBT has made important contributions to chronic pain management, the process by which it is effective is still unclear [55,102,117]. The interventions in most CBT programs for chronic pain are not strictly derived from one well defined theory, e.g. learning theory. Instead, CBT is very often broadly defined and includes a variety of techniques based on several different theoretical assumptions [172]. This results in difficulties with identifying the working mechanism(s), which in turn may contribute to the development of comprehensive multimodal treatments with unnecessary components [172].

Thus, more studies are needed to investigate the effectiveness of CBT oriented interventions with specific groups of patients, e.g. WAD and severely disabled children and adolescents. Moreover, a larger emphasis should be placed on identifying the relevant treatment components and change processes in CBT-oriented interventions for chronic pain. This requires evaluations of well defined, theory driven, interventions, and the use of instruments to assess the hypothesized change processes (process measures).

2.6. Learning theory applied to chronic pain

Many patients with chronic pain engage in behaviors that do not contribute to physical or mental well-being. Such behaviors can be both overt (i.e. can be seen by others) and covert (i.e. can not be seen by others, such as thoughts, emotions, and physiological responses). As an example, behaviors that reduce pain and distress can be adaptive in the acute phase. However, over time, behavior patterns that are oriented toward (short-term) symptom alleviation, i.e. avoidance, tend to gradually decrease functioning and life quality often without any sustained decrease in symptoms [177,209].

A functional relationship between longstanding pain and disability can be explained using learning theory [39]. According to a learning theory model, avoidance of situations associated with unpleasant experiences (e.g. pain, fatigue, fear) is central to the understanding of pain related disability, and explained by both *respondent* and *operant* conditioning mechanisms.

2.6.1. Respondent conditioning

Respondent (also referred to as classical or Pavlovian) conditioning occurs when a neutral stimulus is presented with a significant (unconditioned) stimulus in close temporal proximity. After repeated presentations, or pairings, of the two stimuli, the neutral stimulus will then begin to elicit similar behavioral responses as the unconditioned stimulus. Thus, if a certain activity is associated with a nociceptive stimulus, this previously neutral stimulus (activity) will now increase pain and/or distress [174,188]. Respondent conditioning deals with the learning of automatic, or involuntary, responses and focuses on antecedents (i.e. factors occurring before the behavioral response). A painful injury (e.g. twisting the knee while running) elicits an automatic distress response (i.e. sympathetic activation). This could be referred to as an unconditioned stimulus and response [209]. Through processes of respondent conditioning, neutral stimuli (e.g. a soccer ball, running) will adopt similar psychological functions as the event that inflicted pain and distress (i.e. the injury).

Thus, the previously neutral stimuli are now conditioned and provides an aversive context for the individual, resulting in similar sympathetic reactions (conditioned responses) as the unconditioned stimulus [122].

2.6.2. Operant conditioning

In contrast to respondent conditioning, operant conditioning concerns the modification of voluntary behaviors, and is focused on the consequences following the behavior. Thus, when individuals operate within a context, behaviors will result in certain consequences. For example, a boy with abdominal pain asks his dad "Can you drive me to school? I don't want to take the bus, my stomach hurts." The boy's verbal behavior will affect the context in many ways. For example, his mother (overhearing the conversation) comes out from the kitchen to check if he is alright, his older sister says "Poor you, you can borrow my iPod today if it feels better", and his dad answers "Ok, I can drop you off on my way to work." Put simply, the consequences following a certain behavior may be experienced as reinforcing or punishing. Depending upon the consequence(s) of the behavior, the probability that this behavior will be repeated in a similar situation will either increase or decrease. Positive reinforcement refers to an increase of desired consequences (borrow iPod), and negative reinforcement represents a decrease of aversive events (worries about having to take the bus disappears, removal of anticipated pain, decrease in current pain). Although negative reinforcement appears to be of major importance, positive reinforcement (e.g. increased attention from parents or siblings after leaving school early due to pain) also contribute to the development and retention of behavior patterns in chronic pain patients.

In the operant behavioral pain treatment model, formulated by Fordyce in the 1970's, social and environmental factors that increase pain behaviors (e.g. asking for help, complaining, taking medications) are identified. Following a functional analysis of the target behavior, operant principles (i.e. reinforcement, punishment, extinction) are then used to alter the target behavior(s) [39]. After 35 years, the operant conditioning paradigm is still of great importance for several reasons. One, there are still no effective strategies to effectively achieve sustained symptom alleviation in chronic pain syndromes. Two, the weak relationship between pain intensity and overt pain-related behaviors [77] also implies that improvements in functioning requires that behavioral strategies are specifically and directly addressed [146].

2.6.3. Pain as an interoceptive stimulus

Pain is normally seen as a response, e.g. to noxious stimulation. However, it should be noted that pain can also be considered an *interoceptive stimulus* [12]. Furthermore, the interoceptive stimuli may be unconditioned (e.g. nociceptive pain) or conditioned (e.g. a physical sensation). A severe pain experience provides a context for learning. Following a more or less traumatic event, internal bodily sensations (nausea, fatigue, muscle tension) that accompanied the onset of the severe pain experience may now be associated with the full experience. For example, a patient with idiopathic recurrent abdominal pain started out with a clearly identified organic cause of the pain (e.g. inflammatory process). Over time, repeated pairings between gastrointestinal sensations and nociceptive pain have occurred. After two years, the boy presents with idiopathic recurrent abdominal pain without any nociceptive component. Following a conditioning process, somatic sensations that were previously ignored have now been conditioned and result in hypervigilance, thoughts about hospital, and increases in pain and distress.

Moreover, some types of stimuli do not require previous learning [122]. Stimuli that have been related to survival threats elicit fear, especially in aversive contexts. Pain may likely represent such an interoceptive stimulus that automatically result in fear and attempts to escape or avoid both the experience itself as well as situational factors associated with it.

2.7. The fear-avoidance model

A large number of studies have shown that pain related fear plays an important role in the development of avoidance patterns and disability [209]. In the fear-avoidance model of chronic pain and disability, anticipation of pain is emphasized because it elicits a fear response that leads to avoidance of the situation, which in turn is negatively reinforced by a reduction of the negative stimuli [209]. Thus, the fear-avoidance model incorporates respondent as well as operant conditioning mechanisms. Over time, this leads to impaired functioning without a corresponding decrease in pain or discomfort [176,209]. A severe form of this phenomenon is referred to as kinesiophobia (fear of movement). Kinesiophobia has been extensively investigated, and several studies have demonstrated its association with self-reported disability and poor behavioral performance [20,208]. Interventions derived from the fear-avoidance model are aimed at reducing fear through correcting inaccurate predictions about avoided situations [22], mainly through the process of exposure (i.e. increased contact with previously avoided stimuli without escape or avoidance, or a gradual increase in behaviors previously avoided due to e.g. pain and distress) [205].

2.8. From learning theory to Relational Frame Theory

2.8.1. Beyond direct learning experiences

As previously described, over time many patients that suffer from chronic pain or other symptoms develop extensive patterns of avoidance behaviors that dramatically limit the space in which life is lived. Learning theory provides a frame for understanding the impact of previous experiences on present behaviors. Humans are indeed very clever animals and we learn not just from our own experiences but also from watching or listening to people around us. Commonly, peoples' behaviors can be explained by *direct learning experiences*, in the sense that respondent and/or operant conditioning processes can be identified. However, people sometimes react and behave in ways that are not readily explained by such direct learning experiences, such as worrying about events that they have no previous experience of.

Although learning theory generally is a highly useful theoretical framework, there are circumstances where classical and operant conditioning appears insufficient in explaining the relation between different stimuli, as well as between stimulus and response. When stimuli that become associated have never been presented simultaneously, and do not share important physical properties, respondent conditioning (in the traditional sense) cannot be said to have occurred. Neither can we refer to operant conditioning if the behavioral response that follows the stimuli has not previously been reinforced. Therefore, to better understand the complexity of human behaviors and suffering from a learning theory perspective, we need to move beyond the traditional use of respondent and operant conditioning.

2.8.2. External and internal stimuli

With our sophisticated cognitive abilities we can relate to our "inner representations of the external world" in much the same way as we relate to external events themselves. Thus, thinking about something funny we heard yesterday can make us laugh today. Similarly, thoughts can make us anxious or sad, even in a way that goes beyond direct learning experiences. Due to our ability to link thoughts to other thoughts, we become emotionally vulnerable. Furthermore, when our own thinking causes emotional suffering, it is a common reaction to try to reduce or avoid the painful thoughts or emotions, just the way we avoid external situations associated with pain or distress. Unfortunately, there is an overwhelming magnitude of stimuli (both external and internal) that may inflict e.g. fear or sadness.

Consider the following examples. Reading in the paper that a former colleague has been promoted may result in feelings of worthlessness. Watching "Sex and the City" may lead to the conclusion that "All clothes in my closet are out of fashion and I have no taste." Being asked "What do you want to do in the future?" may feed the ever present idea that "I'm not capable, and trying means failing so I better take it as it comes instead of setting up any goals." As can be seen, in almost any situation there are stimuli that may elicit negative psychological reactions, and result in avoidance behaviors.

Several years with chronic pain, repeated treatment failures, disappointments, sleep difficulties, etc. may have resulted in a large "cognitive bank account" with at least as many negative predictions about the future as there are painful memories from the past. Given the cognitive abilities, the amount of situations that may elicit negative thoughts or emotions is almost endless. Thus, to fully understand the suffering experienced by, for example, patients with chronic pain we need to look more closely at "inner stimuli" and how thoughts may be related to other thoughts. In other words, we need to consider the specific characteristics of *verbal behavior*.

2.8.3. Refining the learning theory model

Although a learning theory framework provides a basic formulation for treatment, the complexity of human suffering indicates a need to refine our models to better account for the links between pain and disability, in order to improve the analysis and treatment.

Recently, within the behavioral paradigm, a treatment approach emphasizing acceptance of pain and distress has been suggested, for example in Acceptance and Commitment Therapy (ACT). In ACT, acceptance is emphasized as a means to decrease avoidance and instead increase valued activities, even when experiencing pain and distress. This model represents a rather sharp contrast to previous psychological interventions focused on increasing the patient's control over maladaptive thoughts, emotions, and overt behaviors [97]. The theoretical rationale for ACT is found in classical and operant conditioning principles, as formulated in basic learning theory and in Relational Frame Theory (RFT).

RFT builds on traditional learning theory and provides an attempt to explain some of the complex human behaviors that may be difficult to account for by traditional learning theory models. In RFT, respondent and operant conditioning principles are used to explain behaviors that are due to direct learning experiences, but also behaviors that appear to result from the more complex phenomenon of *derived learning*. As such, learning theory and RFT provides the theoretical framework for ACT [50,51,55].

RFT, as an extension of traditional learning theory, is an attempt to use a behavioral approach to explain the complexity of human suffering by taking into account unique characteristics of human language and cognition [51]. In other words, there are certain differences between animal and human cognition that may represent keys to understanding human intelligence as well as psychopathology. Specifically, RFT is a well-defined and empirically supported theory that accounts for why and how stimuli may acquire functions and elicit responses that were not explicitly trained, i.e. derived learning (the stimulus has not been classically conditioned, and the response has not previously been reinforced) [9,51]. Tentatively, RFT has the potential to improve the understanding and treatment of disorders characterized by rigid and highly treatment resistant maladaptive behavior patterns, as illustrated by subgroups of patients with e.g. obsessive-compulsive disorder, generalized anxiety disorder, or severe depression. Also, RFT may be a key to a more thorough understanding of the extensive avoidance patterns seen in some people with chronic pain.

2.8.4. Our cognitive ability - a blessing and a curse

Humans' use of language represents a highly sophisticated skill that facilitates communication and complex thinking, for example when planning future events; "I should bring an extra sweater in case it gets colder than expected", or comparing different alternatives; "If I pick this job instead of the other, I'm more likely to get promoted soon." Advantageous as this is, these same skills also have certain negative effects, such as considering the future or the past when it does not serve us well; "I'll fail just as I did the last time, there is no use in trying", "Why did she do that to me, I need to understand in order to move on". Similarly, comparisons are not always helpful to us; "I'm the worst therapist in the clinic"; "I should do better than this."

Due to our cognitive abilities, we can engage in problem solving behaviors that are useful when there is an actual problem to be solved, such as repairing the car, or asking someone for feedback before submitting an application. However, the same type of problem solving behaviors can also be applied to problems that mainly exists "in our heads", in the sense that there is no practical problem to which a solution can be found. For instance, we worry about things long before they happen even if we cannot influence the outcome. Therefore, we suffer in the present from future events on which we cannot act. Or, following a traumatic event we go over what happened again and again, despite the fact that this is painful and interferes with other activities (e.g. leading to withdrawal from social situations). Thus, our sophisticated cognitive apparatus (i.e. language and cognition) is useful but sometimes entangles us in rather unproductive processes that result in considerable suffering.

From this perspective, ACT as a clinical application of learning theory and RFT can be described as a therapeutic approach aimed at improving people's ability to relate to the cognitive processes in a more constructive way, so that negative thoughts and feelings do not interfere with acting in accordance with personal values.

2.8.5. Stimulus equivalence

In learning theory, a stimulus class refers to two or more stimuli that result in similar responses. When the physical properties are very similar, this can be explained as *stimulus generalization* (e.g. two different dogs both result in a similar fear response) [4]. Following training (applying operant contingencies to reinforce the subject when appropriately pairing some of the presented items), we can achieve *functional stimulus classes* [52]. However, when the physical properties are not at all similar and no

previous training has occurred, and a stimulus still results in the same behavioral response, we need to consider mechanisms such as *stimulus equivalence*. In a number of experiments where stimuli-stimuli relations were trained, Sidman and others showed that more associations between different stimuli were acquired than what had been explicitly trained [54,148-150]. In short, this means that if the associations between A and B is trained, as well as the relation between A and C, the subject will automatically (without training) associate B with A, C with A, B with C, and C with B. Such a *generative process* is central to the understanding of how it is possible to associate stimuli that have not previously been presented together [51,149].

2.9. Relational Frame Theory (RFT)

2.9.1. Basic theory and applications to pain

There are several different theories to explain stimulus equivalence. In contrast to Sidman's theories, RFT considers the emergence of equivalence relations between stimuli fundamentally a behavioral process [51]. In other words, *relating* or "framing" stimuli is considered to be a learned behavior under *contextual control* (occurring in certain contexts but not in others). As such, the "relating behavior" is developed through multiple exemplar training (repeated presentations of the stimuli) and shaped by the consequences following the behavior. Importantly, "relational frames" are not latent cognitive constructs but behaviors (framing events or stimuli relationally) that occur in given situations and depend on the context.

According to RFT, we relate stimuli in many different ways. Equivalence (as in stimulus equivalence) or "same as" is just one type of relational framing between stimuli, which in RFT-terms is labeled a *frame of coordination*. A slightly more complex type of framing occurs when learning that "hot" is the opposite to "cold", or that "winner" is the opposite to "loser", which in RFT-terms is called a *frame of opposition*. However, there are several other ways we can relate different stimuli, such as "before-after" (in RFT-terms temporal framing), "smaller-larger" and "better-worse" (comparison framing or a frame of comparison), and "if – then" (frame of causation) [27.52].

The focus in RFT is on the *relations* between stimuli rather than on certain properties of the associated stimuli [51]. The discrimination (detecting, responding to) of stimuli is a central feature of behavior theory, and this can also be applied to the relations between stimuli. In RFT, *relational responding* refers to discriminating relationships between stimuli [9]. Learning that elephants are larger than mice (a relation) includes more than specific information about the elephant and the mouse. We have also acquired knowledge that makes it possible to discriminate which one of these animals is "larger".

As previously described, human learning involves a generative process. In addition to the direct learning experience, *derived learning* is illustrated following multiple exemplar training [51]. In RFT, there are two central terms used to describe this. *Mutual entailment* means that, in any given context, A is related to B the same way B is related to A. If an individual has learned that A is similar to B, this also means the opposite: that B is similar to A. *Combinatorial entailment* implies that if training has established that A is similar to B and that A is similar to C, it will be derived that B is similar to C and C is similar to B. Thus, following the direct learning of two relations, the individual will end up with six relations, of which four are acquired through derived learning. Figure 2.1. illustrates the explicit (or direct) and derived learning that has occurred.

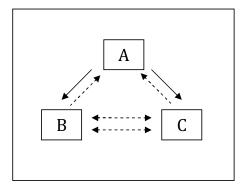


Figure 2.1. Explicit training and derived learning. First, the participant is reinforced for choosing B among several different letters (e.g. L, B, K), when presented with A. Then, with a new set of letters, the participant is reinforced for choosing C, when presented with A. Mutual entailment refers to the bidirectionality of the learning process: when presented with B, A will be picked among a number of letters without this having been directly trained. Similarly, when presented with C, A will be picked. In addition, combinatorial entailment is illustrated: B and C will be related to each other without having explicitly trained this, meaning that C will be picked among a number of letters when presenting B, and B will be picked when presenting C. Broken lines represent the derived learning, i.e. that was not explicitly trained.

An important aspect of RFT is that learning is based not only on physical properties that can be directly seen, heard, smelled, touched, or tasted (non-arbitrary relations) [9,51]. Learned relations can also be based on situational factors or social conventions (non-arbitrary relations). A commonly used example is the value of money [51]. For a young child, a nickel is "bigger than" (frame of comparison) a dime due to physical properties. However, after discussing the value of money with an older sibling, she or he will learn that a dime (ten cents) is "bigger than" a nickel (five cents) due to its monetary value. According to mutual entailment, a dime will be considered "bigger than" a nickel just as well as a nickel will be considered "smaller than" a dime. Adding a penny (one cent) to the relational network, combinatorial entailment implies that: if a penny is less than a nickel, and a nickel is less than a dime, this means that a penny is less than a dime.

Derived stimulus relations (mutual and combinatorial entailment) have been extensively investigated in a large number of well controlled laboratory studies [51]. Also, in one of the rare longitudinal studies available, the successive development of relational responding was observed in a young child [82]. Later studies have shown that this ability develops gradually over time [110], and that it is reduced in some children with autism [138].

When a stimulus that is involved in a relational network has acquired certain psychological functions (e.g. fear, sadness), a *transformation of functions* will occur so that other stimuli within the network will take on similar psychological functions [51]. However, the emotional response that is elicited by presenting the related stimuli depends on the type of relation. For a child that has used a nickel to buy candy, the coin will likely elicit "excitement" (a psychological function). This psychological function will now be transformed to the other stimuli involved in the relational network. Given the relationship between the coins (a dime is bigger than a nickel which is bigger than a penny), the psychological function of a dime will be "more excitement", while a penny

will result in "less excitement". Thus, related stimuli will result in responses depending upon their relationship with the original stimuli. In other words, the psychological function of the stimulus is also derived.

The ability to relate stimuli also accounts for verbal stimuli (i.e. spoken or written words, thoughts). The word "car" is related to an actual car by frames of coordination (roughly the same as stimulus equivalence), which means that the word "car" may elicit similar responses as the actual car (e.g. memories from the accident, sympathetic activation, leaving the room). Similarly, discussing or thinking about future events ("I need to start running again.") may elicit the same psychological function (anxiety) as the real event (running) because the thought "running" is in a frame of coordination with actual running. Also, these thoughts are related to other thoughts ("re-injury", "rehabilitation") that may elicit responses such as interoceptive focusing or interrupting running. Over time, we create large relational networks of verbal stimuli by direct experiences or by derived learning, i.e. through mutual or combinatorial entailment. In fact, we constantly relate stimuli to other stimuli. Though beyond the scope of this text, it appears as if the ability to relate arbitrary symbols is central to the development of human language [51].

Conceptualizing the detrimental effects of chronic pain seen in many patients requires more than analyzing pain per se. From an RFT perspective, pain can be seen as an interoceptive stimulus that is related to a large number of verbal stimuli (thoughts) as part of a complex network of cognitions. Pain in itself may be framed in coordination with thoughts like "I must be careful" and "There is something wrong with me." Other types of framing may be occurring as well: "If I make plans for the weekend, then I will end up getting disappointed" (causation) or "Increased pain now means unbearable pain tomorrow" (temporal). Furthermore, most people have learned that "injury" causes "pain", and from this follows (mutual entailment) that "pain" is an effect of "injury". This, in turn, may be in coordination with "dangerous to future health" and "must rest". From this follows that "pain" and "must rest" can become intimately related through combinatorial entailment. Obviously, most people have also learned through direct experiences that pain tends to decrease when resting (negative reinforcement). Thus, both direct learning and derived relational responding contributes to pain related avoidance behaviors.

Consider the following example in which a rather non-dramatic suggestion elicit thoughts not easily explained by direct learning experiences, and results in seemingly illogical emotional reactions and avoidance behaviors. The physician says: "It might be good for you to start a rehabilitation program" (an external stimulus). The thought about rehabilitation (verbal stimuli) is related by frames of coordination (same as) to many other thoughts, such as "physical strains" and "go back to work". These, in turn, are related by frames of causation (if - then) with e.g. "increased pain" and "failing". Furthermore, thoughts about failing may be framed in coordination with "being considered lazy", "getting fired", "loosing friends", "becoming depressed", "my wife will leave me", "being alone", and "having no life" (see Figure 2.2.). Given the transformation of stimulus functions, psychological functions are "carried over" to other stimuli based on how they are related. Thus, "going back to work" may elicit similar psychological functions as "having no life" (e.g. despair). It is possible, or even likely, that such a strong emotional reaction results in avoidance behaviors, such as finding another doctor, stating that "It is impossible for me to go back to work, you can't make me do that!", demanding more medications, etc. Also, in this situation "me" is likely in a frame of coordination with "pain patient" and "taking heavy medications". These verbal stimuli are framed in opposition with "healthy people" and "not taking

medication", which in turn are in coordination with "independent", "successful", and "planning the future". Thus, if this person is framing him/herself accordingly, this may result in many different sorts of avoidance behaviors (to reduce the psychological reaction that follows the verbal stimuli), such as working extremely hard to prove the thoughts wrong (i.e. controlling the thoughts), giving up a qualified job to avoid risks of failure, or deciding to not plan ahead to avoid disappointments. Figure 2.2. illustrates this example. Although direct learning experiences could explain some of the behaviors seen, derived learning may account for the rather farfetched associations made between e.g. "rehabilitation" and "my wife is going to leave me", or "I shouldn't plan ahead".

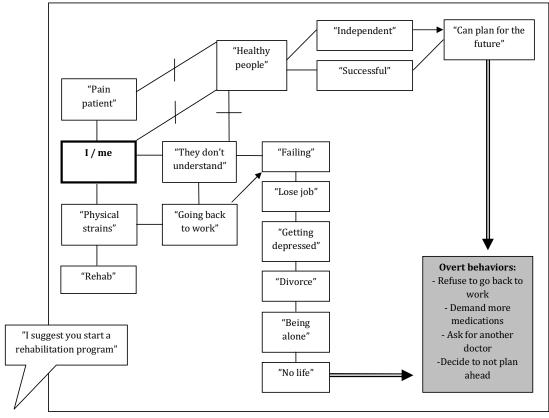


Figure 2.2. A person with chronic pain is suggested by his physician to start a rehabilitation program (external stimulus). Thoughts about "physical strains" and "going back to work" (inner verbal stimulus) are elicited. These are, in turn, in a frame of causation (if – then) with "failing", which is related to other verbal stimuli (e.g. "divorce", "having no real life") that may be difficult to explain by direct learning experiences. The thoughts result in psychological functions such as despair, and overt behaviors to avoid this verbally construed threat of "having no life". "Me" is also framed in coordination with "pain patients", that is in opposition with "healthy", "independent", "successful", "can plan for the future" etc. Following this thread of thoughts may help explaining difficulties with e.g. planning ahead. Three types of relational frames are illustrated: frames of coordination (—), opposition (—), and causation (—). Most people relate thoughts with "acting on them", which may indicate a frame of causation between thoughts and overt actions.

It should be noted that these avoidance behaviors are in line with the content of the thoughts. Central to the understanding of avoidance behavior is the notion that most, or all, people tend to apply a frame of causation relating "inner experiences" (thoughts, emotions, or bodily sensations) with "acting on them". This is likely something we learn from early on in life (if you feel hungry then eat, if you feel tired then go to sleep etc). As most of us relate "pain" with "bad", and "must reduce", this implies that "If I feel pain, then I must act to reduce it." Also, this message is sometimes communicated by friends and family; "If you don't feel like going, you really shouldn't", or from the health care system; "Take this medication when the pain gets worse." Thus, avoidance behaviors result from both an activated network of verbal stimuli and their acquired psychological functions, but also from a context which reinforces behaviors aimed at avoiding or reducing pain and distress (the behaviors are under contextual control).

2.9.2. Clinical implications of RFT

RFT has some important clinical implications that set the stage for ACT [50,55]. Specifically, RFT illustrates the likelihood that people become entangled with verbal behavior, in ACT-terms referred to as cognitive fusion, and provides an explanation how this may occur even without direct learning experiences. Cognitive fusion is tightly linked to rule-governed behavior and although a comprehensive explanation of rule-governed behavior is beyond the scope of this thesis, a brief description of how this may be conceptualized is warranted [167].

Through our ability to relate things to other things, we learn to follow rules even without any direct experiences from the situation that the rule describes. For example, applying the relational frames of e.g. coordination (same as) and causality (if-then), we learn that some mushrooms should not be eaten because doing so might make us sick. Someone describes a particular mushroom which is considered the "same as" a real mushroom. Then, the person tells us "If you eat those, then you will get very sick", which places eating that particular mushroom in a frame of causation with getting sick. (In fact, when the word "sick" is mentioned, this is also framed in coordination with memories from previous experiences of being sick, although not from eating mushrooms. Also, the words may come from someone that is considered an expert compared to me, i.e. a frame of comparison, which further increases the likelihood that I will follow the rule instead of trying to find out myself.) Thus, rules are words that can strongly affect our behaviors even when we lack direct experiences from similar situations

This ability to learn from instructions, or rules, is adaptive in most situations. Exceptions exist; the most apparent example is the *insensitivity to contingencies* that occur when rules are presented [167]. In laboratory studies, people that are given rules about how to respond (e.g. "When you hear the sound, push the button") perform better than those who are not given this instruction or rule but instead have to learn through trial and error. Thus, the behavior "pushing button when hearing the sound" is reinforced. However, if the system is changed and no information about this is provided, the group that was given the rule is much slower in adapting to the new contingencies (e.g. when hearing the sound, not pushing the button for ten seconds is reinforced) [167].

Insensitivities to contingencies can also be seen in pain patients, as in the following example. Immediately following an injury, a person is about to move a couch from the bedroom to the living room. He experiences pain (interoceptive stimulus) and continues with this physically demanding task (behavior), which is followed by increased pain and

re-injury (punishment). In addition, people tell him to be careful and not do things that increase pain. Over time, a rule is established: "I should not do anything physically demanding because then my pain will increase and I will never get better." After eight months, the injury has healed but the pain is unfortunately still present. Now, the contingencies have changed; physical activities are no longer harmful. However, the behavior remains the same (physical activities are consistently avoided). He is now relatively insensitive to contingencies in the environment and changes in behaviors do not come easily. The overt behavior is more guided by the existing rule(s) than the actual consequences of the behavior; he has been avoiding physical activities for eight months and is still not better, and due to the pattern of avoidance behaviors he also misses many important social events. Thus, verbally constructed rules may explain why some patients with extensive avoidance patterns are particularly reluctant to engaging in exposure-based interventions. Using ACT-terms, this phenomenon can be conceptualized as cognitive fusion, which may need to be specifically addressed to facilitate exposure and behavior change.

Also, RFT highlights the tendency to escape or avoid negative experiences even when doing so results in significant harm (experiential avoidance). People go to great lengths to avoid painful memories or any thoughts associated with emotional suffering, such as taking strong medication with severe side effects, using drugs or alcohol, spending no time with sick relatives, or even attempting suicide. In addition, we may engage in direct *suppression of thoughts*, such as trying not to think about what could happen. The problem with such strategies is that they tend to work rather poorly. A large body of literature supports the fact that it is counterproductive to deliberately try to suppress negative thoughts and emotions [1]. The avoided private experiences tend to become more frequent and, even more alarming, increase the impact on overt behaviors.

Furthermore, RFT provides an explanation to why extinction of verbal behavior (i.e. reduction in negative thoughts) is neither an adequate goal in treatment nor necessary to achieve overt behavior change. Relational networks are extremely difficult to break up, given the large number of other relations available to maintain and even reestablish the links [50]. Thus, established relational networks may only be further elaborated through new learning experiences. However, by changing the context we can undermine the link between thoughts/emotions/bodily sensations and overt behaviors, and by this altering the *functions* of stimuli without necessarily changing the content of the e.g. thought. For example, it hurts and I have the thought that I must stop *and* I keep doing what I planned to do. Thus, the clinical implications of RFT point directly to the importance of implementing strategies aimed at acceptance and defusion to facilitate a process of values-oriented exposure. [50].

2.10. Acceptance and Commitment Therapy (ACT)

2.10.1. Developments within CBT

The development of CBT may be divided into different phases based on common and/or dominant assumptions, methods, and goals, sometimes referred to as "waves" or generations [50]. Briefly, the first phase consisted of behavior therapists emphasizing that theories should be built on scientifically well-established principles. Basic principles of respondent and operant conditioning were applied to achieve changes in target behaviors, such as increases in pressing a button when hearing a certain sound, or reducing the sympathetic response in the presence of a snake.

Later, a more cognitively oriented approach (second phase) received increased attention, much due to concerns for variables that were difficult to observe but nevertheless appeared clinically relevant (e.g. motivation). The drawback was that the connections to basic learning theory became blurred. Mechanistic models were built using hypothetical internal constructs (e.g. "cognitive schemas") as mediators to explain behaviors. However, the focus on change remained but was now applied to the newly developed constructs as well. For example, irrational thought patterns should be detected and subsequently restructured, and negative self-images should be corrected. Clinically, many began to combine traditional behavior principles with interventions and techniques that were derived from the cognitive models. Thus, the combination "cognitive-behavior therapy" includes both behavioral and cognitive principles, and is largely aimed at obtaining changes in overt or covert (e.g. cognitions) behaviors [50,102,206].

The third phase has emerged from both the behavioral and the cognitive traditions and includes therapeutic approaches such as ACT, Dialectical Behavior Therapy, Functional Analytic Psychotherapy, and Mindfulness-Based Cognitive Therapy [56]. Although somewhat different, they share common features. For example, they have incorporated areas previously not emphasized in behavior therapy, such as acceptance and mindfulness. Also, there is a focus on central concepts in behavior theory, such as a functional analysis of the target behaviors, skill building procedures, and direct modification of behaviors through application of operant contingencies (shaping) [56].

2.10.2. The philosophical foundation: functional contextualism

Based on RFT, ACT is the result of an attempt to further develop behavior therapy into an approach that more adequately accounts for human cognition, while retaining the principles of behavior analysis and learning theory (i.e. classical and operant conditioning) [55]. The philosophical roots of ACT are found in functional contextualism [57]. According to contextualism, psychological experiences are ongoing activities that occur within a specific context (and cannot be seen as separate from the context other than for analytical purposes). The individual's context consists of a set of situational (environmental, e.g. the people in the room) and historical (i.e. previous experiences brought into the situation, such as memories) factors. Because psychological events are contextually controlled they cannot, in a given situation, be directly changed. Also, psychological events are not causally related to overt behaviors, but mediated by contextual factors. From this follows that covert or overt behaviors can only be predicted and influenced by focusing on manipulable variables in their context. However, by altering the context, changes in private experiences are likely to occur. Moreover, the pragmatic truth criterion states that the value of an idea is measured by how well it works rather than how well it resembles reality. In ACT, workability (how well something works) is emphasized as a truth criterion and the person's own life values are used as the criteria to assess the workability of a particular strategy.

2.10.3. An ACT-oriented analysis

In an ACT-oriented analysis, the assumption is that every person is capable of living a vital life in the presence of pain and distress [55]. From an ACT-perspective, it is argued that, in contrast to pain control per se, the patients' ability to act effectively in the presence of pain and distress constitutes a key factor in functioning and pursuing a valued life. In an ACT model of debilitating chronic pain, avoidance of unpleasant experiences (i.e. *experiential avoidance*) such as pain, fear, negative thoughts is of

central importance when describing the functional relationship between symptoms and disability. Therefore, the initial behavior analysis seeks to clarify avoidance behaviors that prevent the patient from living a vital life. Importantly, to an important extent avoidance results from an experienced need to reduce or control symptoms (pain, fatigue, anxiety etc) in order to live a valued life. As a consequence, patients commonly become engaged in activities that produce short-term relief but that are less active, stimulating, and meaningful. Expressed differently, avoidance occurs primarily when negative thoughts and emotions have excessive or inappropriate impact on behavior, denoted as cognitive fusion. As a result, over time behavior patterns become narrow and inflexible. Another aspect of avoidance and cognitive fusion is the patient's unwillingness (or lack of acceptance) to experience pain and other related symptoms. This is illustrated when patients do not engage in valued activities in order to avoid experiences associated with pain (e.g. fear of pain, failures, disappointments) [142]. Experiential avoidance, cognitive fusion, and unwillingness represent three key concepts in the ACT-conceptualization of debilitating conditions such as chronic pain, and results in what is referred to as psychological inflexibility. Psychological inflexibility represents the central theoretical construct in ACT and is defined as the inability to act effectively in accordance with personal values in the presence of negative private experiences, such as pain and distress [55]. Psychological inflexibility also implies that negative thoughts and emotions tend to interfere with ongoing activities, which may result in difficulties with staying presenting the moment. Rather than being aware of what is actually happening in the present moment (e.g. a piano concert), the client's focus is oriented towards the content of thoughts; "These seats really make my pain worse", "I wonder how much longer I can sit here", "Tomorrow will be awful."

2.10.4. An ACT-oriented intervention

Following a functional analysis of relevant target behaviors (avoidance behaviors that interfere with valued living), the therapist seeks to assist the patient in identifying personal values, i.e. an important direction in life (e.g. "being a supportive friend"), and to help the patient to direct his or her efforts to achieve this. Commonly, patients report that pain and discomfort prevent them from behaving in accordance with their values (i.e. "I can't do it because I'm in pain"). Exposure to previously avoided private experiences is considered the core intervention, emphasizing a wider and more flexible behavior repertoire. In this process, acceptance of what cannot be directly changed (e.g. pain, fatigue, negative thoughts and emotions) is emphasized as a means to recognize and change the things that can (i.e. behaviors directed towards a valued life) [57]. Thoughts ("If I work out, my pain gets worse") are powerful and tend to point in a direction away from expressed values such as "playing soccer, being part of the team" (cognitive fusion). Therefore, by helping the patient to recognize and acknowledge private experiences for what they are (i.e. thoughts are thoughts, rather than exact and fully reliable predictions of the future), the therapist tries to help the patient to defuse, or distance, him- or herself from the thoughts, not by discussing whether they are correct but by functionally analyzing the consequences of acting upon them. Throughout the treatment, the patient is taught and encouraged to stay present in the moment, or to be more mindful, and to gradually learn to notice and acknowledge the unpleasant experiences in a non-judgemental, non-elaborative, and non-controlling way [55]. With this skill, patients are then better able to identify and pursue their goals, and not be as controlled by their psychological events (e.g. pain, fear of anticipated pain). The expressed goal of ACT is to increase psychological flexibility, i.e. to help patients

consistently choose to act effectively in alignment with their values, in the presence of difficult or interfering private experiences, such as pain or fear [50,55]. This is in sharp contrast to a symptom reduction approach, which has been dominant in chronic pain management [30,118]. A more detailed description of the ACT-oriented intervention used in the treatment studies in the present thesis will be presented in the chapter on methodology.

2.11. Empirical status of ACT

The empirical base for ACT has increased rapidly over the past ten years. To date, ACT has successfully been used in a number of various clinical areas other than pain, such as psychotic symptoms [5,42], depression [216], diabetes [46], epilepsy [85], substance abuse [59], and work-related stress [11]. Review articles summarizing the existing ACT-studies have supported the usefulness of this model [55,56].

However, in a recent meta-analysis evaluating the empirical support for interventions referred to as "third-wave" [50], the author concluded that there is a need for more empirical evaluations of ACT and similar approaches, especially RCT's [219]. Unfortunately, a number of recent RCT's, as well as a couple of uncontrolled but large studies, with pain were not included (see below). Furthermore, although ACT has been described as a novel treatment [55], others have argued that ACT is not distinct from CBT, and that it is fully compatible with the traditional CBT model of psychological functioning [62]. To date, existing research on ACT suggest that it works through different processes than other treatments, including other CBT-approaches [55]. However, similarities and differences between ACT and other interventions should be further explored in e.g. component analyses.

ACT has also been applied to children, adolescents, and parents in several different settings, although research in this area is still limited [45,119]. In an RCT, the usefulness of acceptance in reducing high risk sexual behaviors was shown [114]. ACT-oriented interventions have also been used with e.g. adolescents who are at risk for dropping out of school [121], and a case study illustrates how ACT was applied in the treatment of an adolescent with anorexia [60]. The application of ACT to pediatric chronic pain is described in more detail later, but the usefulness of this approach has been previously discussed [196,199] and illustrated in a case report [198], a case series [202], and an RCT [201]. Furthermore, the use of ACT in the work with parents to children with autism has also been described [10].

2.12. Acceptance and pain

To date, a relatively large number of studies have investigated the relationship between acceptance and pain. Tables 2.1.-2.3. present an overview of these papers, categorized as correlational studies (Table 2.1.), experimental laboratory-based studies (Table 2.2.), or treatment evaluation studies (Table 2.3.). These three sets of studies are summarized below.

2.12.1 Correlational studies

The link between acceptance and pain adjustment was first investigated ten years ago, when a study by McCracken showed that greater acceptance of pain was associated with lower pain, depression, and disability [92]. Since then, several studies have supported these findings and illustrated that variables related to acceptance are associated with e.g. quality of life, depression, work status, and less medication use in people with chronic pain [91,92,101,103,203]. The relationship between acceptance and

other types of pain-adjustment behaviors have also been investigated. As previously described, coping refers to strategies aimed at better control over maladaptive thoughts, emotions, and overt behaviors [171]. Interestingly, coping strategies (e.g. distraction, ignoring, coping self-statements) have been found to be rather weakly related to acceptance of pain [95,97]. These studies also showed that acceptance explained significantly more variance than coping in various measures of patient functioning. Furthermore, a recent study described that although acceptance contributes to pain related impairment, coping and catastrophizing influence pain and distress [32]. However, acceptance has previously been found to predict mental well-being beyond pain and catastrophizing [194], and one study have shown that acceptance explains more variance than fear of movement [203]. Also, associations between acceptance and mindfulness-related variables were analyzed using the Mindful Attention Awareness Scale (MAAS) [99]. Relatively moderate correlations were seen between measures of acceptance (CPAQ) and MAAS. When controlling for background variables and CPAQ, mindfulness accounted for significant variance in depression, anxiety, and disability. The associations between acceptance and mindfulness within the pain context are not yet fully understood, but appear to overlap considerably. Moreover, in a series of studies using a prospective design, patients were assessed twice during a period of approximately four months (no intervention). In one of these, greater acceptance, but not pain, at baseline was indicative of better emotional, social, and physical functioning three months later [96]. Also, over time acceptance strategies appear to be more strongly associated with better functioning than control strategies [107]. Furthermore, when a measure of values-based action was added to the acceptance questionnaire, both of these were important predictors of functioning [104].

2.12.2. Laboratory studies

In several papers, results from laboratory studies have reported on the usefulness of applying acceptance strategies. Foremost, acceptance has been found to be more effective than control oriented coping techniques in increasing pain tolerance when experiencing experimentally induced pain [32,48,53,111]. In a well-designed study, people suffering from chronic low-back pain received different instructions before performing a variety of physical tasks. The pain acceptance group demonstrated significantly better functioning than the pain control group [215]. Also, one study has suggested possible gender differences, in favor of women, with regards to the utility of acceptance strategies in healthy subjects, [73]. Recently, the importance of values has been investigated, indicating the importance of this component in promoting acceptance of pain [125,126].

2.12.3. Treatment evaluation studies

There are still relatively few clinical treatment evaluations performed with regards to acceptance and pain. Several large but uncontrolled studies have successfully incorporated acceptance strategies into a comprehensive, multidisciplinary, cognitive behavioral program with adult pain patients [100,106,211]. The treatments evaluated in these studies were performed in a tertiary care rehabilitation unit and consisted of full-day treatment activities during three to four weeks. To control for spontaneous recovery, assessments were in some studies made three months before as well as at the beginning of treatment, indicating stability in reported pain and functioning. Results clearly suggest the effectiveness of this approach referred to by the authors as contextual cognitive behavioral therapy. In contrast to this comprehensive treatment program, a brief outpatient program with weekly sessions based on exposure and acceptance

strategies has been evaluated in a small RCT with adult patients suffering from chronic pain and WAD. Results from a ten-session protocol indicate the utility of this type of treatment [197]. The methodology and results from this study is presented in more detail later. A pilot study using a brief ACT-oriented outpatient program with weekly sessions was recently conducted, showing that the intervention was useful [210]. Also, an ACT- approach has been evaluated with people at risk for sick leave due to stress and pain, indicating that this treatment can be helpful in preventing long-term sick leave [21]. Interventions based on exposure and acceptance have also been developed for use with pediatric pain patients [198,199], and results from treatment evaluations have indicated the effectiveness of this approach (see study 1 and 4 in the present thesis) [201,202]. The methodology and results from the pilot study [202], and the RCT [201], are presented in more detail later. In studies investigating the processes in acceptanceoriented treatments with pain, acceptance has been found to predict positive affect and to moderate the associations between pain and negative affect [76]. Also, in a recent study acceptance also mediated the effects of catastrophizing in e.g. depression, fear, and disability [213].

In sum, correlational, laboratory, and treatment evaluation studies illustrate the importance of acceptance in explaining the link between pain and disability. In fact, there are more studies investigating acceptance and related theoretical constructs in the area of pain than with any other condition. The advances within this field provide opportunities to refine the research questions, but this also requires well-defined and reliable instruments.

2.13. Measuring acceptance in chronic pain

As noted above, psychological (in)flexibility is conceptualized as a combination of different processes [55]. To further explore the nature of this theoretical construct, there is a need for theoretically and clinically adequate measures of each of these processes (e.g. avoidance, acceptance, cognitive fusion). To investigate psychological flexibility, a generic instrument called Acceptance and Action Questionnaire (AAQ) has been validated [58] and used in several studies [34,40]. To date, however, there are few instruments which assess processes related to psychological flexibility in people with chronic pain, such as the Chronic Pain Acceptance Questionnaire (CPAQ) [105] or the Psychological Inflexibility in Pain Scale (PIPS) [204]. The PIPS was developed at the Pain Treatment Service by our clinical research group and evaluated as part of this thesis, and the instrument, methodology, and results will be further presented in the chapter on methodology. In the development of CPAQ, 34 items were generated, largely by modifying the item pool for the AAQ, to reflect acceptance of pain. Initially, 24 items were retained with adequate psychometric properties [43], and a four-factor solution was considered appropriate although one factor seemed to diverge from the overall construct [93]. Later psychometric evaluations resulted in a two-factor solution with 20 items forming subscales labeled activity engagement and pain willingness [105]. Previous studies with CPAQ suggest that the instrument has predictive ability, although results have been somewhat divergent [76,96,104,105,120,194]. However, this divergence may reflect that studies investigating acceptance with the CPAQ have used different versions of the instrument [91]. Specifically, the pain willingness subscale has been criticized as not being as robust as activity engagement [120]. Recently, a Swedish translation of CPAQ was evaluated with 611 participants reporting chronic pain and symptoms of WAD [203]. In this study, exploratory factor analyses supported the previously suggested two-factor solution, but recommended exclusion of item 16 due to low intercorrelations with other items. Furthermore, confirmatory factor analyses (CFA) illustrated an adequate model fit which was significantly improved by removing item 16, thus resulting in a 19-item version of the instrument. This study also investigated the relationships between the two theoretical constructs acceptance, as measured with CPAQ, and kinesiophobia, as measured with Tampa Scale of Kinesiophobia (TSK). Hierarchical regression analyses illustrated that CPAQ explained a larger proportion of variance than TSK in pain, disability, life satisfaction, and depression, thus suggesting that CPAQ is a better predictor of pain adjustment than TSK.

Preliminary data have indicated the utility of both the Brief Pain Coping Inventory [103] in which items concerning psychological flexibility have been included, and the Chronic Pain Values Inventory [108] which addresses another central ACT concept (i.e. values). Furthermore, several different self-report assessments regarding mindfulness have recently been developed [6]. Nevertheless, this paucity of measures clearly shows the need for more instruments to assess relevant aspects of psychological (in)flexibility, such as avoidance and cognitive fusion.

Table 2.1. Summary of studies on acceptance and pain – correlational design.

Authors	Title	Participants (N)	Summary of results
Wicksell et al., under review [200]	The Psychological Inflexibility in Pain Scale (PIPS) - validation and confirmatory factor analysis of an instrument to assess avoidance and cognitive fusion in longstanding pain.	From patient organization for people reporting chronic pain and WAD (611).	PCA and CFA support a 2-factor solution. Construct validity supported. Adequate relationships with criteria variables.
Mason et al., 2008 [91]	Accepting low back pain: Is it related to good quality of life?	Chronic low-back pain, outpatients (86).	General qol was associated with acceptance. Pain and acceptance made modest contribution to psychological and social aspects of qol. SF-CPAQ is preliminarily supported.
McCracken and Vowles, 2008 [104]	A prospective analysis of acceptance of pain and values-based action in patients with chronic pain.	Chronic pain patients at pain clinic (115).	Acceptance- and values measures at time 1 were sign. correlated with functioning at time 2.
Vowles et al., 2008 [214]	The Chronic Pain Acceptance Questionnaire: Confirmatory factor analysis and identification of patient subgroups.	Two samples. Chronic pain patients at pain clinic (333 + 308).	CFA on CPAQ support a 2-factor solution. People with low CPAQ scores showed lower functioning than people with high scores on CPAQ.
Wicksell et al., 2008 [203]	The Chronic Pain Acceptance Questionnaire (CPAQ)-further validation including a confirmatory factor analysis and a comparison with the Tampa Scale of Kinesiophobia.	From patient organization for people reporting chronic pain and WAD (611).	Inter-item correlations suggest the removal of one item. PCA and CFA support a 2-factor solution. CPAQ explains more variance than TSK in disability, life satisfaction and depression.
Wicksell et al., 2008 [204]	Avoidance and cognitive fusion-central components in pain related disability? Development and preliminary validation of the Psychological Inflexibility in Pain Scale (PIPS).	Chronic pain - from pain clinics and patient organizations (203).	PCA suggests a 2-factor solution of PIPS with subscales for avoidance and cognitive fusion. Adequate relationships with criteria variables.
Esteve et al., 2007 [32]	Adjustment to chronic pain: the role of pain acceptance, coping strategies, and pain-related cognitions.	Chronic pain patients at pain clinic (117).	Results from SEM shows that acceptance contributes to impairment, although coping and catastrophizing influenced distress and pain.
McCracken et al., 2007 [99]	The role of mindfulness in a contextual cognitive- behavioral analysis of chronic pain-related suffering and disability.	Chronic pain patients at pain clinic (105).	MAAS accounted for sign amounts of variance in depression, anxiety, and disability.

Authors	Title	Participants (N)	Summary of results
McCracken et al., 2007 [107]	A prospective investigation of acceptance and control-oriented coping with chronic pain.	Chronic pain patients at pain clinic (120).	When assessing coping and functioning at 2 time points, activity persistence was associated with better functioning over time while control-oriented responses were associated with greater difficulty.
McCracken and Vowles, 2007 [103]	Psychological flexibility and traditional pain management strategies in relation to patient functioning with chronic pain: an examination of a revised instrument.	Chronic pain, consecutive patients at pain clinic (260).	The subscale with items reflecting psych. flex. explained more variance than the pain management subscale in functioning.
Feldner et al., 2006 [34]	The role of experiential avoidance in acute pain tolerance: a laboratory test.	Non-clinical (70).	Experiential avoidance (AAQ) predicted e.g. pain tolerance and endurance but not intensity.
McCracken and Eccleston, 2006 [97]	A comparison of the relative utility of coping and acceptance—based measures in a sample of chronic pain sufferers.	Chronic pain patients at pain clinic (230).	CPAQ explains more variance in functioning than CSQ.
McCracken and Yang, 2006 [108]	The role of values in a contextual cognitive- behavioral approach to chronic pain.	Chronic pain patients at pain clinic (140).	Results on the Chronic Pain Values Inventory correlated with avoidance acceptance, and disability, depression and anxiety.
Nicholas and Asghari, 2006 [120]	Investigating acceptance in adjustment to chronic pain: is acceptance broader than we thought?	Chronic pain patients at pain clinic (271).	CPAQ did not predict pain or disability. Activity engagement predicted depression, but data suggest that the pain willingness is not robust.
McCracken, 2005 [94]	Social context and acceptance of chronic pain: the role of solicitous and punishing responses.	Chronic pain patients at pain clinic (228).	Punishing responses from significant others were negatively associated with acceptance of pain.
McCracken et al., 2005 [98]	Clinical assessment of behavioral coping responses: preliminary results from a brief inventory.	Chronic pain patients at pain clinic (200).	Preliminary data supports temporal consistency and validity of BPCI, which predicted functioning.
McCracken and Eccleston, 2005 [96]	A prospective study of acceptance of pain and patient functioning with chronic pain.	Chronic pain, consecutive patients at pain clinic (118).	Acceptance, but not pain, at time 1 was related to better emotional, social, and physical functioning at time 2.

Authors	Title	Participants (N)	Summary of results
Zettle et al., 2005 [217]	Differential strategies in coping with pain as a function of level of experiential avoidance.	Non-clinical (25).	High avoiders were less tolerant of pain and reported more dysfunctional coping, but did not differ from low avoiders in pain.
McCracken et al., 2004 [105]	Acceptance of chronic pain: component analysis and a revised assessment method.	Chronic pain patients at pain clinic (235).	Further analyses of CPAQ suggest a revised version with 2-factors.
McCracken and Eccleston, 2003 [95]	Coping or acceptance: what to do about chronic pain?	Chronic pain patients at pain clinic (230).	Coping variables were weakly related to acceptance and functioning. Acceptance was associated with less pain, disability, depression and anxiety.
Rankin and Holtum, 2003 [136]	The relationship between acceptance and cognitive representations of pain in participants of a pain management program.	Chronic pain patients at pain clinic (116).	Acceptance correlated with severity, consequences, and identity but not with beliefs about cause, expected duration, control or cure.
Viane et al., 2003 [194]	Acceptance of pain is an independent predictor of mental well-being in patients with chronic pain: empirical evidence and reappraisal.	Chronic pain patients at pain clinic (120) + self-help group with fibromyalgia, pain clinic (66).	Acceptance predicted mental well-being beyond pain and catastrophizing and was related to normal life activities. Moderate relation b/w CPAQ and ICQ, indicating that different aspects of acceptance are assessed.
McCracken, 1999 [93]	Behavioral constituents of chronic pain acceptance: Results from factor analysis of the Chronic Pain Acceptance Questionnaire.	Chronic pain patients at pain clinic (230).	Factor analyses suggested 4 components of the CPAQ.
McCracken et al., 1999 [101]	Behavioral dimensions of adjustment in persons with chronic pain; pain-related anxiety and acceptance.	Chronic pain patients at pain clinic (190).	Dysfunctional patients reported more anxiety and less acceptance, indicating a behavioural dimension of adjustment to chronic pain.
McCracken, 1998 [92]	Learning to live with the pain: acceptance of pain predicts adjustment in persons with chronic pain.	Chronic pain patients at pain clinic (160).	Higher acceptance was associated with lower pain, anxiety and avoidance, depression, and disability, more uptime, and better work status.

Table 2.2. Summary of studies on acceptance and pain - laboratory studies with experimental design.

Authors	Title	Participants (N)	Summary of results
McMullen et al., 2008 [111]	Acceptance versus distraction: Brief instructions, metaphors and exercises in increasing tolerance for self-delivered electric shocks.	Non-clinical (80).	Acceptance condition including metaphors and exercises increased task tolerance. Both acceptance conditions reduced believability of thoughts.
Páez-Blarrina et al., 2008 [125]	The role of values with personal examples in altering the functions of pain: comparison between acceptance–based and cognitive-control-based protocols.	Non-clinical (30).	An ACT-values instruction increased tolerance as compared with pain control-values instruction.
Páez-Blarrina et al., 2008 [126]	Coping with pain in the motivational context of values: comparison between an acceptance–based and a cognitive-control-based protocol.	Non-clinical (20).	Both acceptance and control increased pain tolerance and reduced pain. Believability decreased more with acceptance.
Masedo and Esteve, 2007 [90]	Effects of suppression, acceptance and spontaneous coping on pain tolerance, pain intensity and distress.	Non-clinical (219).	Acceptance increased pain tolerance and decreased pain recovery ratings as compared to suppression and spontaneous strategies.
Vowles et al., 2007 [215]	Effects of pain acceptance and pain control strategies on physical impairment in individuals with chronic low back pain.	Chronic low back pain (91).	Acceptance instructions significantly enhance pain tolerance and behavioral persistence as compared with pain control.
Keogh et al., 2005 [73]	Comparing acceptance- and control-based coping instruction on the cold-pressor pain experiences of healthy men and women.	Non-clinical (62).	Acceptance lowered pain, affective pain lowered for women.
Gutiérrez et al., 2004 [48]	Comparison Between an Acceptance-Based and a Cognitive-Control-Based Protocol for Coping With Pain.	Non-clinical (40).	Participants showed significantly higher pain tolerance and lower believability of experienced pain following acceptance as compared with control instructions.
Minoru et al., 2002 [115]	Acceptance Rationale and Increasing Pain Tolerance: Acceptance Based and FEAR Based Practice.	Non-clinical (28).	Acceptance including exercise was significantly better than information and placebo on pain tolerance.
Hayes et al., 1999 [53]	The impact of acceptance versus control rationales on pain tolerance.	Non-clinical (32).	Significant difference in pain tolerance following acceptance as compared with control.

Table 2.3. Summary of studies on acceptance and pain - clinical treatment evaluations.

Summary of results	Improvements following ACT in both trials, improvements seen also in the CBT-condition.	Significantly better than multidisciplinary treatment incl. amitriptyline at post- and follow-up assessments in e.g. perceived functional ability, pain, and distress.	Significant improvements in pain, depression, disability, acceptance and values-based action. Most improvements retained after 3 months.	ACT + TAU was significantly better at post- and follow-up in e.g. disability, life satisfaction, and psychological flexibility.	Sign improvements following treatment in e.g. disability, depression, acceptance. Most retained after 3 months. Average efect size (d): 7.5.	Sign improvements following treatment in e.g. disability, depression (retained after 3 months). Acceptance, catastrophizing, and pain associated with treatment changes.
Follo w-up	Š.	3.5 and 7 mo.	3 mo.	3.5 and 7 mo.	3 mo.	3 mo.
Treatment setting, intervention, no. of hours	Outpatient, weekly sessions, 12 hours (8 x 1.5 h).	Outpatient (weekly sessions), values-based exposure, acceptance and defusion, 13 hours.	Multidisciplinary, residential. ACT-principles including mindfulness, 97.5-130 hours of treatment.	Outpatient (weekly sessions), values-based exposure, acceptance and defusion, 10 hours.	Multidisc.,residential. ACT-principles, mindfulness Approx. 80 hours of treatment.	Multidisciplinary, residential. ACT-principles, mindfulness, 97.5-130 hours of treatment.
Design	Within- grp + non- rand.ctrl	RCT	Withingrp, grp, process analysis	RCT	Within- grp	Withingrp, grp, process analysis
Participants (n)	Chronic pain patients (11), and veterans (11).	Adolescents with chronic pain, consecutive patients at pain clinic (32).	Chronic pain (187).	Chronic pain and WAD, recruited from patient organization (22).	Chronic pain (severely dis.), cons. pat. at pain clinic (53).	Chronic pain, consecutive patients at pain clinic (252).
Title	Targeting acceptance, mindfulness, and values-based action in chronic pain: findings of two preliminary trials of an outpatient group-based intervention.	Evaluating the effectiveness of exposure and acceptance strategies to improve functioning and quality of life in longstanding pediatric pain - A randomized controlled trial.	Acceptance and values-based action in chronic pain: a study of treatment effectiveness and process.	Can exposure and acceptance strategies improve functioning and life satisfaction in people with chronic pain and whiplash-associated disorders (WAD)? A randomized controlled trial.	Contextual cognitive-behavioral therapy for severely disabled chronic pain sufferers: effectiveness and clinically significant change.	Processes of change in treatment for chronic pain: the contributions of pain, acceptance, and catastrophizing.
Authors	Vowles et al., in press [210]	Wicksell et al., 2009 [201]	Vowles and McCracken, 2008 [211]	Wicksell et al., 2008 [197]	McCracken et al., 2007 [100]	Vowles et al., 2007 [212]

Summary of results	Significant improvements in disability, school attendance, catastrophizing, and pain. Retained at follow-up.	Sign improvements following treatment in e.g. physical and disability, depression, acceptance. Most retained after 3 months.	ACT reduces no of sick days, retained after 6 months.	Acceptance mediates effects of catastrophizing in e.g. depression, fear, and disability.	Acceptance predicts positive affect and moderates associations b/w pain and negative affect.	Improvements were seen in e.g. disability and pain.
Follo w-up	3 and 6 mo.	3 то.	6 то.	1	1	6 то.
Treatment setting, intervention, no. of hours	Outpatient (weekly sessions), values-based exposure, acceptance and defusion, 10 hours.	Multidisciplinary, residential. ACT-principles, mindfulness, 97.5-130 hours of treatment.	4 hours			Values-based exposure, acceptance and defusion strategies, weekly sessions, 13 hours of treatment.
Design	Within- grp	Within- grp	RCT	Corr., mediator	Within- grp	Case
Participants (n)	Adolescents with chronic pain, consecutive patients at pain clinic (16).	Chronic pain, consecutive patients at pain clinic (142).	At risk for sickleave due to stress or pain (19).	Chronic pain, consecutive patients at pain clinic (344).	Osteoarthritis and fibromyalgia (125).	Adolescent with chronic pain at pain clinic (1).
Title	Exposure and acceptance in the rehabilitation of adolescents with idiopathic chronic pain - a pilot study.	Acceptance-based treatment for persons with complex, long standing chronic pain: a preliminary analysis of treatment outcome in comparison to a waiting phase.	Acceptance and Commitment Therapy and the treatment of Persons at risk for long-term disability resulting from stress and pain symptoms: a preliminary randomized trial.	Mediator and moderator analyses Vowles et al., Patient functioning and catastrophizing 2008 [213] in chronic pain: the mediating effects of acceptance.	Pain acceptance moderates the relation between pain and negative affect in female osteoarthritis and fibromyalgia patients.	Using Acceptance and Commitment Therapy in the rehabilitation of an adolescent female with chronic pain: a case example.
Authors	Wicksell et al., 2007 [202]	McCracken et al., 2005 [106]	Dahl et al., 2004 [21]	Mediator and mo Vowles et al., 2008 [213]	Kratz et al., 2007 [76]	Case reports Wicksell et al., 2005 [198]

3. ASSUMPTIONS AND AIMS

3.1. Assumptions

The development and evaluation of the proposed clinical model was based on several assumptions.

First, pain-related avoidance behavior is considered central to the development of disability in pain syndromes of unclear organic origin, and the relationship between chronic pain and disability is mediated by avoidance behaviors. Thus, an intervention aimed at improving functioning and quality of life should focus on behavior modification of pain-related avoidance behaviors.

Second, exposure (i.e. to gradually increase behaviors previously avoided due to negative private experiences such as pain and distress) is considered to be the core intervention as well as the hypothesized working mechanism in successful CBT, and should therefore be emphasized in the development of a clinical model.

Third, pain reduction does not have a clear causal relationship with disability and is not required to achieve improvements in functioning and quality of life.

Fourth, pain related disabilities are largely related to psychological inflexibility (e.g. avoidance, fusion, unwillingness).

Fifth, psychological flexibility can be increased following a change in context (from non-acceptance to acceptance of negative private experiences such as pain) even if a change in content is not achievable (i.e. no change in pain intensity).

Sixth, a behavior modifying intervention for chronic pain patients should be based on a behavior medicine approach (i.e. modern learning theory and pain physiology), and can be effectively administered by a coordinated team consisting of a CBT-trained psychologist and a physician specialized in pain treatment.

Seventh, an increase in psychological flexibility and functioning can be achieved using a low intensive intervention program (i.e. weekly sessions during a period of three to four months).

Eighth, the effectiveness of a new intervention should be evaluated by comparing it to an adequate treatment alternative (i.e. an individualized multidisciplinary approach including pharmacotherapy) or as an add-on to usual treatment.

Ninth, further improvements of the clinical model require that the working mechanisms are identified. From this follows a need to develop an instrument to assess central aspects of the treatment objective (i.e. increased psychological flexibility).

3.2. General and specific aims

The present thesis includes five different studies with two general aims: 1) to investigate the effectiveness of an intervention based on values-oriented exposure and acceptance strategies (ACT), and 2) to evaluate the psychometric properties of a self-report instrument designed to assess psychological flexibility in people with chronic pain. The specific aims of each respective study were as follows:

Study 1: Exposure and acceptance with adolescents - a pilot study.

- To investigate if an exposure and acceptance-based approach could increase functioning as well as decrease pain for adolescents with chronic debilitating pain of idiopathic character.
- 2. To analyze if improvements seen immediately after the ACT-oriented intervention were sustained three and six months following end of treatment.

Study 2: Preliminary validation of the PIPS.

- 1. To develop a new and theoretically relevant instrument to assess central aspects of psychological flexibility in people with chronic pain.
- 2. To test the statistical adequacy of this instrument, labeled Psychological Inflexibility in Pain Scale (PIPS).

Study 3: Exposure and acceptance with WAD - an RCT.

- 1. To investigate if an exposure and acceptance-based approach could increase functioning and life satisfaction in adults with chronic pain and symptoms of WAD.
- 2. To analyze if improvements seen immediately after the ACT-oriented intervention were sustained four and seven months following end of treatment.
- 3. To investigate if the exposure and acceptance intervention delivered in addition to treatment as usual (TAU) could increase functioning and life satisfaction in people with WAD, as compared to a control group receiving only TAU.
- 4. To investigate if psychological flexibility, as measured by PIPS, changed following an exposure and acceptance oriented intervention.

Study 4: Exposure and acceptance with children and adolescents - an RCT.

- 1. To further evaluate the effectiveness of an intervention based on exposure and acceptance strategies (ACT) for children and adolescents with longstanding debilitating pain syndromes.
- 2. To analyze if improvements seen immediately after the ACT-oriented intervention were sustained 3.5 and 6.5 months following end of treatment.
- 3. To investigate the relative effectiveness of exposure and acceptance as compared to a multidisciplinary treatment approach including amitriptyline (MDT).

Study 5: Evaluation of psychometric properties and model fit of the PIPS.

- 1. To evaluate the psychometric properties of PIPS by examining the factor structure, internal consistency, and concurrent criteria and construct validity.
- 2. To test the model fit of the instrument using confirmatory factor analyses.

4. METHOD

4.1. General outline of the project

Each of the five studies included in the thesis were conducted with different samples. Paper 1, 3, and 4 are clinical treatment outcome studies, and paper 2 and 5 are psychometric evaluations of a new process measure. To provide a clear overview of the project, the three treatment outcome studies will be described collectively with regards to design, participants, assessment, intervention, and statistical analyses. Similarly, the methodology of the two psychometric evaluations will be presented together.

In studies 1 and 4, participants were children and adolescents (consecutive patients) referred to the Pain Treatment Services (PTS). Participants in studies 3 and 5 were adults recruited from a patient organization for people with WAD (The Swedish Association of Survivors of Traffic Accidents and Polio), and in study 2 the sample was people recruited from either different pain clinics or from patient organizations. Tables 4.1. and 4.2. summarize the sample characteristic and methodology for the respective studies.

4.2. Treatment outcome studies - papers 1, 3, and 4

4.2.1. Participants

Participants in study 1 and 4 consisted of consecutive pediatric patients (in study 1: ten to 20 years, in study 4: ten to 18 years) with longstanding idiopathic pain referred to the PTS at Astrid Lindgren Children's Hospital, Karolinska University Hospital. In study 3, participants were adults recruited from a patient organization for people with WAD.

4.2.2. Procedure

In the pilot study (paper 1), no control group was used. Flowcharts for the randomized controlled trials (3 and 4) are presented in Figures 4.1. and 4.2.

4.2.3. Eligibility and inclusion/exclusion criteria

In studies 1 and 4, children and adolescents referred to the PTS with pain duration of more than three months were considered eligible for inclusion in the study. In study 3 (adults), eligibility was based on those people who responded to the letter of information administered by the patient organization, and reported pain duration of more than six months.

In general, patients were excluded from studies 1, 3, or 4 if: a) pain was associated with an identified ongoing nociceptive process (e.g. arthritis, cancer, inflammatory bowel disease), b) co-existing psychiatric or psychosocial issues were considered more relevant to reduced functioning than pain. (This also included risk for suicide that was assessed in the psychological screening interview), c) having a reduced proficiency in Swedish, d) suffering from major cognitive dysfunctions resulting in difficulties following a conversation and/or understanding the description of the study, e) currently participating in another rehabilitation program based on CBT.

Table 4.1. Summary of sample characteristics and methodology: treatment outcome studies.

Papers	Study 1	Study 3	Study 4
Study aim	Preliminary evaluation of treatment over time.	Evaluation of treatment + TAU in relation to TAU only.	Evaluation of treatment in relation to other active treatment.
Sample	Consecutive patients at pain clinic.	Patient organization.	Consecutive patients at pain clinic.
Design	Case series	RCT	RCT
Sample size	16	22	32
Dropouts	2	1	2
Participant characteristics			
Female gender	78%	76%	77%
Age (years): range, mean	13-20, m=17.0 years	33-66, m=51.5 years	10-18, m=14.8 years
Pain duration (months): range, mean	7-108, m=52.6 months	29-170, m=83.0 months	6-96, m=32.4 months
Pain type/diagnosis	Idiopathic pain	Chronic pain and WAD	Idiopathic pain
Intervention			
Experimental condition	Values oriented exp. and acc.	TAU + Values oriented exp. and acc.	Values oriented exp. and acc.
No. of sessions (pre-post): mean (sd)	Patients: m=14.4 (6.6) Parents: m=2.4 (2.9)	10 (0)	Patients: m=10.3 (3.6) Parents: m=1.7 (sd 0.6)
Control condition		TAU	MDT + amitriptyline
Assessment and statistical analyses			
Main dependent variables	FDI, school absence	PDI, SWLS, PIPS	FDI, PAIRS, Pain interference, SF-36
Data collection	Pre, post, follow up (3 and 6 mo.)	Pre, post, follow-up (4 and 7 mo.)	Pre, post, follow-up (3.5 and 6.5 mo.)
Dropout strategy	Results based on completers, ITT did not change results	Results based on completers, ITT did not change results	ITT-analyses
Missing value replacement	Replaced with series mean	Last value carried forward	Imputed with Expectation- Maximization likelihood method
Main statistical analyses	ANOVA-repeated (1x4)	ANOVA-repeated (1x4); ANCOVA (pre-treatment data as covariates)	ANOVA-repeated (1x4); ANCOVA (pre-treatment data as covariates)
Effect size measure	Cohen's d	Partial eta-squared (η_n^2)	Partial eta-squared (η_n^2)

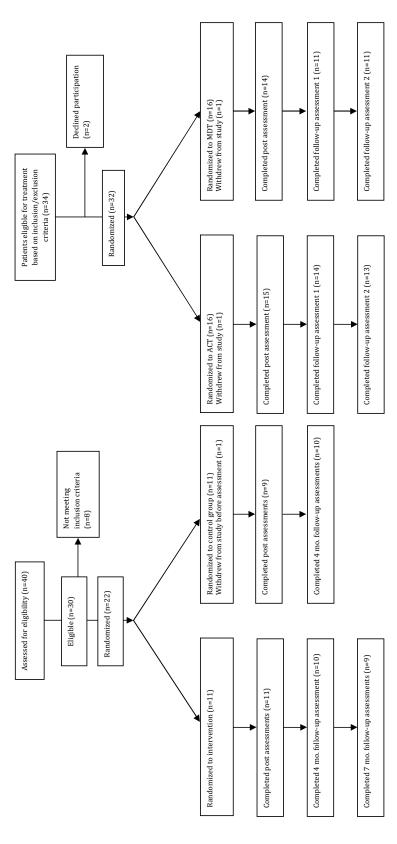


Fig 3.1. A flow diagram of study 3. One participant in the control group withdrew before collection of baseline data, and one during the treatment period. Only the treatment group completed seven months follow-up assessments.

Fig 3.2. A flow diagram of study 4. One participant in each group withdrew from the study during the intervention period.

4.2.4. Assessment

All participants completed questionnaires and daily ratings during one to three weeks (different baseline lengths in the three studies) prior to treatment, immediately following treatment, at follow-up 1 (three to four months after post-treatment assessments), and at follow-up 2 (six to seven months after post-treatment assessments). In studies 3 and 4, pretreatment assessments were performed subsequent to the randomization. With the exception of the pilot study, assessments were conducted by a nurse who was not involved in delivering the treatment protocol.

4.2.5. Randomization

In studies 3 and 4, a simple randomization technique was used with the participants as a single block (22 and 32 respectively). In study 4, participants meeting the criteria for inclusion were continuously randomized during the 26 months recruiting period. After inclusion, a sealed envelope (prepared by a secretary who was blind to the objective of the study) containing a code for the experimental or the control condition was opened, assigning the participant to one of the two groups.

4.2.6. Dependent variables

Pain related functioning (e.g. Functional Disability Inventory, Pain Impairment Relationship Scale) and quality of life (e.g. Short Form-36, Satisfaction With Life Scale) were considered primary outcome variables in the three studies. Assessments also included secondary outcome variables, such as kinesiophobia and pain intensity. In study 3, a process measure (PIPS) was included to assess target variables in the intervention protocol. See paragraph 3.4. for a description of all instruments used in the studies.

4.2.7. Intervention – the experimental condition

In total, two psychologists and one physician carried out the interventions provided in the experimental condition. The psychologists were trained in CBT. Both the psychologists and the physician had some experience and formal training in ACT (e.g. participation in experiential workshops, supervision), although skills and experiences increased over time and, thus, differ between the studies. To maintain treatment fidelity, treatment content and progress were discussed continuously within the clinical research group in all studies.

The intervention was conducted individually with weekly sessions. Treatment length and number of sessions varied somewhat between the studies. In general, the intervention protocol consisted of 10-14 sessions (60 minutes) performed during a period of 8-16 weeks. Approximately, 80% of the sessions were conducted by psychologists, and 20% by a physician specialized in pain. In studies 1 and 4, the intervention also included one to three sessions with parents.

Exposure to previously avoided situations and private experiences was considered the core intervention, with an emphasis on acceptance of negative reactions that cannot be directly changed, as a means to facilitate the exposure process. The central objective was to improve the patients' functioning and quality of life by increasing the ability to act in accordance with long term goals and values, in the presence of interfering pain and distress (i.e. psychological flexibility). The intervention protocol used in the treatment outcome studies was, in short, as follows:

Pain education – altering the context in which pain occurs

Initially, the physician explains the mechanisms involved in idiopathic longstanding pain syndromes and how this differs from acute (nociceptive) pain, clarifying that pain is not necessarily caused by a potentially harmful disease or injury. Thus, the dysfunctional character of chronic idiopathic pain is emphasized (e.g. indicating harm without existing tissue damage), as well as the lack of effective treatments to reduce pain of non-nociceptive character. Although not an ACT-intervention per se, this information is aimed at altering the context in which pain is experienced, and serves to facilitate a shift in perspective from symptom reduction to valued living. It is neither particularly meaningful nor necessary to accept, or defuse from, wrong information or misunderstandings. In other words, helping the patient to understand the nature of pain syndrome sets the stage for exposure and acceptance strategies. Thus, the purpose is to facilitate an increase in activity by clarifying that exposure may increase pain without being harmful.

Values assessment/clarification

A thorough assessment of individual values in important life domains is performed early, initiating a shift in focus from symptom alleviation to valued life in the presence of possible negative private events (pain, fear, negative thoughts). Distinctions between values as a life orientation (e.g. being a good friend, learning more in school) and goals (e.g. making a phone call to my friends at least twice a week, missing less than five classes a week) are discussed, although to various degrees depending on factors such as the patient's age. Behaviorally oriented goals are also generated (i.e. values oriented behaviors were operationalized). Furthermore, discussing values provides, in itself, a context for exposure (see below).

Shifting perspective

Values clarification is followed by an exercise in which the workability of previous strategies (e.g. pain medications, rest, avoiding risk situations) to reduce pain and distress are collaboratively evaluated, emphasizing both short and long term effects as well as the impact on functionality/valued life. Normally, short term symptom relieves (negative reinforcement) maintain behaviors even if no long term effects are seen. In addition, to reduce these symptoms people tend to engage in behaviors (e.g. remaining still or not going out of doors) that prevent them from activities required to produce life satisfaction (e.g., visiting friends, working, or playing sport). Since previous strategies (such as avoidance) generally have not reduced pain over time, and still brought the patient farther from important activities, most patients experience this exercise as emotionally challenging. However, this collaborative evaluation of previous strategies also reveals the possibility of increasing functionality and vital activities by instead accepting a certain amount of pain and distress. Figure 4.3 illustrates the "patient's dilemma", i.e. struggling to achieve symptom reduction or control while at the same time striving towards a more vital life.

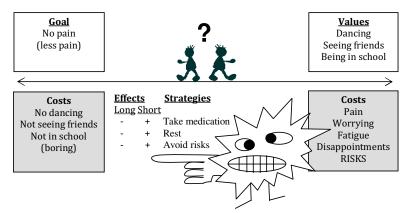


Figure 4.3. "The Line", illustrating the patient's dilemma, is used when collaboratively exploring the workability of previous strategies to reduce pain. Subsequently, workability is discussed in relation to personal values. This can be used as an experiential exercise to facilitate what is referred to as "creative hopelessness" or a shift in perspective from symptom reduction to valued living in the presence of pain and distress. The pain monster is used as a metaphor for discussing private experiences, representing thoughts, emotions, and bodily sensations that tell you to act to reduce pain and distress.

Values-based exposure

As previously stated, exposure is the core process in this treatment approach. Following the discussion about previously used strategies and their effectiveness, the therapist introduces the idea of accepting a certain amount of pain and distress to enable engagement in values oriented behaviors. Patients are then encouraged to perform gradual values-based exposure to increase frequency of values-directed behaviors and *psychological flexibility* in moments with pain and distress, situations that previously have resulted in pain-related avoidance. The gradual increase in relevant activities is mainly carried out by the patients between sessions.

Also, for most patients, discussing values (for example making up plans for the future) generates discomfort, such as negative thoughts and emotions about pain, failure etc. and efforts to avoid the topic. This is addressed in therapy using exposure and acceptance strategies (see below).

Acceptance/willingness and defusion

As previously mentioned, an ACT model of debilitating chronic pain includes the patient's unwillingness to have pain, as illustrated in patients that do not engage in valuable activities in order to avoid negative experiences such as pain and fear [142]. (The terms acceptance and willingness are used interchangeably throughout the text.) Disability (here defined as the avoidance of valued activities) is considered to occur when actions are guided by internal psychological events (thoughts, emotions, bodily sensations) rather than the external contingencies of reinforcement that operate in a given situation. Cognitive fusion, in the context of ACT, can be described as the process by which thoughts about an event become merged with the actual event. The thought about the event then evokes the same emotional reaction as the event itself; leading to behaviors that would follow if the thought was a fact. Thus, when cognitive fusion occurs, verbal processes ("My pain prevents me from going") have excessive or improper impact on the behavior (stays home to avoid pain) [55]. Thus, negative private experiences that functionally are leading to avoidance of values-oriented actions, such

as driving the car in the presence of severe back pain, are addressed. In session, the participant's ability to acknowledge and accept these negative psychological events for what they are (e.g. a thought is a thought) without acting on its content instead of trying to control, suppress, or avoid the private experience is discussed. By repeatedly helping the participant to distinguish between experiencing a thought and buying into its content, she or he can defuse, or distance, her/himself from the private events that previously determined avoidance behaviors. Thus, acceptance of what cannot be directly changed is emphasized to help the patient act in alignment with values, even while experiencing pain at the same time.

When discussing the concepts of acceptance and defusion, illustrations and metaphors are sometimes used to clarify the difference between e.g. accepting and distracting from a negative thought. For example, in the "sunset metaphor", a boy or girl intends to have a barbecue with his or her friends at the beach while watching a beautiful sunset. However, the sunset turns out to be rather ugly and the boy/girl is left with the option to either try to "fix" the sunset or accept it as it is. By accepting the ugly sunset, as well as feelings of disappointment, without efforts to change, control or reduce, he or she can direct his or her behaviors towards engaging fully in the barbecue and the social interactions. Since acceptance of pain, fear, thoughts etc. is counterintuitive, metaphors can play a role in illustrating how the patient can relate to these experiences in an alternative way. In this case, instead of making an effort to control something that might be uncontrollable, the patient can notice and acknowledge the pain *and* behave in accordance with values (e.g. spending time with friends, being engaged in meaningful conversations).

Behavioral activation with ACT-oriented problem solving

As explicitly stated, the ACT approach seeks to assist the patient in increasing values-oriented behaviors. Following a shift in perspective, the (new) treatment objective is contextually different (i.e. vitality in the presence of pain/distress) from before (i.e. reduce pain, a vital life with no pain). In this later phase of the intervention, session content is focused on behavioral activation and the therapist's role is to support this process in various ways. For example, values-based exposure is continuously suggested (prompted) by the therapist, psychologically flexible behaviors are reinforced, and when obstacles occur and trouble-shooting is needed the therapist provides a context for what can be described as an ACT-oriented problem-solving (emphasizing values, exposure, acceptance and defusion).

Everything, always

Importantly, the presented clinical model is an approach that is based on a set of principles which are applied individually throughout the treatment. The intervention protocol describes certain, more or less distinct, components. However, it should be noted that although each session has a pre-specified theme, the therapist behaves in accordance with the ACT-approach in each therapeutic moment. Consider the following example. The values-clarification work is facilitated if the therapist initiates the discussion by first mentioning the possibility that this may elicit negative emotions (exposure), and that these may be accepted for what they are: "Given all your previous failures, it seems likely that talking about what you really want in life may give rise to thoughts like 'I'm not going to be able anyway, so why bother to think about it'. I'm wondering if it would be an option to notice those thoughts when they show up. You could even let me know when they show up, but not do as they tell you to do. For

example, the thought 'stop describing what you want in life'. That way we could let them come and go, without having them interfere with what we are about to do today. What do you think?"

A number of different ACT-related processes are hypothesized to be involved. First, this may increase the ability to clarify important values. Second, the suggestion to notice the thoughts can be seen as a defusion exercise. Third, this brief conversation clearly points to how and why acceptance provides an alternative to other types of coping with unpleasant thoughts and emotions. Fourth, this is an opportunity to illustrate psychological flexibility, i.e. to act constructively in alignment with long term goals in the presence of negative personal experiences. Thus, the therapist may be described as doing "everything always", with the intent to facilitate the exposure process and increase the psychological flexibility.

4.2.8. Control conditions in studies 3 and 4

Study 3 - Treatment as usual

In this study, an add-on design was adopted, meaning that all participants received treatment as usual (TAU) (e.g. medication, acupuncture, physiotherapy, naprapathy, osteopathy) during the course of the study. Thus, randomization to "waitlist" meant continuous treatment as usual. Participants who were randomized to the waiting list condition were offered an ACT-oriented intervention starting four months following end of the treatment phase (results not included in the study design).

Study 4 - Multidisciplinary treatment including amitriptyline (MDT)

The MDT was performed by a psychiatrist, a child psychologist, a physiotherapist and a pain physician, all experienced in working with longstanding pediatric pain. The clinical model followed routines developed during 15 years of clinical work with this population, thus representing the standard treatment in this particular tertiary care setting. Within this approach, participants were seen by the different health care providers based on individual needs. A biobehavioral model of longstanding pain provided a general theoretical framework for this clinical approach, emphasizing perceived stress in everyday life as an important factor predicting the severity of longstanding pain and disability. The biobehavioral approach is supported in several articles and summarized in the biobehavioral model of pediatric pain [180,187].

Amitriptyline doses were increased by 10 mg every week up to 50 mg, and then by 25 mg up to a maximum of 100 mg, with median maximum doses=50 mg (mean 64.3, sd 27.5). The increase of doses was stopped when severe side effects appeared (e.g. sedation, dry mouth). Amitriptyline was administered during a period of 1.2 months to 19.6 months (mean 10.3, sd 5.9). Average time between pre and post assessments was 5.5 months (sd 1.9).

During this period the participants in the MDT were seen for an average of 10.6 sessions (sd 4.7), equally divided between the physician, physiotherapist and psychiatrist/psychologist. Importantly, following post assessments, participants received a number of additional sessions (mean 11.7, sd 11.9). In addition, given that participants received amitriptylin for approximately ten months, the pharmacological treatment also continued well beyond post assessments. At follow-up 2, the MDT group had received an average of 22.8 sessions (sd 15.4), divided between the physician (mean 11.1, sd 9.1), physiotherapist (mean 3.6, sd 4.0), psychologist/psychiatrist (mean 6.7, sd 6.7), and other (mean 1.4, sd 2.1).

4.2.9. Data analyses

Research questions

Two main research questions were addressed in the statistical analyses. First, did participants in the ACT-based intervention improve over time? Second, how did the effects seen in the ACT condition compare with the results from the control condition (studies 3 and 4)? However, because the participants in the MDT condition (study 4) received a substantially greater amount of treatment after post assessments, the groups were not fully comparable at follow-up. Thus, in this study a comparison across conditions required additional analyses based on pre- and post-treatment assessments only.

Missing values

To ascertain that data were absent at random, missing values were analyzed (e.g. using Little's MCAR test in the Missing Values Analysis module in SPSS 15). Subsequently, empty cells were replaced, for example by using the expectation-maximization-likelihood method (EM) as in study 4 (see Table 4.1.).

Statistical methods and considerations

In studies 3 and 4, comparability of the experimental and control conditions at pretreatment was investigated using analyses of variance (ANOVA). To detect possible therapist effects, the interaction between therapist and time was analyzed with ANOVA, 2x4 mixed design (two therapists, four assessment points). Prior to running parametric tests, the data set was analyzed to detect possible violations of assumptions (normal distribution or homogeneity of variance). In analyses where the sphericity assumption was violated, degrees of freedom were adjusted using the Greenhouse-Geisser correction [37]. The presented results are based on intent-to-treat analyses (ITT).

The effects from the ACT-intervention were analyzed using ANOVA, repeated measures (including pre-, post- and follow-up assessments). In study 1, following the recommendations of a 30% reduction in pain [26,33], the proportion of patients with a clinically important change in pain (i.e. intensity and interference respectively) was calculated. To maximize power in the relatively small samples, ANCOVA (with pre-treatment data as covariate) was used when comparing the experimental group with the control group [184,195]. The level of statistical significance was set at p<0.05, but exact p-values were presented to facilitate interpretations of the results. Statistical analyses were performed using SPSS 15.0.

Effect size

As measures of effect size, Cohen's d (study 1) and partial eta-squared (η_p^2) (studies 3 and 4) were used. According to Cohen's criteria, d=0.2 represents a small effect size, d=0.5 constitutes a medium effect size, and d=0.8 a large effect size. For eta-squared, $\eta_p^2=0.01$ is considered a small effect, $\eta_p^2=0.09$ a medium effect, and $\eta_p^2=0.25$ indicates a large effect [18].

Statistical power

Reports of effect sizes for CBT-oriented treatments with chronic pain patients vary between different review studies. In the study by Flor and colleagues, very large effect sizes (Cohen's d=1.51) were found when comparing pre- and post-assessments for the

treatment group [38]. Other studies provide more modest effect sizes. In the review by Morley et al., effect sizes of 0.5 (Hedges g) are reported when comparing the treatment to a waiting list control condition [118]. The Cochrane review on behavioral treatment for chronic low-back pain found effect sizes between 0.23 and 0.59 (Cohen's d), depending upon outcome type, when comparing operant therapy as well as combined respondent and cognitive therapy to waiting list controls [124].

In our pilot study with adolescents, large effect sizes were found (Cohen's d between 1.05 and 1.27) in three measures of functioning (primary outcome variables). Therefore, either a medium or a large effect size could be assumed in calculating the adequate sample size for the two RCT's. With a power of .80 and an alpha level set at p<.05, a medium effect size (partial eta squared, η_p^2 =0.09) requires a sample size of n=100. If a large effect size (η_p^2 =0.138) is assumed, about 45 participants would be needed to ascertain the power of the analyses. However, such large samples were not possible to include in the present outcome studies. Both studies with adolescents included consecutive patients referred to the PTS. To include 32 participants in the RCT took approximately 26 months, and it was not considered reasonable to extend this period. Instead, a second RCT with improved design and methodology was planned. In study 3, approximately 140 members of a patient organization were invited to participate in the treatment study. Thirty of those who responded were considered eligible. Thus, a large enough sample was not obtainable from this procedure. Consequently, the results from the present studies need to be interpreted with caution and the reader should keep in mind potential type-II errors resulting from lack of power due to small samples.

4.3. Measurement development studies - papers 2 and 5

4.3.1. Participants and data collection

In study 2 and 5, participants were recruited from pain clinics (study 2) and/or patient organizations (studies 2 and 5). The questionnaires, a letter with written information, and a consent form were administered by a designated person at each clinic or patient organization to protect the confidentiality of those who declined participation. Thus, only the completed questionnaires and consent forms were returned to the research team

In study 2, the contact persons were instructed to include people over 18 years of age, with pain duration longer than three months, and fluent in Swedish with adequate reading and writing skill. People who primarily suffered from pain due to cancer were not included in the study. When participants were recruited from pain clinics, questionnaires were completed prior to initiation of the treatment/rehabilitation program. In study 5, the participants were recruited through a Swedish patient organization for people with WAD. Two administrators not involved in, and blind to the objective of, the study selected 1000 people from the membership directory for participation. No randomization device was available and the membership directory did not contain any systematic information except names. Thus, the participants were selected non-systematically.

The response rates were approximately 52% in study 2 (n=203) and 61% in study 5 (n=611). Due to limitations in the data collection procedures (study 2) and membership files (study 5), information concerning those who declined participation could not be obtained. Table 4.2. presents a summary of sample characteristics and methodology for studies 2 and 5.

4.3.2. Statistical analyses/analytic approach

In both studies, starting with the initial pool of items, a series of analyses was performed to develop and evaluate the questionnaire. Factor structures and internal consistencies were investigated, as well as the concurrent criterion and construct validities of the questionnaire. Also, in study 5, the suggested factor structure was tested by confirmatory factor analysis (CFA) using Amos 16.0 in SPSS. Specifically, the development of the questionnaire involved the following steps.

Missing values

Different strategies were employed to replace missing values. In study 2, to identify patterns in missing data, t-tests were performed to analyze differences between participants with missing and non-missing values on the subscales. The principal component analyses (PCA) were conducted with missing values replaced by variable means. In the validation procedure, variables with missing values were excluded pairwise (bivariate correlations) and listwise (ANOVA, regression analyses). In study 5, a missing value analysis was performed (Little MCAR's test) to identify patterns in missing data. Following the recommendation by e.g. Tabachnick and Fidell, missing data was subsequently imputed using EM-methods [164].

Item-analysis

Initial considerations included examination of the adequacy of the sample size and the factorability of the correlation matrix. Frequency distributions were analyzed to identify items with extremely skewed response distribution or low variability. Inter-item correlations were examined to ascertain that variables correlated with a sufficient number of items, but were not too strongly correlated with other items. Item-total statistics were also analyzed to detect and remove items showing low correlations with the overall score of the questionnaire (lower than .3 in study 2, and lower than .25 in study 5).

Factor structure and internal consistency

A PCA was performed to examine the underlying factor structure among the remaining items. Given that the factors were assumed to be related, a direct oblimin (oblique) rotation with delta = 0 was used. The rotated factor structure was investigated to find items with weak factor loadings (lower than .4) or cross loadings (second loading higher than .3).

Internal consistencies of the total scale and the subscales, as measured by Cronbach's alpha, were analyzed to ascertain that no item contributed negatively to the scales' alpha. Also, intercorrelations between subscales as well as the total variance explained by the components were calculated.

Table 4.2. Summary of sample characteristics and methodology: measurement development studies.

Papers	Study 2	Study 5
Study aim	Development and preliminary psychometric evaluation.	Examination of factor structure, internal consistency, model fit, and validity.
Sample	Pain clinics (74%) and patient organizations (26%)	Patient organization (WAD)
Sample size	203	611
Response rate	52%	61%
Participant characteristics		
Female gender	80.8%	74.8%
Age (years): range, mean	19-70, m=45.5	17-84, m=49.0
Pain duration (months): range, mean	8-600, m=132	9-576, m=120
Pain type/diagnosis	Various (e.g. fibro. 31%, headache 21%, WAD 15%)	WAD, pain: neck 99%, headache 58.6%, low-back 48.6%
Assessment and statistical analyses		
Missing values replacement	Series mean	Expectation-maximization-likelihood (EM)
Main criteria variables	MPI, SF-12	PDI, SWLS, CPAQ, TSK
Main statistical analyses	PCA, bivariate and partial correlations, ANOVA, hierarchical regression analyses	PCA, CFA, bivariate correlations, hierarchical regression analyses

Concurrent criterion validity

The concurrent criterion validity of the scales were investigated by analyzing the relationships with variables such as pain intensity and patient functioning (medication use, work absence), as well as instruments assessing e.g. disability, life satisfaction, anxiety, depression, kinesiophobia, and acceptance. A series of regression analyses were performed to investigate the contribution of the subscales in predicting the criteria variables. In each of the regression analyses, relevant background variables (age, gender, education, and time since pain onset) were entered first (step 1) followed by the two PIPS-subscales (step 2). In addition, different groups of participants, i.e. gender and marital status, were compared on scores from the PIPS subscales using ANOVA.

Confirmatory factor analyses (CFA)

In study 5, the factor structure suggested from the PCA's in both studies 2 and 5 was tested by CFA using Amos 16.0 in SPSS. In the CFA, only items that were repeatedly retained (in both studies 2 and 5) were included. For the CFA, model fit was assessed with χ^2 (although sensitive to sample size and consequently interpreted with caution), the goodness-of-fit index (GFI), the root mean square error of approximation (RMSEA), and the comparative fit index (CFI). Different cut-off levels for the indices have been suggested [164]. However, $\chi^2/df < 2$ is generally considered as an acceptable fit of the model. Regarding the RMSEA, values below 0.06 are considered a good-fitting model, values below 0.08 are indicative of an adequate fit, and values above 0.10 suggest a poor-fitting model. For the CFI, values above .90 indicate an acceptable fit and values above .95 a close fit. A GFI greater than .90 indicate a good fit to the data. To compare the model fit for different factor solutions, chi-square difference tests were performed. In addition to the model fit indices, the amount of explained variance in life satisfaction was used to evaluate the utility of the model. In other words, both the fit of the model and its ability to predict a relevant dependant variable were used to decide whether or not an item contributed to the model. Furthermore, to ascertain that the findings are valid across different samples, a CFA with the final version of the instrument was conducted using the data set from the preliminary validation study (n=203) [204].

4.4. Measures

In addition to the questionnaires described below, background information was also collected. The instruments are presented in alphabetical order. Table 4.3. summarizes the questionnaires with references to the paper(s) in which they were used.

Center for Epidemiological Studies Depression Scale for Children

The Center for Epidemiological Studies Depression Scale for Children (CES-DC) [189] was administered to assess symptoms of depression in young patients. The reliability and validity of the measure has been established, especially with adolescents between 12-18 years [35]. The CES-DC has been translated to Swedish and shown adequate reliability [123]. In study 1, a standard cut-off score of 30 was used (range 0-60) [123] when analyzing the data.

Children's Depression Inventory

The Children's Depression Inventory (CDI) [75] is another measure of depression used with children and adolescents. In the analyses in study 1, a standard cut-off score of 19 was used (range 0-54) [25].

Chronic Pain Acceptance Questionnaire

The Chronic Pain Acceptance Questionnaire (CPAQ) was originally developed as a 34-item instrument to assess acceptance in chronic pain patients [43], largely by modifying the item pool for the Acceptance and Action Questionnaire [58]. Early psychometric evaluations supported a four-factor solution of the scale [93]. However, the revised version of the instrument consists of two subscales measuring the degree of engagement in life activities regardless of pain (activity engagement) and the willingness to experience pain without efforts to avoid or control it (pain willingness) [105]. The reliability and validity of the CPAQ have been demonstrated in several studies [105,214]. Also, its' ability to predict functioning among people with chronic pain has been shown repeatedly [96,107]. Participants rate the items on a scale from 0 (never true) to 6 (always true), with higher scores indicating more activity engagement/pain willingness. A recent analysis with a Swedish version of CPAQ, including a CFA, further supports the psychometric properties of the two-factor solution. In this study, CPAQ was also found to be a better predictor than TSK in life satisfaction, functioning, and depression [203].

Functional disability inventory

The Functional Disability Inventory (FDI) was designed to be applicable to a broad range of illnesses and varying levels of severity [16,182]. Both the child and the parent form of FDI were administered. The forms are similar with fifteen items regarding different functional abilities (e.g. "walking up stairs", "being at school all day", "going shopping") to be rated by the participants on a 0-4 scale from "No trouble" to "Impossible". Results are expressed as total scores. The psychometric properties of the instrument have been found satisfactory. Previous studies have shown a significant correlation between child and parent ratings, with slightly lower scores for the adults [16]. However, pre-treatment scores in study 1 indicated a potential risk for floor effects [202], and the instrument does not specifically address pain related impairments [16].

Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HAD) has shown to be a reliable instrument for detecting anxiety and depression among patients in medical settings [218]. The instrument consists of 14 items, rated on a four-point Likert scale, with subscales for anxiety and depression. The measure has good reliability, and scores are independent of physical complaints. The psychometric properties of a Swedish version of the instrument have been found satisfactory [83]. Cut-off scores for both subscales indicate that 0-7 = normal, 8-10 = mild anxiety/depression, 11-14 = moderate anxiety/depression, and 15-21 = severe anxiety/depression [3,218].

Impact of Event Scale

The Impact of Event Scale (IES) was used to assess the degree of posttraumatic stress symptoms. This questionnaire was designed to assess distress related to a specific event. IES consists of 15 items addressing intrusive symptoms and avoidance. Participants were asked to rate on a four-point scale how often each of the items had occurred in the past week. IES has shown good reliability and validity [64,162].

Medication use

In study 1, the use of pain medication (paracetamol, NSAID, codein, tramadol, gabapentin) was rated by the patients on a 0-3 scale (almost never, 1-3 times/month, 1-3 times/ week, almost everyday). In study 5, participants also rated the frequency of using prescribed medication using a four-point scale (from "daily" to "never").

Multidimensional Pain Inventory - Swedish version

The West Haven-Yale Multidimensional Pain Inventory (WHYMPI) was developed to assess various aspects of chronic pain and disability [74]. In MPI-S, the subscales of part 1 and 2 have been translated to Swedish and psychometrically tested. The factor structure was confirmed with minor changes, and internal consistencies for the subscales were satisfactory (0.66-0.86) [8]. The subscales included in study 2 were: pain severity (two items, measures pain intensity, currently as well as during the past week), interference (11 items, pain interference with work, chores at home, and social activities), life control (four items, perceived control over pain, stressful situations, and daily activities), affective distress (three items, mood, irritability, tension, and anxiety during the past week), support (two items, attention and support from significant others). All items were rated on a 0-6 scale, higher scores indicating more pain, interference, control, distress, and support.

Pain

In the treatment outcome studies, pain intensity and interference (i.e. prevented from doing things, experiencing bad mood or negative thoughts due to pain) were rated daily by the participants on a 100 mm visual analogue scale (VAS) during a period of 1 (study 3) or two to three weeks (study 1 and 4). The daily ratings were used to calculate each individual's mean for the assessment period. In study 1, assessments were made 4 times a day based on a preset schedule, and in study 3 and 4 ratings were made only once a day and scores represented an average pain experience for that day. In the measurement development studies pain intensity was assessed by asking the participants to rate their current pain experience on a seven-point scale from "not at all" to "very much", using an item from the MPI.

Pain Coping Questionnaire

The Pain Coping Questionnaire (PCQ) [139] is a self report instrument for children and adolescents from age eight to measure how often a particular coping strategy is used on a scale from 1 (never) to 5 (very often). Internalizing/catastrophizing is a five-item subscale that assesses one aspect of coping with negative emotions that likely impair the use of more adaptive strategies [139]. This particular subscale has previously been considered relevant to this population [29].

Pain Disability Index

Pain Disability Index (PDI) is a brief instrument developed to assess the degree to which chronic pain interfere(s) with daily activities [166]. Seven items regarding various activities are rated by the patients on a 0-10 scale from "no trouble" to "total disability". Several studies support the reliability and validity of the PDI [165,166]. A Swedish version of the PDI has been used with WAD-patients, showing good reliability [154].

Pain and Impairment Relationship Scale

The Pain and Impairment Relationship Scale (PAIRS) was developed to assess patients' beliefs and attitudes regarding pain, or the ability to function despite discomfort [140]. Psychometric evaluations of the instrument have shown adequate internal consistency [151]. Also, PAIRS reliably discriminated between pain and non-pain groups, and the instrument was significantly related to impairment even after pain intensity, duration, and severity of spine dysfunction were controlled for [151]. PAIRS scores have been shown to change significantly following a CBT-oriented treatment, indicating the instrument's sensitivity to change in this type of treatment [47]. The PAIRS consists of 15 statements reflecting thoughts, attitudes and opinions about pain, such as "As long as I am in pain, I'll never be able to live as well as I did before." The degrees to which the participant agreed or disagreed with each statement was rated on a seven-point Likert scale (higher scores indicating greater tendency to associate pain with impairment and to restrict functioning in the presence of pain). In study 4, an age appropriate adaptation was made in one item by changing the wording from "work" to "school".

Pain interference index – a composite score

Due to a lack of adequate instruments for children, we constructed the Pain Interference Index (PII) as a measure of pain interference with everyday life for use in study 4. The Multidimensional Pain Inventory, Interference scale (MPI) [74] and the Brief Pain Inventory, pain interference items (BPI) [17] have been suggested as measures of pain related functioning [26]. Both of these instruments are short measures with certain advantages, e.g. the inclusion of items assessing sleep. Based on these two measures, a brief inventory was assembled to assess pain interference in adolescents. The six questions closely resembled the items in MPI and BPI although age-appropriately formulated. A composite score of pain interference was calculated by averaging the 6 items addressing interference with schoolwork, activities outside school (leisure activities), seeing friends, mood, physical ability, sleep. The items were rated on a VAS-scale from "not at all" to "completely".

Pain related discomfort

Previous studies have shown that worrying about longstanding pain is more distressing, difficult to dismiss, and distracting as compared with non-pain related worrying [28]. However, there were no measurements readily available to assess this in pediatric pain patients. Thus, in study 4, to assess the extent to which the participants were thinking of, or worrying about, pain and disability five questions were generated: 1) How often do you worry about pain or related symptoms? 2) How often do you think about having pain or other symptoms? 3) How often are you angry or sad because of pain or related symptoms? 4) How often do you worry about not being able to do things because of pain or related symptoms? 5) How often do you worry about not being able to do things in the future because of pain or related symptoms? The questions were rated using a VAS scale from "never" to "always". A composite score (i.e. mean) was calculated based on the five questions, with higher scores indicating more discomfort.

Psychological Inflexibility in Pain Scale

The Psychological Inflexibility in Pain Scale (PIPS) is developed to assess *psychological inflexibility* in relation to chronic pain. In developing PIPS, an initial pool of 38 items was generated by the authors to reflect some of the core processes

underlying psychological (in)flexibility: avoidance (12 items), acceptance (7 items), cognitive fusion (14 items), and values orientation (5 items). Furthermore, items were generated to be relevant in the context of chronic pain (i.e. reflecting descriptions from patients in treatment) and were modeled after previous ACT-related instruments (i.e. AAQ and CPAQ). Items consisted of different statements that were considered to be related to chronic pain, psychological inflexibility, suffering, and disability (coherent with ACT theory). Participants were asked to rate how true these statements were on a seven-point Likert-type scale that ranged from "never true" to "always true", with higher scores indicating higher psychological inflexibility. Two studies support the psychometric properties of a two-factor solution [200,204], with subscales labeled avoidance and cognitive fusion based on item content. The revised version of the instrument based on both exploratory and confirmatory factor analyses is included in the thesis as an appendix.

Quality of life – single item

A single item was included to assess perceived quality of life. The item was stated: "Rate your current level of life quality by marking one of the following alternatives." Participants were presented with seven alternatives from "very low quality of life" to "very high quality of life".

Satisfaction With Life Scale

Satisfaction With Life Scale (SWLS) is a five-item scale measuring global life satisfaction [24]. Items are rated on a seven-point scale from "strongly disagree" to "strongly agree", with higher scores indicating greater life satisfaction. SWLS has repeatedly shown to have good psychometric properties [131] although a Swedish version of the SWLS is yet to be validated.

School attendance

To assess school attendance, patients in study 1 were asked to rate their school absence due to pain using a 0-3 scale (no absence, 1-4 h/month, 5-10 h/month).

Short Form-36 Health Survey

The Short Form-36 Health Survey (SF-36) is a well-developed 36-item measure assessing health related quality of life [186]. The instrument is extensively evaluated and has shown good psychometric properties [109]. The SF-36 provides summary scores for two subscales: the physical component scale (PCS) and the mental component scale (MCS), with higher scores indicating better functioning. The instrument was developed for use with subjects from age 14, and a Swedish version of SF-36 has been validated showing adequate psychometric properties [161].

Short Form-12 Health Survey

SF-12 is a 12-item measure based on the SF-36 to assess health related quality of life [186]. As with SF-36, two different subscales measure physical and mental functioning, with larger scores indicating a higher level of functioning. Internal consistencies for the two subscales were 0.77 and 0.80 respectively in a large sample of patients with back pain [87]. A Swedish version of SF-12 has been validated and shown to adequately predict scores on SF-36 [41].

Tampa Scale of Kinesiophobia

The Tampa Scale of Kinesiophobia (TSK) assesses the participants' fear of (re)injury by physical movement/activity, or kinesiophobia [163,208]. The scale consists of 17 items, rated on a four-point scale from "strongly disagree" to "strongly agree" with higher scores indicating stronger fear of (re)injury. The TSK has shown to be a reliable assessment tool for longstanding pain in several studies, especially low-back pain [20,207], and a recent study have supported a two-factor solution with subscales for activity avoidance and somatic focus [144]. Also, analyses of the psychometric properties including Dutch, Canadian, and Swedish samples with several different pain types showed that the factor structure was stable across pain diagnoses and nationalities [145].

Work absence

Self-reported work absence (number of missed workdays) was measured using an item from the Örebro Screening Questionnaire (on a nine-point scale from "0" to "181-365") [80].

4.5. Ethics

All studies included in the thesis were approved by the Ethical Review Board in Stockholm, Sweden.

Table 4.3. Summary of questionnaires used in the different studies.

Questionnaire	In studies	Subscales used	Scale	# of items	Key references
Center for Ep. Studies Depr. ScChildren (CES)	1, 4		09-0	20	Fendrich et al. 1990; Olsson and von Knorring 1997; Weissman et al. 1980
Children's Depression Inventory (CDI)	1		0-54	27	Doerfler et al., 1988; Kovacs, 1985
Chronic Pain Acceptance Questionnaire (CPAQ)	5	Activity engagement Pain willingness	0-66	11 8	McCracken et al. 2004; Vowles et al., 2008; Wicksell et al. 2008
Functional disability inventory (FDI)	1,4		09-0	15	Claar and Walker 2006; Walker and Greene 1991
Hospital Anxiety and Depression Scale (HAD)	3, 5	Anxiety Depression	0-21	7	Lisspers et al. 1997; Zigmond and Snaith 1983
Impact of Event Scale (IES)	3		09-0	15	Horowitz et al. 1979; Sundin and Horowitz 2002
Pain Coping Questionnaire (PCQ)	1, 4	Catastrophizing	5-25	5	Reid et al. 1998
Multidimensional Pain Inventory (MPI-S)	7	Pain severity Interference Life control Affective distress Sumort	0-12 0-66 0-24 0-18	2 T 4 E C	Kerns et al. 1985; Bergstrom et al. 1998
Pain and Impairment Relationship Scale (PAIRS)	4	-	06-0	İ	Riley et al. 1988; Slater et al. 1991
Pain Disability Index (PDI)	3,5		0-70	7	Soderlund et al. 2000; Tait et al. 1987; 1990
Pain interference index (PII)	4		0-10	9	Wicksell et al., in press (study 4)
Pain related discomfort (composite score)	4		0-10	5	Wicksell et al., in press (study 4)
Psychological Inflexibility in Pain Scale (PIPS) 2 versions: 16 and 12 items	2, 3, 5	1: Avoidance (10) 1: Cognitive fusion (6) 2: Avoidance (8) 2: Cognitive fusion (4)	10-70 6-42 8-56 4-28	10 6 8 4	Wicksell et al. 2008 (study 2); under review (study 5)
Satisfaction With Life Scale (SWLS)	3,5		5-35	5	Diener et al. 1985; Pavot et al. 1991
Short Form-36 Health Survey (SF-36)	4	Mental component Physical component	0-100	Total: 36	McHorney et al. 1993; Sullivan et al. 1995; Ware and Sherbourne. 1992
Short Form-12 Health Survey (SF-12)	2	Mental well-being Physical well-being	0-100	Total: 12	Gandek et al. 1998; Ware et al. 1996
Tampa Scale of Kinesiophobia (TSK) 2 versions: tot. scale (17) or 2 subscales (8+5)	3, 4, 5	1: Total scale (17) 2: Activity avoidance (8) 2: Somatic focus (5)	17-68 8-32 5-20	17 8 5	Roelofs et al. 2004; 2007; Swinkels-Meewisse et al. 2003; Vlaeyen et al. 1995

5. EMPIRICAL STUDIES WITHIN THE RESEARCH PROJECT

5.1. Treatment outcome studies

The effects of treatment for the experimental condition (i.e. the exposure and acceptance intervention) in studies 1, 3, and 4 are summarized in Table 5.1. The results from the studies were, in short, as follows.

5.1.1. Study 1: Exposure and acceptance with adolescents - a pilot study.

Aim

To investigate if an exposure and acceptance-based approach could increase functioning as well as decrease pain for adolescents with chronic debilitating pain, and if the effects were retained six months following the end of treatment.

Major findings

Substantial and stable decreases in functional disability, pain intensity, pain interference, school absence and internalizing/catastrophizing were seen following treatment, continuing during post-treatment periods (see Table 5.1.). Effect sizes were generally large for the outcome variables (Cohen's d>.80). ITT analyses (i.e. with the two dropouts included in the analyses) did not change the results presented. Importantly, no patient reported an increase in pain intensity following treatment despite a substantial increase in functionality (i.e. functional ability and school attendance). For a majority of patients, a clinically important reduction in pain (i.e. intensity and interference) was seen following treatment and at follow-ups.

Methodological considerations

Several methodological shortcomings were noted that clearly limited the possibility to draw any conclusions from this pilot study. First and foremost, the lack of a control group prevented comparisons with other treatments or spontaneous recovery. Also, as this study was conducted within an ongoing process of developing a clinical model, the structure and sequence, as well as the therapeutic skills, changed successively. In addition, the number of sessions varied greatly. Importantly, treatment was based on individual needs and continued until goals set in therapy were achieved. In combination with the lack of a control group, such "success criteria" obviously made it difficult to evaluate the effectiveness of this intervention. Also, this study did not evaluate a standardized treatment protocol but rather an approach based on a set of principles applied individually reflecting each patient's specific difficulties and needs, as perceived by the therapist.

Conclusion

The improvements seen following treatment tentatively suggested that exposure and acceptance strategies may be used to increase functional ability as well as reduce pain. The results were of particular interest given the difficulties to achieve clinically meaningful and sustained effects for this group of patients. Although the study had important methodological limitations, the results were promising and merited further studies to empirically evaluate the effects of this type of rehabilitation for pediatric and adult patients disabled by chronic idiopathic pain.

5.1.2. Study 3: Exposure and acceptance with WAD - an RCT.

Aim

To investigate if exposure and acceptance delivered in addition to TAU (experimental group) could increase functioning and life satisfaction in people with WAD, and to compare this with a control group receiving TAU only. Also, the relationship between improvements in functioning and changes in psychological flexibility was investigated.

Major findings

Following treatment, improvements were seen in all measures but pain intensity. Statistically significant differences between the groups, in favor of the experimental condition, were seen in the primary outcome variables (pain disability and life satisfaction), secondary outcome variables (e.g. fear of movement, posttraumatic stress symptoms), and in the process variable (psychological inflexibility). Large effects ($\eta_p^2 >$ 0.25) were obtained in several measures including the primary outcome variables, as shown in Table 5.1. Pairwise contrasts indicated that the improvements mainly occurred during the treatment phase. The pattern of results implied that reported increases in functional ability and life satisfaction were not due to a corresponding decrease in pain. In contrast, changes in psychological inflexibility (i.e. avoidance and fusion subscales) corresponded well with improvements in life satisfaction and functioning. This suggested that psychological flexibility may have been an important mediator of change, and this should be explored in future studies. ITT analyses, i.e. including the participant that dropped out from the control group, did not change the results. Also, no differences were seen between the two therapists involved in the study. In addition, no participant dropped out of treatment, which is a fact that tentatively suggested that the clinical model was well received by participants.

Methodological considerations

The small sample and the selection of participants (recruited from a patient organization) may have limited the external validity of the results. A 12- or 24-month follow-up assessment would have provided valuable information regarding the sustainability of the improvements. Exclusive reliance on self-report measures as well as the lack of validated Swedish versions of several of the included instruments constituted further limitations. The lack of video/audiotape prevented direct observation and assessment of therapist competence and protocol adherence.

Conclusion

The results from this relatively small RCT were promising and merited further studies to investigate the effectiveness of exposure and acceptance strategies to increase functioning and life satisfaction in people with debilitating chronic pain and WAD.

Aim

To evaluate the effectiveness of an intervention based on exposure and acceptance strategies (ACT) for children and adolescents with longstanding debilitating pain syndromes, and to compare this with a multidisciplinary treatment approach including amitriptyline (MDT).

Major findings

As illustrated in Table 5.1., the exposure and acceptance group showed substantial and sustained improvements in all measures, with mostly large effects sizes. Thus, these results supported previous findings that an approach based on exposure and acceptance may be effective in the treatment of longstanding pediatric pain. The MDT group improved significantly on several measures, implying that an active and generally useful treatment was used as a control condition. Comparisons between the two conditions including follow-up assessments showed that the exposure and acceptance group performed significantly better on perceived functional ability in relation to pain (PAIRS), fear of re/injury or kinesiophobia (TSK), pain intensity and pain related discomfort. Analyses based on post-treatment assessments (before groups diverged in extent of treatment) also illustrated significant differences between the groups in favor of the exposure and acceptance condition in pain interference (PII) and quality of life: mental scale. Analyses of the differences between the groups showed moderate to large effect sizes (η_p^2 =.13-.34).

Methodological considerations

The prolonged treatment in the MDT group complicated comparisons between groups at follow-up assessments. Although consecutive patients were used, the relatively small sample may have limited the external validity of the findings. It was suggested that future trials include audio/video recordings of sessions to facilitate formal assessments of therapist competence and protocol adherence. Also, the use of dependant variables other than self-report measures would have strengthened the results obtained. The lack of validated Swedish instruments for pediatric pain was unfortunate and resulted in the use of several measures that were not psychometrically validated with a relevant population, for example the PAIRS. A potential floor effect was noted in the FDI, indicating a need to either refine or develop instruments to assess specific pain related disabilities among pediatric patients. For example, the PII appeared promising but the reliability and validity need to be explored.

Conclusion

Improvements seen in the exposure and acceptance condition, as compared with the MDT including amitriptyline, supported previous findings and suggested the effectiveness of this intervention. Thus, the results illustrated that this treatment approach can lead to important benefits in pain adjustment, functioning, and quality of life with pediatric patients suffering from debilitating longstanding pain. However, the methodological concerns should be noted and larger scale studies are warranted, as well as the validation of an adequate instrument to assess psychological flexibility in pediatric patients with chronic pain.

Table 5.1. Summary of results for the experimental conditions in the treatment outcome studies (ANOVA, repeated 1x4). Effects over time in primary, secondary, and process variables following an intervention based on exposure and acceptance are illustrated.

			- J.E.	()				1. P.	
Study	Dependent variables	Pre	Post	Means (su) Follow-up 1	Follow-up 2	F-value	p-value		10°2
Primary 1	Primary outcome measures 1 FDI (0-60) School absence (0-3)	20.7 (12.4)	7.6 (11.6)	5.4 (7.9)	3.3 (4.2)	18.0	<.001	1.05	
	PDI (0-70) SWI S. (5-35)	37.1 (12.3)	24.3 (14.0) 23.7 (6.2)	31.6 (14.3)	31.4 (14.3)	6.7 1.11	.017		0.28
, 44	PAIRS (0-90) SF-36: mental (0-100)	50.5 (14.8) 34.6 (10.8)	34.5 (14.9) 42.9 (12.2)	31.3 (18.1) 40.9 (10.1)	28.5 (19.3) 42.7 (9.6)	13.3 4.3	<.001 .027	000	0.47
Seconda:	Secondary/process measures 1 Pain interference – daily ratings (0-10) 1 Catagoralization (5, 25, 27)	5.3 (2.2)	2.5 (2.3)	1.7 (1.9)	0.7 (1.1)	24.0	, c.001	1.27	
	TSK (17-68) PIPS-avoidance (10-70)	33.4 (9.4)	29.0 (6.1)	28.7 (6.4)	28.3 (6.2) 26.7 (9.7)	3.7	.059		0.27
w 44	PIPS-tusion (6-42) TSK (17-68) Pain related discomfort (0-10)	32.1 (4.9) 39.7 (8.4) 5.3 (2.2)	22.3 (8.5) 31.2 (6.4) 2.6 (1.8)	23.0(8.9) 29.9(8.7) 2.6(2.7)	22.2 (8.5) 29.3 (8.0) 2.3 (2.5)	7.3 19.4 10.9	.007 <.001 .003	Ö ÖÖ	0.42 0.56 0.42
Pain intensity 1 Pa 3 Pa 4 Pa	e nsity Pain intensity (0-10) Pain intensity (0-10) Pain intensity (0-10)	5.6 (1.7) 5.3 (1.0) 5.3 (1.8)	3.0 (2.4) 4.8 (2.1) 3.6 (2.3)	2.7 (1.9) 5.2 (1.9) 3.1 (2.5)	2.0 (1.7) 5.2 (2.2) 3.1 (2.7)	21.15 0.3 8.2	<.001.816.004	1.53	0.03

Notes. Effect sizes are interpreted as follows [18]. Size (1.8) (2.3) (2.3) Notes. Effect sizes are interpreted as follows [18]. Cohen's d: d=.2 (small effect), d=.5 (medium effect), d=.8 (large effect). Partial et a squared: $\eta_p^2=.01$ (small effect), $\eta_p^2=.09$ (medium effect), $\eta_p^2=.25$ (large effect).

5.2. Measurement development studies

The results from the measurement development studies are summarized in Tables 5.2. and 5.3. Standardized regression weights of the PIPS obtained with CFA are shown in Figure 5.1. Furthermore, the final 12-item version of the instrument is provided as an appendix, including scoring instructions.

5.2.1. Study 2: Preliminary validation of the PIPS.

Aim

To develop and test the internal consistency and criterion related validities of a new instrument to assess important aspects of psychological flexibility in adults with chronic pain.

Major findings

Principal component analyses supported the reliability and validity of a two-factor solution with subscales for *avoidance* and *cognitive fusion*. As illustrated in Table 5.2., the subscales demonstrated adequate internal consistencies and intercorrelation. Furthermore, background variables were controlled for, PIPS contributed significantly to the prediction of pain severity, interference, life control, and affective distress (MPI subscales), physical and mental well being (SF-12 subscales), and quality of life (single item). The individual contribution to explaining variance in the dependant variables was larger for avoidance than for cognitive fusion (see Table 5.3.).

Methodological considerations

The lack of longitudinal data prevented analyses of the causal relationship between PIPS and e.g. decreased quality of life. The criterion validity was based on self-report measures and objective data in the form of medication use, work absence etc. would have added to the validity of the measure. The lack of systematic data from people who declined participation also limited the validity of the results.

Conclusion

Although tentative, data from the present study demonstrated satisfactory psychometric properties for this 16-item version of the PIPS, with subscales for avoidance and cognitive fusion. More data was needed to further test the factor structure and validity of the questionnaire. Replicating the study with a different sample would, thus, support the validity of the questionnaire.

5.2.2. Study 5: Evaluation of psychometric properties and model fit of the PIPS.

Aim

To examine the psychometric properties of the instrument including factor structure and internal consistency, as well as the criterion and construct validities, and to investigate the model fit of the subscales across two different samples.

Major findings

Exploratory factor analyses (i.e. PCA) supported the previously suggested two-factor solution. Internal consistencies were good for the subscales (avoidance and cognitive fusion) as well as the total scale. As seen in Table 5.3., hierarchical regression

analyses illustrated adequate relationships with the criteria variables (e.g. disability and life satisfaction). Construct validity was supported by strong correlations with CPAQ and the activity avoidance subscale of the TSK. Furthermore, CFA was performed with the 14 items that were retained in both the preliminary validation and in the present study, and this resulted in the removal of two more items. By considering the model fit as well as the amount of explained variance in relevant criteria variables, a final version of the instrument was established using eight (avoidance) and four (cognitive fusion) items in the two respective subscales (see Figure 5.1.).

Methodological considerations

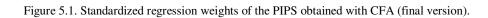
Participants in the present study were members of a patient organization and reported symptoms of WAD but no diagnostic information. Thus, scores on the subscales may not generalize to a clinical population. Lack of a formal randomization procedure for selection of participants was unfortunate. Also, the lack of systematic data about the members prevented any analysis of those who declined participation. The sole use of self-report measures was another limitation, and objective data would have added to the validity of the measure. Furthermore, the criterion validity of the questionnaire was evaluated by correlations with other measures, preventing causal inferences.

Conclusion

The psychometric properties of this 12-item version of the instrument were supported, with CFA indicating an acceptable fit of the model. The instrument was, thus, suggested as an adequate measure of avoidance and cognitive fusion among adults with chronic pain (see appendix).

Table 5.2. Summary of the results from the measurement development studies. Data for each subscale as well as the total scale from the two studies are illustrated, including explained variances and internal consistencies (Cronbach's alpha).

Scale	Final no. of items	Mean (sd)	Explained variance	Alpha (α)	Correlation bet	ween subscales Raw score
Study 2 - Development	and prelimina	ry validation				
Avoidance	10	41.7 (12.0)	39.0%	.90	22	46
Cognitive fusion	6	31.3 (6.0)	12.7%	.75	.33	.46
Total scale	16	73.0 (15.8)	51.7%	.89		
Study 5 - Psychometric	evaluation and	l model testing				
Avoidance	8	31.4 (10.0)	42.1%	.89	22	20
Cognitive fusion	4	21.2 (4.2)	13.7%	.66	.33	.39
Total scale	12	52.6 (12.3)	55.8%	.87		



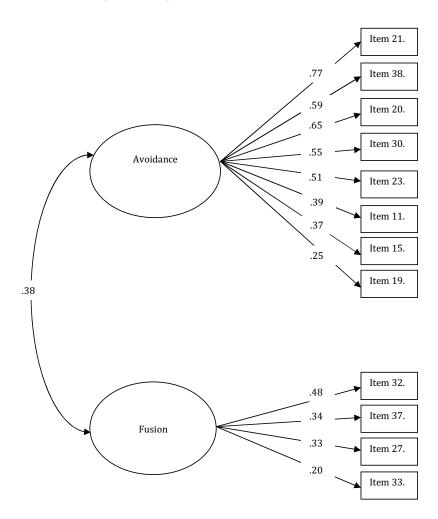


Table 5.3. Summary of the results from the measurement development studies - concurrent criterion and construct validity.

			,	,			Standard	Standardized Coefficients Beta	ents Beta
Dependent variables	Step	Predictor variables	R ²	R' change	F change	Sig. F Change	Beta	.	Sig. Beta
Study 2 - Development and preliminary validation	d preliminary	validation							
MPI - Pain severity	-	Background variables	.100	.100	6.741	<.001			
		Age					053	755	.452
		Education					185	-2.636	600.
		Pain duration					.234	3.306	.001
	2	PIPS	.170	.071	7.731	.001			
		Avoidance					.173	2.183	.030
		Cognitive fusion					.154	2.028	940.
MPI - Interference	-	Background variables	.193	.193	7.172	<.001			
		Age					295	-3.051	.003
		Education					051	524	.602
		Pain duration					.277	2.903	.005
	2	PIPS	.601	.408	44.930	<.001			
		Avoidance					909.	7.120	000.
		Cognitive fusion					.199	2.563	.012
MPI - Affective distress	-	Background variables	.153	.153	11.055	<.001			
		Age					287	-4.192	000
		Education					105	-1.549	.123
		Pain duration					.202	2.955	.004
	2	PIPS	.307	.154	20.248	<.001			
		Avoidance					.402	5.556	000.
		Cognitive fusion					.025	.352	.725

;	į	;	?	,		į	Standard	Standardized Coefficients Beta	nts Beta
Dependent variables	Step	Predictor variables	¥	R' change	F change	Sig. F Change	Beta	t	Sig. Beta
SF-12: physical scale		Background variables	.037	.037	2.124	660:			
		Age					.036	.473	.637
		Education					065	846	399
		Pain duration					179	-2.339	.021
	2	PIPS	.181	144	14.544	<.001			
		Avoidance					361	-4.448	000.
		Cognitive fusion					084	-1.074	.284
SF-12: mental scale	-	Background variables	620.	620.	4.776	<.001			
		Age					.087	1.163	.246
		Education					.191	2.567	.011
		Pain duration					160	-2.135	.034
	2	PIPS	.268	.189	21.304	<.001			
		Avoidance					447	-5.818	000.
		Cognitive fusion					034	458	.648
Study 5 - Psychometric evaluation and model testing	aluation and	model testing							
Pain intensity	_	Background variables	.013	.013	8.27 (1,605)	.004			
		Age					12	-3.15	.002
	2	PIPS	.106	.092	31.05 (2,603)	<.001			
		Avoidance					.22	5.28	<.001
		Fusion					.14	3.30	.001
SWLS		Background variables	.026	.026	7.93 (2,605)	<.001			
		Age					.13	3.82	<.001
		Education					.05	1.35	.177
	2	PIPS	.283	.258	108.30 (2,603)	<.001			
		Avoidance					47	-12.47	<.001
		Fusion					09	-2.30	.022

							Standardi	Standardized Coefficients Beta	ents Beta
Dependent variables	Step	Predictor variables	~	R² change	F change	Sig. F Change	Beta	t	Sig. Beta
PDI	-	Background variables	.016	.016	4.90 (2,605)	800.			
		Age					10	-2.98	.003
		Education					02	48	.632
	2	PIPS	.324	308	137.34 (2,603)	<.001			
		Avoidance					.55	15.11	<.001
		Fusion					.01	.34	.732
TSK-activity avoidance	1	Background variables	.047	.047	14.90 (2,606)	<.001			
		Gender					.17	4.82	<.001
		Education					90:-	-1.79	.074
	2	PIPS	.311	.264	115.50 (2,604)	<.001			
		Avoidance					.43	11.71	<.001
		Fusion					.16	4.34	<.001
CPAQ-activity engagement	-	Background variables	.044	.044	6.74 (4,590)	<.001			
		Age					.12	3.71	<.001
		Gender					07	-2.23	.026
		Education					90.	1.33	.183
		Time since pain onset					.07	2.01	.045
	2	PIPS	.472	.429	238.90 (2,588)	<.001			
		Avoidance					61	-18.75	<001
		Fusion					10	-3.08	.002
CPAQ-pain willingness	1	Background variables	600.	600.	5.34 (1,607)	.021			
		Education					.00	.81	.416
	2	PIPS	.546	.537	357.46 (2,605)	<.001			
		Avoidance					58	-19.34	<.001
		Fusion					28	-9.48	<.001

6. GENERAL DISCUSSION

6.1 Treatment evaluations

6.1.1. Summary of the treatment outcome studies

In the present thesis, a clinical model emphasizing exposure and acceptance strategies to increase psychological flexibility and thereby improve functioning and life satisfaction was developed and evaluated. Traditionally, CBT conducted with pain patients have addressed reductions in, or control of, pain and distress by e.g. relaxation/biofeedback techniques, stress management strategies, and decatastrophizing [22,89,175]. In contrast, no intervention in the present study was aimed at reducing or controlling pain. Instead, the focus was on increasing the patients' psychological flexibility, i.e. the ability to choose values-oriented behaviors in the presence of pain and distress. Thus, the rationale for this exposure and acceptance based approach is conceptually different from most CBT programs used with chronic pain patients. The emphasis on values and the use of acceptance and defusion represent other differences between this approach and more traditional forms of CBT.

In summary, the treatment evaluation studies included in the thesis suggest that a clinical approach based on values-oriented exposure and acceptance can improve functioning and quality of life in people with chronic debilitating pain syndromes. Tentatively, results suggest that improved functioning and life quality may be tightly linked to changes in psychological flexibility. Thus, based on the present studies it is argued that, in contrast to pain control per se, the patients' ability to act effectively in the presence of pain and distress constitutes a key factor in functioning and quality of life. Clearly, these studies have methodological limitations that need to be considered before generalizing the results. Such limitations are small samples and heavy reliance on self-report measures. However, the findings are relatively consistent across three studies, and significant effects were obtained despite small samples, supporting the validity of the findings. The results also support previous research on acceptance and pain (see Tables 2.1. to 2.3.). Large, although uncontrolled, treatment studies have indicated the usefulness of a comprehensive multidisciplinary treatment based on similar theoretical principles [106,211]. In correlation studies, acceptance has repeatedly been shown to predict pain adjustment and quality of life [92,97,203]. Laboratory studies have provided further support for the utility of accepting rather than trying to control pain [111,215]. Thus, the presented studies contribute to the growing empirical base for interventions based on exposure and acceptance.

In contrast to most clinical outcome studies with CBT for pain, the interventions used in the present studies are derived from, and closely related to, one well-defined theory (i.e. learning theory). Also, the protocols used did not include a large number of different treatment components. This is important given the need to further explore the mechanism(s) of action and change processes in successful CBT. Recently, studies have shown that acceptance mediates the effects of catastrophizing in e.g. depression, fear, and disability [213], and is highly associated with treatment changes [212].

As previously stated, pain intensity was neither considered a primary outcome measure nor a target in these treatment evaluations. Yet, we were interested in exploring whether a change in context (from a non-accepting to an accepting posture) would alter the experience of pain. Interestingly, in both studies with adolescents we found a decrease in pain intensity despite the fact that no intervention was aimed at pain

reduction. Rather, the emphasis on exposure to pain-related activities could be expected to result in increased pain. In contrast to these findings with adolescents, there was no change in pain intensity across time in the treatment study with adults. It should be noted, though, that the reported increase in activity did not result in a corresponding pain increase.

6.1.2. Clinical implications

Although a large body of literature supports CBT for people with chronic debilitating pain, there is still an extensive number of patients that are not offered such treatment within the regular health care system. This is somewhat difficult to understand given the large direct and indirect costs for chronic pain, the relative ineffectiveness of medical interventions for chronic pain syndromes, and the well-known usefulness of CBT for this group. Although comprehensive, CBT-oriented rehabilitation programs may be well worth the money, as shown by studies illustrating the cost-effectiveness of CBT as compared with usual care and information [81]. However, it may be that brief and less intensive interventions are more easily incorporated into existing health care organizations. It should be noted that the results in the presented studies were obtained using a small behavior medicine team consisting of a psychologist and a pain physician (trained in CBT and ACT or currently under training) and weekly sessions during a period of three to five months. Also, the results from these brief interventions are comparable with similar but more extensive programs [106], indicating a need to explore the arguments for and against these, undoubtedly more expensive, comprehensive treatments.

In addition to providing structured ACT/CBT interventions to a larger number of chronic pain patients, a paradigm shift for this group seems warranted. Although certain subgroups of patients benefit from various medical treatment options, such as opiates or spinal cord stimulations, there is enough empirical evidence to conclude that the link between reductions in pain intensity and increased functioning is rather weak [174]. Thus, even if medical interventions are provided with the intent to reduce pain, behavioral activation needs to be specifically addressed to achieve improved functioning. Also, increases in healthy behaviors such as social interactions or physical activities may mediate the effects of the medical interventions.

Learning theory, behavior therapy, and ACT should be seen as approaches to 1) understand important links between pain and disability, and 2) tailor the support provided to people with debilitating conditions, in order to assist them in improving functioning. As such, this is a framework to be used for all people involved in these patients. Expressed differently, ACT is not as much a particular psychotherapeutic intervention or technique as it is a team approach.

The behavioral medicine approach to pain and disability appears essential to achieve improvements in functioning among people with chronic and severe somatic symptoms. Given the large emphasis on psychological aspects, it may seem as if the presented intervention is mainly provided by the psychologist. This is, however, not the case. The role of the physician in the behavioral medicine team should be to facilitate the exposure process by providing correct information regarding the benign character of the pain, and closing the door to further medical assessments or treatments. By doing this, she or he is altering the context in which pain is experienced. From a contextual and RFT perspective, the physician as a pain expert is central to a process where new relational framing may occur. Frames of coordination may develop between stimuli that were previously not related by "sameness", but rather framed as "opposite". For

example, "having pain" may (gradually) start to be seen as compatible with "perform physical activities" (i.e. not "opposite as"). Similarly, "being in pain" AND "living a vital life" may be possible, as well as "being a pain patient" AND "plan for the future".

The relational frames that previously resulted in cognitive fusion and experiential avoidance are undermined due to modifications in the relational network (following new learning experiences). Thus, a (behavior medicine oriented) pain physician may be an extremely important behavior therapist that plays a central role in modifying dysfunctional behavior patterns. This process also includes refraining from reinforcing behaviors in line with cognitive fusion and experiential avoidance. Saying no to further assessment or treatments aimed at decreases in pain is obviously difficult for the patient, as well as for the physician. Nevertheless, it is a vital part of shifting the patients' perspective towards acceptance of pain and values-oriented exposure.

Subsequently, through values clarification, workability and creative hopelessness, acceptance and defusion exercises, goal setting and behavioral activation etc. the patient acquires new information (through direct experiences and derived learning). In this continuous process, the relational framing of verbal stimuli in the network of verbal stimuli is gradually modified. Consequently, previously well established ideas such as "pain needs to be reduced" may no longer be taken for granted. When such a verbal stimuli is framed differently, the psychological functions are changed. For example, the function of "I can not do this, due to my pain" is further undermined following a (successful) process of exposure and defusion. Moreover, when starting to behave differently in the presence of thoughts like "there is no use in trying" or "it hurts too much, I can't go", the behavior repertoire starts to expand. If such behaviors are reinforced by meaningful experiences, they may generalize to other situations. A larger behavior repertoire is built, and the patient becomes more flexible in using it (increased psychological flexibility). Thus, rather than learning to control negative thoughts, emotions, and bodily sensations, the objective of this clinical approach is to assist the patient in generating and increasing values oriented behaviors in the presence of pain and distress.

In addition, the values work appears essential when targeting behavior change in patients with chronic pain. In contrast to anxiety, pain is unlikely to be substantially reduced following an exposure based intervention. Thus, the rationale for the exposure process must be different (i.e. not primarily desensitization). Importantly, the shift in perspective (or creative hopelessness) from symptom reduction to valued living establishes a context that facilitates exposure. Using RFT-terms, by frequently discussing personal values and long term goals, the therapist can help the patient to bring future effects into a frame of causation with present behaviors. That way, the psychological function of the present behavior may shift from e.g. "it will hurt, I shouldn't do it" to "it will hurt and this is in the service of being a good parent". Expressed differently, the values work is motivational in the sense that it illuminates the incentives to repeatedly engage in behaviors that are likely to increase pain and distress.

Clearly, the empirical support for ACT and related treatment approaches is growing rapidly and the utility of these interventions is of particular interest within the field of behavioral medicine and treatment-resistant somatic conditions. Besides chronic pain, there is a substantial number of patients suffering from longstanding somatic symptoms, with or without a clear etiology, for which effective medical treatments are lacking. Many times, these symptoms lead to deterioration and reduced quality of life. For these patients, it appears as if interventions such as values-oriented exposure, acceptance, and defusion may be beneficial. Although research in this area is greatly needed, some

studies exist. As previously mentioned, ACT interventions have been evaluated with stress [11], epilepsy [84-86] and diabetes [46]. Recent studies have also indicated that acceptance oriented interventions may have an important role to play for patients with tinnitus [192,193], and treatment outcome studies are eagerly awaited. Also, in a small study conducted with women diagnosed with breast cancer, acceptance- and control based interventions were compared [127]. Due to a small sample size, results were tentative but indicated the usefulness of the acceptance approach and this appears to be a relevant area for future research.

In the previously mentioned study on diabetes, the ACT intervention resulted in better diabetes self-care [46]. This is of particular interest given the difficulties with treatment compliance seen among subgroups of patients with e.g. diabetes or cystic fibrosis [156]. For these individuals, not behaving in accordance with the selfmanagement program may lead to serious or even fatal consequences. Although skills training may be one important dimension of a self-care program, it seems plausible that emotional distress and avoidance may constitute barriers that may be addressed with an exposure and acceptance oriented intervention. Furthermore, based on these and previous findings, it appears reasonable to think that a behavior medicine model based on ACT would be beneficial to patients with e.g. chronic fatigue syndrome, unclear neurological symptoms, secondary sleep disorder (resulting from e.g. chronic pain), and in patients with complex somatic conditions. It may also provide a useful treatment approach for patients presenting with somatic disorders and severe psychiatric comorbidity. Sometimes a medical treatment is successfully applied (e.g. to cancer) and the patient is cured but continues to experience somatic symptoms such as nausea, headache, or fatigue. Additional distress related to fear of remission may be present. In total, the successfully treated patient may continue to suffer from both anxiety and somatic symptoms that can result in depression as well as decreased social and physical functioning. For this group, it appears as if an ACT-oriented program aimed at improving valued living in the presence of interfering somatic and psychiatric symptoms can be useful.

6.2. Measurement development

6.2.1. Summary of the measurement development studies

The present thesis includes two studies conducted to develop and evaluate a process measure assessing central and discernible components of psychological flexibility. Initially, 38 items reflecting avoidance, fusion, values, and acceptance were generated. All items appeared theoretically relevant for one of these components. Following exploratory and confirmatory factor analyses, a 16-item version and later a 12-item version was suggested, with subscales for avoidance and cognitive fusion. In both sets of data, the instrument illustrated adequate internal consistencies as well as concurrent criterion and construct validities. Thus, data suggest that PIPS can be used as a reliable and valid measure to assess key components in psychological inflexibility in adults with chronic pain.

6.2.1. Clinical implications

It is suggested that the results of this study have clinical implications. It should be possible for the clinician to refine the behavior analytic case formulation by using the questionnaire and thereby get a better understanding of the patient's pain related difficulties. The information provided by PIPS can subsequently guide the clinician in

tailoring the intervention to address the patient's difficulties. Specifically, it may be possible to identify different subgroups based on the results from instruments such as PIPS. Possibly, these subgroups of patients may benefit from different types of interventions. Thus, it may be important to investigate whether certain components of the ACT-model (e.g. defusion or behavioral activation) should be emphasized with some patients.

6.3. Future directions

6.3.1. Treatment evaluations

The empirical base for an exposure and acceptance oriented interventions is growing. However, there is a need to further investigate the effectiveness of exposure and acceptance oriented treatments with chronic pain patients, especially children and adolescents. The need for more empirical evaluations of ACT and similar approaches, especially RCT's, has been raised in a recent meta-analysis [219]. Notably, this metaanalysis did not include a several studies with pain patients. With regards to pain, more and larger randomized trials are needed and preferably with standardized interventions in both the experiment and the control conditions to optimize the internal validity. Moreover, the effectiveness of group interventions may be investigated and compared with individual treatment. Previous research has indicated that differences between treatment (multidisciplinary) and control conditions at post-treatment assessments tend to deteriorate during the following year [67]. Thus, given the promising results from exposure and acceptance oriented treatments, there is a great need for long term followup assessments (18-36 months following end of treatment). Results from one of the studies in the present thesis illustrate that although improvements in general were maintained for the treatment group seven months following end of treatment, declines were seen in some measures. This implies that a longer intervention program, e.g. 14-16 sessions extended over six months might be preferable and should be tested in future studies. Booster sessions could be dispersed over an extended period to maintain and further increase activity engagement and psychological flexibility.

Although a number of relevant lab-studies have been conducted recently, there is still a need to clarify the importance of separate components in ACT-oriented treatments. Ideally, this type of studies should include physiological measures to explore the biological dimensions of these psychological constructs, e.g. acceptance. Imaging techniques, such as fMRI and PET may also provide new insights with regards to the working mechanisms in acceptance strategies.

As pointed out in previous research on CBT interventions for chronic pain, behavior change and physical improvements are (to some extent) two different objectives demanding different types of interventions [209]. Thus, the patterns of pain related avoidance seen among these patients should be individually analyzed using a learning theory framework, and subsequently targeted with behavior therapeutic strategies such as exposure. From this perspective, the mechanism of action in successful treatments based on exercise and increases in physical activities may in large be conceptualized as exposure (i.e. a frequent and gradually increase of pain eliciting stimuli without trying to reduce or alter the experience).

For patients with e.g. WAD, interventions to improve strength, balance, and mobility are important but difficult. The results from study 3 suggest that acceptance strategies may be included to facilitate engagement in physical exercises perceived as potentially painful but critical to improving strength and mobility. Thus, the probability

of achieving sustainable improvements in functional abilities may be increased if physical training is combined with individually tailored behavior therapy focusing on exposure as well as acceptance strategies. Future studies might test whether an exposure and acceptance based intervention performed prior to a physiotherapeutic intervention could enhance the effectiveness of the latter.

The importance of family factors to the child's pain and disability is today well known [128,130,179]. However, further studies are needed to explore if family functioning and parents' behaviors (e.g. general style of communication, attending to pain symptoms) have a direct influence on pain and/or functional disability or whether more complex relationships exist [130]. Thus, it is suggested that the parents' roles as mediators and moderators on treatment effects is addressed in future studies.

Few studies have investigated costs involved in caring for children with longstanding pain, but economic benefits from developing effective treatments for this group is clearly indicated [152]. The participants in the MDT group received, on average, twice as many sessions as the participants in the ACT group. This indicates that the results obtained should be evaluated in relation to the costs involved in delivering the intervention. However, the difference in treatment length in study 4 was unintended and the data needed for such an analysis could not be systematically obtained retrospectively. Tentatively, results imply that an ACT approach may be a cost-effective intervention for these patients, but it is suggested that future studies set up the data collection procedures to facilitate such analyses.

6.3.2. Measurement development

In future research, PIPS may be used in longitudinal studies to explore the role of psychological flexibility in the transition from acute to chronic pain and related disability. Subsequently, PIPS may provide information about patients with subacute pain who may be at risk for developing chronic pain and e.g. long-term sick leave. One such project is currently underway. As a first step, the instrument's predictive validity will be explored in a longitudinal study. People reporting chronic pain and WAD (same group as in study 5) have completed assessments three years following baseline assessments.

The successive refinement and increasing empirical support for instruments such as PIPS and CPAQ have provided possibilities to further explore psychological flexibility and its relationship to other well-established constructs, such as kinesiophobia [203]. Future studies need to examine the relationship between PIPS and other measures of psychological inflexibility such as CPAQ. The values items included in the original pool of data appeared to constitute a separate construct but did not correlate highly enough with the other items in PIPS to be included as a third component. However, these items may be developed as a separate four or five item instrument to assess values orientation and should then be psychometrically examined [204]. Furthermore, the development of psychometrically adequate instruments to assess different dimensions of the overarching construct psychological flexibility provides the opportunity to test the relevance of a theoretical model, using for example structural equation modeling.

The importance of PIPS as a process measure needs to be further explored. Although major differences between pre- and post assessments were seen following a ten-session protocol [197], more data from outcome studies will further clarify the questionnaire's sensitivity to change and its role as a mediating variable.

To date, questionnaires to assess dimensions related to psychological flexibility, such as the PIPS [204] and the CPAQ [105,203], have only been developed and

validated with adult pain patients. This implies an urgent need to investigate the usefulness of e.g. PIPS with younger pain patients. Most likely, age-appropriate adaptations of these instruments will be needed, at least for patients younger than 14 years.

6.4. Conclusions

To conclude, the results from the present thesis indicate the effectiveness of a relatively brief intervention based on exposure and acceptance for children and adults with chronic debilitating pain. Although relatively small samples were used, effects from treatment are fairly consistent across the three samples, which support the validity of these findings. Following the pilot study, two RCT's showed that the exposure and acceptance intervention was effective in comparison to both treatment as usual and a multidisciplinary treatment including a pharmacological intervention. Based on these and other recent studies with similar findings, it is suggested that interventions emphasizing exposure and acceptance are provided as part of the standard treatment for these patients. Future research should include larger scale randomized trials, especially with young patients, as well as studies to clarify the mechanisms of action in this type of treatment. Furthermore, results from two studies support the psychometric properties of a newly developed self-report questionnaire to assess central components of psychological inflexibility in people with chronic pain (PIPS). Data also indicate the importance of avoidance and cognitive fusion in explaining pain related disabilities and reduced life satisfaction. Thus, it is suggested that the instrument is a useful clinical tool in the analysis of pain related disabilities, and that it can be used to further explore the theoretical construct of psychological flexibility.

APPENDIX

The Psychological Inflexibility in Pain Scale (PIPS)

Below you will find a list of statements. Please rate how true each statement is for you by circling a number next to it.

1	2	3	4	5	6	7
Never true	Very rarely true	Seldom true	Sometimes true	Often true	Almost always true	Always true

- 1. I cancel planned activities when I am in pain.
- 2. I say things like "I don't have any energy", "I am not well enough", "I don't have time", "I don't dare", "I have too much pain", "I feel too bad", or "I don't feel like it".
- 3. I need to understand what is wrong in order to move on.
- 4. Because of my pain, I no longer plan for the future.
- 5. I avoid doing things when there is a risk it will hurt or make things worse.
- 6. It is important to understand what causes my pain.
- 7. I don't do things that are important to me to avoid feeling my pain.
- 8. I postpone things on account of my pain.
- 9. I would do almost anything to get rid of my pain.
- 10. It's not me that controls my life, it's my pain.
- 11. I avoid scheduling activities because of my pain.
- 12. It is important that I learn to control my pain.

Scoring

Add the items for each subscale as well for the total scale. No reversing is necessary.

Avoidance:

Item nr: 1,2,4,5,7,8,10,11

Fusion:

Item nr: 3,6,9,12

APPENDIX

The Psychological Inflexibility in Pain Scale (PIPS)

Här nedan hittar Du några påståenden. Vi vill veta hur ofta Du tycker att varje påstående stämmer in på Dig, så som Ditt liv ser ut nu. Välj det alternativ som passar bäst för varje påstående.

1	2	3	4	5	6	7
Stämmer aldrig	Stämmer mycket sällan	Stämmer sällan	Stämmer ibland	Stämmer ofta	Stämmer mycket ofta	Stämmer alltid

- 1. Jag ställer in planerade aktiviteter de dagar jag har ont.
- Jag använder meningar i stil med: "Jag orkar inte", "Jag är inte tillräckligt bra",
 "Jag har inte tid", "Jag vågar inte", "Jag har för ont", "Jag mår för dåligt" eller
 "Jag har inte lust".
- 3. Jag måste förstå vad som är fel för att kunna gå vidare.
- 4. På grund av min smärta planerar jag inte längre framtiden.
- Jag undviker att göra saker när det finns en risk att det kommer göra ont eller bli värre.
- 6. Det är viktigt att förstå orsaken till smärtan..
- För att undvika smärta låter jag bli att göra saker som egentligen är viktiga för mig.
- 8. Jag skjuter upp saker på grund av min smärta.
- 9. Jag skulle göra nästan vad som helst för att bli av med min smärta.
- 10. Det är smärtan som bestämmer i mitt liv, inte jag själv.
- 11. På grund av min smärta undviker jag att planera in aktiviteter.
- 12. Det är viktigt att jag lär mig kontrollera min smärta.

Rättningsanvisning

Delskalorna summeras separat (ingen reversering av poängen behövs). Poängen för respektive delskala kan summeras för att få fram en totalpoäng.

Undvikande (avoidance): Item nr: 1,2,4,5,7,8,10,11

Fusion:

Item nr: 3,6,9,12

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Although I knew early that the clinical research we conducted was going to result in a doctoral thesis, this was not a primary objective. Rather, to complete the next study, to figure out the best way to address the patients' problems, to come up with a model for conceptualizing "creative hopelessness" in a way that can be understood by children, to work out a way to communicate the importance of exposure even when this may not result in symptom reduction, to find a way to address health care providers that are mainly oriented towards symptom reduction, to understand why missing values should not be replaced with series means or why ANCOVA is preferable to ANOVA in small samples, to fully comprehend in what way a discussion of values provide a context for exposure, those were true incentives to engage in this work.

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