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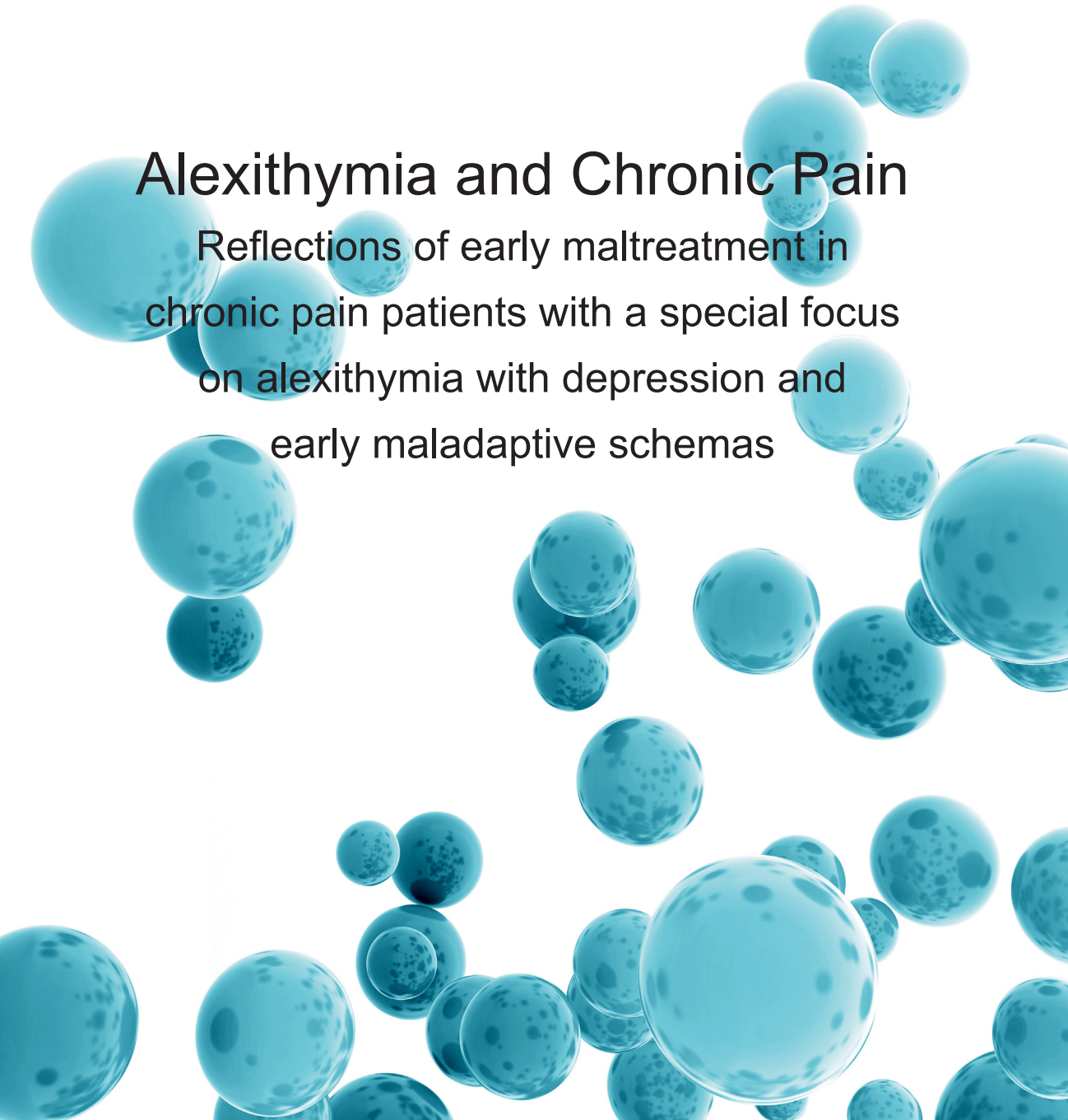
Reflections of early maltreatment in chronic pain patients with a special focus on alexithymia with depression and early maladaptive schemas



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ACADEMIC DISSERTATION
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UNIVERSITY OF TAMPERE

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To all those innocent animals (especially to rats), who have sacrificed their lives to teach the human race not to neglect their offspring.

ABBREVIATIONS

ACTH	adrenocorticotropic hormone
BDI-II	Beck Depression Inventory
CES-D	Center for epidemiological studies – depression scale
CRPS	complex regional pain syndrome
CRH	corticotrophin-releasing hormone
DDF	difficulties describing feelings
DIF	difficulties identifying feelings
EMS	Early Maladaptive Schema
EOT	externally oriented thinking style
fMRI	functional magnetic resonance imaging
HADS	Hospital Anxiety and Depression Scale
HPA-axis	hypothalamus-pituitary-adrenal axis
IASP	The International Association for the Study of Pain
IBQ	Illness Behavior Questionnaire
LBP	low back pain
MPQ	McGill Pain Questionnaire
MRI	magnetic resonance imaging
NRS	Numeric Rating Scale
PD	personality disorder
PDS	Pain Disability Scale
PDI	Pain Disability Index
PET	positron emission tomography
PM	psychological mindedness
PTSD	posttraumatic stress disorder
SCL-90-R	Symptom Check List Revised
SF-MPQ	Short Form McGill Pain Questionnaire
STAI-Y	State-Trait Anxiety Inventory Form Y
STAXI-2	State-Trait Anger Expression Inventory-2
VAS	Visual Analogue Scale
VRS	Verbal Categorical Rating Scale
TAS-20	The 20-item Toronto Alexithymia Scale

ABSTRACT

Chronic pain is a complex biopsychosocial phenomenon with numerous sufferers causing a significant burden on the health care system. Alexithymia is a manifestation of problems in identifying and describing feelings, externally oriented thinking style and restricted imaginative ability. Early Maladaptive Schemas (EMSs) describe internal patterns which have developed in response to adverse childhood experiences. Depression frequently co-occurs with chronic pain, but also with alexithymia and EMSs. Chronic pain, alexithymia, EMSs and depression have been found to be associated with early maltreatment.

The aims of the present study were to explore the relations and effects of alexithymia, EMSs and depression in a sample of chronic pain patients using cross-sectional and longitudinal study designs and thus indirectly to estimate the influence of childhood adversities on chronic pain. EMSs have not been studied among alexithymic chronic pain patients and longitudinal studies on alexithymia and chronic pain are rare.

The study participants were consecutive first-visit chronic pain patients recruited in 2004-2005 from six Finnish pain clinics. The first follow-up data was collected one year after the first visit to the pain clinic and the second follow-up was done eight years after baseline. The data was based on self-report questionnaires containing pain and psychological variables measuring pain intensity, pain disability, alexithymia, depressiveness and EMSs. The follow-up questionnaires were supplemented by questions assessing treatment interventions.

At baseline one fifth of chronic pain patients were defined as alexithymic. The alexithymic group reported more pain disability, pain intensity and depressiveness at baseline and at both follow-ups. Depressiveness mediated the effect of alexithymia on pain disability in cross-sectional and longitudinal settings. Alexithymia and depressiveness correlated significantly with most EMSs and alexithymic, depressive patients scored highest on EMSs. Almost all alexithymic patients were depressive and the association between alexithymia and depression remained strong and actually increased during follow-up. Both alexithymia and EMSs showed stability during the eight-year follow-up period.

None of the treatment interventions proved superior in achieving better outcome regarding pain intensity and pain disability. Poorer outcome was related to higher pain intensity and pain disability at baseline, but also to alexithymia and depressiveness. Additionally, alexithymia and depressiveness were associated with higher consumption of opioids. The patients showed a clear polarization: nonalexithymic patients recovered better than alexithymic patients who mainly remained depressive with disturbing pain. Men tended to have a less favourable outcome than women.

The study results highlighted the importance of psychological factors in the course and outcome of chronic pain. Co-existence of severe and treatment resistant pain situation with alexithymia, EMSs and depression may suggest emotional dysregulation and psychosomatic problems that are masked by pain symptoms. Furthermore, their co-occurrence probably reflects early adversities as initial predisposing factors. Maladaptive coping styles related to alexithymia, depression and EMSs maintain and exacerbate pain problems. Opioid therapy associated with alexithymia and depression may be a sign of mental problems and unrecognized emotional malaise treated with narcotics.

Assessment of alexithymia, depression and EMSs among chronic pain patients helps to identify those pain patients with poor prognosis. Pain patients therefore need individually tailored treatment options according to their overall biopsychosocial situation.

TIIVISTELMÄ

Krooninen kipu on monimutkainen biopsykososiaalinen ilmiö, joka aiheuttaa kärsimystä lukemattomille ihmisille ja kuormittaa merkittävästi terveydenhuoltoa. Aleksitymia tarkoittaa ongelmia tunteiden tunnistamisessa ja kuvailemisessa, ulkoisesti ohjautuvaa ajattelumallia ja rajoittunutta mielikuvitusta. Varhaiset haitalliset mallit ovat sisäistettyjä tulkinnallisia kaavoja, jotka ovat kehittyneet vasteena haitallisille lapsuuden kokemuksille. Masennus liittyy usein krooniseen kipuun mutta myös aleksitymiaan ja varhaisiin haitallisiin malleihin. Krooninen kipu, aleksitymia, varhaiset haitalliset mallit (tunnelukot) ja masennus ovat yhteydessä varhaisiin traumaattisiin kokemuksiin.

Tämän tutkimuksen tarkoitus oli tutkia aleksitymian, varhaisten haitallisten mallien ja masennuksen välisiä suhteita ja vaikutuksia kroonisilla kipupotilailla poikittaisessa ja pitkittäisessä tutkimusasetelmassa ja täten epäsuorasti arvioida lapsuudenaikaisten traumaattisten kokemusten vaikutusta krooniseen kipuun. Varhaisia haitallisia malleja ei ole tutkittu aleksitymisilla kroonisilla kipupotilailla ja pitkittäistutkimukset aleksitymiasta kroonisessa kivussa ovat harvinaisia.

Tutkimukseen rekrytoitiin kuuden kipupoliklinikan peräkkäiset ensikävijät vuosina 2004–2005. Ensimmäinen seurantatutkimus kerättiin vuosi alkuperäisotoksen jälkeen ja toinen seurantatutkimus tehtiin kahdeksan vuotta ensimmäisen aineiston keruun jälkeen. Tutkimusmateriaali kerättiin lomaketutkimuksena. Potilaat vastasivat kyselylomakkeeseen, joka sisälsi strukturoidut kyselyt kivun voimakkuudesta, kivun aiheuttamasta haitasta, aleksitymiasta, depressiosta ja varhaisista haitallisista malleista. Seurantakyselyssä kartoitettiin myös saadut hoitointerventiot.

Joka viides kipupotilas voitiin määritellä aleksitymiseksi. Aleksitymiset potilaat raportoivat enemmän kivun aiheuttamaa haittaa, kipua ja masennusta sekä alkutilanteessa että seurannoissa. Masennus toimi välittäjänä aleksitymian ja kivun aiheuttaman haitan välillä sekä poikittaisessa että pitkittäisessä asetelmassa. Aleksitymia ja masennus korreloivat merkittävästi useimpien varhaisten haitallisten mallien kanssa siten, että aleksitymisilla, masentuneilla potilailla oli korkeimmat arvot. Melkein kaikki aleksitymiset potilaat olivat masentuneita. Aleksitymian ja masennuksen välinen suhde pysyi korkeana ja jopa kasvoi koko seuranta-ajan.

Kahdeksan vuoden seurannassa aleksitymia ja varhaiset haitalliset mallit osoittivat pysyvyyttä.

Mikään hoitomenetelmistä ei osoittanut paremmuutta kivun voimakkuuden tai sen aiheuttaman haitan lieventymisessä. Huono hoitovaste oli yhteydessä perustason kivun voimakkuuteen ja kivun aiheuttamaan haittaan mutta myös aleksitymiaan ja masennukseen. Aleksitymiaan ja masennukseen liittyi myös suurempi opioidien kulutus. Seuranta-aikana kävi ilmi selkeä polarisaatio; ei-aleksitymiset toipuivat paremmin kuin aleksitymiset potilaat, joista suurin osa jäi masentuneeksi ja kipeäksi. Hoitovaste oli miehillä naisia huonompi.

Tutkimus toi esille psykologisten tekijöiden merkittävän yhteyden kipusairauden kulkuun ja siitä toipumiseen. Aleksitymian, varhaisten haitallisten mallien ja masennuksen yhteisvaikutus näkyi hankalana ja hoidolle huonosti reagoivana kiputilana, joka todennäköisesti heijasteli kipuoireiden peittämää emotionaalista dysregulaatiota ja psykosomaattisia ongelmia sekä niiden lisäksi lapsuuden haitallisia kokemuksia yhteisenä altistavana taustatekijänä. Aleksitymiaan, masennukseen ja varhaisiin haitallisiin malleihin liittyvät hankalat toimintamallit ylläpitävät ja pahentavat kipuongelmia. Opioidien käyttö aleksitymian ja masennuksen yhteydessä voi olla merkki psyykkisistä ongelmista ja lääkkeiden käytöstä turruttamaan emotionaalista pahoinvointia.

Aleksitymian, masennuksen ja varhaisten haitallisten mallien tutkiminen kroonisilla kipupotilailla auttaa tunnistamaan ne potilaat, joilla on huono ennuste. Tällöin kullekin kipupotilaalle voidaan valita biopsykososiaalisen tilanteen mukaisia, yksilöllisesti suunniteltuja hoitokeinoja.

TABLE OF CONTENTS

LIST OF ORIGINAL PUBLICATIONS

The dissertation is based on the following original publications.

I Saariaho AS, Saariaho TH, Mattila AK, Karukivi MR and Joukamaa MI (2013): Alexithymia and depression in a chronic pain patient sample. Gen Hosp Psychiatry 35:239-245.

II Saariaho AS, Saariaho TH, Mattila AK, Karukivi MR and Joukamaa MI (2015): Alexithymia and Early Maladaptive Schemas in chronic pain patients. Scand J Psychol 56:428-37.

III Saariaho AS, Saariaho TH, Mattila AK, Ohtonen P, Joukamaa MI and Karukivi MR (2017): Alexithymia and depression in the recovery of chronic pain patients: a follow-up study. Nord J Psychiatry 71:262-269.

IV Saariaho AS, Saariaho TH, Mattila AK, Joukamaa MI and Karukivi MR (2016): The role of alexithymia: An 8-year follow-up study of chronic pain patients. Compr Psychiatry 69:145-154.

Some unpublished data are also presented (5.5).

1 INTRODUCTION

The interactions between an individual and the environment produce multiple health related outcomes. In a novel based on clinical experiences in a remote rural area six decades ago, the doctor facing his patients with various disorders in various life situations asked repeatedly the same silent question in his mind, *"why have you selected this particular disease?"* (Schulze 1978). At that time, the term "biopsychosocial" in the medical context had not yet been established but in clinical practice the multifaceted nature of different disorders was obvious and tangible. The present study stems from similar tacit questions arising in clinical practice with chronic pain patients; *"Why do these patients suffer so much? What are these pains for? What do they represent?"* The incompetence and helplessness of biomedical approaches to alleviate suffering among chronic pain patients and expanding scientific knowledge concerning the development of chronic pain motivated the author to explore psychological factors contributing to the chronic pain that is the topic of the present study.

The quality of the human brain is attributed with enormous learning capacity and memory and with an adaptive characteristic called neuroplasticity (Pascual-Leone et al. 2005, Pascual-Leone et al. 2011). The interactions between a developing individual (an unborn foetus, an infant or a child) and the environment and in particular those circumstantial factors which are the closest, most important or intensive or repeated often enough compose the base of biopsychosocial learning (Kolb and Gibb 2011, Kolb et al. 2013). The consequences of this process depend on the nature of these interactions, genetic factors and personality and temperamental features of the individual in question.

Early adversities, childhood maltreatment, especially during vulnerable periods of the development of the nervous system, have longlasting effects on health and wellbeing throughout the lifespan (Sullivan et al. 2006). Several studies in different areas of human sciences have demonstrated the connections of a great number of health related disorders with early maltreatment, neglect and abuse (Felitti et al. 1998, Teicher et al. 2003, Anda et al. 2006, Pollak 2015). The mechanisms through which early experiences modify the biopsychosocial entity of an individual have been widely explored, and include theories and research results which link

biological epigenetic contingencies, neurophysiological alterations and psychosocial learning processes in the personal development of the individual (Taylor et al. 2011).

Emotions are a major part of our biological heritage and their importance in survival and adaptive processes is crucial (Greenberg and Paivio 1997). Affective development, i.e. emotional maturation and regulation, takes place step by step in childhood in reciprocal interactions and learning with significant caregivers (Taylor et al. 1997). The ability to interpret consciously bodily felt emotional states, to symbolize feelings in words and to express emotions is conducive to good health (Greenberg 2002). Emotional inhibition, repression and dysregulation play an important part in the development of several psychiatric and somatic diseases (Keefe et al. 2001, Dvir et al. 2014). Disturbances in emotional maturation during childhood are associated with insecure attachment and various early adversities and moreover, cause problems later in life in situations needing emotional adaptation (Krause et al. 2003, Charuvastra and Cloitre 2015).

Chronic pain is a worldwide unsolved health problem with millions of sufferers (Breivik et al. 2006, Johannes et al. 2010). The course of chronic pain in general population studies has confirmed its persistent nature (Elliott et al. 2002, Andersson 2004). No definite advantage of biomedical interventions in the treatment of chronic pain has been achieved. The modern concept regards chronic pain as a multifaceted phenomenon consisting of biopsychosocial and interrelated factors (Gatchel et al. 2007). Traumatic childhood experiences have been reported in studies of chronic pain patients (Davis et al. 2005, Stickley et al. 2015). Emotion processing dysregulation and involvement of emotion encoding brain areas are of interest in the research of chronic pain (Lumley et al. 2011). The co-occurrence of alexithymia and depression in chronic pain syndromes represents problems linked with emotional regulation (Keefe et al. 2001).

Alexithymia, a deficit or disorder of emotional regulation, has been considered to originate in the defective development of the cognitive-emotional domain (Bagby and Taylor 1997a). The predisposing factors for alexithymia include genetic susceptibility (Picardi et al. 2011) but also childhood adversities with insecure attachment (Honkalampi et al. 2004, Joukamaa et al. 2008, Pedrosa et al. 2008, Carpenter and Chung 2011, Aust et al. 2013). The developmental process achieving emotional maturity has not proceeded successfully, resulting in a person with difficulties in identifying and describing feelings and with a limited imagination and ability for fantasy (Bagby and Taylor 1997a, Lumley et al. 2007). The bodily felt emotional states are misinterpreted, leading to a tendency to somatization (Mattila

et al. 2008a). A wide range of health related conditions, such as chronic pain, personality disorders, inflammatory bowel disease and anxiety disorders among others, have been shown to be associated with alexithymia (Lumley et al. 2007) but the prognostic value of alexithymia in health disorders is contradictory (Kojima 2012).

During childhood, one creates the most permanent and durable concepts of oneself, others and the world. These concepts produce internal patterns, schemas and coping models by which one automatically interprets life experiences, and which guide the behaviour and modes of action (Beck et al. 1979, Beck et al. 1990**,** Young et al. 2003). The schemas developed by traumatic (toxic) early experiences may later in lifecourse expose to thinking, feeling and behavioural styles which are maladaptive to the situation and exacerbate one's problems and psychological imbalance. These schemas are called Early Maladaptive Schemas (EMSs) (Young et al. 2003). There are studies reporting of a co-occurrence of EMSs with depression (Renner et al. 2012), chronic pain (Saariaho et al. 2011) and alexithymia (Lawson et al. 2008).

Depression is regarded as a mental disorder with several manifestations characterized by diminished or altered performance and both mental and somatic malaise. Its predisposing/risk factors include a wide range of life events and circumstances as well as personal health characteristics (Bottomley et al. 2010). Its origin has also been connected with traumatic experiences with insufficient adaptive psychological adjustment (Kinderman et al. 2013). A traumatic experience may be an abusive childhood or a bereavement, such as a death of a close person, unemployment or contracting a serious disease. Depression is a concomitant feature in several health related conditions (Moussavi et al. 2007) and is closely associated e.g. with chronic pain (Bair et al. 2003) and alexithymia (Honkalampi et al. 2000). Individuals with a high degree of active EMSs are often more depressive than individuals without active EMSs (Renner et al. 2012).

Chronic pain, alexithymia, EMS and depression are widely studied phenomena. Their important connecting factor is a history of childhood adversities which have probably predisposed to subsequent morbidity. They all include characteristics which appear to be similar or parallel and reflect problems in personal cognitive-emotional domains and coping skills. Globally, chronic pain is still mostly deemed as a biomedical problem and the majority of treatment interventions are based on that concept. However, there is growing evidence confirming the involvement of biopsychosocial individual factors in each patient's personal pain situation (Gatchel et al. 2007, Flor and Turk 2011a). In spite of decades of research concerning the

connection between alexithymia and chronic pain, the effect of alexithymia on pain conditions is not generally measured or evaluated in clinical situations in pain clinics (author's empirical observation, no research data available). Follow-up studies assessing alexithymia, chronic pain and depression are rare. Cross-sectional studies have shown that alexithymia and chronic pain are related to each other and alexithymia is related to depression but the prognostic value of alexithymia in chronic pain needs to be evaluated in a longitudinal study design.

2 REVIEW OF THE LITERATURE

2.1 Childhood maltreatment

"Time does not heal, time conceals" (Felitti 2009)

2.1.1 Childhood adversities and health

There is compelling research evidence that childhood adversities, physical and/or psychological abuse, any kind of neglect and maltreatment, have an influence on the development of the child and thus later on adult life (Cozolino 2006, Kessler et al. 2010). Research on the impact of early stress and adversities extends to psychology, neuroimaging, neuroendocrinology, genetics, epigenetics, immunology and epidemiology. The link between childhood negative experiences and subsequent outcome, especially various health related disorders, has been confirmed in numerous aspects of research (Felitti et al. 1998, Teicher et al. 2003, Anda et al. 2006, Pollak 2015). Early adversities have been found to be associated with dysfunction of the stress response system (Hunter et al. 2011), immunological responses (Fagundes et al. 2013), chronic depression (Klein et al. 2009), depressiveness (Korkeila et al. 2005) anxiety disorders (Spinhoven et al. 2010), chronic pain (Lampe et al. 2003, Sach-Ericsson et al. 2007, Stickley et al. 2015), alexithymia (Joukamaa et al. 2008, Aust et al. 2013) and eating disorders (Johnson et al. 2002) among others.

In a cross-sectional community survey of adults in ten countries, childhood adversities were associated with subsequent poor physical health (Scott et al. 2011). A large general population study of parental childhood physical abuse predicted poorer mental and physical health even decades after the abuse (Springer et al. 2007). There is evidence that the quality and quantity of the negative experiences are important factors determining outcome: A study exploring childhood experiences and depression showed that parental loss did not predict subsequent depression, but emotional neglect and any kind of abuse did (Hovens et al. 2012).

Most studies support the concept that early adversities are connected with health related consequences but not unanimously. The results depend on the study design selected (especially the method used to elicit the past adversities). A retrospective study of cancer patients found no differences in adversities between the patients and the controls (Korpimäki et al. 2010). Another population-based study (using different questions) found connections between adult cancer and childhood adversities and suggested that the risk for cancer was increased by early stress (Kelly-Irving et al. 2013). The discrepancy between the results of different studies may be understood by the different measures and designs used to demonstrate the link between childhood adversities and acquired health problems. Re-call of past events in self-report questionnaires varies, and cross-sectional epidemiological studies in particular may yield mixed results.

2.1.2 The mechanism of childhood maltreatment in health related disorders

In a review of childhood abuse and its relation to adult health problems (Sachs-Ericsson et al. 2009), the authors referred to several possible mechanisms through which childhood abuse increases the risk of poorer health outcomes: Childhood abuse survivors have been found to exhibit high-risk behaviours such as substance abuse, binge-eating, overweight, smoking, exercise avoidance, risky sexual behaviour, drunk driving. Abuse may cause also injuries, for example traumatic brain injury or sexually transmitted diseases. The review highlighted the impact of early adversities on the developing brain, concomitant psychiatric disorders with a range of problems such as low self-esteem, poor coping skills, disturbed self-identity, poor interpersonal skills, insecure attachment styles and increased vulnerability to stress. Childhood abuse works as a stress factor affecting the stress regulation system and immune functions (see 2.1.3 and 2.1.4). Maltreated children are prone to dysregulation of emotions and therefore also to subsequent health disorders (Alink et al. 2009). The consequences of early maltreatment may lead to vicious circles, for example childhood maltreatment is connected with insecure attachment styles and difficulties in healthy social relationships, causing a lack of social support which may predispose to mental problems (Cloitre et al. 2008). Social support has been found to be a protective factor for psychiatric disorders (Grav et al. 2012), especially depression, which in itself may restrict social functioning.

The adverse experiences during the vulnerable periods of the development and the maturation of the central nervous system give rise to neurobiological events, which can even produce enduring changes in the brain (Sullivan et al. 2006). These changes consist of structural, neurohumoral and functional components and are connected with subsequent negative health outcome, but also with emotional and cognitive disturbances (Teicher et al. 2003, Hart and Rubia 2012, Blanco et al. 2015). Epigenetics has become an important research area connecting genetic heritage with environmental factors. Animal studies have shown prenatal stress to cause long-term effects on the behavioural and neuroendocrine response to stressors (Darnaudéry and Maccari 2008). Early adversities act as environmental factors influencing genetic expression (Gudnsnuk and Champagne 2011) and increasing the risk for health disorders (Radtke et al. 2015, Romens et al. 2015).

2.1.3 Stress regulation system

The human stress system is based on complex neuronal and neuroendocrinological interactions and is modified by learning processes. The interpretation of a stimulus, if it is a threatening one, is primarily automatic but also a subject of learning by responsive conditioning. The amygdala receives a stressful stimulus and activates the stress response system, which entails the activation of the sympathetic nervous system, increased vigilance, avoidance behaviour and cortisol release. Via the stria terminalis the amygdala activates the hypothalamus and thus the important part of the stress response system called the hypothalamus-pituitary-adrenal (HPA) axis. The hypothalamus produces corticotrophin-releasing hormone (CRH), which causes the anterior pituitary to release adrenocorticotropic hormone (ACTH) and finally cortisol (a glucocorticoid) is released from the adrenal cortex in response to an elevated level of ACTH. Cortisol is responsible for several physiological changes which prepare for "fight-or-flight" responses including glucose metabolism, suppression of immune function and memory procedures. In normal acute stress situations, the stress response is controlled by glucocorticoid receptors in the hippocampus responding to the high circulating cortisol level, and as a feedback response suppressing the release of CRH. In the case of chronic stress, the stress regulation system becomes overloaded and cortisol production becomes inappropriate, with multiple consequences in the immune system and in neuroendocrinology. Experimental animal studies have shown that a continuous exposure to cortisol, as in the case of chronic stress, can cause neural loss in the

hippocampus. In human studies, patients with post-traumatic stress disorder have been found to have a decrease in the volume of the hippocampus (Bear et al. 2007a).

2.1.4 Neurobiological consequences of early stress

Human and animal studies have confirmed the connection between early stress and atypical functioning of the HPA-axis. Dysfunction of the HPA-axis manifests as inappropriately increased or decreased cortisol levels or as an abnormality in the diurnal fluctuation of cortisol level (van der Vegt et al. 2009). A study assessing cortisol response to stress tasks found patterns of dysregulation of the HPA axis in participants exposed to early life adversities. Those who had had early stress and had recurrent psychological distress during adulthood had impaired cortisol responses when compared with participants without early stress, while the participants with early stress but without or with only minimal psychological distress during adulthood showed elevated baseline cortisol level, greater cortisol production and prolonged responses to stress (Goldman-Mellor et al. 2012). A lower cortisol awakening response has been found in alexithymic individuals when compared with nonalexithymics. Furthermore, the values correlated negatively with perceived stress (Alkan Härtwig et al. 2013). Dysfunction of the HPA-axis is also connected with chronic pain (Mc Beth et al. 2007), depression (Heim et al. 2008) and post-traumatic stress disorder (Gunnar and Quevedo 2008).

Comparing major depressive patients and healthy controls, researchers found a decrease in the hippocampal volume of participants reporting childhood maltreatment irrespective of depression (Chaney et al. 2014). Healthy adults with or without a history of childhood maltreatment got a strong emotional stimulus (a threatening facial expression) to activate the amygdala response. The participants with childhood maltreatment had functional (limbic hyperresponsiveness) and structural (reduced hippocampal volume) changes in their brains (Dannlowski et al. 2012). Reduced hippocampal volume has been connected with a risk of developing stress related psychopathology (Gilbertson et al. 2002), memory dysfunctions and depression (Hickie et al. 2005) and dementia (den Heijer et al. 2010). A structural MRI study of hippocampus showed that in a general population sample maltreatment was connected with volume reductions in the hippocampal subfields proposed to be sensitive to neurogenesis suppression caused by stress exposure (Teicher et al. 2012). A review of the possible neurobiological consequences of

childhood maltreatment concluded that the research evidence shows a link between early stress and atypical HPA-axis functioning and between maltreatment and different structural and functional changes in the brain (McCrory et al. 2011). However, genetics may also influence individual differences in outcomes associated with maltreatment.

One mechanism of early maltreatment in subsequent health disorders has been suggested to be the dysregulation of immune response (Gonzalez 2013). Early adversity causes stress-induced autonomic and neuroendocrine activation and thus affects the immunological system (Fagundes et al. 2013). Abnormal immune responses have been found in alexithymic individuals (Lumley et al. 2007, Honkalampi et al. 2011). Immunological mechanisms have been suggested to contribute the development and maintenance of chronic pain (Maletic and Raison 2016, Zouikr et al. 2016) and depression (Cattaneo et al. 2015).

2.1.5 Early adversities and epigenetics

Epigenetics explores changes in gene expression due to the environmental, external factors which influence on the transcription of the genes – how the genetic code is "opened and read". Research in epigenetics has changed the previous formulation of a question "nature *or* nurture" in the development of the child to the new "nature *and* nurture" level. The functions of epigenetic mechanisms are regarded as adaptive processes between the individual and the environment. The term "adaptation" in this context must be understood in the neutral, biological meaning. Epigenetics provides the biological explanation for how the impact of early adversities is transferred to a physiological level, causing structural and functional changes which may predispose to and are connected with dysregulation of stress and immune response systems (Meaney and Ferguson-Smith 2010, Murgatroyd and Spengler 2011).

2.1.6 Victimization

The consequences of early adversities observed in psychological functions and operations are partly due to learning and partly due to adaptive processes. The psychological and social consequences are an important part of the impact of childhood maltreatment. In the early years the child in interactions with the environment learns the basic concepts of the self, the others and the world and

how to adapt and cope with the life situations (Beck et al. 1979, Young et al. 2003). In other words, the abused and maltreated child may develop a self-image of a poor self. The victim of maltreatment implicitly regards him/herself to be responsible for the victimization – "*I deserve to be abused because I am not good enough*" (Street et al. 2005). The result may be an individual who struggles to be good enough by achievements or alternatively becomes an abuser. In both cases, the self-esteem is low and the self is experienced as bad. Other consequences are problems in close relationships; the early maltreated person has difficulties in committing to and trusting others. As the abused child has learnt to be a victim, the victimization may continue in later life and the choice of partner may be based on earlier experiences (Murphy 2011). A systematic review of childhood maltreatment and psychological adjustment showed that exposure to maltreatment had negative effects on self-esteem, peer relationships, academic performance and social competence (Pacheco et al. 2014).

2.1.7 Developmental trauma disorder

Childhood interpersonal trauma refers to the outcome of physical, sexual or psychological abuse and any kind of neglect caused by other people, especially parents or significant others. The symptoms of this trauma have been suggested to occur in five domains: 1. affect and impulse dysregulation, 2. disturbances in attention, cognition and consciousness, 3. distortions in self-perception and systems of meaning, 4. interpersonal difficulties and 5. somatization and biological dysregulation. The severity and occurrence of symptoms vary between traumatized individuals. It has been suggested that the combination of symptoms be called developmental trauma disorder (van der Kolk and d'Andrea 2010).

A child will confront numerous negative experiences causing stress reactions during the growth period. It is impossible to bring up a child without sad events, losses, trauma, health problems or other negative experiences. However, the crucial factor, how these experiences affect the child, is the quality of close interpersonal relationships which may save or disturb the child. An example of the importance of supporting and comforting role of parents: preterm infants during a heel lance got pain relief with the method called for "facilitated tucking by parents" – so a comforting mother during the painful procedure diminished the stress reaction (Axelin 2010). The absence of the mother is associated with more pain and fear and may have an effect on the developing stress system. Childhood trauma is not

visible in adulthood, but is masked in many forms of ill-being, affective and somatic disorders and behaviour styles and often forgotten in clinical situations.

2.2 Early Maladaptive Schemas

2.2.1 The schema concept

The term "schema" originates from Greek and is defined as "a diagrammatic presentation, a structured framework or plan and a mental codification of experience that includes a particular organized way of perceiving cognitively and responding to a complex situation or set of stimuli" (Merriam-Webster 2016). The term has been widely used in psychology starting with Piaget (1947), who used it to explain the cognitive development of the child and later in cognitive therapy (Beck 1964, Young et al. 2003) to describe the cognitive and emotional patterns of the human mind. In the following section the development of schemas as results of learning is illustrated (by the author) with examples based on the theories of Piaget, Beck and Young:

> *The nature of the learning human brain is to organize and categorize life experiences and to form patterns, models and concepts which help to interpret new experiences which will be assimilated to existing models, patterns and concepts which will be enriched and modified. The quality, emotional colour and context of experiences and their recurrence adjust their effectiveness as well as the individual personality, intelligence and temperament. This learning process happens in the reciprocal and interpersonal context and consists of cognitions, emotions and behavioural responses. Two different simplified examples illustrate this process: An infant sees a lamp, points it and the caring mother gives the answer "it is a lamp, my sweetheart", this lamp episode will be repeated hundreds of times with different lamps and finally builds the category "lamps", which will be used lifelong to recognize a certain type of object as belonging to the "lamp category", even a unique design lamp never seen before. The second, more complicated example: A child is brought up by abusive and neglecting adults and experiences daily fear and violence and builds a category "close relationships are frightening and unsafe" and in future relationships closeness may be avoided as it is categorized as a dangerous matter. The categorization builds schemas which are understood as internal "keys" to conceptualize and to guide coping with different life situations.*

A schema is reinforced by repeated learning, is triggered automatically and encodes the event accordingly. Schemas represent the economic and ecological side of conscious processes as they help to create a rapid situation analysis with its emotional colour and coping style. However, schema driven observations and interpretations may be misleading as the new situation is not necessarily a repetition of the past.

2.2.2 Concept and origin of Early Maladaptive Schemas

Schematherapy is based on the hypothesis that toxic childhood experiences produce schemas which reflect the developmental circumstances and predispose to later psychological disturbances, especially to personality disorders. These schemas are called Early Maladaptive Schemas (EMSs) and defined as "*a broad, pervasive theme or pattern; comprised of memories, emotions, cognitions, and bodily sensations; regarding oneself and one's relationships with others; developed during childhood or adolescence; elaborated throughout one's lifetime; dysfunctional to a significant degree*" (Young et al. 2003). EMSs describe the internal models organizing thoughts, emotions and interpretations of life events. According to the theory of schema therapy, EMSs are consequences of childhood adversities and form a core theme for personality disorders (Young et al. 2003, Carr and Francis 2010). EMSs exert influence over various other psychiatric maladies (Young et al. 2003, Nordahl et al. 2005) and over psychological problems such as interpersonal problems (Thimm 2013).

According to schematherapy theory, based on empirical work, there are now eighteen different schemas in five main domains, each describing and representing a specific part of "unmet emotional needs" of the child and reflecting rearing circumstances and parenting styles (Table 1). Unconditional schemas represent developmentally early structures and conditional schemas are considered "adaptive" trials to cope with unconditional schemas.

Table 1. Schema domains, their descriptions and early maladaptive schemas (Young et al. 2003)

Schema domain	Description	Early Maladaptive Schema
Disconnection and rejection	The belief that one's needs for security, safety, stability, nurturance, empathy, sharing of feelings, acceptance or respect will not be met.	Abandonment/Instability* Mistrust/Abuse* Emotional Deprivation* Defectiveness/Shame* Social Isolation/Alienation*
Impaired autonomy and performance	The belief that one's ability and capacity to separate, survive, cope independently or perform successfully is impaired.	Dependence/Incompetence* Vulnerability to Harm or Illness* Enmeshment/Underdeveloped Self* Failure*
Impaired limits	Difficulties in setting internal limits, feel responsibility or set long-term goals.	Entitlement/Grandiosity* Insufficient Self-Control/Self-Discipline*
Other-directedness	The needs, desires or responses of others are over respected and taken into account at the expense of one's own needs.	Subjugation** Self-Sacrifice** Approval-Seeking/Recognition-Seeking**
Overvigilance and inhibition	The spontaneous feelings and impulses are suppressed and replaced by rigid, internalized rules about performance and behaviour.	Negativity/Pessimism* Emotional Inhibition** Unrelenting Standards/Hypercriticalness** Punitiveness*

*Unconditional schema, **Conditional schema

Earlier research has shown the co-occurrence of EMSs and adverse childhood experiences and their impact on later problems. In depressive adolescents, the relation between childhood adversity and anhedonic symptoms was mediated by loss or worthlessness presenting schemas while schemas connected with catastrophes and fears mediated the relation between anxious symptoms and childhood adversities (Lumley and Harkness 2007). Maladaptive interpersonal styles and childhood traumatic experiences were associated and the relation was mediated by EMSs (Tezel et al. 2015). A study of college students found that the connection between childhood emotional maltreatment and later symptoms of anxiety and depression was mediated by certain EMSs, namely Vulnerability to Harm, Defectiveness/Shame and Self-Sacrifice schemas (Wright et al. 2009). A longitudinal study showed that insecure childhood and adult attachment styles were associated with EMSs (Simard et al. 2011). A cross-sectional study on undergraduates found relations between EMSs and attachment avoidance and anxiety (McLean et al. 2014).

2.2.3 Early Maladaptive Schemas and health disorders

EMSs were initially recognized and identified in patients with personality disorders (PD) and schematherapy was planned for their treatment (Young 1990). EMSs and

schema driven beliefs and behaviour have also been observed in various disorders such as depression, posttraumatic stress disorder, eating disorders, substance abuse, alexithymia and chronic pain.

Different types of personality disorders have been found to be related to specific schema representations, e.g. narcissistic PD was positively associated with Impaired Limits schema domain and negatively with Other Directedness schema domain while paranoid PD was associated with Disconnection and Rejection and Impaired Autonomy and Performance schema domains (Corral and Calvete 2014). In a clinical study, borderline personality disorder (BPD) patients scored high on Dependence/Incompetence, Defectiveness/Shame and Abandonment schemas, obsessive-compulsive PD patients had high scores on Unrelenting Standards schema domain and avoidant PD patients showed most activity in Emotional Inhibition schema domain (Jovev and Jackson 2004). According to a review exploring the relations between BPD and EMSs, BPD was associated with schemas of Disconnection/Rejection schema domain (Barazandeh et al. 2016).

EMSs are connected with susceptibility to depression. Depressive patients and even formerly depressed patients scored more on EMSs than did never depressed individuals, and severity of depression was related to certain schemas (Halvorsen et al. 2009). A clinical follow-up study of depressive patients concluded that EMSs are significant vulnerability markers for depressiveness (Wang et al. 2010). Stability of EMSs was found in a study of depressive patients, even after evidence-based depression treatment. In the same study the authors found that depression symptom severity was related to specific schema domains, namely the Impaired Autonomy and Performance domain and the Disconnection and Rejection domain (Renner et al. 2005) but the treatment intervention for depression was not schema focused. A study of suicidal adolescents concluded that tendency to attempt suicide was based on the interactive dysfunctional psychological factors; EMSs which were associated with depression, hopelessness and alexithymia (Hirsch et al. 2001).

Posttraumatic stress disorder (PTSD) was connected with EMSs (and alexithymia) in adult women with a history of childhood sexual abuse (Zlotnick et al. 1996). Vietnam War veterans with PTSD had higher EMSs than veterans without PTSD (Cockram et al. 2010). In the same study, schema focused psychotherapy was found to be more effective for PTDS symptoms and anxiety, and those veterans who had EMSs and got schematherapy moreover recovered better than those with EMSs and no schematherapy. Schematherapy also helped to reduce the EMSs.

Eating disorders have been found to be associated with EMS (Anderson et al. 2006, Unoka et al. 2010) as also have addiction disorders (Shorey et al. 2013). Substance abusers with eating disorder scored higher on EMSs than users without eating disorder (Elmqvist et al. 2015). This may reflect multiple childhood adversities with more difficulties to control negative emotions and cognitions. In a study investigating EMSs in treatment-seeking obese adults with normal-weight controls found that obese patients had overall more EMSs than the controls, but also more mood disturbances (Anderson et al. 2006).

There are few studies connecting alexithymia and EMSs. A study investigating alexithymia and core beliefs (EMSs) among a sample of women with eating disorders showed that alexithymia factor difficulties identifying feelings (DIF) was associated with Entitlement schema and alexithymia factor difficulties describing feelings (DDF) was associated with Abandonment and Emotional Inhibition schemas (Lawson et al. 2008). Defectiveness/Shame and Entitlement/Grandiosity schemas and alexithymia factors DIF and DDF were found to have predictive value in irritable bowel syndrome (Phillips et al. 2013). The concept of psychological mindedness (PM) and its measurement by a self-report questionnaire or a clinical interview has been used to evaluate healthy personality constructs. A study exploring college adjustment by PM and EMSs belonging to the Disconnection and Rejection schema domain found that EMSs were inversely associated with both college adjustment and PM (Cecero et al. 2008). Earlier it has been found that PM scores were negatively correlated with alexithymia (Shill and Lumley 2002).

Chronic pain is associated with EMSs, a study measuring EMSs showed that almost 60% of chronic pain patients had meaningful EMSs and those having EMSs had greater pain and disability and that schema driven behaviour exacerbated the pain situation (Saariaho et al. 2010). Chronic pain patients scored higher on EMSs (incapacity to perform independently, catastrophic beliefs and pessimism) than the controls, and the most disabled patients had higher scores on EMSs belonging to the Disconnection and Rejection schema domain (Saariaho et al. 2011). The patients also differed from the controls in higher order schema factors and their schema factor showing defectiveness, shame, social isolation, failure, emotional inhibition and deprivation was associated with depressiveness (Saariaho et al. 2012a). Early maladaptive schema factors predicted depressiveness among chronic pain patients, and depressiveness predicted pain disability more than pain intensity when pain duration was over two years (Saariaho et al. 2012b).

2.3 Alexithymia

Alexithymia refers to a personality construct involving a deficit in emotional processing (Bagby and Taylor 1997a) which may predispose to health disorders or then its co-occurrence has an impact on the course of the illness. In a Finnish general population study the prevalence of alexithymia was 9.9% - men 11.9% and women 8.1% (Mattila et al. 2006). There was a difference between age groups, in the youngest group the prevalence was 2.7% and in oldest group 28.8%. In Finnish adolescents, 9.5% of girls and 6.9% of boys were alexithymic (Joukamaa et al. 2007). Another study found a prevalence rate of alexithymia of 7.3% among adolescents (Honkalampi et al. 2009). Elevated prevalence rates of alexithymia have been observed in several health disorders (see 2.3.5).

2.3.1 The concept of alexithymia

2.3.1.1 History of the alexithymia concept

The development of the alexithymia concept (Timoney and Holder 2013): The features, which now are generally regarded as alexithymic characteristics, have long been recognized in the clinical observations of psychosomatic medicine and psychiatry. The development of symptoms and characteristics of psychosomatic patients were mainly explained by the psychoanalytic framework. In 1948 Ruesch classified psychosomatic patients with poor ability to recognize and describe their emotional arousals and states, as "infantile personalities". More observations were made among psychiatric patients with no emotional awareness and they were deemed "emotional illiterates" (Freedman and Sweet 1954). The concept of "la pensée opératoire" (M'Uzan 1974) was use to refer to the pragmatic mental style of psychosomatic patients. These early findings and clinical observations of psychosomatic patients and their inability to find words to describe their feelings led Sifneos (1973) to conduct a study on 25 psychosomatic patients with controls. The results showed that a majority of psychosomatic patients had "*marked constriction in experiencing emotions*" with less fantasy life and difficulties in describing their emotions. These characteristics were coined by Sifneos, as he expressed it in his study abstract: "*For lack of a better term, I call these characteristics 'alexithymic'*", borrowing the word from Greek (Sifneos was a Greek). Literally alexithymia means

"no words for feelings", and since 1973 the term alexithymia has become established.

2.3.1.2 Characteristics and properties of the alexithymia concept

The well-known and scientifically accepted definition of alexithymia according to its characteristics consists of the following typical attributes: difficulties identifying feelings and their bodily felt sensations, difficulties describing feelings, externally oriented cognitive style and limited capacity for imagination (Bagby and Taylor 1997a, Lumley et al. 2007). Additionally, many alexithymic individuals are described as anhedonic, i.e. showing vague negative affectivity and lacking joy and happiness (Bagby and Taylor 1997a). Poor empathizing ability has been considered to be a part of emotional dysfunction in alexithymic individuals (Moriguchi et al. 2007, Messina et al. 2014). The psychopathological definition of alexithymia refers to its developmental origin as "*a deficit in the cognitive-experiential domain of emotion response systems*" (Parker et al. 1997). Impaired emotion recognition ability measured by the Perception of Affect Task, which covers seven emotions; happiness, sadness, fear, anger, surprise, disgust and neutral, was documented in alexithymic participants in all tested items (Lane et al. 2000).

Alexithymic individuals may vary in their personal mode "of being alexithymic". An interesting cluster analysis study by Chen et al. (2011) using the alexithymia factors of the 20-item Toronto Alexithymia Scale (TAS-20, see 2.3.3.2), namely difficulties identifying feelings (DIF), difficulties describing feelings (DDF) and externally oriented thinking style (EOT), to distinguish subtypes of alexithymia, found four different groups: extrovert-high alexithymia, general-high alexithymia, introvert-high alexithymia and non-alexithymia groups. The groups differed from each other in emotional status, emotional expression and regulation. Latent profile analysis exploring different facets of alexithymia among alexithymic adults showed three different clusters: "low" having lower loading on all facets, "mixed" with a pronounced facet in identifying feelings and "high" with high loadings on all facets. The psychological distress differed between the groups; "mixed" profile being most linked with distress (Alkan Härtwig et al. 2014).

The terms primary and secondary alexithymia refer to the proposed aetiology (Freyberger 1977). Primary alexithymia is regarded as a disposition based on biological mechanisms ("inborn alexithymia") and secondary alexithymia has developed as a consequence of a stressful situation caused by a traumatic experience like chronic illness predisposing to the dysfunction of the emotional

regulation. There is substantial research evidence to suggest that traumatic events in later life may induce alexithymia. Patients suffering from posttraumatic stress disorder have been found to have alexithymic features (Badura 2003), but it is difficult to establish whether or not the patient has initially been alexithymic. Brain injury may result in alexithymia and it has been suggested that the term "organic alexithymia" should be used when alexithymia occurs after brain injury (Messina et al. 2014).

Alexithymia is a dimensional construct, thus people may be more or less alexithymic, and its individual grade and severity may vary to some extent. Depression has an influence on alexithymia causing a fluctuation in its severity (Honkalampi et al. 2001). The variation in the level of alexithymia has caused scientific debate between "state or personal trait"-assumptions concerning the stability and origin of alexithymia. In a sample of pregnant women, alexithymia did not predict depression and subjects' of TAS-20 scores increased with depression and decreased after recovery, supporting the notion of alexithymia being a state-dependent phenomenon (Marchesi et al. 2008). In a 4-year follow-up study on adolescents mean scores on the TAS-20 and its factors showed a mixed variation in decrease and stability in the whole sample, in females and in males. As the effect sizes of statistically significant changes remained low and correlations between baseline and follow-up were large in size, the authors concluded that the results supported the concept of the relative stability of alexithymia (Karukivi et al. 2014). A large general population follow-up study showed that stability of TAS-20 scores over a 10-year period and depression or anxiety disorders had no predictive value for alexithymia scores at follow-up (Hiirola et al. 2015).

The most popular conclusions of research favour the relative stability of alexithymia (Parker et. al 1991, Luminet et al. 2001, Tolmunen et al. 2011, de Haan et al. 2012, Karukivi et al. 2014). However, alexithymic individuals in appropriate psychotherapy are capable of learning to recognize their feelings and to improve their emotional skills (Samur et al. 2013), which challenges the concept of stability. The neuroplastic properties of the central nervous system support and afford opportunities for learning emotional knowledge.

The independence of the alexithymia construct has also been criticized. Lack of emotional expression and emotional numbness have been connected with an individual's defence system using repression, denial, inhibition or avoidance as a method to cope with painful or traumatic emotions. A study on combat veterans examining similarities between the numbing symptoms of posttraumatic stress disorder (PTSD) and alexithymia found significant positive correlations between

measures of PTSD, alexithymia and combat exposure, and according to the principal components analysis there was a lack of independence between PTSD subscale and alexithymia. The author therefore concluded that alexithymia is a matter of emotional numbing, not a distinct construct (Badura 2003). Defensive processes bear a superficial resemblance with alexithymic features but the difference between defensive mechanisms and alexithymia lies in the dynamics; defensive processes are active procedures reducing emotionally painful experiences and alexithymia is a passive inability to recognize emotional states (Lumley et al. 2007). High correlations between alexithymia and depression measures have generated a logical suspicion as to whether they are distinct or overlapping constructs. Two studies using factor analyses with the items of both alexithymia (TAS) and depression (BDI) scales found that the factor loadings corresponded to the distinct constructs between the scales (Parker et al. 1991). In a general population factor analysis study alexithymia (TAS-20) and depression (BDI-21) appeared as different constructs in nonalexithymic, nondepressive subjects but in alexithymic, depressive subjects item loadings were overlapping (Hintikka et al. 2001). The relations between alexithymia (TAS-20), depression (BDI-II), dissociation (the Dissociative Experiences Scale) and somatization (somatization part of Symptom Check List-90) were explored using principal component analysis. The results suggested that in spite of considerable correlations between the study objects, they nevertheless represent distinct constructs (Lipsanen et al. 2004).

2.3.2 Origin of alexithymia

2.3.2.1 Childhood adversities and insecure attachment

According to the main theory of the origin of alexithymia, the deficit in emotional processing emerges from the childhood growth environment consisting of elements which disrupt healthy emotional maturation. The caregivers are emotionally unavailable or misleading in interactions crucial for learning the conceptualization, expression and regulation of affective states (Bagby and Taylor 1997a) and the child has neither opportunities nor support to learn to describe and to express emotional states in an appropriate and adaptive manner. The insecure attachment styles found in alexithymic individuals reflect a growth environment without sufficient emotional guidance (Troisi et al. 2001). Interactions with caregivers may be abusive, emotionally neglectful or absent or otherwise negative

and thus produce insecure attachment styles. Several studies have shown the connections between alexithymia and childhood adversities (Honkalampi et al. 2004, Joukamaa et al. 2008, Pedrosa et al. 2008, Carpenter and Chung 2011, Aust et al. 2013). Higher scores on TAS-20 and especially on DIF were associated with a greater number of types of childhood adversities in substance dependent patients (Evren et al. 2009). Alexithymia mediated the relation between emotional maltreatment in childhood and subsequent somatic complaints in a sample of undergraduates (Smith and Flannery-Schroeder 2013). Maternal overprotection, which is not usually defined as maltreatment but may impede normal emotional maturation, was associated with TAS-20 total score and factors DIF and DDF have been observed in late adolescents (Karukivi et al. 2011).

2.3.2.2 Developmental deficiencies

It has been observed that children with congenital cardiac malformations have psychosocial, alexithymic features (Bellinger 2008) embodied in verbal performances (as storytelling) and communication (Bellinger 2010). Inadequate speech development documented at the age of five years predicted alexithymia in males in adolescence (Karukivi et al. 2012). In an earlier study, early speakers, examined by the extent of vocabulary at the age of one year, scored lowest on the alexithymia scale (TAS-20) at the age of 31 years (Kokkonen et al. 2003). However, impairment of cognitive function in language found in adult fibromyalgia patients was associated with history of childhood abuse (Ortiz et al. 2016).

Alexithymic individuals have several physiological and neuroanatomical alterations (see 2.3.4). Their impact on the developmental origin of alexithymia is unclear – for example early adversities have consequences established in the brain structure, stress and immunological systems (see 2.1.3 - 2.1.5). The vulnerability of the developing nervous system and neuroplasticity may lead to findings which now are connected with alexithymia and which may also be a part of the health problems associated with alexithymia.

2.3.2.3 Genetics

Genetic influence on alexithymia has mainly been investigated by general population twin studies (Valera and Berenbaum 2001, Jørgensen et al. 2007, Picardi et al. 2011). Other mental health factors such as depression or anxiety associated

with alexithymia may confound the results. An Italian twin study found that heredity accounted for 42% of alexithymia. However, when depression was included in the genetic structural equation model, the share of genetic factors in alexithymia was 33% and unshared environmental factors accounted for most of the variation (Picardi et al. 2011). The results of Jörgensen et al. (2007) are parallel, but in the study by Valera and Berenbaum (2001), only alexithymia factor EOT was linked with genetics.

2.3.3 Assessing alexithymia

Alexithymia, like other human psychological characteristics, is difficult to measure objectively. Several different methods have been developed, and the questions of the validity of measure criteria and overlapping phenomena with controversial research findings confuse the reliability of assessments. A projection scale, observation scales, self-rating scales and scales for children and adolescents are in use for screening for alexithymia in clinical and research purposes.

2.3.3.1 Interview and observation methods

The original method for evaluating alexithymic features was a clinical interview and the determination of the presence or absence of alexithymia was made by the interviewer. The method needs an experienced interviewer, the results are difficult to compare and it is time consuming. The interview method is best for a single patient in the clinical situation. Typically the patient has a lot of somatic complaints which he/she describes in detail (even to the extent of being boring) but the answers concerning his/her feelings are brief detached phrases. The lack of emotional expressions makes his/her story sound like a technical description of a machine. In the clinical interview it is possible to get a diagnostic impression of the possibility of alexithymia but this method lacks specific criteria, psychometric properties and the replicability needed for diagnostic confidence and research work (Lumley et al. 2007).

The first alexithymia scale was the Beth Israel Hospital Psychosomatic Questionnaire (BIQ), generated by Sifneos (1973). This is a structural observation scale consisting of questions intended to evaluate the impressions of the interviewer about the observations of the patient. The interviewer rates his/her opinions dichotomously as no or yes answers and then the scores are calculated.

The advantage of the method is that the interviewers have to focus on similar elements and the disadvantage is the subjective rating depending on the interviewer. The problems of low inter-rater reliabilities of BIQ caused a need to modify the scale. The new scale, the Modified Beth Israel Questionnaire (M-BIQ) had additional items, and the rating style has been changed to a seven-point Likert-type scale (Bagby and Taylor, 1997b). The reliability and the validity of M-BIQ have been confirmed to be adequate.

The California Q-set Alexithymia Prototype (Haviland and Reise 1996) is an observation scale, mainly for professional use, and it has a brief "layman version" Observer Alexithymia Scale (OAS) which has been confirmed to assess "clinically relevant expressions of alexithymia" from an observer point of view. The observer may be a family member, a friend or a therapist. The scale has a five-factor structure divided into easily identified characteristics: distant, uninsightful, somatizing, humourless and rigid, which have been estimated to belong to alexithymic personality (Haviland et al. 2000). OAS total score correlates moderately and significantly with two other alexithymia scales; TAS-20 and BVAQ (Berthoz et al. 2007).

The Toronto Structured Interview for Alexithymia (TSIA) is a semi-structural interview method which has shown an acceptable level of reliability and a modest and significant correlation with TAS-20 score (Bagby et al. 2006).

The benefit of interview and observation based methods to assess alexithymia is the lack of respondent bias and the aim of an objective method; on the other hand, the result depends on the interviewer's ability to observe diagnostic criteria, and altogether, interviews are time consuming, which restricts their effective use. In Finnish language, no official psychometric evaluation has been performed for the observation and interview based alexithymia assessment methods.

The Rorschach Alexithymia Scale (RAS) is a projection scale developed for estimating alexithymia scores (Porcelli and Mihura 2010). However, the interpretation needs lot of experience, the overall reliability of Rorschach tests has been questioned, and finally, the RAS does not provide any benefits when compared with the TAS-20.

2.3.3.2 Self-report questionnaires

The Toronto Alexithymia Scale (TAS) is a self-report questionnaire. A 26-item scale was first developed (Taylor et al. 1985). A modified Finnish version has been validated and used in alexithymia research (Kauhanen et al. 1991 and 1992). The

original TAS was later modified and followed by the most used version of TAS, with twenty items, the TAS-20. It has been scrutinized for psychometric research and according to the results, the scale demonstrates good internal consistency, test-retest reliability and validity (Bagby et al. 1994a, Bagby et al. 1994b, Parker et al. 2003, Taylor et al. 2003). The scale comprises three subscales representing three main facets of alexithymia. The subscales are difficulties identifying feelings (DIF, seven items), difficulties describing feelings (DDF, five items) and externally oriented thinking style (EOT, eight items). The interpretation of the scale is simple: higher score represents a higher degree of alexithymia, but there are also cut-off points for categorical use. The recommended cut-off points used in research and clinical practice are as follows: score 20-51 means no alexithymia; 52-60 is borderline/moderate alexithymia and score over 60 means alexithymia (Bagby and Taylor 1997b). TAS-20 score is widely used in research work and the questionnaire has been translated into several languages with confirmation of its psychometric properties. The Finnish version of TAS-20 is validated and has been found to have reliable psychometric properties (Joukamaa et al. 2001). TAS-20 has become "a gold standard" in measuring alexithymia, and is probably the most used alexithymia assessment tool in research. However, TAS-20 lacks items on restricted fantasy.

The Amsterdam Alexithymia Scale, later better known as the Bermond-Vorst Alexithymia Questionnaire (BVAQ) is a self-report questionnaire consisting of five subscales (inability to differentiate between emotions, inability to verbalize emotions, inability to analyse emotions, inability to fantasize and inability to experience emotions). These five subscales according to the higher order factor analyses have two higher dimensions called an alexithymia cognitive factor and an alexithymia affective factor. The interpretation of the BVAQ is at the subscale level. The BVAQ correlates modestly with the TAS-20 and its psychometric properties have been shown to be reliable and valid (Vorst and Bermond 2001). There is no validated Finnish version of the BAQ.

2.3.3.3 Assessment problems and possibilities

The problem of different types of alexithymia assessments is uncovered when they are compared with each other – the correlations between different scales may be low or modest (Zech et al. 1999, Morera et al. 2005) and lead to uncertainty concerning the validity of measures. However, a psychological study design is difficult to build up to resemble laboratory conditions and the presence of confounding (and missing) factors is notable. The current state of comparability

favours the use of the TAS-20 as it is the most widely validated and has shown factorial stability across cultures and languages, although there is criticism concerning its subscales, especially EOT, which does not always show good psychometric properties (Kooiman et al. 2002).

It has also been suggested that alexithymic features should be measured and compared with an "opposite" scale to estimate emotional awareness. The Level of Emotional Awareness Scale (LEAS, Lane et al. 1990) may be helpful. Unfortunately, the psychometric properties of the LEAS were found not to correlate with those of the TAS-20 (Waller and Scheidt 2004).

The results of neuroimaging studies have shown various structural differences in the brains of alexithymic people (see 2.3.4.1). In a voxel-based morphometry the study participants had neuroanatomical differences in brain mapping according to their alexithymia subtypes (Goerlich-Dobre et al. 2015). However, the samples have been small and the study designs varied, and repeated comparisons made with non-alexithymic persons are lacking. In explorative laboratory conditions alexithymic and nonalexithymic individuals have been found to have different responses to emotional stimuli in functional brain imaging (Karlsson et al. 2008). In the future, neuroimaging with machine learning technique could become a possibility to assess alexithymia in a biometrically objective manner.

2.3.4 Alexithymia in biomedical findings

2.3.4.1 Neurological studies

The neurological base of alexithymia has been proposed to lie in dysfunctional activity of the brain hemispheres – diminished right side activity and salient left side activity with or without interhemispheric transfer deficit (Parker and Taylor 1997). However, transfer deficit has remained without proof as there are controversial results – alexithymia has been connected to facilated transcallosal inhibition (Grabe et al. 2004) and reduced transcallosal inhibition (Romei et al. 2008). The current research interest is focused more on emotion processing areas of the brain, not in differences in hemisphere functions.

Neuroimaging techniques have been used in exploring if there are morphological and/or functional differences between alexithymic and nonalexithymic individuals. Alexithymia is mainly measured by TAS-20 total score. Several brain imaging studies have found differences between alexithymic and

nonalexithymic persons in the experimental circumstances - the usual procedure is to show pictures or films which may arouse specific emotional and/ or cognitive states and then appraise the activation in different brain areas.

The anterior cingulated cortex has an important task in affect regulation and a voxel-based morphometry study of 54 female volunteers revealed that participants with TAS-20 score > 60 (n=14), had smaller grey matter volume in the anterior cingulate cortex (Borsci et al. 2009). The same type of study of 33 high alexithymic and 31 low alexithymic (according to the TAS-20 score) healthy right-handed males did not show any morphological differences between the groups explored (Heinzel et al. 2012).

Fear is a strong feeling and the amygdala and premotor cortex are activated when a fearful stimulus is observed and these brain areas prepare for an adaptive response. In an experimental study healthy right-handed men (13 high and 12 low alexithymic participants) observed fearful body expressions and fMRI was performed. The authors found that right amygdala activity (a response to fearful stimuli) correlated negatively with DIF, activity in the anterior cingulate cortex was greater in high alexithymic participants and premotor cortex activity was connected with reduced subjective emotional reactivity. The differences were explained by overregulation of emotional state among high alexithymic individuals (Pouga et al. 2010). An emotional stimulus (sad, neutral, amusing films) administrated to alexithymic and non-alexithymic healthy women provoked different activation modes between the groups, the alexithymic participants having more activation in sensory and motor cortices (Karlsson et al. 2008). An fMRI study of emotion perception and emotion regulation in healthy participants showed that alexithymia was correlated with lower activation in emotional attention and recognition networks, but no difference from nonalexithymic participants was found in emotion regulation areas (van der Welde et al. 2015).

Kano and Fukudo (2013) proposed that the link between alexithymia and physical disorders is based on lower reactivity of emotional brain regions in alexithymic individuals, meaning a lack of adaptive emotional processes to cope with different (physiological) stimuli. Instead of that, alexithymics show pronounced activation in somatosensory brain areas. In the case of visceral pain, there was hyperactivity in the visceral perception areas but hypoactivity in pain processing areas. The authors suggested that deficiency of emotional regulation causes hypersensitivity to unpleasant painful bodily sensations and pain related distress. A study of the connectivity of the default mode network of brain areas showed differences between alexithymic and nonalexithymic healthy volunteers,

alexithymics having diminished connectivity in those brain areas suggested to be involved in emotional awareness and self-referential processing, and higher connectivity in areas associated with emotional suppression and a more action-oriented focus (Liemburg et al. 2012).

In a study using triangle animation (a theory of mind task) and neuroimaging, alexithymic individuals showed hypoactivity in the right medial prefrontal cortex which was related to impairment in taking a perspective different from self and thus, in understanding the mental states of self and others (Moriguchi et al. 2006).

A review of neuroimaging studies on alexithymia summarized that alexithymia is related to reduced neural responses to external affective stimuli in the limbic and paralimbic systems, in the posterior cingulate cortex during an imaginary task, reduced activation in the medial prefrontal cortex when engaged in cognitive processes needed for social tasks and increased neural response to stimuli having somatosensory or sensorimotor processes. The authors concluded that neuroimaging studies support the characteristics of alexithymia (Moriguchi and Komaki 2013).

2.3.4.2 Immunological studies

Stress induces immunological changes (Segerstrom and Miller 2004). Immunological consequences have been found to be associated with early stress and possibly predispose to depression (Cattaneo et al. 2015). Emotions and immunity have a bi-directional relation (Brod et al. 2014). Poor ability to deal with negative emotions may indirectly contribute to immune dysregulation; coping styles such as denial or repression are connected with altered immunity (Kiecolt-Glaser et al. 2002). In repeated studies inflammatory markers have been associated with depression (Valkanova et al. 2013). These findings among others have given indirect evidence that alexithymia, too, may be connected with immunological alterations.

It has been proposed that immunological findings (cytokine imbalance) observed in alexithymic subjects refer to a situation similar to chronic stress (Guilbaud et al. 2003). Previously it was found that alexithymic individuals' dexamethasone suppression tests were positive indicating dysregulation in the stress system (Lindholm et al. 1990) but the number of alexithymic test participants was low. Alexithymic men showed impaired cellular immunity when compared with nonalexithymic men (Dewaraja et al. 1997). A study with healthy females found a positive association between alexithymia and inflammatory marker

interleukin-4 (Corcos et al. 2004). Depressed cell-mediated immunity was found in alexithymic women (Guilbaud et al. 2009). In a general population study, the levels of inflammatory markers (high-sensitivity C-reactive protein and interleukin-6) were higher in alexithymic subjects, and according to logistic regression analysis, elevated hs-CRP predicted alexithymia (Honkalampi et al. 2011). However, a clinical study (patients referred for upper endoscopy), alexithymia predicted lower levels of interleukin-4 and -6 (Mandarelli et al. 2011). Alexithymic subjects have been shown to have lower levels of adiponectin (which has an anti-inflammatory effect) than their nonalexithymic controls (Honkalampi et al. 2014). Alexithymia has also been found to be associated with autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematous (Vadacca et al. 2014). A review of studies on alexithymia and immunological markers concluded that the studies suggest significant relations between stress, alexithymia and immunological dysregulation (Uher 2010).

2.3.4.3 Physiological responses

Alexithymia has been found to be associated with sympathetic overactivity or inappropriate sympathetic function (Martin 1986, Fukunishi et al. 1999) and with a tendency to hypertension (Jula et al. 1999). Alexithymic individuals have been found to have higher pulse rate, higher electrodermal activity and lower oxygen consumption during normal or resting periods but during the acute stress, alexithymic individuals show unchanged sympathetic activity or at least lower state than nonalexithymic individuals (Lumley et al. 2007). However, no recent studies are available on differences in physiological responses *per se* between alexithymic and nonalexithymic individuals.

More recent studies have measured and compared stress responses between alexithymic and nonalexithymic subjects. An experimental study measuring cortisol release before and during social stress test found that alexithymia (especially factor DDF) was associated with higher basal anticipatory level of cortisol but not with the cortisol values during the test (de Timary et al. 2008). Another social stress study showed that both before and during the test alexithymic participants had higher cortisol values than nonalexithymic participants and that the result was mainly related to alexithymia factor DDF (Hua et al. 2014). Hyperarousal (a sign of overactivity of the sympathetic nervous system) was connected with alexithymia and its factor DIF in a clinical study on posttraumatic distress (Declercq et al. 2010).

2.3.5 Alexithymia and health related disorders

The characteristics of alexithymia have attracted scholarly attention and its prevalence and influence have been explored in several somatic and psychiatric disorders and diseases. Some examples of these studies are described in this chapter, but pain and alexithymia (see 2.5) as well as depression and alexithymia are addressed separately (see 2.3.6).

Alexithymia is overrepresented in psychiatric samples and has its own impact on different mental disorders. A Korean study (Son et al. 2012) showed notable proportions of alexithymia in patients with depressive, somatoform, anxiety or psychotic disorders (42.2%, 35.9%, 33.3% and 35.3% respectively). In a psychiatric out-patient sample, posttraumatic stress disorder and borderline personality disorder contributed independently to the severity of alexithymia (Zlotnick et al. 2001). In a study on young female anorexia nervosa patients with a control group the prevalence of alexithymia was 62.5% in patients while in the control group it was 12.5% (Torres et al. 2011). Most studies concerning alexithymia among anorexia nervosa patients have shown high prevalence, suggesting that emotional dysregulation plays an important part in this disorder. Obsessive-compulsive disorder has been found to be associated with alexithymia (Roh et al. 2011).

A longitudinal study on patients suffering from multiple sclerosis reported elevated prevalence of alexithymia: 30.6% at baseline and 29.5% at five-year follow-up (borderline alexithymia 30.6% and 31.8% respectively). In this sample, alexithymia factors DIF and DDF were associated with anxiety and depression (Chahraoui et al. 2014). Patients with psoriasis (n=108) were compared with healthy controls (n=100). The results showed that patients differed from controls in alexithymia: 32.4% of patients were alexithymic (assessed by TAS-20) and 22.2% were classified as borderline. Mean TAS-20 score among controls was 39.6 and in patients 52.6. In general, higher scores on alexithymia were associated with higher anxiety and depression levels, so that DIF was associated with both but DDF was related only to anxiety (Korkoliakou et al. 2014). Coronary heart disease patients showed a prevalence of 21.0% of alexithymia (measured by TAS-20). In this sample alexithymia was not associated with cardiovascular risk factors or exercise capacity, but with self-rated depression and diminished life satisfaction (Valkamo et al. 2001). However, a long follow-up study on Finnish males (20 years) found a notable association between alexithymia and cardiovascular mortality (Tolmunen et al. 2009). Previously it was found that middle-aged men with high alexithymia scores had a threefold greater risk of a traumatic death and a twofold greater risk of

any cause of death compared to men with lower alexithymia scores (Kauhanen et al. 1996).

A review of epidemiological studies concerning alexithymia as a prognostic risk for health problems reported among nonclinical studies contradictory results: Adverse effects on health outcomes were found in three studies out of seven studies reviewed, one showed a beneficial influence and three studies lacked associations. In clinical samples, 18 studies out of 38 reviewed showed adverse effects of alexithymia on health outcomes, while 15 studies showed no associations and five studies reported a favourable effect of alexithymia (Kojima 2012).

The mechanisms through which alexithymia contributes to health related disorders include physiological, psychological and behavioural aspects. A main theory suggests that emotional dysregulation with alterations in autonomic nervous system and in immune and endocrine responses predisposes to different kinds of diseases. Additionally, maladaptive coping styles and unhealthy behaviour have been observed in alexithymic individuals increasing the risk for health problems (Lumley et al. 2007).

2.3.6 Alexithymia and depression

Alexithymia and depression co-occur and create an important force in a number of disorders, their co-occurrence generally exacerbating the disorder. Exploring their relations has been a subject of numerous of studies.

In a general population study with 2 018 subjects, the prevalence of alexithymia was 12.8% in men and 8.2% in women. In the same study, screening for depression showed that the prevalence of alexithymia was 32.1% in subjects having depression scores over the cut-off value for depression, while only 4.3% of nondepressive participants were alexithymic (Honkalampi et al. 2000). The prevalence of depressiveness was 58% among alexithymic adolescents (Honkalampi et al. 2009). In a prospective study both major depression patients and controls demonstrated an association between TAS-20 and BDI-II scores, and that the change in TAS-20 score caused a parallel change in BDI-II score (Honkalampi et al. 2001). In a one-year follow-up study on 120 major depression outpatients, depression and distress decreased during the follow-up period but total TAS-20 scores did not. Examination of the subscales showed that DIF and DDF changed apace with mood changes, but that EOT showed stability (Saarijärvi et al. 2001). In a cross-sectional study on 150 depressive patients, total alexithymia

scores were related to the severity of depressiveness, and DIF and DDF scores were associated with BDI-II scores (Bamonti et al. 2010). In a longitudinal general population study alexithymia at baseline (without depression) predicted depressiveness at follow-up, after both four and eleven years (Tolmunen et al. 2011). An earlier prospective general population study (Honkalampi et al. 2010) did not support alexithymia but supported depressiveness as a predictor of major depressiveness. However, the assessment of depressiveness in alexithymic subjects by BDI-II has been criticized for an overlapping effect producing too high scores on BDI-II and an adjusted scale has been recommended (Mattila et al. 2008b).

The results of a meta-analysis (Lin et al. 2015) concerning the relation between alexithymia (measured by TAS-20) and depression (different measures) summarized that TAS-20 total score and its emotional factors, DIF and DDF, were moderately related to severity of depressiveness. The correlation rates varied according to the sample type (general population or depression patients) and the measure used to estimate depression, self-rating questionnaires producing higher correlations than observer ratings.

The relative similarity of some features, co-occurrence and high correlations between psychometric instruments (TAS-20 and BDI) have raised the question if alexithymia and depression should be defined as distinct constructs or as overlapping phenomena. A factor analysis of TAS-20 and BDI performed among university students and repeated in psychiatric outpatients yielded evidence that alexithymia is indeed distinct and separate from depression (Parker et al. 1991). Neuroimaging studies also have found differences between nondepressive alexithymic individuals and patients with depression, which has been taken as evidence of separate phenomena (Wiebking and Northoff 2015).

It has been suggested that "alexithymic depression" differs from "normal depression" as alexithymic depressive patients have more somatic complaints (Sayar et al. 2003), more suicidal ideation (Hintikka et al. 2004) and a poorer response to antidepressants (Ozsahin et al. 2003). A study based on the hypothesis of "alexithymic depression" yielded preliminary results that alexithymic depressive patients had more somatic-affective symptoms of depression and their interpersonal functioning was more distant than in nonalexithymics (Vanheule et al. 2007a).

The effect of alexithymia on depression was mediated by poor functioning relationship in a general population study of couples (Foran and O'Leary 2013). In chronic pain patient samples, depression has been found to be the mediating factor of the effect of alexithymia on the pain condition (Lumley et al. 2002, Makino et al.

2013). A study exploring illness perception in systemic lupus erythematous patients showed that illness perception was influenced by alexithymia and some aspects of this link were mediated by depression (Barbasio et al. 2015).

Childhood trauma has been found in the background of both alexithymia and depression. In a study on patients with major depressive disorder childhood emotional neglect and abuse predicted the presence of alexithymia and somatization (Güleç et al. 2013). In a sample on young women with eating disorder both alexithymia and depression mediated the association between eating disorder and childhood trauma (Mazzeo and Espelage 2002). The co-occurrence of depression and alexithymia and difficulties to define their distinct features may be based on their common origin in the psychopathology of emotional dysregulation.

2.4 Pain

Pain is a common reason for seeking medical help. A Finnish study showed that pain was a reason in 40% of visits to primary health care (Mäntyselkä et al. 2001). Chronic widespread pain predicted elevated number of consultations in family practice in the United Kingdom (Kadam et al. 2005). The prevalence of chronic pain (also defined as persistent pain) in general population studies is decidedly high, 19% in Europe and also 19% in Finland (Breivik et al. 2006) and likewise 19% in the United States (Kennedy et al. 2014). According the study by Breivik et al. (2006), only 2% of chronic pain sufferers have access to pain specialists.

2.4.1 Definition of pain

The definition of pain depends on the context: pain in the fictive literature is a wider concept referring both physical and mental suffering while in medical settings pain is generally regarded as a physical sensation of disease or disorder. The English word "pain" originates from Latin word *"poena"* which means punishment (it is interesting that pain patients often reason about their pain using the phrase "*I feel I am punished*", author's observation).

According to the Cartesian concept, pain is directly related and correlated with tissue damage, and in the body-mind dichotomy perceived pain is regarded as a message (a perception) from the pathological process of the body transferred via the afferent nerve system to consciousness (Flor and Turk 2011b). However, this

view describes more nociception than the pain phenomenon. Nociception is a sensory neural process including the activation of the nociceptors at the nerve endings caused by different stimuli related to potential tissue damage, and the transduction of this information to the central nervous system. Nociception is not a synonym for pain but rather a process emitting signals to trigger pain (Bear et al. 2007b). In the case of acute pain, the tissue damage or threat thereof is often obvious and also treatable by biomedical knowledge. In the case of chronic pain, the situation is more complex. The tissue damage itself is lacking, or it has been long time ago and/or it is not related to the pain experience, but the threat of it persists in the (dualistic) minds of patients and health care personnel. The token similarity of chronic pain (=bodily felt unpleasant sensation) to acute pain has guided medical examinations and treatment trials. Chronic pain syndrome with a fear of an unknown dangerous disease has led to the "hunting of the real reason" for pain, causing costs, frustrations and delay in the treatment of chronic pain. (Flor and Turk 2011b).

Pain is a feeling or a perception of an unpleasant sensation, and the pain experience is an individual conscious summary of perceived pain influenced by a wide spectrum of sensory, emotional, cognitive and behavioural components. It has been suggested that the pain experience consists of three different dimensions: sensory-discriminative (location, physical characteristics), affective-motivational (emotions, behaviour) and cognitive-evaluative (meaning giving) (Lumley et al. 2011). According to the International Association for the Study of Pain (IASP), pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Merskey and Bogduk 1994).

In his book "The Management of Pain" (1953), Bonica defined chronic pain as "*pain persisting beyond normal healing time*" (Dunn et al. 2012). Nachemson and Anderson (1982) assessed low back pain as a chronic pain condition if it lasts over three months. Later the definition was elaborated by the IASP: "*Chronic pain is defined as pain lasting beyond the normal healing time, usually defined between 3-6 months*" (IASP 1986). However, the definition by duration has been criticized as chronic pain consists of multidimensional features more important for the prognosis than just the duration of pain. Loeser and Melzack (1999) proposed that "*it is not the duration of pain that distinguishes acute from chronic pain*".

An alternative definition for chronic pain is based on an idea of "*a prognostic approach*" (Dunn et al. 2012). The prognostic risk score of the patient will be evaluated and pain syndrome defined to be probably chronic if the calculation

shows "*the risk of having clinically significant pain to be present one or more years in the future*". The suggested risk score scale consists of the following items: average pain intensity, worst pain intensity, current pain intensity, interference with usual activities, interference with work/household activities, interference with family/social activities, days of activity limitation due to pain in the preceding three months, depression score, number of pain sites and number of days with index pain in the preceding six months. The items are ranked by score levels and scores added up to the total risk score interpreted as the procentual risk of having clinically significant pain at one year. This kind of conceptualization of chronic pain caters for the aspects of the multidimensionality of the pain experience and early identification of patients at risk, respecting neurophysiological and somatosensory mechanisms. The "prognostic approach" to define chronic pain is related to the biopsychosocial model of chronic pain and highlights the basic developmental differences between acute and chronic pain and the individual features involved.

2.4.2 Acute pain versus chronic pain

Almost all people have pains. Acute pain is mostly connected to tissue damage (such as trauma or a consequence of a disease process) and it has a protective and warning, i.e., a logical meaning. The fate of individuals having congenital analgesia (a rare sensory disorder lacking the ability to sense painful events) proves the lifesaving value of acute pain as sufferers with this disorder usually die in early adulthood because of trauma and the ensuing complications (Kalso 2009). Chronic pain may also be connected with a tissue injury, at least in the initial phase of pain disease, but the existence of active tissue pathology is not necessary for the persistence of pain symptoms. In fact, identical injuries or pathological disease states may or may not cause chronic pain (Mansour et al. 2013). In neuroimaging studies, the distinct nature of acute and chronic pain is established; acute pain is more linked to sensory processing brain areas while chronic pain activates brain regions which encode emotional and motivational states (Baliki et al. 2006, Apkarian et al. 2011).

The current concept regards chronic pain as a multifaceted, complex phenomenon influenced by several interrelated biological and psychosocial factors (Gatchel et al. 2007, Apkarian et al. 2009, Flor and Turk 2011c). Numerous predisposing, maintaining, exacerbating or alleviating factors have been found or

implicated in the development and persistence of chronic pain. Chronic pain lacks any obvious useful function and its pathological effect is best understood by assessing its various biopsychosocial aspects (Dansie and Turk 2013). Despite the modern concept of chronic pain, the discrepancy between the subjective pain experience and "objective" biomedical findings still influences attitudes towards chronic pain and the patient encounters the Cartesian dualism (at home, in work and in the office) that impairs patient-healthcare relationships and leaves the sufferer alone with his/her pain problem (Ojala et al. 2015).

2.4.3 Assessment of pain

The nature of pain makes objective measurement impossible. Pain is an individual and subjective experience and thus beyond any objective measuring methods and instruments (Younger et al. 2009). Yet measuring pain is important for communication, treatment and research purposes (Farrar et al. 2001, Dworkin et al. 2008). To some extent the intensity of acute pain can be estimated indirectly by its physiological responses, such as elevated heart rate and blood pressure or visible pain behaviour, but such measures describe only one limited part of the entire pain experience. In a study comparing self-rated pain intensity and physical pain symptoms, no correlation was found between pain intensity and pulse rate or blood pressure (Lord and Woollard 2011). However, when assessing pain in babies and young children, these observational methods are important (Büttner and Finke 2000). Several measurements and questionnaires have been developed for estimating pain experience.

2.4.3.1 Pain intensity scales

Most instruments used to measure pain intensity are the Numeric Rating Scale (NRS), the Visual Analogue Scale (VAS) and the Verbal Categorical Rating Scale (VRS). They are practical, easily available and patients quickly learn to use them. The scales measure the experienced pain intensity from 0 to 10 (NRS) or from 0 millimeter to 100 millimeters (VAS) or use a four-point categorical rating scale (VRS). NRS scores are divided into four categories describing no pain (0), mild pain (1-4), moderate pain (5-6) and severe pain (7-10). On the VAS 0 describes no pain and 100mm the "worst pain imaginable". A clinical study to estimate "how many millimeters represent moderate pain" concluded that VAS score over 30 mm

corresponds to at least moderate pain (Collins et al. 1997). In practice, the VAS follows the interpretation scale of the NRS. The VRS has four verbal categories: no pain, mild, moderate and severe pain. The NRS and VAS have been shown to have almost identical values in the same patient, but the VRS was not as accurate. The NRS and VAS have been found to be superior to the VRS, and thus are preferable for use in clinical work and in research. The benefit of these methods is time and situation dependency; they are best for "right now" until "in the past week" estimates and for acute pain (Breivik et al. 2000, Breivik et al. 2008, Hawker et al. 2011).

Assessment of chronic pain by such a simple measure has been regarded as insufficient as it consists of multiple facets (Breivik et al. 2008). However, in practice, current pain intensity is often estimated using the NRS or VAS or by verbally, and these measurements are widely used in pain research (Ferreira-Valente et al. 2011). Measuring pain intensity has been criticized for not correctly expressing "the real intensity" as a chronic pain patient may sit peacefully reporting pain intensity NRS 8-9 while a patient with the same score in acute pain displays explicit pain behaviour in concordance with the reported scores. In chronic pain research pain intensity measured by a simple numerical method has nevertheless been proven to describe the change in the pain situation when compared with a parallel verbal statement (Farrar et al. 2001). Additionally, a pain intensity measure gives a predictive value of the course of a pain condition, e.g. high pain intensity in the initial phase of distal radius fracture was associated with persistence of pain (Mehta et al. 2015).

2.4.3.2 Pain assessment according to the suspected origin

A traditional pain assessment has included the classification of pain according to the suspected or diagnosed tissue pathology (Vainio 2009). Nociceptive pain refers to pain originating from tissue damage caused, for example, by inflammation, ischaemia or tumour growth. Neuropathic pain is pain originating from dysfunction or damage of the nerve system. Visceral pain is a type of nociceptive pain transferred from the internal organs via activation of the autonomic nerve system. Idiopathic pain describes pain without salient tissue damage or origin. Psychogenic pain refers to bodily experienced pain with no organ pathology source in some mental disorders such as in delusions, conversion symptoms or severe depression. The classification works well in acute pain, but in chronic pain syndromes the presence of tissue damage is not decisive. The tissue origin may be

unclear or totally absent, and the central nervous system sensitization has taken place in the pain experience (Latremoliere and Woolf 2009).

2.4.3.3 Qualitative assessment of pain

Pain quality assessments have been developed to facilitate diagnostics and to define the pain experience in verbal descriptions. Assessments are based on the perception that different kinds of pain are connected with a certain pain (tissue damage) origin or a type of pain (see the classification in 2.4.3.2). The McGill Pain Questionnaire (MPQ) is a multidimensional questionnaire which measures pain intensity and the sensory, affective and evaluative sides of pain (Melzack 1975). It contains 78 pain descriptor items divided into four subscales for different aspects of pain (= the Pain Rating Index) and a present pain intensity scale. The MPQ has been evaluated to be reliable to use in an immediate, "right now", situation (Graham et al. 1980). The MPQ is widely used to evaluate pain interventions and in chronic pain syndromes (Hawker et al. 2011). As the MPQ is time-consuming and possibly too complicated for use in clinical situations, a short form has been developed (SF-MPQ). It contains 15 descriptors of pain qualities rated from zero to three according to their severity. The short form has been demonstrated to be as sensitive as the original MPQ in clinical situations (Melzack 1987). The MPQ and SF-MPQ and its revised version, the SF-MPQ-2, provide a combination of a quantity and quality measure.

Various questionnaires have been developed to distinguish neuropathic pain symptoms and signs. These include the Neuropathic Pain Symptom Inventory (NPSI) and the Neuropathic Pain Scale (NPS). The Pain Quality Assessment Scale (PQAS) includes the NPS with additional pain qualities (Jensen and Karoly 2011). Most of the pain clinics in Finland use local or national applications of these above mentioned questionnaires.

Assessments of pain qualities (if the pain is dull, sharp, burning etc.) and spatial characteristics (perceived depth, location in the body) are used for diagnostic purposes but whether a certain type of pain description is related to functioning is uncertain (for example, if a sharp pain disturbs sleeping more than a dull or burning pain). A study of pain qualities and spatial characteristics (Jensen et al. 2006) found that none of the typical descriptors of pain was superior to physical or emotional dysfunction, but it was possible to find some typical descriptors for pain syndromes, for example in neuropathic pain, sharp, sensitive, itchy and deep pain was connected with dysfunction.

2.4.3.4 Pain assessment and neuroimaging

The recent findings of neuroimaging have shown that distinct chronic pain syndromes have both similarities in brain activation areas and also their own typical activation markers (Baliki et al. 2011). It is possible that in the future the pain condition can be objectively assessed and classified by neuroanatomical and neurofunctional findings in brain imaging (Apkarian et al. 2011). Furthermore, the development of brain imaging techniques and learning computer programs (machine learning) have inspired researchers to conduct experimental trials to objectively measure pain stimulus in the brain. The results have shown that it is possible to assess and to predict if the stimulus administrated, such as heat, is painful (Brown et al. 2011). The measuring of an experimental physical pain stimulus in healthy persons in functional magnetic resonance imaging (fMRI) illustrated brain areas associated with heat stimulus (Wager et al. 2013). Voxel-based brain mapping has shown the activities of the brain areas associated with certain stimuli. In the future the development of brain biomarkers by machine learning may give opportunities to explain the neurophysiology of pain and to predict outcome in pain disease (Wager 2015). These techniques may give an objective evaluation of different pain conditions and pain syndromes in their neurophysiological base. However, such research is still very far from the clinical use of the brain imaging for measuring even acute pain and especially chronic pain. The results of imaging studies prompt questions, such as how the whole pain experience is related to these findings. As Flor and Turk (2011d) stated: *"The association between physical pathology and reported pain is, however, far from perfect"*.

2.4.4 Assessment of factors influencing the pain experience

Measuring the intensity and the type or the qualitative dimensions of pain probes only one facet of pain experience as subjective pain experience is based on one's biopsychosocial entity and life history. For example, in a case of spinal stenosis, a depressive pain patient exhibits a pain experience with remarkable pain disability, restricted coping styles with pessimistic pain beliefs, while a patient with a positive attitude and self-efficacy experiences pain in a completely different way, and the patients also have different prognoses, even in cases of similar pathology (Sinikallio et al. 2009). The assessment of pain experience may include evaluation of pain disability, mood and affect state, fear of pain, cognitive factors such as

catastrophizing and pain beliefs and factors related to coping skills such as self-esteem and self-efficacy.

In spite of the wide spectrum of different measures available to estimate pain experience related factors, in clinical reality the most used are scales defining pain intensity, pain disability and mood. Pain assessment methods are needed for evaluating the outcome of clinical treatment trials but there has been a lack of standards. A consensus meeting of pain researchers recommended that in the case of chronic pain, four core outcome domains should be measured: pain intensity, physical functioning, emotional functioning and overall improvement. The questionnaires recommended for use are the NRS, the Multidimensional Pain Inventory and the Brief Pain Inventory Interference Scales, the Beck Depression Inventory and the Profile of Mood States and Patient Global Impression of Change Scale. The aim has been to provide standards to compare different treatment protocols (Dworkin et al. 2008).

Assessing the pain experience of chronic pain patients is demanding as the pain experience is both subjective and multidimensional, involving biomedical, psychosocial and behavioural factors. Successful treatment and rehabilitation of a pain problem needs evaluation and understanding of all these three domains using available instruments such as self-report questionnaires to estimate pain intensity, functioning, cognitions, beliefs, expectations and emotional distress (Dansie and Turk 2013).

2.4.4.1 Pain disability

Pain disability refers to different aspects of life disrupted by the pain condition. Several self-report questionnaires have been developed to evaluate the degree of disability in normal life activities. The Pain Disability Index (PDI) has seven different categories for different important parts of life, including family and home responsibilities, hobbies, social activity, occupation, sexual behaviour, self-care (as taking a shower, driving, getting dressed) and life-support activities (such as eating, sleeping, breathing). The Scale for each part ranges from zero to ten, and higher scores mean higher disability (Pollard 1984, Tait et al. 1990, Chibnall and Tait 1994). Most of the other pain disability measurements in use are comparable and developed for national, local or research use. There are also disability assessments

for specific pain syndromes like back pain: The Owestry Disability Index (Fairbank et al. 1980, Fairbank and Pynsent 2000).

2.4.4.2 Pain catastrophizing

The definition of pain catastrophizing can be expressed *"as an exaggerated negative "mental set" brought to bear during actual or anticipated pain experience"* (Sullivan et al. 2001). The concept of catastrophizing originates from cognitive-behavioural psychotherapy framework, where it has been used to describe the maladaptive thinking styles of anxious or depressive patients (Turner and Aaron 2001). Pain catastrophizing modifies the pain experience. It is a factor increasing pain severity, having a negative influence on pain regulation in the central nervous system, impairing pain coping skills and affecting social relationships unfavourably (Quartana et al. 2009). There is a scientific debate concerning the independency of pain catastrophizing as to whether it is a unique feature in chronic pain situation or a consequence of general negative affect or depression (Leung 2012).

The Pain Catastrophizing Scale (PCS) is one of the most widely used scales for measuring pain related catastrophizing (Sullivan et al. 1995). It contains three different subscales: rumination, magnification and helplessness.

2.4.4.3 Depression

Assessment of depression belongs to pain experience evaluation because depression and chronic pain occur frequently together (Holmes et al. 2013), and some of their concomitant features are overlapping (e.g. sleep disturbances, fatigue, difficulties with concentration). The Beck Depression Inventory – Second edition (BDI-II) has been proven appropriate for depression assessment in chronic pain (Harris and D'Eon 2008). The Hospital Anxiety and Depression Scale (HADS) has been shown to be valid for measuring both depressiveness and anxiety in somatic and psychiatric patients (Bjelland et al. 2002) and it is widely used in pain research.

2.4.5 Future pain assessments

Pain assessment is traditionally and usually based on structural interviews or self-report questionnaires, which have proven to show reliable psychometric properties.

Neuroimaging and machine learning techniques are set to find evidence of the pain experienced (Wager 2015). The empirical research framework used in medicine supports endeavours to reach objectivity of findings, and in this framework the very subjective nature of the pain experience has been challenged. However, there are other frameworks available to assess and understand the pain experience. Philosophy is rarely connected with medicine, but concepts based on mereology and phenomenology may be helpful to broadly comprehend the unique pain experience of a single individual (Thacker and Moseley 2012, Ojala et al. 2015).

In the case of chronic pain, it has been suggested that pain intensity measures should be discontinued as they may promote a focus on drug (opioid) use trials instead of understanding the distress and suffering of the chronic pain patient, as summarized by Ballantyne and Sullivan (2015): "*But no quantitative summary of these measures will adequately capture the burden or the meaning of chronic pain for a particular patient. For this purpose, nothing is more revealing or therapeutic than a conversation between a patient and a clinician, which allows the patient to be heard and the clinician to appreciate the patient's experiences and offer empathy, encouragement, mentorship, and hope".*

2.4.6 Factors associated with the development and maintenance of chronic pain

2.4.6.1 Genetics and epigenetics

Chronic pain patients often explain their symptoms to be hereditary; "*my back is aching just like my father always complained*". Genetic background, an inheritable susceptibility, as a causative factor would to some extent explain the variance of chronic pain. There is a group of rare monogenic pain disorders such as familial hemiplegic migraine disorders and neurological channelopathies producing paroxysmal pain disorders (Drenth and Waxman 2007). These disorders are rarities in clinical practice. Animal studies have been carried out to identify "pain genes" and some evidence has been found to support the concept. Genes, which encode proteins involved in response to injury and central pain modulation, have been proposed to have effects on susceptibility to pain symptoms. The results of pain gene studies have yielded cumulative but scattered information on "pain genes" (mostly in mice) responsible for variance in pain experience and in the outbreak of pain disease, but the real causative links between genes and common pain disorders have not been detected (Mogil 2012).

Population-based twin studies or studies of a patient group with a certain pain disorder have been performed to explore the share of heredity in chronic pain. In a study of familial occurrence of fibromyalgia (FM) the offspring of FM patients had a higher prevalence of FM than that in general population, independent of anxiety or depression (Buskila et al. 1996). A modest genetic influence on chronic widespread pain was found in a general population twin study (Kato et al. 2006). Twin studies have shown statistical proof for heritability in pain syndromes including migraine, chronic pelvic pain and chronic widespread musculoskeletal pain (Vehof et al. 2014). However, epidemiological studies cannot demonstrate the biological link between genes and chronic pain syndromes and the effect of confounding factors remains unclear since the studies use different designs and different statistical tools. It is also possible that coping with pain and reasoning of pain is learnt by other family members. If the adult family members in the case of any pain provide models of catastrophizing and fear-avoidance, the offspring may learn similar models, which have been shown to contribute the development of chronic pain (Vlayen and Linton 2000).

Gene research has given a vague indication of heredity as a part of chronic pain mechanisms, but epigenetics may explain more about the link between genes, the environment and the outcome. Pain induces changes in neural pathways and networks. The ability of the nervous system to adapt (or in other words, to learn) is called neuroplasticity (Pascual-Leone et al. 2005, Pascual-Leone et al. 2011). At neurophysiological level neuroplasticity means changes in individual molecules, synapses, cellular function and network activity based on changes in gene transcription. Epigenetic mechanisms are involved in the regulation of gene expression needed for neuroplastic changes and it has been suggested that noxious stimulation launches epigenetic modifications (Géranton 2012). It is possible that epigenetic responses are both involved in the development of chronic pain and also in the consequences of chronic pain (Sibille et al. 2013).

2.4.6.2 Early pain experience

Painful procedures during infancy influence the developing pain system but also stress regulation and immunological systems (Fitzgerald 2012, Beggs 2015, Walker et al. 2016). Preterm babies especially, who during their first weeks are exposed to repeated painful and stressful procedures, are at risk of having altered brain microstructure and stress hormone levels associated with longstanding effects on neurodevelopment (Vinall and Grunau 2014). It is interesting that even in infants

the affective quality of the pain experience depends on the context, "facilated tucking" has been proven to reduce pain expression in premature infants during their painful procedures (Hartley et al. 2015).

2.4.6.3 Early adversities

Based on his clinical observations Engel (1959) presented the concept of "the pain prone patient" to describe patients "among whom psychic factors play the primary role in the genesis of pain, in the absence as well as in the presence of peripheral lesions". He proposed that pain is a psychological phenomenon and remarked that patients susceptible to pain have "aggression, suffering and pain" in their early family relationships.

Early life stress caused by physical or mental abuse, neglect, maltreatment and emotional deprivation have widespread and long lasting effects. The evidence of the consequences of early stress is discovered in the cortisol response of the stress system (see 2.1.3) and in brain imaging (Teicher et al. 2012). Other, indirect measures, such as life history inventories, psychological questionnaires and epidemiological studies have linked health disorders with early adversities (see 2.1.2). Chronic pain patients have been found to have insecure attachment styles (Davies et al. 2009), alexithymia (see 2.5.3) and Early Maladaptive Schemas (Saariaho et al. 2011), all of which have associations with childhood adversities.

The connection between adult chronic pain disease and childhood adversities has been found repeatedly (Jones et al. 2009). A meta-analytic review provided evidence that individuals reporting neglectful or abusive childhood experiences were more likely to have a chronic pain disorder than individuals without these adversities, and individuals with chronic pain, reported more early adversities than individuals without pain syndrome (Davis et al. 2005). Fibromyalgia patients have reported childhood adversities (Imbierowicz and Egle 2003). A study concerning trauma induced stress reactivity in the development of fibromyalgia showed associations between fibromyalgia, stress reactivity and childhood abuse (Lee 2010). Fibromyalgia also occurs with alexithymia (Di Tella and Castelli 2013) and it has been found that fibromyalgia patients having suffered childhood abuse had lower pain pressure threshold and more tender points than nonabused patients (Ortiz et al. 2016). In 1993 Schofferman et al. published a paper on low back pain patients and reported them to have a high number of childhood adversities (>50% of patients). Nickel et al. (2002) tried to reproduce the study but they did not reproduce the findings.

In a general population study, the physically and sexually abused individuals reported more health problems including more pain problems than did other subjects, even if depression was controlled for (Sachs-Ericsson et al. 2007). A review study on childhood abuse stated that in adult survivors reporting health and pain-related problems, current life stress exacerbated the effect of childhood abuse on health problems and the victims of early abuse also had psychiatric disorders, which exacerbated pain and other health problems (Sachs-Ericsson et al. 2009).

2.4.6.4 The neurophysiological and neuroanatomical side

The neurophysiological explanation for the transition from acute pain to chronic pain regards the prolongation/persistence of the pain condition as a failure of the repair mechanisms of the pain modulating neurocircuits. Instead of the normal course of healing processes (= pain diminishes as expected after an injury or surgical trauma), secondary neurochemical and neurophysiological mechanisms take place and generate peripheral and central sensitization of the nervous system which maintain and increase the pain experienced (Voscopolous and Lena 2010).

Postsurgical or posttraumatic pain may persist and become a chronic pain syndrome. In the initial phase there are markers which predict subsequent problems. Preoperative moderate or severe pain, high acute postoperative pain, signs of neuropathic pain early in the postoperative phase and the extent of surgical trauma were connected with having pain after one year in a prospective study of breast cancer surgery patients (Andersen et al. 2015). In distal radius fracture patients higher initial pain intensity was associated with chronicity of pain (Mehta et al. 2015).

Pain intensity and its relation to the further development of chronic pain need some explanations. In laboratory conditions in acute pain provocations, the standard noxious heat stimulus shows variability between individuals from almost zero ratings until near maximal scores eliciting differences of pain sensitivity. In a study of pain thresholds, various stimuli (thermal, electrical and mechanical) showed that the pain thresholds were subject, not stimulus-dependent (Neddermayer et al. 2008). Fibromyalgia patients having suffered childhood abuse had lower pain pressure threshold and more tender points than nonabused patients (Ortiz et al. 2014). Thus it seems that experienced pain intensity depends on individual properties and life history.

Neuroplastic mechanisms are involved in the development and maintenance of chronic pain (Schmidt-Wilcke and May 2015). Neuroimaging studies have shown

that chronic pain is associated with both peripheral and central nervous system reorganization with various brain activities and neuroanatomical alterations which are pain disorder specific. These changes are associated with persistence of pain and regarded as pain maintaining neural network (Apkarian et al. 2009, Apkarian et al. 2011). Impaired pain inhibition or conditioned pain modulation has been suggested to be involved in pain pathophysiology. Low pain inhibition has been found in idiopathic pain syndromes such as fibromyalgia and tension type headache (Yarnitsky 2010). A proportion of morphological pain related neuroanatomical and neurophysiological alterations in the central nervous system (CNS) may disappear when the pain condition has been successfully treated (Seminowicz et al. 2011). The theory of initiating stimuli to provoke the learning process of neural system leading to CNS alterations which maintain and modify chronic pain has been challenged by a neuroimaging study. The authors found that structural abnormalities in brain white matter were present before the transition from acute low back pain to chronic low back pain and the presence of these alterations predicted persistence of pain (Mansour et al. 2013).

2.4.6.5 Psychosocial factors

The development of chronic pain can also be understood through the individual learning processes of the central nervous system. Pain experience is mostly implicitly learnt, consists of behavioural, cognitive and emotional memory structures and is maintained by circular reinforcement. The learning process causes structural and functional changes in the brain with an altered body-image (Flor 2012).

According to cognitive psychotherapy depressive patients have a "primitive thinking style" (instead of adaptive thinking) which helps to maintain maladaptive information processing (Beck et al. 1979). Pain catastrophizing (see 2.4.4.2) means negative evaluation of experienced pain by overestimating its significance and consequences. It is linked to negative affectivity and is automatically triggered by a suitable stimulus. Catastrophizing contributes to pain intensity, pain disability and pain related distress (Severeijns et al. 2001) explaining 7-31% of the variance of pain severity (Sullivan et al. 2001). Catastrophizing modifies cognitions and behavioural choices and strengthens and maintains pain related fear-avoidance beliefs. Furthermore, catastrophizing has been regarded as a dysfunctional coping strategy (avoidant) to suppress negative emotions related to pain (Flink et al. 2013). In a sample of chronic myofascial pain patients alexithymia was associated with

catastrophizing and less self-efficacy, suggesting poorer coping, and also independently with depression and affective pain (Lumley et al. 2002). A cross-sectional study comparing fibromyalgia patients with healthy controls obtained parallel results and concluded that deficit in emotional processing with catastrophizing and fear of pain predisposes to emotional distress contributing to pain severity (Martínez et al. 2015).

Fear-avoidance is a pain maintaining coping style: an initial pain experience (related to trauma or illness or perception of bodily felt unpleasant sensation) is interpreted as a threatening symptom (=catastrophizing) that is a consequence of (catastrophizing) thinking style based on negative affectivity. The cognition "threat" is linked with emotion "fear" and the behavioural solution is to "avoid" any possible presumed pain triggering action. Fear-avoidance leads to inactivity, disability and depressiveness with a focus on pain experience and thus to pain maintaining circular reinforcement (Vlayen and Linton 2000) and increased "pain learning". It was observed in an explorative neuroimaging study that *expected* pain intensity modified the pain experience and was identified in brain activation (Koyama et al. 2005) supporting in a concrete way the fear-avoidance model. Placebo research has contributed more evidence of how the central nervous system works in an anticipatory and predicting mode. Expectation of pain experience or pain relief activates the brain network to feel pain or accordingly to experience alleviation (Ingvar 2015, Medoff and Colloca 2015), thus catastrophizing and fear of pain engage a pain feeling network. Behavioural responses in fear-avoidance; inactivity and immobilization have been shown to produce cortical changes, even during a short period of immobilization (Langer et al. 2012). Fortunately, studies have confirmed that the brain changes are mostly reversible.

In a population study in rural Alabama the researchers found a race-associated pain intensity and pain interference, namely the African-Americans scoring higher on pain variables. In the same study, pain catastrophizing mediated the effect of primary literacy on experienced pain intensity (Day and Thorn 2010). Low level of education has been connected with more health problems, including chronic pain (Klijs et al. 2014). The psychological and social work factors (quantitative demands, role conflict, social climate, decision control, empowering leadership) had a role in onset and persistency of neck pain in a four-year follow-up study of 1250 employees (Christensen and Knardahl 2014).

2.4.6.6 The role of emotions in chronic pain

Pain is one of the first primitive emotions and feeling pain causes stress to seek help. Emotions are related to chronic pain in several different aspects. The most popular concept highlights that experienced (physical) pain produces negative emotions. However, it has been observed that negative affects in turn increase pain severity. The psychosomatic concept regards bodily felt pain as a substitute for emotions as in the case of emotional suppression and avoidance. Difficulties in describing and identifying emotions may cause bodily felt emotional states to be interpreted as painful signs of physical illness. The pain history is also present in the emotional context of the pain experience; previous pain-related strong emotions, like fear or hopelessness, are automatically triggered in the current pain event.

Research has produced evidence for all the above mentioned concepts. Negative affect associated with chronic pain has been regarded as a factor exacerbating the pain experience (Janssen 2002). According to Keefe et al. (2001), emotional dysregulation and disturbances in emotional processing; like inhibition and/or avoidance of emotions, alexithymia and depression, are important factors increasing pain and distress. Emotional dysregulation has been suggested to link chronic pain and depressiveness (Linton and Bergbom 2011). Negative emotional states increase pain and cause poor adjustment and conversely, inhibition of negative emotions is connected with greater pain and disability. The apparent conflict represents maladaptive coping and dysregulation of emotions: Awareness and expression of primary emotions (such as anger) have been suppressed and replaced by secondary maladaptive emotions (such as guilt or shame), somatic symptoms and pathological physical states (via the autonomic nervous system, stress and immune systems) which in turn may predispose, maintain and increase chronic pain (Lumley et al. 2011). Other studies support the contribution of emotional dysregulation in chronic pain. A study of fibromyalgia patients revealed that patients had both elevated levels of negative emotions and increased emotional avoidance with decreased level of positive emotions (van Middentorp et al. 2008). Emotional numbing (with pain intensity) predicted chronic pain and pain disability six months and twelve months after thoracotomy (Katz et al. 2009a). A longitudinal study showed synchronic changes in anxiety, depression and pain symptoms suggesting the importance of mood disorders in the pain experience (Gerrits et al. 2015).

2.4.7 Chronic pain and depression

Depression is a mood disorder characterized by a bundle of affective, cognitive, behavioural and somatic symptoms. The list of symptoms includes low mood, feeling sad or empty, diminished interest or pleasure, eating and sleeping disorders, psychomotor agitation or retardation, feeling guilty or worthless, difficulties in thinking or concentrating, indecisiveness, thoughts of death, suicidal ideation or attempts (American Psychiatric Association 1994). Its severity fluctuates as does the combination of symptoms in individuals and between individuals. The suspected origin of depression is also multifactorial, including childhood adversities, remarkable negative life events, work exhaustion, physical morbidity and substance abuse among others.

According to the concept of cognitive therapy, "*early experiences provide the basis for forming negative concepts about one's self, the future and the external world*" (Beck et al. 1979). Furthermore, these concepts may be hidden and activated by experiences resembling the earlier predisposing events. Numerous studies have provided evidence that childhood adversities are connected with susceptibility to depression in later life (Korkeila et al. 2005, Widom et al. 2007, Klein et al. 2009, Spinhoven et al. 2010). A recent study revealed that among 349 chronically depressed patients, 76 % reported having experienced childhood traumas, sexual and emotional abuse showed remarked influence on depression, and symptom severity was associated with multiple traumatic exposures (Negele et al. 2015). The type of negative experience influences the development of depression; according to the study by Hovens et al. (2012), sexual, physical, psychological abuse and particularly emotional neglect predicted the occurrence of depression but parental loss did not. Early maladaptive schemas (see 2.2), which represent consequences of toxic childhood experiences, have been considered to be important predisposing factors for later depression (Young et al. 2001). Depression linked with childhood trauma has been proven to be less responsive to pharmacotherapy but responds better to psychotherapy (Nemeroff et al. 2003). The disturbances in the stress regulating system are considered to be involved in depressive disorder caused by childhood adversities (Heim et al. 2008). On the developmental and neuroendocrinological side, both depression and chronic pain have been connected with the dysfunction of the HPA-axis and thus with early stress as a shared aetiological ground (Blackburn-Munro and Blackburn-Munro 2001).

In chronic pain syndromes the prevalence of depression depends on evaluation methods and study design. In an old literature review (France 1987), the rate of

depression was reported to vary from 10% to 100% among chronic pain patients, and conversely the occurrence of pain symptoms in depressive patients was reported to vary from 30% to 80%. A more recent literature review concluded that from 5% to 85% of pain patients are depressive, while on average, 65% of depressive patients experience pain symptoms (Bair et al. 2003). Furthermore, in a general population study Ohayon (2004) found that almost half of the participants with major depressive disorder also had chronic painful physical conditions associated with more adverse symptoms and longer duration of depression. In general the depression rate rises when the study population changes from primary health care to the tertiary level, i.e. pain clinics.

Co-occurrence of chronic pain and depression has been a source of speculation concerning their causative relations. The following hypotheses have been proposed: The antecedent hypothesis states that depression precedes chronic pain. The consequence hypothesis regards depression as a reactive consequence of chronic pain. According to the scar hypothesis there have been episodes of depression before the onset of pain and these episodes are predisposing factors to depression occurring with pain. The cognitive mediation hypothesis highlights the interaction of maladaptive coping styles or catastrophizing between depression and chronic pain. Finally, there is the independent hypothesis by which depression and chronic pain are distinct phenomena sharing some common pathology (Fishbain et al. 1997). The research has found proof for all the hypotheses presented, and it can be concluded that the origin of depression in a single chronic pain patient is based on individual life history.

There are some typical features of the relations between chronic pain and depression. It has been noted that patients with multiple pain symptoms are three to five times more likely to be depressed, and also that greater number of pain episodes and longer pain duration are associated with depression. Furthermore, increased pain severity is connected with more depressive symptoms and depressiveness with higher disability. There is also evidence of a biological link between depression and pain from their shared pathways, neurotransmitters and genetics (Gambassi 2009, Han and Pae 2015). A systematic review exploring whether depressive symptoms are prognostic for the course of low back pain, showed that the majority of the studies reviewed suggested that depression has an adverse effect on the prognosis of low back pain (Pinheiro et al. 2016). Structural equation modelling used to explore the effect of depression on the fear-avoidance model of chronic pain showed that depressive symptoms have a great impact on

fear-avoidance beliefs and avoidance behaviour suggesting the importance of depression in maintenance of chronic pain (Seekatz et al. 2016).

Engel (1959) suggested that chronic pain with depression is a specific syndrome, mainly psychiatric with the problem of somatization. Since Engel, similar ideas have been proposed. Hudson and Pope (1989) claimed that fibromyalgia could belong to the "affective spectrum disorder"-category. Goldenberg (2010) proposed the term "pain-depression dyad" based on observations of fibromyalgia patients. Somatic complaints including pain are common in depression, thus chronic pain has been suggested to be a masked form of depression (Blumer and Heilbronn 1982). However, in general, clinicians and researchers tend to perceive chronic pain and depression as separate entities.

2.4.8 Biopsychosocial model of chronic pain

Emerging knowledge concerning the complexity of the chronic pain phenomenon has inspired models to describe its predisposing, developmental and maintaining interactive processes. A diathesis-stress model of chronic pain proposes that pain disorder is a result of noxious experiences with the presence of predisposing genetic, personal and psychological factors (Turk 2002, Martin et al. 2010). The model regards experienced pain as a trauma and psychological and behavioural responses such as fear of pain, pain avoidance, anxiety and catastrophizing as pain maintaining and exacerbating factors. Fear-avoidance model has similar components with addition of negative affect (Vlayen and Linton 2000, Vlayen and Linton 2012). The vulnerability (diathesis) to the above-mentioned responses to pain symptoms is based on previous life history and personal characteristics. In these models the pain symptom is the starting point and the outcome is chronic pain disorder. The models have been tested by pain patients and they explain part of the mechanism through which chronic pain develops in learning processes (negative feedback).

According to current state of the art, the biopsychosocial model of chronic pain is an approach to understand the contributions and dynamic interactions of physiological, psychological and social factors to experienced pain. As each chronic pain patient has his/her own life history and co-factors influencing the pain situation, to create one simple model would be difficult as Gatchel et al. (2007) admitted: *"a comprehensive conceptual model of the biopsychosocial interactive processes involved in pain can be quite complex*".

2.5 Alexithymia and pain

There is a discrepancy between somatic symptoms and somatic findings in chronic pain patients (Katz et al. 2015) and alexithymic individuals have a tendency to somatization (Mattila et al. 2008a) and somatic amplification (Kosturek et al. 1998, Nakao et al. 2002, Nakao and Barsky 2007). These observations have raised interest among alexithymia researchers to consider the role of emotional dysregulation as a part of the chronic pain syndrome.

The following review of alexithymia and pain is based on regular internet based information seeking with different permutations of the following keywords: alexithymia, pain, chronic pain, pain disability, depression, longitudinal, early maladaptive schema.

2.5.1 Alexithymia in experimental pain studies

In experimental conditions (see Table 2) most studies, but not all showed that alexithymia was associated with hypersensitivity to unpleasant (painful) stimulation. However, the samples were small, consisting of healthy volunteers with a small number of alexithymic individuals.

Table 2. Alexithymia and pain, laboratory studies

Author, year of publishing	Sample	Measures	Results	Conclusions
Nyklíček and Vingerhoets 2000	41 healthy females and males	alexithymia (TAS-20), threshold of painful electric stimulus	alexithymia factors (DIF and EOT) predicted pain threshold level	alexithymia is related to hypersensitivity to an unpleasant stimulus
Jackson et al. 2002	114 college undergraduates	alexithymia (TAS-20), cold pressor test	no correlation between TAS-20 score and cold pressor pain	alexithymic people are not hypersensitive to cold stimuli
Kano et al. 2007	45 healthy females and males,)	alexithymia (TAS-20), pain intensity (numeric scale) measuring the effect of colonic distension (visceral pain), levels of plasma adrenaline, noradrenaline, serum cortisol and ACTH, positron emission tomography (PET)	DIF score was related to stronger pain and symptoms of unpleasantness TAS-20 score was related to greater activation in the pregenual anterior cingulated cortex, right insula and midbrain and to adrenaline level	alexithymia is associated with hypersensitivity to visceral stimulation , the results support somatosensory amplification in alexithymics
Katz et al. 2009b	67 undergraduate students	alexithymia (TAS-20), anxiety (anxiety sensitivity index), fear of pain (fear of pain	sex, fear of pain and alexithymia predicted average heat pain intensity	emotion regulation difficulties affect the pain experience

		questionnaire III),pain catastrophizing (pain catastrophizing scale),pain anxiety (pain anxiety symptoms scale-20), heat pain stimuli		
Pollatos et al. 2015	50 healthy female participants	alexithymia (TAS-20), emotional state (Zerssen Mood Scale), thermal stimulation, pain intensity, sensory and affective (VAS), the Pain Sensation Scale, every day pain experience in last 2 months	DDF was related to hyposensitivity to pain, DIF was related to higher everyday pain , EOT was related to lower everyday pain, mean alexithymia score 39.7 (SD 9.1)	different facets of alexithymia are related to alterations in pain processing

2.5.2 Alexithymia and pain in general population studies

Research on alexithymia and chronic pain among general population samples (Table 3) has yielded positive results concerning their co-occurrence. In the Northern Finland Birth Cohort 1966 Study participants with orofacial pain symptoms were more alexithymic (TAS-20 score >60) than asymptomatic subjects (Sipilä et al. 2001). A study on city transit operators (Mehling and Krause 2005) found a positive connection between alexithymia and low back pain. A large Finnish population study investigated a subsample of participants with shoulder pain complaints and showed that pathological clinical findings were associated with work-load and diabetes, but that shoulder pain without any medical diagnosis was associated with the TAS-20 factor difficulties describing feelings (DIF) and depression and burnout situation (Miranda et al. 2005). A Japanese study found that high TAS-20 scores predicted the occurrence of chronic pain. Pain intensity, pain disability, depression and anxiety increased in parallel with TAS-20 scores and life satisfaction decreased simultaneously (Shibata et al. 2014). Mehling and Krause (2007) explored in a longitudinal study design (7.5-year follow-up time) the effect of alexithymia on compensated work disability because of low back pain and found no association. The researchers suggested that the unexpected result was a consequence of possible feelings of shame being laid off (but it is also conceivable that alexithymic workers with low back pain complaints lacked adequate physical findings supporting the need for sick leave, author's comment).

The results of general population studies mainly supported associations between alexithymia and pain disorders. Two studies (Miranda et al. 2005, Shibata et al. 2014) also reported connection between alexithymia and depression.

Table 3. Alexithymia and pain, general population samples

Author, year of publishing	Sample	Measures	Results	Conclusions
Sipilä et al. 2001	Northern Finland Birth Cohort 1966, 4893 subjects in 1997	alexithymia (TAS-20), depression (Symptom Checklist-25 = SCL-20). self-report inquiry to report temperomandibular disorder symptoms, oro-lingual and dental pain	proportion of subjects scoring TAS-20 >60 was higher with those among orofacial symptoms than asymptomatic	alexithymia is associated with orofacial pain
Mehling and Krause 2005	a cohort study, 1180 city transit operators	alexithymia (TAS-20) medical record of low back pain (LBP)	31.4% of drivers had LBP, upper quartile of TAS-20 scores was associated with twofold higher odds of LBP, DIF factor had strongest association TAS-20 mean 38.3 (9.4) in LBP participants	alexithymia and LBP are associated
Miranda et al. 2005	The Health 2000 Survey, 3909 participants among chronic rotator cuff tendinitis sample and 3525 participants among nonspecific shoulder pain sample	health check-up, an interview, questionnaires including TAS-20, BDI-II, work-related questionnaires	chronic rotator cuff tendinitis was associated with work load and diabetes but nonspecific shoulder pain was associated with burnout, depression and alexithymia	pain complaints without clinical findings indicate the presence of psychological and psychosocial factors in pain condition
Mehling and Krause 2007	a cohort study of 1207 transit operators, 7.5 year follow-up	alexithymia (TAS-20), diagnosed LBP in compensation data	alexithymia did not predict the duration of compensated work disability	alexithymia was negatively associated with compensated low back pain claims, the result was explained by possible shame and reporting behaviour
Shibata et al. 2014	927 adults participating The Hisayama Study (a cohort study for cardiovascular disease and its risks)	alexithymia (TAS-20), negative affect (SCL-90-R), pain intensity (VAS), disability (VAS). anxiety and depression (SCL-90-R), life satisfaction (VAS)	higher scores indicating alexithymia were associated with a higher risk of having chronic pain, and higher scores of TAS-20 were associated with diminished life satisfaction and increased pain intensity, disability, depression and anxiety	in general population, alexithymia is associated with a higher risk of having chronic pain, early identification of alexithymia and negative affect may prevent chronic pain

2.5.3 Alexithymia and chronic pain in clinical studies

Clinical cross-sectional studies on chronic pain and alexithymia included for review (Table 4) consisted of 27 studies published during the period 1994-2016. The studies varied in design and in clinical diagnosis. Measuring alexithymia was mainly performed by TAS-20 (21 studies), and the remaining six used TAS-26. Clinical populations were as follows: chronic pain (without location or a specific diagnosis); five studies (Lumley et al. 1997, Kosturek et al. 1998, Gregory et al. 2000, Ak et al. 2004, Makino et al. 2013), fibromyalgia; three studies (Pedrosa et al. 2008, Huber et al. 2009, Martinez et al. 2015), chronic low back pain; one study (Pecukonis 2009), fibromyalgia and rheumatoid arthritis; one study (Sayar et al. 2004), fibromyalgia, rheumatoid arthritis; and general medicine; one study (Steinweg et al. 2011), fibromyalgia and chronic low back pain; one study (Tuzer et al. 2011), somatoform pain disorder; three studies (Cox et al. 1994, Burba et al. 2006, Celikel and Saatcioglu O, 2006), migraine or chronic headache; three studies (Villain et al. 2010, Yalug et al. 2010, Vieira et al. 2013), tempero-mandibular disorder or oro-facial pain; four studies (Glaros and Lumley 2005, Castelli et al. 2013, Haas et al. 2013, Mingarelli et al. 2013), myofascial pain; one study (Lumley et al. 2002), muscular dystrophy; one study (Hosoi et al. 2010), cancer pain; one study (Porcelli et al. 2007), rheumatoid arthritis; one study (Kojima et al. 2014) and complex regional pain syndrome and low back pain; one study (Margalit et al. 2014). The number of participants varied from 30 participants (Lumley et al. 1997) to 465 (Villani et al. 2010). Healthy controls were used in nine studies.

In general, chronic pain patients were more alexithymic than their controls except in two studies having psychiatric patients as controls (Kosturek et al. 1998, Gregory et al. 2000). It was interesting that among chronic pain patients fibromyalgia sufferers were more alexithymic than their controls with rheumatoid arthritis (Steinweg et al. 2011) or low back pain (Tuzer et al. 2011). Furthermore, among alexithymic rheumatoid arthritis patients severity of pain was not related to the state of inflammation as it was among nonalexithymic patients (Kojima et al. 2014).

Alexithymia factors were explored separately in some studies: A study with healthy controls showed that chronic pain patients scored more on DIF (Ak et al. 2004, Sayar et al. 2004). A similar finding was reported in a study on painful temperomandibular disorder patients who scored higher on DIF than healthy controls or patients without pain disorder, but this association was lost in statistics when controlling for depression. However, in the same study TAS-20 total score

and factor EOT correlated with pain severity (Lumley and Glaros 2005). Fibromyalgia patients scored higher than healthy controls on DIF and DDF (Martinez et al. 2015) and among cancer patients DIF predicted pain condition (Porcelli et al. 2007). Two studies explored emotional expression (anger) and found that alexithymia correlated with suppression of anger (Sayar et al. 2004, Castelli et al. 2013).

Table 4. Alexithymia and chronic pain, cross-sectional clinical studies

Author, year of publishing	**Sample**	**Measures**	**Results**	**Conclusions**
Cox et al. 1994	55 motor vehicle accident survivors with chronic pain and somatoform pain disorder	alexithymia (TAS-20)	prevalence of alexithymia was 53%, no differences between alexithymic and nonalexithymic patients in pain severity or pain location, alexithymic used more words to describe their pain	alexithymic people have a diffuse style in describing their pain experience
Lumley et al. 1997	30 patients with chronic pain, 32 patients with nicotine dependence and 25 patients with moderate obesity	alexithymia (TAS-26, the Alexithymia Provoked Response Questionnaire, (APRQ), personality test (Minnesota Multiphasic Personality Inventory-2,MMPI-2)	chronic pain patients were more alexithymic than two other groups and they had more features of psychopathology in MMPI-2	alexithymia is more common among chronic pain patients and alexithymia may contribute to psychopathology
Kosturek et al. 1998	50 patients with chronic pain referred for psychiatric consultation, 50 controls selected randomly from patients referred for psychiatric consultation	alexithymia (TAS-20), anxiety and depression (the Brief Symptom Inventory =BSI), somatic amplification (the Somatosensory Amplification Scale =SAS)	the control group scored higher on anxiety, depression, TAS-20 and SAS , there were no differences between subsamples of chronic pain group with pain disorder or without, linear regression analysis with all participants (n=100) showed that SAS-scores were predicted by anxiety, depression and alexithymia but not by chronic pain	the results may be influenced by the psychopathology of the control group but it is possible that alexithymia in chronic pain patients is associated with mood disorders, not with pain disease

Gregory et al. 2000	220 patients referred for psychiatric consultation, 140 having chronic pain and 80 patients without pain for controls	alexithymia (TAS-20),anxiety and depression (subscales of Brief Symptom Inventory),somatosensory amplification (SAS), counterdependency (CDS), DSM-IV diagnoses by interview of psychiatrists	major depressive disorder was the most common disorder in both groups, no difference in alexithymia scores between the groups, back and extremities pain was associated with higher counterdepency	psychopathology but not chronic pain is associated with alexithymia in psychiatric patients
Lumley et al. 2002	80 patients with chronic myofascial pain	alexithymia (TAS-20), self-efficacy (CPSS),catastrophizing (CSQ), depression (CES-D),sensory and affective pain (MPQ), physical impairment (WHYMPI)	alexithymia correlated with depression, lesser self-efficacy and greater catastrophizing and depression, was related to affective pain but regression analysis showed that depression accounted for relation of alexithymia with affective pain	alexithymia may lead to depression which mediates the relation of alexithymia to affective pain, physical impairment is connected to alexithymia via self-efficacy and catastrophizing
Ak et al. 2004	30 chronic pain patients, 30 healthy controls	alexithymia (TAS-20),somatosensory amplification (SAS),Counter-Dependency Scale (CDS)	chronic pain patients amplified their somatic sensations, they had more difficulties identifying their feelings and distinguishing bodily sensations than healthy controls, psychiatric history increased the phenomenon,no differences between the groups in counter-dependency	individuals focusing their bodily sensations are more prone to have chronic pain
Sayar et al. 2004	50 fibromyalgia (FM) patients, 20 rheumatoid arthritis(RA)patients, 42 healthy controls, all females	alexithymia (TAS-20), depression (The Beck Depression Inventory), anxiety (The Beck Anxiety Inventory), fibromyalgia (The Fibromyalgia Impact Questionnaire), pain intensity (VAS), anger (State-Trait Anger Expression Inventory)	FM patients were more alexithymic, scored more on DIF, and were more depressive and anxious than healthy controls, fibromyalgia patients were more alexithymic, anxious and showed more anger supression	alexithymia and anger are important in the psychopathology of fibromyalgia, alexithymia factor DIF is associated with alexithymia

			than RA patients	
Glaros and Lumley 2005	49 patients with painful temperomandibular disorder (TMD), 24 pain-free somatic controls, 28 healthy controls	alexithymia (TAS-20),depression (the depression subscale of SCL-90-R), pain severity (ESM=experience sampling methodology, the mean of pain ratings from 0 to 10 during one week)	no differences between pain-free and healthy controls, painful TMD patients scored higher on DIF but the result accounted for depression, after controlling for depression, TAS-20 total score and EOT correlated with pain severity	alexithymia factors should be examined separately, TMD pain and alexithymia are related to each other
Burba et al. 2006	120 adolescents with somatoform pain disorder and 60 healthy controls	alexithymia (TAS-20), anxiety and depression (HADS)	prevalence of alexithymia was 59% in somatoform pain disorder patients versus 1% in healthy controls, the rate of anxiety was also higher (62% versus 15%), rate of depression was low in both groups	alexithymia and anxiety are associated with somatoform pain disorder in adolescents
Celikel and Saatcioglu 2006	30 female psychiatric outpatient with diagnosis of somatoform pain disease and 37 healthy matched controls	alexithymia (TAS-26), anxiety (STAI),pain intensity (VAS), pain duration	chronic pain patients were more alexithymic than controls, TAS score correlated with pain duration but not with pain intensity or anxiety	alexithymia may be an important subjective factor in pain condition
Porcelli et al. 2007	108 cancer patients divided into those with pain (n=45) and those without pain (n=63) groups	alexithymia (TAS-20), pain intensity (BPI=Brief Pain Inventory),coping with cancer (MAC=Mental Adjustment to Cancer Scale), illness behavior (IBQ=Illness Behaviour Questionnaire)	pain was associated with tumour sites and status, poor adjustment with cancer, higher disease conviction and perception, not with global alexithymia but with DIF, which predicted pain and correlated with quality descriptors of pain	DIF factor may be involved in pain experience as well as maladaptive coping and abnormal illness behaviour
Pedrosa et al. 2008	40 female fibromyalgia patients	alexithymia (TAS-26), parenteral style (FDEB = a German version of the Measure of Parental Style)	15% of patients were alexithymic, a positive association between TAS total score and maternal abuse was found, paternal indifference	unsecure parental style was associated with higher alexithymia scores

			predicted higher DIF scores	
Huber et al. 2009	68 female fibromyalgia patients	alexithymia (TAS-20), pain intensity (VAS), pain questionnaire (Questionare Italiono del Dolore,QUID),psychological distress; depression (CES-D) and anxiety (STAI-Y), illness behaviour (IBQ)	alexithymia factor DIF was related to affective pain, relation diminished when controlling for psychological distress or illness behaviour, DIF scores were predictive for hypocondrial illness behaviour	alexithymia is related to increased affective pain and it is mediated via psychological distress and illness behaviour, alexithymia is related to hypocondrial illness behaviour
Pecukonis 2009	59 women with chronic low back pain, 53 control subjects	alexithymia (TAS-26), Physical Self-Efficacy Scale	chronic pain patients scored significantly more in TAS-26 and had less perceived physical presentation confidence than controls, no differences in perceived physical abilities	emotion dysregulation is connected with chronic low back pain, lack of confidence may disturb rehabilitation
Hosoi et al.2010	129 patients with muscular dystrophy and chronic pain	alexithymia (TAS-20), pain intensity (NRS), pain interference (The Brief Pain Inventory, BPI), mental health and vitality (Mental health and vitality subscales from the Short Form Health Survey) were examined	TAS-20 total score, DIF, DDF and EOT correlated significantly with higher pain intensity and pain interference and TAS-20, DIF and DDF negatively with vitality and mental health. After partial correlation controlling for mental health the associations diminished; TAS-20 and EOT correlated with pain intensity and DIF negatively with vitality	alexithymia is associated with pain related variables in chronic pain, association is influenced by mental health
Villani et al. 2010	465 migraine patients of whom 70 were repeaters = visiting emergency department at least 3 times within six months	alexithymia (TAS-20) depression (BDI-II), anxiety (STAI), disability (migraine disability assessment scale (MIDAS), personality (the Tridimensional Personality Questionnaire=TPQ)	repeaters were more alexithymic (TAS-20 mean score 61.1 vs. 47.2 and the prevalence of alexithymia was 53.6% vs. 14.3%), more depressive (BDI-II mean score 18 vs. 13.7), more	the profile of repeaters differs from non-repeaters needing psychometric evaluation and more specific treatment

			anxious and scored more on harm avoidance on TPQ than non-repeaters	
Yalug et al. 2010	165 patients with episodic migraine (EM) and 135 patients with chronic migraine (CM)	alexithymia (TAS-20), depression (BDI-II), anxiety (STAI),pain characteristics	CM patients scored more in BDI-II, TAS-20 score correlated with age and education, TAS-20 correlated with anxiety and depression in both groups	migraine patients have positive associations between anxiety, depression and alexithymia
Steinweg et al. 2011	50 fibromyalgia patients, 50 general medicine patients, 50 arthritis rheumatoid patients	alexithymia (TAS-20),depression (BDI)	prevalence of alexithymia was 44% in the fibromyalgia group, 21% in the rheumatoid arthritis group and 8% in the general medicine group, fibromyalgia patients were significantly more depressive than other patients.	the high prevalence of alexithymia may be due to depressiveness, fibromyalgia patients are more depressive than the other groups explored
Tuzer et al. 2011	70 fibromyalgia patients, 56 chronic low back pain patients, 72 healthy controls	alexithymia (TAS-20),Brief Symptom Inventory, Symptom Interpretation Questionnaire	fibromyalgia patients scored higher in alexithymia, depression, somatization and hostility than back pain patients and controls, DIF and DDF predicted anxiety and depression, both patient groups were more alexithymic than controls	therapeutic processes should plan differently for alexithymic and nonalexithymic patients
Castelli et al.2013	45 female myofascial facial pain patients (MP) and 45 female healthy controls	alexithymia (TAS-20),depression (BDI-SF),anxiety (STAI-Y),distress thermometer (DT), anger (STAXI-2)	patients had higher TAS-20 score than controls, patients had more depression, anxiety, suppression of anger and emotional distress, alexithymia correlated with anger expression-in scale (internalized anger) and anxiety	MP patients had high prevalence of alexithymia, depression, anxiety and tendency to suppress anger

Haas et al. 2013	20 patients with temporomandibular disorder (TMD) and 20 controls	alexithymia (TAS-26), the Facially Expressed Emotion labeling (FEEL), the Screening for Somatoform Symptoms, the German Pain Questionnaire and 21-item Hamilton Depression Rating Scale	patient group was more alexithymic, had more somatoform symptoms and higher depression scores and they scored lower in FEEL, alexithymia and somatization explained 31% of the variance of FEEL	patients with TMD have impaired facial emotion recognition which is partially explained by alexithymia and somatization
Makino et al. 2013	128 chronic pain patients attending psychosomatic outpatient clinic	alexithymia (TAS-20, DDF),pain intensity (NRS), pain interference (BPI), depression and anxiety (HADS), pain catastrophizing (PCS)	TAS-20 total score and DDF were associated with pain interference, catastrophizing and negative affectivity, associations became nonsignificant when negative affectivity was controlled for	alexithymia influences indirectly on patients' functioning by negative affectivity
Mingarelli et al. 2013	133 patients with temperomandibular disorder (TMD)	alexithymia (TAS-20),Research Diagnostic Criteria for Temperomandibular Disorders Questionnaire	alexithymia and age explained 10% of pain, 31% of poor health and alexithymia explained 7% of social difficulty, alexithymic patients had more pain than nonalexithymic	alexithymia predicts pain, poor health and social difficulties in patients with TMD
Vieira et al. 2013	40 female outpatients from specialized headache hospital services and 33 general population controls	alexithymia (TAS-26), Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), a questionnaire of alcohol related disorders, self-reflection and insight scale, self report questionnaire for neurotic and psychotic disorders, quality of life (WHOQOL-BREF)	migraine patients had higher levels of alexithymia, anxiety and depression and lower levels of quality of life, self-reflection and insight compared with controls, quality of life was predicted by depression and alexithymia factor with poor ability to express emotions and fantasies in the migraine group, in the control group quality of life was predicted by a	migraine patients have psychological factors which have to be considered in health care practice

			concrete thinking style	
Kojima et al. 2014	213 rheumatoid arthritis patients	alexithymia (TAS-20), depression (BDI-II), pain intensity (VAS), inflammation (CRP)	patients without alexithymia showed linear association between pain severity and CRP level, depression was associated with pain severity, alexithymic patients had no such linear association, depressive and alexithymic patients reported severe pain even at low CRP levels	alexithymia and depression have a substantial role in pain perception
Margalit et al. 2014	Comparison of 30 patients with complex regional pain syndrome (CRPS) with 30 gender- and age-matched low back pain (LBP) patients	alexithymia (TAS-20) Hospital Anxiety and Depression scale (HADS) two subscales of the McGill Pain Questionnaire (MPQ)	There were no differences in pain variables but CRPS patients had higher scores for psychological distress and alexithymia than their controls, their pain severity was related to higher levels of alexithymia and psychological distress, DIF may predict pain condition	CRPS patients need an early diagnosis and consideration of psychological distress and alexithymia in their non-physical treatment
Martínez et al. 2015	Comparison of 97 fibromyalgia women with 100 healthy controls	TAS-20: DIF, DDF, EOT Short-Form McGill Pain Questionnaire (SF-MPQ) Pittsburgh Sleep Quality Index (PSQ) Impairment and Functioning Inventory (IFI) Hospital Anxiety and Depression Scale (HADS) Pain Catastrophizing Scale (PCS) Pain Anxiety Symptoms Scale-20 (PASS-20) Pain Vigilance and Awareness Questionnaire (PVAQ)	fibromyalgia patients scored significantly higher on all variables except EOT, high correlations were found between DIF and anxiety, depression, fear of pain, catastrophizing, between DDF and anxiety, catastrophizing, between pain experience anxiety, depression, catastrophizing and fear of pain. Pain vigilance correlated most with pain catastrophizing and fear of pain.	fibromyalgia patients have emotional processing problems (DID and DDF), these problems with fear of pain and catastrophizing predispose to emotional distress which contribute to increased pain experience

Depressiveness and anxiety were the most explored psychological co-factors with alexithymia (Lumley et al. 2002, Villani et al. 2010, Yalug et al. 2010, Steinweg et al. 2011, Tuzer et al. 2011, Castelli et al. 2013, Vieira et al. 2013, Kojima et al. 2014, Margalit et al. 2014. Martinez et al. 2015). Pain catastrophizing, fear of pain, poor self-efficacy, hypocondrial illness behaviour and poor quality of life were found to be related to chronic pain and alexithymia. Some studies showed that depressiveness was a mediator between other psychopathology or pain severity/affective pain and alexithymia (Lumley et al. 2002, Makino et al. 2013). One study found a positive association between maternal abuse and alexithymia (Pedrosa et al. 2008).

The negative influence of alexithymia on the course of pain disorder was reported in both longitudinal "alexithymia and pain disorder"-studies (Table 5). Pain disability and poor response to rehabilitation were related to alexithymic features (Julkunen et al. 1988) and the duration of postoperative pain was predicted by alexithymia (Baudic et al. 2016).

Table 5. Alexithymia and pain disorder, longitudinal clinical studies

Author, year of publishing	Sample	Measures	Results	Conclusions
Julkunen et al. 1988	One year of follow-up on low back pain female patients attending the back school (n=95) with controls without intervention (n=93)	neurotic features (The Middlesex Hospital Quesionnaire), hostility (the Roschach test), pain intensity, low back pain index, the bumber of pain attacks	the poor responders showed less cognitive capacity and poorer emotional regulation	patients having alexithymic features did not recover but had more disability after one year
Baudic et al. 2016	One year postoperative follow-up study on breast cancer patients, 96 participants	alexithymia (TAS-20),emotional repression (from the Weinberger Adjustment Inventory, the self-restraint and defensiveness measures), anxiety (STAI), depression (BDI), catastrophizing (the Pain Catastrophizing Scale), locus of control (The Cancer Locus of Control Scale), the Body Image Scale	body image and catastrophizing predicted acute or subacute pain at 2 months, anxiety predicted pain at 3 months, while alexithymia predicted pain at 3, 6 and 12 months, emotional repression did not predict pain	alexithymia was the only significant predictor of pain during the 12-month postsurgical period, emotional dysregulation is involved in the development of postsurgical pain

The reviews of alexithymia and chronic pain (Table 6) supported, with reservations, the association between chronic pain and alexithymia, but not unambiguously. The lack of repeated studies with an identical design impeded the evaluation. Depression emerged as a mediator between alexithymia and pain symptoms and possible different pain syndromes have a different "alexithymia profile". Alexithymia factor DIF in particular was found to be important in chronic pain syndromes.

Table 6. Alexithymia and chronic pain, reviews

Author, year of publishing	Sample	Measures	Results	Conclusions
DiTella and Castelli 2013	a review of seven studies concerning the relation between alexithymia and fibromyalgia (FM)	alexithymia (TAS-20)	in three studies FM patients had significantly higher scores in TAS-20 than controls, one study showed no difference between FM patients and healthy controls, in three studies without controls, FM patients showed slight to moderate higher prevalence of alexithymia than expected	unclear results, study designs vary
Di Tella and Castelli 2016	a review of studies between November 2012-September 2015 found in the PubMed and Ovid databases by keywords "alexithymia&chronic pain&emotional processing"	a critical discussion on alexithymia in different chronic pain conditions	chronic pain is associated with alexithymia features, especially with DIF, alexithymia may enhance disability, however, associations between pain intensity and alexithymia were not clear or were mediated by other factors, especially by depression	more accurate measures to assess alexithymia and pain are needed, chronic pain conditions may differ as regards presence/absence of alexithymia and its effect on pain situation

2.6 Conclusions based on the literature reviewed

The aim of the literature review was to elucidate and conceptualize the complex development and characteristics of alexithymia and chronic pain with their relations to depression and Early Maladaptive Schemas. The human development occurs in multiple levels which are interrelated and influence each other; e.g. neurophysiological development is influenced by genes and environmental factors which produce different outcomes in regulation systems which in turn encode the reactions of an individual to internal or external changes.

The differentiation between body and mind as well the differentiation between "nature and nurture" has been challenged by modern research. The early experiences modify both physiological and psychological facets of the individual. The development of the whole personality with its individual features is a complex learning process based on neuroplasticity and influenced by genetics, epigenetics and environmental factors. The consequences are concretized and to some extent discernible in neurobiological findings, in properties of the stress regulation system and immunological alterations. Psychological outcome manifests in behavioural, cognitive and emotional responses.

The research on early adversities highlights the importance of the quality of child treatment during the early years and the longstanding effects of mistreatment. However, there is still a long way from "bench to bed" and from statistics to the individual level. Our knowledge is collected from various research attempts and the empirical data about brain alterations or stress system adjustment is confined to small explorative studies or animal studies. Epidemiology and statistics point in the health problem direction but their results are indirect and depend on the methods used. The probability of a direct line from childhood adversities to adult health problems still has many concerns. We are inclined to consider human development as a linear time bound process from childhood to adulthood and aberrations in this process as (health) problems. It is possible that "development" is not linear, but consists of different paths, steps, stops and retrograde movements. The results of childhood adversities may also be explained as adaptive processes and/or protective strategies and in any case, as a logical outcome emerging from the given circumstances.

Science is determined by seeking the facts and the objectivity. Psychological phenomena are highly subjective in nature and their assessment according to the demands of objectivity is difficult. Questionnaires and interview based methods used to assess alexithymia, pain as well as depressiveness and EMSs face these

difficulties. The reliability and the validity of the methods depend on their chosen contents, repeatability, comparability and usefulness. Self-report questionnaires and interview based assessments have demonstrated their sufficient properties but invariably involve the very problem of response and interpretation bias. Brain scanning of psychological properties is still in its infancy.

Chronic pain has long been regarded as an extension of acute, somatic pain. There is now mounting evidence that chronic pain is a distinct disorder, although sometimes its initial stage seems to be associated with acute pain, which probably triggers the chronic pain syndrome. Susceptibility to chronic pain, however, is multifactorial and chronic pain itself consists of various pain disorders. The onset of chronic pain depends on the life history and predisposing life events. Every chronic pain patient has his or her own subjective pain experience which represents that individual's life trauma or adaptation to life events.

Early Maladaptive Schemas reflect early adversities and psychological adjustment to them. There is some evidence that certain EMSs may at least predispose to chronic pain through the coping styles associated with EMSs. Connections between alexithymia and EMSs have not been widely studied but their coexistence has been noticed in some psychological problems, such as in posttraumatic stress disorders. Theoretically, alexithymia and EMSs originate from the same breeding ground and may represent different facets and outcomes of early adverse experiences.

Depression occurs frequently with chronic pain, alexithymia and EMSs and its severity and effect on them varies. In chronic pain patients, depression manifests mainly as the psychological side of chronic pain and helps to maintain the pain problem. Fear-avoidance and pain catastrophizing can be considered as working models of depression in chronic pain.

Alexithymia has been proposed as a risk factor for chronic pain but its effect on the development of chronic pain is unclear. Only a proportion of chronic pain patients are alexithymic but those who suffer from chronic pain and are alexithymic usually report more pain and have more pain exacerbating factors such as low mood and catastrophizing. In chronic pain samples, alexithymia is associated with depressiveness, and depressiveness has been shown to mediate the effect of alexithymia on the variables describing the pain situation (pain intensity, pain disability). It is also unclear if chronic pain and depressiveness jointly predispose together to alexithymia or vice versa. The involvement of emotion dysregulation in chronic pain highlights the role of alexithymia with depression as factors which exacerbate the pain situation and impede possible recovery. It is also

possible that depressive alexithymic pain patients do not actually have a pain disease but that the amplified somatic symptoms and somatization representing emotional dysregulation are misinterpreted and treated as pain disorder without proper cure.

3 AIMS OF THE STUDY

The memories of early trauma may be inaccessible but their effect may manifest in their consequences. As chronic pain, alexithymia, depression and Early Maladaptive Schemas have connections with childhood adversities, their co-occurrence in adulthood may reflect the long-term effects of childhood trauma on health status.

The aim of the present study is to increase the understanding of the role of alexithymia in the context of chronic pain phenomena by exploring the relations of experienced pain, alexithymia, depression and Early Maladaptive Schemas in a sample of chronic pain patients in cross-sectional (Study I and II) and longitudinal study (Study III and IV) designs.

The concrete aims of the study are as follows:

Study I

1. To assess the prevalence of alexithymia in a clinical sample of chronic pain patients
2. To measure differences in pain variables and depression between alexithymic and nonalexithymic patients
3. To evaluate relations of alexithymia, depression and pain disability

Study II

1. To explore alexithymia, depression and Early Maladaptive Schemas and to estimate their combined effect on pain experience
2. To ascertain if alexithymic chronic pain patients have some typical Early Maladaptive Schemas or schema domains

Study III

1. To explore in a one-year follow-up the changes in pain variables, alexithymia and depression in a sample of chronic pain patients
2. To investigate the differences in pain variables and depression between alexithymic and nonalexithymic patients at baseline and at follow-up
3. To evaluate how baseline alexithymia and depression influence treatment choices

4. To evaluate the possible predictive value of baseline variables and the treatment selected on the outcome of the pain situation

Study IV

1. To evaluate in an eight-year follow-up the changes in the pain situation, alexithymia and depression in a sample of chronic pain patients
2. To explore the effect of basic characteristics, baseline pain variables, alexithymia and depression on the outcome of the pain situation
3. To investigate the relations between depression and alexithymia in the chronic pain situation

4 MATERIAL AND METHODS

4.1 Study design and participants

The present study is the second part of a larger study named "*The survey of the psychic profile of pain patients"* to explore psychological factors influencing the individual pain experience. The results of the first part have been published in the dissertation entitled "*Chronic pain, depressiveness and pain disability*" (Saariaho T 2012).

The study participants were chronic pain patients from six pain clinics in northern and central Finland. The data for the study was gathered by self-report questionnaires in the period 2004-2012. The study comprised cross-sectional and longitudinal sections. Participation in the study was on a voluntary basis.

4.1.1 Participants

In six pain clinics, successive chronic pain patients referred to their first pain clinic visit during a one-year period (2004 – 2005) were recruited for the study. Sources of referral were various medical specialists or primary health care facilities. The inclusion criteria were as follows: first consultation in the pain clinic, chronic non-malignant pain defined by its duration as a pain disorder lasting three months or longer, age 18-65 years and absence of psychosis or serious cognitive impairment. The study protocol information letter and the study questionnaire were sent to the patients before their first visit to the pain clinic. The patients completed the questionnaire at home and brought it with them when coming for their consultation. There were 318 eligible patients, 47 (15%) refused to take part in the study, so the first sample comprised 271 chronic pain patients. This sample was used in the cross-sectional study designs (Studies I and II).

One year after their first visit to the pain clinic, the follow-up study questionnaire was sent to the home addresses of all 271 patients who had participated in the first part of the study. Of these patients, 154 (57%) returned the study questionnaire and comprised the one-year follow-up sample (Study III).

In 2012 the second follow-up questionnaire was sent to all 271 patients who took part in the study in 2004-2005. The postal services returned 23 wrongly addressed letters and four relatives of patients reported their deaths. Out of 244 eligible patients, 83 (34%) returned the questionnaire and comprised the eight-year follow-up sample (Study IV).

Pain clinics were not involved in the data collections of either follow-up samples and the medical records of the patients were not used in any part of the study. Thus all collected data reflected concepts and assessments experienced and reported by the patients themselves.

4.1.2 Basic characteristics of the participants

In Studies I and II there were 271 subjects (male/female 127/144). Their mean age was 47.0 years (SD 1.6) and education in years 11.1 (SD 1.6). In Study III there were 154 subjects (male/female 68/86). At baseline their mean age was 47.9 years (SD 9.0) and education in years 11.1 (SD 1.8). In Study IV there were 83 participants (male/female 34/49). At baseline (2004-2005) their mean age was 49.5 years (SD 7.1) and education in years 11.3 (SD 1.8).

4.1.2.1 Comparisons between responders and nonresponders in the one-year follow-up study

The results of comparisons of basic characteristics and baseline study variables between the patients who responded and did not respond to the one-year follow-up questionnaire showed no significant differences (Table 7).

Table 7. Comparisons of basic characteristics and baseline study variables between responders and non-responders in the one-year follow-up study. Values presented in means (SD).

	Responders(n=154)	Nonresponders(n=117)	Sig.	Effect size
M/F	68/86	59/58	.305[a]	.062[c]
age (years)	47.9 (9.0)	46.0 (9.5)	.084[b]	.205[d]
education (years)	11.1 (1.8)	11.0 (1.4)	.426[b]	.062[d]
pain duration (years)	9.4 (9.0)	9.3 (8.6)	.918[b]	.011[d]
VAS	5.9 (1.3)	5.8 (1.1)	.296[b]	.083[d]
PDS	16.3 (4.9)	16.7 (5.2)	.573[b]	.079[d]
number of pain sites	2.2 (1.3)	2.1 (1.3)	.765[b]	.076[d]
TAS-20	47.6 (12.2)	47.2 (13.0)	.800[b]	.031[d]
DIF	15.7 (6.3)	15.4 (6.4)	.696[b]	.047[d]
DDF	11.1 (4.4)	11.3 (4.6)	.836[b]	.044[d]
EOT	20.7 (4.6)	20.5 (5.1)	.735[b]	.041[d]
BDI-II	15.7 (10.8)	15.7 (9.4)	.968[b]	.000[d]

Note: VAS= pain intensity in Visual Analogue Scale, PDS = Pain Disability Scale, TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II= Beck Depression Inventory, [a]Chi-Square, [b] Student's *t*-test, [c] φ coefficient, [d] Cohen's d

Table 8. Comparisons of basic characteristics and baseline study variables between responders and nonresponders in the eight-year follow-up study. Values presented in means (SD).

	Responders(n=83)	Nonresponders (n=188)	Sig.	Effect size
M/F	34/49	93/95	.196[a]	.079[c]
age (years)	49.5 (7.1)	45.9 (9.9)	<.01	.418[d]
education (years)	11.3 (1.8)	11.0 (1.5)	.116[b]	.181[d]
pain duration (years)	10.0 (9.0)	9.0 (8.8)	.380[b]	.112[d]
VAS	5.7 (1.2)	5.9 (1.3)	.241[b]	.160[d]
PDS	16.3 (4.6)	16.5 (5.3)	.807[b]	.040[d]
number of pain sites	2.2 (1.4)	2.1 (1.2)	.517[b]	.077[d]
TAS-20	46.9 (13.2)	47.7 (12.2)	.622[b]	.063[d]
DIF	15.5 (6.7)	15.6 (6.1)	.828[b]	.016[d]
DDF	11.0 (4.6)	11.3 (4.4)	.601[b]	.065[d]
EOT	20.4 (5.1)	20.8 (4.7)	.611[b]	.082[d]
BDI-II	14.8 (10.8)	16.1 (9.9)	.344[b]	.125[d]

Note: VAS= pain intensity in Visual Analogue Scale, PDS = Pain Disability Scale, TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II= Beck Depression Inventory, [a]Chi-Square, [b] Student's *t*-test, [c] φ coefficient, [d] Cohen's d

4.1.2.2 Comparisons between responders and nonresponders in the eight-year follow-up study

The results of the comparisons of basic characteristics and baseline study variables between the patients who responded and did not respond to the eight-year follow-up questionnaire showed no significant differences except that nonresponders were younger on average (Table 8).

4.2 Methods

4.2.1 Study questionnaires

The study questionnaires were planned for the study entitled "*The survey of the psychic profile of chronic pain patients*".

4.2.1.1 Baseline study questionnaire

The baseline study questionnaire consisted of questions concerning basic characteristics (age, gender and occupation), pain and illness history, pain mapping, pain attributes and pain related concepts. Pain intensity was measured on the Visual Analogue Scale (VAS) and pain disability (PDS), alexithymia (TAS-20), depression (BDI-II) and Early Maladaptive Schemas (EMSs) were elicited.

4.2.1.2 Follow-up study questionnaires

Both follow-up questionnaires included the same pain (VAS, PDS) and psychological variables (TAS-20, BDI-II, EMSs) as the baseline questionnaire. Additionally, there were questions concerning quality and quantity of treatment interventions.

4.2.2 Measures

4.2.2.1 Pain intensity, pain duration and pain mapping

The Visual Analogue Scale (VAS) was used to measure pain intensity. The VAS is a 100mm line segment where 0mm represents no pain and 100mm the worst pain one (the patient him/herself) can imagine. In the present study, 0mm was assigned a numerical value 0 and 100mm a numerical value 10. The patients were asked to rate their current maximal and minimal pain, and the mean value of these two ratings was regarded as their average pain intensity. The interpretation of the VAS values was changed to follow the interpretation of the numerical scale (Jensen et al.

2003): 0=no pain, 1-4 mild pain, 5-6 moderate pain, 7-10 severe pain. Pain intensity ≤ 4 was regarded as an acceptable level of pain according to common clinical practice. In pain treatment interventions, a 10-20% decrease in pain intensity level is regarded as a minimal improvement and a decrease of 30-33% as a moderate improvement (Farrar et al. 2001, Jensen et al. 2003). Pain duration was calculated in years according to the patient's answer to the question: "when did your present pain condition start"? The patients were asked to colour their pain sites in the body map provided. The number of different pain sites was calculated according to the pain map regions coloured. The pain sites were divided into six categories: head, neck-shoulder, lower back, abdominal region, thorax and limbs.

4.2.2.2 Pain disability

The Pain Disability Scale (PDS) is a self-report inquiry developed for the "*The survey of the psychic profile of pain patients"* to evaluate the interference of the pain disease in various life sectors. The PDS consists of seven direct statements ("my pain is disturbing my sleep", "…my hobbies", "…my sex life", "…my work", "…my mobility", "…my economy", "…my social contacts") and two inverted statements ("I can enjoy my life despite my pain" and "I can control my pain"). The items were rated by a Likert-type 0-3 scale: 0 = not at all, 1 = to some extent, 2 = significantly and 3 = very much. The total score indicates the level of the severity of pain disability (a score 0-4 = no disability, a score 5-13 = mild disability, a score 14-22 = remarkable disability and a score 23-27 = severe disability). The reliability and validity of the PDS were tested in a pilot study of 103 chronic pain patients by comparing the correlation between the PDS and the Pain Disability Index (PDI) (Tait et al. 1987, 1990). The correlation between the PDS and the PDI was .81, and furthermore, their correlations with the Beck Depression Inventory-II (r=.56 and r=.58, respectively) and with the VAS (r=.62 and r=.62, respectively) were almost identical. The results of the pilot study supported the reliability and validity of the PDS.

4.2.2.3 Treatment variables

In the follow-up questionnaires the patients were asked to report the quality and the number of their treatment interventions, the number of their visits to the pain clinic during one year and their drug therapy. Pain treatment methods were divided

into two categories: invasive methods such as surgery, anaesthesiological procedures and acupuncture and noninvasive methods such as drug therapy, physiotherapy, psychotherapy and pain groups. Invasive methods reflect more passive treatment methods than noninvasive methods needing more active involvement of the patient. The number of visits to the pain clinic was categorized into two classes: few visits (1-2 visits) and moderate or frequent visits (three or more visits). The drug use was defined by following groups: anti-inflammatory analgesics (NSAID) and paracetamol, antiepileptic drugs, sleeping pills, opioids, low-dose antidepressants and treatment dose antidepressants.

4.2.2.4 Alexithymia

Alexithymia was measured by the 20-item Toronto Alexithymia Scale (TAS-20), which is clearly the most used and tested method to measure alexithymia. It is also the most used measurement of alexithymia in chronic pain research (see 2.3.3). Its psychometric properties; internal consistency, reliability, test-retest reliability and convergent, discriminant and concurrent validity have been proven to be satisfactory (Bagby et al. 1994a, Bagby et al. 1994b, Parker et al. 2003, Taylor et al. 2003). The Finnish version used in this study has proven to have good psychometric properties (Joukamaa et al. 2001). The items of the TAS-20 are twenty statements on a Likert-type scale from 1 (strongly disagree) to 5 (strongly agree). Five items are inverted. The scores are added up and the result indicates the level of alexithymia. Scores ranges from 20 to 100. The cut-off point TAS-20 > 60 for alexithymia, was initially based on a study of a small sample of students (Bagby and Taylor 1997b) but in research work it has become a standard routine to make a distinction between alexithymic subjects and nonalexithymic subjects. In the present study, the patients were dichotomized to alexithymic and nonalexithymic using the cut-off point TAS-20 > 60. TAS-20 contains three factors describing different facets of alexithymia: difficulties identifying feelings (= Factor 1, DIF, 7 items), difficulties describing feelings (= Factor 2, DDF, 5 items) and externally oriented thinking style (= Factor 3, EOT, 8 items).

4.2.2.5 Depression

Depression was estimated by the revised 21-item version of the Beck Depression Inventory (BDI-II, Beck et al. 1996). Its psychometric properties have been

confirmed to be valid in Finnish (Beck et al. 2004). BDI-II has been proven suitable to measure depressiveness in chronic pain patients (Poole et al. 2006, Harris and D'Eon 2008, Corbière et al. 2011). It consists of 21 self-rated items which are ranked from 0 to 3 and then summed for the total score. The range of scores is from 0 to 63 and severity of depressiveness is estimated as follows: a score of 0-13 = no or minimal depressiveness, 14-19 = mild depressiveness, 20-28 = moderate depressiveness and 29–63 = severe depressiveness (Beck et al. 1996).

4.2.2.6 Early Maladaptive Schemas

Early Maladaptive Schemas (EMSs) were explored using the Finnish version of the extended Young Schema Questionnaire (= YSQ-S2-extended). The reliability and 18-factor structure have been proven (Saariaho et al. 2009). The YSQ-S2-extended consists of 18 current schemas, each schema containing five items. The schemas are divided into five schema domains (Table 9). Each domain represents one facet of unmet emotional core needs of the child. The schemas are also defined as unconditional or conditional schemas. Unconditional schemas are suggested to develop in early childhood and contain unconditional beliefs about the self, others and the world. Conditional schemas are consequences of unconditional schemas and may mask them. They represent coping attempts to adapt unconditional schemas (Young et al. 2003).

The YSQ-S2-extended is a self-report Likert-type questionnaire. Each schema contains five items which can be rated from 1 (completely untrue of me) to 6 (describes me perfectly). Schema questionnaires have been developed for clinical work and used as an interactive tool between the patient and the therapist in schematherapy. There are no official cut-off points to establish that the patient has or has not a certain schema, but in general higher schema scores indicate the activity and importance of the schema in life events, more maladaptive core beliefs and more schema triggered coping styles and behaviour. It has also been suggested that if a schema has two or more items rated 5 or 6, the schema is active and influences the individual's life (http://www.schematherapy.com/id111.htm). In the present study, the scores for each schema have presented as a mean value of the schema.

Table 9. Schema domains, their descriptions and Early Maladaptive Schemas (EMSs) (Young et al. 2003)

Schema domain	Description	Early Maladaptive Schema
Disconnection and rejection	The belief that one's needs for security, safety, stability, nurture, empathy, sharing of feelings, acceptance or respect will not be met.	Abandonment/Instability (AB)[a] Mistrust/Abuse (MA)[a] Emotional Deprivation (ED)[a] Defectiveness/Shame (DS)[a] Social Isolation/Alienation (SI)[a]
Impaired autonomy and performance	The belief that one's ability and capacity to separate, survive, cope independently or perform successfully is impaired.	Dependence/Incompetence (DI)[a] Vulnerability to Harm or Illness (VH)[a] Enmeshment/Underdeveloped Self (EM)[a] Failure (FA)[a]
Impaired limits	Difficulties in setting internal limits, feel responsibility or set long-term goals.	Entitlement/Grandiosity (ET)[a] Insufficient Self-Control/Self-Discipline (IS)[a]
Other-directedness	The needs, desires or responses of others are overrespected and taken into account at the expense of own needs.	Subjugation (SB)[b] Self-Sacrifice (SS)[b] Approval-Seeking/Recognition-Seeking (AS)[b]
Overvigilance and inhibition	The spontaneous feelings and impulses are suppressed and replaced by rigid, internalized rules about performance and behaviour.	Negativity/Pessimism (NP)[a] Emotional Inhibition (EI)[b] Unrelenting Standards/Hypercriticalness (US)[b] Punitiveness (PU)[b]

[a]unconditional schema, [b]conditional schema

4.2.3 Statistical methods

4.2.3.1 Study I

The scores of the study variables were calculated and expressed in means (SD). Student's *t*-test was used for continuous data and Pearson's Chi-square for categorical data for comparisons between the alexithymic and nonalexithymic groups. For estimating gender differences, study variables were compared between alexithymic men and women, likewise between nonalexithymic men and women. The dichotomization was performed by using the cut-off point TAS-20 total score >60. The patients were also categorized by their BDI-II score into four groups: no or minimal depressiveness (a score of 0-13), mild depressiveness (a score of 14-19), moderate depressiveness (a score of 20-28) and severe depressiveness (a score of 29-63). The percentages of patients in each group were calculated in the total group and separately in the alexithymic and nonalexithymic groups.

Pearson's correlation (r=correlation coefficient) was used to assess the relations between study variables and partial correlation to control depressiveness for. The

correlation was regarded as small if r was ±.1 – ±.29, moderate if r = ±.30 – ±.49 and large if r = ±.50 – ±1.0 (Cohen 1988). Cohen's d-value was used to define the effect sizes for continuous data and the phi coefficient was used for categorical data. The interpretation of Cohen's d by Cohen (1988): .8 = large, .5 = moderate and .2 = small effect size. The interpretation of the phi coefficient is similar to the Pearson correlation coefficient.

The possible mediation of BDI-II between TAS-20 and PDS was calculated by Lisrel path analysis. Mediation is indicated if there is a lower or nonsignificant path coefficient between two variables after the mediating variable is entered into the model. The level of significance in Lisrel path analysis was a path t-value >1.96.

4.2.3.2 Study II

The basic statistical methods were similar to those in Study I (dichotomization to alexithymic and nonalexithymic groups, exploring means of study variables in the whole sample, separately in alexithymic and nonalexithymic groups with their comparisons by Student's *t*-test and Chi-square test and calculating the effect sizes by Cohen's d and phi coefficient). Mann-Whitney U-test was used in the group comparisons between mean values of Early Maladaptive Schemas (EMSs) as the distribution of schema scores was skewed and *r*-value was calculated for measuring effect sizes. For the same reason, Spearman's rho was used in correlations between EMSs, alexithymia, BDI-II and pain variables. Partial correlation was performed in order to control for depressiveness.

Regression analyses were performed with pain intensity as the dependent factor and TAS-20, DIF, DDF, EOT, BDI-II and schema domains as independent factors estimating their predictive value on pain intensity.

An exploration of the effect of different levels of depressiveness on EMSs, pain intensity (VAS) and pain disability (PDS) was performed as follows: The patients were divided according to their BDI-II scores to form four categories: no depressiveness (0-13), mild depressiveness (14-19), moderate depressiveness (20-28) and severe depressiveness (29-63). Means of EMSs, PDS and VAS scores were calculated for each category and separately in alexithymic and nonalexithymic patient groups.

4.2.3.3 Study III

The patients were dichotomized according to the scores indicating an acceptable level of pain intensity (VAS≤4) and pain disability (PDS≤13), no alexithymia/alexithymia (TAS-20≤60) and no depression/depression (BDI-II≤13). The scores at baseline and at follow-up were using the McNemar test to find out the percentual changes in the abovementioned study variables.

Differences between VAS score, PDS score, TAS-20 total score and its factors and BDI-II score at baseline and at follow-up were compared using paired samples t-test. Comparisons were performed among the total patient sample (n=154), and among alexithymic (n=24) and nonalexithymic (n=130) patients. Student's *t*-test was used to compare the scores on the study variables between alexithymic and nonalexithymic patients both at baseline and at follow-up. In these comparisons, dichotomization to alexithymics and nonalexithymics was determined by TAS-20 score at baseline. Influence of baseline alexithymia and depression on treatment choices was explored by comparing treatment variables between alexithymic and nonalexithymic patients and between depressive and nondepressive patients using Chi-Square test (categorical data) and Student's *t*-test (continuous data).

The outcome in the pain situation was estimated by pain intensity and pain disability at follow-up. The patients were dichotomized to poorer and better outcome groups according the level of the mean score on pain intensity (VAS≤4) and the mean score on pain disability (PDS≤13). The groups were compared in terms of basic characteristics, baseline study variables and treatment variables using Chi-Square test and Student's *t*-test. Effect sizes were estimated by phi coefficient for categorical data and by Cohen's d for continuous data. The interpretations of effect sizes are presented in 4.3.1.

An increase in alexithymia scores and relations of baseline alexithymia and depression to follow-up pain disability necessitated two *post hoc* analyses: The patients were dichotomized using TAS-20 total score at follow-up to alexithymic (n=36) and nonalexithymic (n=118) patients and paired samples t-test was performed in both groups between baseline and follow-up variables. Lisrel path analysis was used to ascertain if depressiveness (at baseline) mediated the effect of alexithymia (at baseline) on pain disability at follow-up.

4.2.3.4 Study IV

Comparisons of mean scores of pain variables (VAS, PDS), alexithymia (Tas-20, DIF, DDF and EOT) and depressiveness (BDI-II) between baseline and follow-up values were performed in the total sample using paired samples *t*-test. Both baseline and follow-up scores of study variables were compared between alexithymic and nonalexithymic patients using Student's *t*-test and Chi-Square test. Pearson correlation analyses were performed to show the relations of BDI-II and TAS-20 both at baseline and at follow-up.

To estimate the outcome in the pain situation, the patients were dichotomized to "improvement" and "no improvement" groups according to follow-up scores in pain intensity and pain disability. A decrease of 30% or more in follow-up scores indicated improvement both in pain intensity and pain disability. Baseline study variables were compared between "improvement" and "no improvement" groups with Chi-Square test and Student's *t*-test. Effect sizes were calculated as presented in 4.3.1. Binary logistic regression analyses were performed to estimate the predictive value of baseline variables for outcome in pain intensity and pain disability at follow-up. Three different models of variables were formed consisting of basic characteristics (gender, age, education), pain variables (pain duration, pain intensity, pain disability) and psychological variables (alexithymia and depression). All models were tested and the last model was completed with the best predictors of previous models.

One *post hoc* analysis was done as male gender predicted poorer outcome in pain intensity; the study variables were compared with Student's *t*-test between males and females.

4.3 Ethical approval

All patients gave their written informed consent at all steps of data collection for the study. The study protocol was approved by the ethics committee of the Northern Ostrobothnia Hospital District.

5 RESULTS

5.1 Study I

The prevalence of alexithymia in the sample was 19.2%. There were no differences between alexithymic and nonalexithymic patients in terms of age (46.8 and 47.1 years respectively, p=.853) and education (10.8 and 11.2 years respectively, p=.121). However, in the alexithymic group the male/female ratio showed male predominance; 35/17 versus 92/127 in the nonalexithymic group, p<.01. Alexithymic patients scored significantly higher on pain intensity, pain disability and depressiveness (Table 10). The categorization of pain sites showed that alexithymic patients had more abdominal and low back pain than nonalexithymic patients (p<.01 and p<.05, respectively). In gender comparisons alexithymic men scored higher on pain intensity (VAS) than alexithymic women (p< .01). Nonalexithymic men had higher TAS-20 total score (p<.01) and Factor III score (p<.001) than nonalexithymic women. No other statistically significant differences were found between men and women in both groups.

Table 10. Mean values (SD) of pain variables, alexithymia and depression in the total sample and their comparisons between alexithymic and nonalexithymic patient groups.

	All patients (n=271)	**Alexithymic group (n=52)**	**Nonalexithymic group (n=219)**	**Sig.[a]**	**Effect size[b]**
TAS-20	47.4 (12.5)	66.8 (5.5)	42.8 (8.7)	<.001	2.92
DIF	15.6 (6.3)	24.6 (3.9)	13.4 (4.7)	<.001	2.59
DDF	11.2 (4.5)	17.5 (2.7)	9.7 (3.4)	<.001	2.54
EOT	20.7 (4.8)	24.7 (3.4)	19.7 (4.6)	<.001	1.24
BDI-II	15.7 (10.2)	25.0 (9.3)	13.5 (9.1)	<.001	1.26
PDS	16.5 (5.1)	19.0 (3.8)	15.9 (5.1)	<.001	0.63
VAS	5.9 (1.2)	6.3 (1.3)	5.8 (1.2)	<.01	0.43
Pain duration (years)	9.3 (8.8)	10.2 (9.5)	9.1 (8.6)	.436	0.12
Number of pain sites	2.1 (1.3)	2.3 (1.4)	2.1 (1.2)	.262	0.17

Note: VAS= pain intensity in Visual Analogue Scale, PDS = Pain Disability Scale, TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II= Beck Depression Inventory, [a] Student's *t*-test, [b]Cohen's d

Depressiveness in the total sample measured by BDI-II scores was as follows: 48.3% had no depressiveness, 20.3% mild depressiveness, 18.1% moderate depressiveness and 13.3% severe depressiveness (Table 11). The mean value of depressiveness was significantly higher in the alexithymic group (Table 10) Furthermore, alexithymic patients showed more severe depression levels than nonalexithymic patients as they scored significantly higher ($p<.001$, Chi-Square) on BDI-II levels indicating moderate or severe depressiveness (Table 11).

Table 11. Numbers of patients (with percentages) of BDI-II score levels according to the grade of depressiveness in alexithymic and nonalexithymic patients

	BDI-II score 0-13	**BDI-II score14-19**	**BDI-II score 20-28**	**BDI-II score ≥29**	**Total number of patients**
Total group	131 (48.3 %)	55 (20.3%)	49 (18.1%)	36 (13.3 %)	271
Number of alexithymic patients	6 (11.5%)	7 (13.5%)	19 (36.5%)	20 (38.5%)	52
Number of nonalexithymic patients	125 (57.1%)	48 (21.9%)	30 (13.7%)	16 (7.3%)	219

Pearson's correlation analyses were performed separately in the alexithymic and nonalexithymic groups as presented in Table 12. After partial correlation controlling for BDI-II, the correlations between TAS-20 and PDS and also those between PDS and factor DIF were no more significant in the alexithymic group. The correlations between VAS and PDS and between PDS and the number of pain sites in the nonalexithymic group lost their significance when BDI-II was controlled for.

Table 12. Pearson's correlations between pain variables, depressiveness and alexithymia data in the alexithymic and nonalexithymic pain patient groups

		TAS-20	**DIF**	**DDF**	**EOT**	**BDI-II**	**PDS**	**VAS**	**Pain duration**
Alexithymic pain patient group (N=52)	**BDI-II**	0.510**	0.450**	0.464**	-0.055				
	PDS	0.331*	0.323*	0.195	0.013	0.526**			
	VAS	0.167	-0.035	0.186	0.161	0.168	0.206		
	Pain duration	0.111	0.176	0.087	-0.089	0.344*	0.174	0.104	
	Number of pain sites	0.103	0.188	0.115	-0.138	0.255	0.357**	-0.013	0.193
Non-alexithymic pain patient group (N=219)	**BDI-II**	0.325**	0.382**	0.355**	-0.034				
	PDS	0.154*	0.154*	0.259**	-0.055	0.522**			
	VAS	0.095	0.145*	0.133	-0.065	0.239**	0.318**		
	Pain duration	-0.043	-0.024	0.085	-0.120	0.030	0.187**	0.118	
	Number of pain sites	0.032	0.192*	0.091	-0.20**	0.256**	0.396**	0.171*	0.159*

Notes: TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II= Beck Depression Inventory, PDS = Pain Disability Scale, VAS = Visual Analogue Scale, *Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed)

In Lisrel path analysis TAS-20 predicted PDS by the significant path coefficient (β=0.27, *t*=4.65). When BDI-II was entered into the model, the path from TAS-20 to PDS became nonsignificant (β=-0.02, *t*=-0.36) but the path from TAS-20 to BDI-II was significant (β=0.52, *t*=9.87) likewise the path from BDI-II to PDS (β=0.57, *t*=9.69). The statistical conclusion states that BDI-II was a mediator between TAS-20 and PDS.

5.2 Study II

Alexithymic patients had significantly higher mean values in all Early Maladaptive Schemas (EMSs) than nonalexithymic patients, except for Self-Sacrifice SS) schema (Table 13). The correlation analysis showed a large correlation between TAS-20 total score and Emotional Inhibition Schema (EI). Schema factor DIF correlated in large size with Vulnerability to Harm and Illness schema (VH). Schema factor DDF correlated in large size with Mistrust/Abuse (MA), Emotional Deprivation (ED) and EI schemas. BDI-II correlated in large or moderate size with all EMS, except with SS schema. All the correlations are presented in Table 14.

Table 13. Means (SD) of EMSs in the total sample and in the alexithymic and nonalexithymic pain patient groups with comparisons between alexithymic and nonalexithymic groups.

	All patients n=271	**Alexithymic patients n=52**	**Nonalexithymic patients n=219**	**Sig.[a]**	**r[b]**
Abandonment/Instability (AB)	1.8 (1.0)	2.7 (1.4)	1.6 (0.8)	<.001	0.35
Mistrust/Abuse (MA)	1.7 (0.9)	2.5 (1.3)	1.5 (0.7)	<.001	0.34
Emotional Deprivation (ED)	2.0 (1.6)	3.0 (1.4)	1.7 (0.9)	<.001	0.39
Defectiveness/Shame (DS)	1.6 (1.0)	2.5 (1.4)	1.4 (0.7)	<.001	0.38
Social Isolation/Alienation (SI)	1.9 (1.2)	3.0 (1.5)	1.6 (0.9)	<.001	0.37
Dependence/Incompetence (DI9	1.6 (0.8)	2.3 (1.2)	1.4 (0.6)	<.001	0.39
Vulnerability to Harm or Illness (VH)	1.8 (1.0)	2.7 (1.4)	1.6 (0.8)	<.001	0.37
Enmeshment/Undeveloped Self (EM)	1.3 (0.7)	1.7 (1.1)	1.2 (0.5)	<.01	0.18
Failure (FA)	1.8 (1.1)	2.6 (1.5)	1.6 (0.8)	<.001	0.34
Entitlement/Grandiosity (ET)	1.7 (0.8)	2.2 (1.1)	1.5 (0.7)	<.001	0.29
Insufficient Self-Control/Self-Disclipine (IS)	1.9 (1.0)	2.5 (1.2)	1.8 (0.8)	<.001	0.26
Subjugation (SB)	1.5 (0.8)	2.1 (1.1)	1.4 (0.7)	<.001	0.33
Self-Sacriface (SS)	3.4 (1.1)	3.6 (1.2)	3.3 (1.1)	.076	0.10
Approval-Seeking/Recognition-Seeking (AS)	2.6 (1.1)	3.1 (1.2)	2.5 (1.0)	<.001	0.21
Negativity/Pessimism (NP)	2.4 (1.2)	3.3. (1.2)	2.1 (1.0)	<.001	0.40
Emotional Inhibition (EI)	1.9 (1.0)	2.8 (1.5)	1.7 (0.8)	<.001	0.40
Unrelenting Standards/Hypercriticalness (US)	2.9 (1.2)	3.3 (1.2)	2.7 (1.1)	<.01	0.19
Punitiveness (PU)	2.3 (1.1)	3.0 (1.1)	2.1 (1.0)	<.001	0.29
Schema total	36 (12.7)	49.0 (15.1)	32.8 (9.8)	<.001	0.43
Schema mean	2.0 (0.7)	2.7 (0.8)	1.8 (0.5)	<.001	0.43

[a]Mann-Whitney U Test, [b]effect size

After partial correlation analysis controlling for BDI-II, the sizes of the correlations between alexithymia TAS-20 total score, DDF and DIF with most EMS diminished. There were moderate correlations between TAS total score and EI (.349, p<.001), between DIF and VH (.322, p<.001) and between DDF and EI (.434, p<.001).

Table 14. Spearman's correlations between EMSs, BDI-II and pain variables

	TAS-20	DIF	DDF	EOT	VAS	Pain duration	Pain sites	PDS	BDI-II
AB[a]	.410*	.458*	.430*	.065	.163*	.041	.087	.270*	.504*
MA[a]	.453*	.475*	.517*	.074	.226*	.069	.152	.290*	.498*
ED[a]	.488*	.488*	.517*	.137	.134	.135	.166*	.270*	.533*
DS[a]	.468*	.488*	.442*	.169*	.110	.015	.109	.255*	.560*
SI[a]	.428*	.477*	.464*	.056	.153	.145	.162*	.344*	.628*
DI[a]	.485*	.490*	.431*	.205*	.245*	.011	.123	.369*	.635*
VH[a]	.462*	.512*	.444*	.107	.186*	-.002	.081	.298*	.580*
EM[a]	.246*	.264*	.262*	.080	.128*	-.064	.064	.170*	.379*
FA[a]	.454*	.462*	.432*	.169*	.162*	.029	.083	.225*	.453*
ET[a]	.322*	.370*	.324*	.069	.130	.025	.006	.095	.336*
IS[a]	.365*	.369*	.376*	.113	.106	.052	.077	.204*	.479*
SB[a]	.418*	.407*	.416*	.148	.167*	.074	.162*	.300*	.534*
SS[a]	.150	.162*	.167*	.040	.054	.036	-.034	.129	.172*
AS[a]	.278*	.265*	.258*	.115	.096	.041	-.054	.065	.347*
NP[a]	.480*	.487*	.463*	.165*	.157*	.043	.118	.318*	.671*
EI[a]	.552*	.460*	.612*	.246*	.122	.131	.018	.212*	.479*
US[a]	.150	.181*	.199*	-.004	.078	.019	.017	.060	.334*
PU[a]	.389*	.394*	.405*	.122	.156	.080	.034	.292*	.542*

Note: TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II= Beck Depression Inventory, PDS = Pain Disability Scale, VAS = Visual Analogue Scale, [a] Early Maladaptive Schema abbreviations are presented in Table 13. * Correlation is significant at the 0.01 level (2-tailed)

Regression analyses, having pain intensity as a dependent factor and exploring the predictive value of EMS domains, TAS-20 total score, alexithymia factors and BDI-II showed that the domain "Impaired Autonomy and Performance" (p<.05) and BDI-II (p<.05) predicted pain intensity best, explaining 8% of its variance.

Observation of the compartmentalization by four levels of depressiveness and alexithymia or nonalexithymia showed that higher mean scores of EMSs were observed on higher levels of depressiveness and alexithymic patients mainly had higher scores on EMSs than nonalexithymic patients at different levels of BDI-II. Pain disability and pain intensity also increased slightly in parallel with BDI-II. Due to low numbers of subjects in some of the cells, the observed relations did not reach statistical significance. (Table 15).

Table 15. Means (SD) of Early Maladaptive Schemas (EMSs), pain intensity (VAS) and pain disability (PDS) in alexithymic and nonalexithymic pain patient groups according to the Beck Depression Inventory-II (BDI-II) scores.

	BDI-II <14		**BDI-II 14-19**		**BDI-II 20-28**		**BDI-II >28**	
	non-alexithymic (n=125)	alexithymic (n=6)	non-alexithymic (n=48)	alexithymic (n=7)	non-alexithymic (n=30)	alexithymic (n=19)	non-alexithymic (n=16)	alexithymic (n=20)
AB[a]	1.4 (0.5)	2.4 (2.1)	1.8 (0.8)	1.5 (0.7)	2.1 (1.0)	2.9 (1.3)	2.4 (1.6)	3.1(1.3)
MA[a]	1.4 (0.6)	1.7 (0.9)	1.5 (0.5)	1.4 (0.5)	1.7 (0.6)	2.5 (1.0)	2.4 (1.4)	3.2(1.5)
ED[a]	1.5 (0.7)	1.9 (0.9)	1.9 (0.9)	2.1 (1.0)	1.9 (1.0)	2.8 (1.3)	2.9 (1.6)	3.8(1.2)
DS[a]	1.2 (0.3)	1.7 (1.0)	1.3 (0.4)	1.2 (0.4)	1.6 (0.7)	2.3 (1.2)	2.6 (1.7)	3.3(1.4)
SI[a]	1.3 (0.6)	1.8 (1.5)	1.7 (0.7)	1.7 (0.8)	2.0 (1.0)	2.9 (1.2)	3.1 (1.4)	3.8(1.5)
DI[a]	1.2 (0.3)	1.6 (0.9)	1.5 (0.6)	1.6 (0.5)	1.7 (0.6)	2.1 (0.9)	2.4 (1.2)	2.9(1.4)
VH[a]	1.3 (0.5)	1.9 (1.1)	1.6 (0.7)	1.9 (0.8)	2.0 (1.0)	2.6 (1.2)	2.6 (1.2)	3.3(1.5)
EM[a]	1.1 (0.3)	1.6 (0.9)	1.3 (0.5)	1.2 (0.4)	1.3 (0.5)	1.7 (0.9)	2.0 (1.0)	2.0(1.4)
FA[a]	1.4 (0.5)	2.6 (1.1)	1.6 (0.7)	2.0 (0.8)	1.9 (0.9)	2.1 (1.2)	2.9 (1.6)	3.3(1.6)
ET[a]	1.4 (0.5)	1.8 (0.6)	1.6 (0.6)	1.7 (0.5)	1.7 (0.8)	2.0 (0.9)	2.0 (1.3)	2.8(1.3)
IS[a]	1.5 (0.5)	2.1 (1.3)	1.8 (0.8)	1.8 (0.9)	2.2 (1.0)	2.4 (1.1)	2.6 (1.3)	3.0(1.3)
SB[a]	1.2 (0.4)	1.4 (0.6)	1.3 (0.5)	1.3 (0.4)	1.7 (1.0)	1.9 (0.9)	2.5 (1.3)	2.7(1.2)
SS[a]	3.2 (1.1)	2.0 (1.1)	3.3 (1.1)	3.7 (0.9)	3.7 (1.1)	3.5 (0.9)	3.6 (1.1)	4.0(1.5)
AS[a]	2.3 (1.0)	3.1 (1.6)	2.5 (0.9)	2.5 (0.9)	3.2 (1.0)	2.9 (0.8)	3.1 (1.2)	3.5(1.3)
NP[a]	1.7 (0.7)	2.7 (1.0)	2.3 (0.8)	2.4 (1.2)	2.7 (1.0)	3.3 (1.0)	4.0 (1.2)	3.9(1.2)
EI[a]	1.5 (0.6)	1.5 (0.4)	1.8 (0.8)	2.1 (0.8)	1.9 (0.9)	2.9 (1.1)	2.5 (1.3)	3.4(1.1)
US[a]	2.6 (1.1)	2.1 (1.2)	2.8 (1.0)	2.3 (1.0)	3.2 (1.2)	3.6 (0.9)	3.2 (1.3)	3.8(1.2)
PU[a]	1.8 (0.9)	2.3 (0.9)	2.1 (0.8)	1.9 (0.8)	2.8 (1.0)	2.9 (1.0)	3.3 (1.1)	3.6(1.1)
EMS total	28.6(6.4)	37.2(11.4)	33.7(6.8)	34.3(5.4)	39.0(8.9)	47.3(10.1)	50.2 (15.1)	59.2 (15.4)
EMS mean	1.6 (0.4)	2.1 (0.6)	1.9 (0.4)	1.9 (0.3)	2.1 (0.5)	2.6 (0.6)	2.8 (0.8)	3.3(0.9)
VAS	5.5 (1.1)	5.9 (2.1)	6.1 (1.3)	6.0 (0.8)	6.2 (1.2)	6.4 (1.2)	5.8 (1.5)	6.4 (1.2)
PDS	13.9(4.7)	15.0 (2.8)	17.1(5.1)	17.9(2.6)	19.7(3.8)	18.8 (3.9)	20.4 (3.1)	20.8 (3.4)

Note: [a] Early Maladaptive Schema abbreviations are presented in Table 9

5.3 Study III

There was a significant increase in percentual proportions among patients with better outcome in pain intensity (7.2% at baseline and 26.1% at follow-up, $p<.001$) and pain disability (28.9% at baseline and 44.7% at follow-up, $p<.001$). Alexithymia increased, the proportion of nonalexithymic patients was 85.0% at baseline and 76.5% at follow-up ($p<.05$). There was no significant change in depressiveness (BDI-II≤13); at baseline 51.3% and at follow-up 56.6% ($p=.24$). The paired samples t-test yielded similar results (Table 16).

Alexithymic and nonalexithymic patients showed significant differences in pain disability and depressiveness both at baseline and at follow-up and the alexithymic group included a significant preponderance of males (Table 17).

Table 16. Comparisons of means (SD) of pain, alexithymia and depression variables between baseline and 1-year follow-up in the whole group (n=154), in the alexithymic (at baseline) group (n=24) and in the nonalexithymic (at baseline) group (n=130).

	Baseline	Follow-up	Sig.[a]	Effect size[b]
VAS				
all	5.9 (1.3)	5.1 (1.9)	<.001	.491
nonalexithymic	5.9 (1.3)	4.9 (1.9)	<.001	.614
alexithymic	6.3 (1.4)	5.7 (1.8)	<.01	.372
PDS				
all	16.3 (4.9)	14.3 (6.0)	<.001	.365
nonalexithymic	15.8 (5.0)	13.7 (6.0)	<.001	.362
alexithymic	19.1 (3.2)	17.4 (5.3)	<.05	.388
TAS-20				
all	47.6 (12.2)	49.7 (13.1)	<.01	.166
nonalexithymic	43.8 (8.7)	46.7 (11.3)	.<.01	.288
alexithymic	68.0 (6.3)	66.6 (9.7)	.34	.171
DIF				
all	15.7 (6.3)	16.7 (7.0)	<.05	.150
nonalexithymic	13.9 (4.7)	15.2 (6.1)	<.05	.239
alexithymic	25.5 (4.7)	25.3 (5.5)	>.9	.039
DDF				
all	11.1 (4.4)	12.1 (4.3)	<.001	.230
nonalexithymic	10.0 (3.5)	11.3 (3.8)	<.001	.356
alexithymic	17.6 (3.3)	16.9 (3.9)	.28	.194
EOT				
all	20.7 (4.6)	20.9 (4.4)	.63	.044
nonalexithymic	20.0 (4.4)	20.3 (4.4)	.35	.068
alexithymic	24.9 (3.5)	24.3 (2.7)	.22	.192
BDI-II				
all	15.7 (10.8)	15.4 (11.6)	.58	.027
nonalexithymic	13.6 (9.5)	13.1 (9.6)	.39	.052
alexithymic	27.3 (9.8)	28.7 (12.9)	.46	.122

Note: VAS = pain intensity on Visual Analogue Scale, PDS = Pain Disability Scale, TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II = Beck Depression Inventory, [a]paired samples t-test, [b] Cohen's d

Table 17. Comparisons between means (SD) of study variables of alexithymic (at baseline) patients (n=24) nonalexithymic (at baseline) patients (n=130).

	Alexithymic	Nonalexithymic	sig.	Effect size
Age (years)	46.8 (8.5)	48.1 (9.2)	.51[a]	.147[c]
Gender M/F	17/7	51/79	.<.01[b]	.231[d]
Education (years)	11.1 (2.0)	11.2 (1.7)	.84[a]	.054[c]
Pain duration (years)	11.3 (10.6)	9.0 (8.6)	.25[a]	.238[c]
VAS baseline	6.3 (1.4)	5.9 (1.3)	.12[a]	.296[c]
VAS follow-up	5.7 (1.8)	4.9 (1.9)	.086[a]	.432[c]
PDS baseline	19.1 (3.2)	15.8 (5.0)	.<.01[a]	.786[c]
PDS follow-up	17.4 (5.3)	13.7 (5.9)	<.01[a]	.660[c]
BDI-II baseline	27.3 (9.8)	13.6 (9.5)	<.001[a]	1.420[c]
BDI-II follow-up	28.7 (12.9)	13.1 (9.6)	<.001[a]	1.372[c]

Note: VAS = Visual Analogue Scale, PDS = Pain Disability Scale, BDI-II = Beck Depression Inventory, [a]Student's *t*-test, [b]Chi-Square, [c]Cohen's d, [d]φ coefficient

The analysis concerning the influence of baseline alexithymia and depression on treatment variables showed that alexithymia was associated with more frequent use of opioids ($p<.01$) and antiepileptic drugs ($p<.05$) and depressiveness with more frequent use of opioids ($p<.01$), sleeping pills ($p<.01$) and treatment-dose antidepressants ($p<.05$).

Poorer outcome in pain intensity (VAS > 4) was associated with higher pain intensity ($p<.001$) and higher DIF scores ($p<.05$) at baseline and with more frequent consumption of opioids ($p<.05$) and treatment dose antidepressants ($p<.01$). Poorer outcome in pain disability was associated with male gender ($p<.05$), longer pain duration ($p<.05$) and higher scores on pain intensity ($p<.001$), pain disability ($p<.001$), TAS-20 total ($p<.01$), DIF ($p<.01$), DDF ($p<.001$) and BDI-II ($p<.001$) at baseline and with more frequent consumption of sleeping pills ($p<.001$) and treatment-dose antidepressants ($p<.01$).

Post hoc analyses:

The patients were dichotomized to alexithymic and nonalexithymic groups according to TAS-20 score at follow-up. Comparisons of study variables between baseline and follow-up scores yielded the following results: In both groups pain intensity decreased significantly but pain disability decreased significantly only in the nonalexithymic group. In the alexithymic group was a significant increase in BDI-II and TAS-20 total score, DIF, DDF and EOT scores. In the nonalexithymic group there was a significant decrease in BDI-II score (Table 18).

The Lisrel path analysis showed that TAS-20 score at baseline predicted pain disability (PDS) at follow-up ($\beta=.28$, $t=3.54$) and when BDI-II (at baseline) was entered into the model, the path between TAS-20 and PDS became insignificant ($\beta=0.07$, $t=0.85$). The path from TAS-20 and BDI-II was significant ($\beta=0.50$, $t=7.00$), likewise the path from BDI-II to PDS was significant ($\beta=0.42$, $t=4.96$). This result indicated that BDI-II mediates the effect of TAS-20 on PDS.

Table 18. Comparisons of means (SD) of pain variables, alexithymia and depression between baseline and 1-year follow-up in the alexithymic (at follow-up) group (n=36) and in the nonalexithymic (at follow-up) group (n=116).

	Baseline	Follow-up	Sig.[a]	Effect size[b]
VAS				
alexithymic	6.5 (1.3)	5.8 (1.6)	.<.01	.483
nonalexithymic	5.8 (1.3)	4.8 (1.9)	<.001	.614
PDS				
alexithymic	18.9 (4.1)	17.8 (4.7)	.097	.249
nonalexithymic	15.5 (4.9)	13.2 (5.9)	<.001	.424
TAS-20				
alexithymic	59.6 (11.5)	68.7 (5.5)	<.001	1.009
nonalexithymic	43.8 (9.6)	43.9 (8.4)	.888	.011
DIF				
alexithymic	21.2 (6.3)	26.2 (4.0)	<.001	.947
nonalexithymic	13.9 (5.2)	13.8 (4.7)	.717	.020
DDF				
alexithymic	15.4 (4.5)	17.8 (3.0)	<.01	.627
nonalexithymic	9.8 (3.4)	10.4 (3.0)	<.05	.187
EOT				
alexithymic	22.0 (4.2)	24.7 (2.9)	<.05	.748
nonalexithymic	20.1 (4.5)	19.7 (4.1)	.339	.092
BDI-II				
alexithymic	24.5 (12.3)	27.5 (12.3)	<.05	.243
nonalexithymic	13.0 (8.7)	11.7 (8.4)	<.05	.152

Note: VAS = pain intensity on Visual Analogue Scale, PDS = Pain Disability Scale, TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II = Beck Depression Inventory, [a]paired samples t-test, [b] Cohen's d

5.4 Study IV

During the eight-year follow-up period, pain intensity, pain disability and depressiveness decreased among the participants but alexithymia scores remained largely unchanged. (Table 19).

Table 19. Comparisons of means (SD) of pain variables, alexithymia and depression between baseline and follow-up data of chronic pain patients (n=83).

	Baseline	Follow-up	Sig.[a]	Effect size[b]
VAS	5.7 (1.2)	4.6 (2.0)	<.001	.67
PDS	16.3 (4.7)	11.2 (6.2)	<.001	.93
TAS-20	46.6 (13.1)	46.3 (12.6)	.84	.02
DIF	15.2 (6.7)	14.6 (6.6)	.20	.09
DDF	10.9 (4.6)	11.2 (4.1)	.40	.07
EOT	20.5 (5.2)	20.7 (5.1)	.70	.04
BDI-II	14.7 (11.0)	10.8 (9.1)	<.001	.36

Note: VAS = pain intensity on Visual Analogue Scale, PDS = Pain Disability Scale, TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing

feelings, EOT = externally oriented thinking style, BDI-II = Beck Depression Inventory, [a]paired samples t-test, [b]Cohen's d

Alexithymic patients scored significantly higher than nonalexithymic patients on pain disability (20.1 vs. 15.4, p<.001) and on depressiveness (26.4 vs. 11.9, p=<.001) at baseline and significantly higher on pain intensity (5.6 vs. 4.4, p<.05), pain disability (15.2 vs. 11.1, p<.05) and depressiveness (20.8 vs. 8.5, p<.001) at follow-up. There was a large correlation between TAS-20 and BDI-II both at baseline (r=.612, p<.001) and at follow-up (r=.743, p<.001).

Improvement in pain intensity (a decrease of 30% or more in VAS scores) was reported by 27.7% of participants (n=23). In group comparisons between the "improvement and "no improvement" groups, "no improvement" was associated with male gender (p<.05), baseline TAS-20 total (p<.05) and DDF (p<.05) scores. In the binary regression analysis, "no improvement" in pain intensity was best predicted by TAS-20 total score (p<.05, the model explaining 16.0% of variance). Improvement in pain disability (a decrease of 30% or more in PDS scores) was reported by 43.4% of participants (n=36). "No improvement" was associated with male gender (p<.05) and baseline TAS-20 total score (p<.05). In the binary logistic regression analysis, "no improvement" in pain disability was predicted by male gender (p<.05, the model explaining 15.2% of variance).

The *post hoc* comparison between males and females showed that they had significant differences in TAS-20 total score (50.5 vs. 44.3, p<.05) and EOT score (22.7 vs. 18.9, p<.01) at baseline. Furthermore, at follow-up there was a significant difference in pain disability (13.6 vs. 10.6, p<.05) and almost significant differences in the TAS-20 total score (49.6 vs. 44.0, p=.057), EOT score (22.0 vs. 19.7, p=.057) and in pain intensity (5.2 vs. 4.3, p= .051).

5.5 Supplementary data

5.5.1 Control group

The results showed that alexithymic, depressive chronic pain patients had more Early Maladaptive Schemas, poorer pain situation and poorer outcome. There was a control sample available from "*The survey of the psychic profile of pain patients"* (Saariaho et al. 2009) and alexithymia, depression and EMSs in the general

population sample were explored and compared with chronic pain patients at baseline (see Studies I and II).

The control group was recruited for the basic study of this project from among municipal employees in the Finnish town of Raahe (n=918, 728 women and 190 men) in March 2005. The inclusion criteria were age 18-65 years and being employed as a municipal official. Participation was voluntary and anonymous. The total number of participating employees was 331. They completed a questionnaire containing the same items as those addressed to the pain patients. They were similar in terms of age but the control group differed from patients in having significantly more women ($p<.001$) and having longer duration of education (in years) estimated by the occupation ($p<.001$).

5.5.2 Comparisons between the control group and chronic pain patients

The mean score (SD) on TAS-20 was 47.4 (SD 12.5) among patients and 40.0 (SD 10.7) among the controls ($p<.001$). The prevalence rate of alexithymia was 19.2% among patients and 4.3% among controls ($p<.001$). Depression scores were as follows: patients 15.7(SD 10.2) and controls 6.9 (SD 6.7)($p<.001$).

The mean (SD) score on BDI-II was 12.7 (SD 7.2) among alexithymic controls and 6.6 (SD 6.6) among nonalexithymic controls. Corresponding values among patients were 25.0 (SD 9.3) and 13.5 (SD 9.1). Among the controls there was no difference between alexithymics and nonalexithymics in the severity of depressiveness while among the chronic pain patients alexithymics showed more moderate or severe depressiveness (=BDI-II >19) than nonalexithymic patients (75% vs. 21%).

As the number of alexithymic patients was exceptionally low in the control group (possibly due to the high proportion of females and higher level of education), the second dichotomization was done by using the cut-off point TAS-20 < 52 (Bagby and Taylor 1997b) to form two groups: low alexithymics (LA) and borderline/high alexithymics (BA). Hence there were 269 controls and 173 patients in the LA groups and 43 controls and 98 patients in the BA groups. Score of BDI-II was compared with the above mentioned grouping. The results showed that the BA control group scored significantly higher than the LA control group (11.3, SD 7.0, vs. 6.0. SD 6.2, $p<.001$) but the mean BDI-II score remained under the cut-off point of BDI-II score for depression. The patient BA group also scored significantly higher than the patient LA group (21.2, SD 10.1 vs. 12.6, SD 8.8,

p<.001) on BDI-II. Furthermore, LA patients scored significantly higher than LA controls (p<.001) and BA patients scored significantly higher than BA controls (p<.001) on BDI-II.

Independent samples Mann-Whitney U tests were performed to estimate and to compare the scores on Early Maladaptive Schemas in the above mentioned four groups: There were significant differences among the controls between BA and LA groups on all EMS (p <.001,) except in SS, US and AS schemas, the BA group scoring higher on all EMS. In the patient group, the BA group scored significantly higher on all EMSs (p <.001 except AS schema; p<.01 and EM schema, p<.05) than the LA patient group, except on SS and US schemas. The comparisons between the control LA and the patient LA groups showed that there were significant differences in AB (p<.05), MA (p<.05), DI (p<.05), SB (p<.05) and AS schemas (p<.01). The comparisons between the control BA and the patient BA groups found no differences on EMSs scores between the groups.

5.5.3 Additional explorations of Early Maladaptive Schemas

Alexithymic patients scored significantly higher on all schema domains (p<.001) than nonalexithymic patients. The schema domain "Overvigilance and Inhibition" had the highest mean score value (3.1, SD 1.0) among alexithymic patients.

According to the baseline results, alexithymic men scored significantly higher on all EMSs than nonalexithymic men, except for SS schema. Alexithymic women scored significantly higher than nonalexithymic women on ED, VH, SS, NP and EI schemas but the small number of alexithymic women may violate the statistics (Table 20). The results are also illustrated in Figure 1 to clarify EMSs profiles of chronic pain patients.

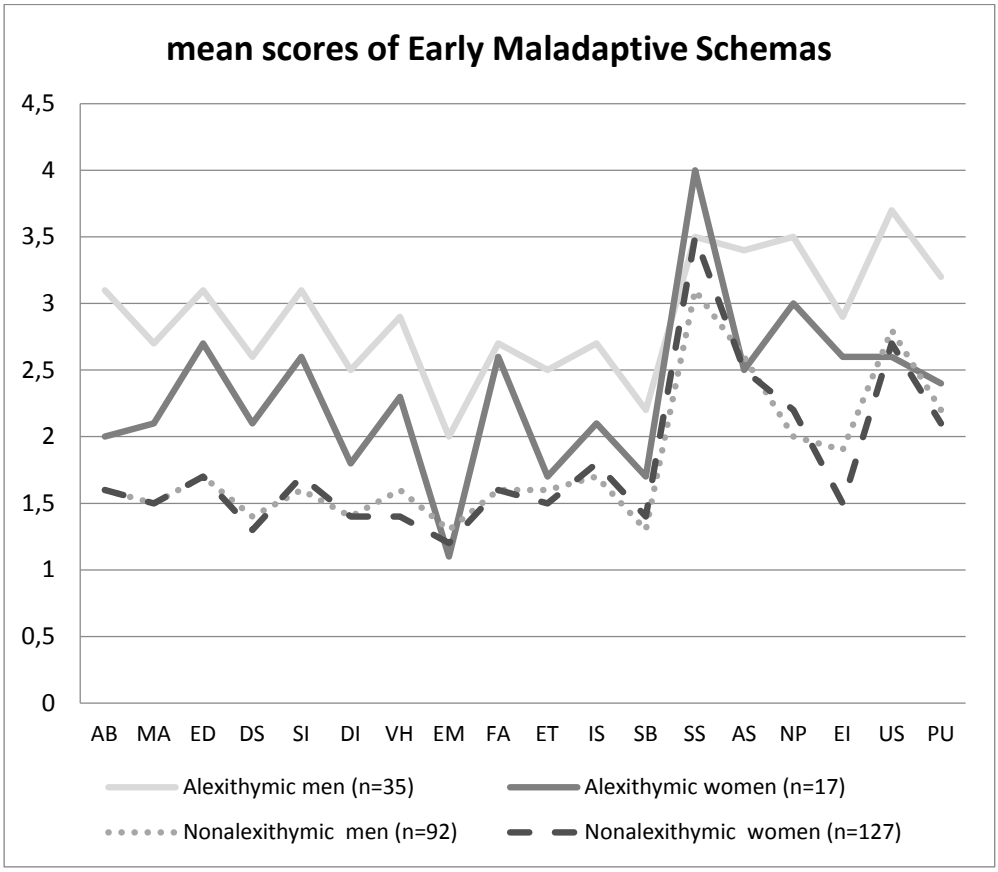
Stability of EMSs was explored by paired samples *t*-test, which was performed between the EMSs scores at baseline and at eight-year follow-up. No significant differences were found between the scores at baseline and at follow-up.

Table 20. Comparisons of means (SD) of Early Maladaptive Schema scores of alexithymic and nonalexithymic men and alexithymic and nonalexithymic women.

	Alexithymic men(n=35)	Nonalexithymic men (n=92)	Sig.[b]	Alexithymic women (n=17)	Nonalexithymic women (n=127)	Sig.[b]
AB[a]	3.1(1.3)	1.6 (0.8)	<.001	2.0 (1.3)	1.6 (0.8)	.293
MA[a]	2.7 (1.3)	1.5 (0.7)	<.001	2.1 (1.3)	1.5 (0.7)	.061
ED[a]	3.1 (1.3)	1.7 (0.9)	<.001	2.7 (1.5)	1.7 (1.0)	<.01
DS[a]	2.6 (1.3)	1.4 (0.8)	<.001	2.1(1.6)	1.3 (0.7)	.064
SI[a]	3.1 (1.3)	1.6 (0.9)	<.001	2.6 (1.9)	1.7 (0.9)	.080
DI[a]	2.5 (1.1)	1.4 (0.7)	<.001	1.8 (1.2)	1.4 (0.6)	.150
VH[a]	2.9 (1.4)	1.6 (0.8)	<.001	2.3 (1.3)	1.4 (0.8)	<.01
EM[a]	2.0 (1.1)	1.3 (0.5)	<.001	1.1 (0,3)	1.2 (0.5)	.073
FA[a]	2.7 (1.2)	1.6 (0.9)	<.001	2.6 (1.7)	1.6 (0.8)	.056
ET[a]	2.5 (1.1)	1.6 (0.8)	<.001	1.7 (0.9)	1.5 (0.6)	.425
IS[a]	2.7 (1.1)	1.7 (0.8)	<.001	2.1 (1.4)	1.8 (0.8)	.958
SB[a]	2.2 (1.1)	1.3 (0.6)	<.001	1.7 (1.0)	1.4 (0.8)	.278
SS[a]	3.5 (1.3)	3.1 (1.1)	.146	4.0 (1.2)	3.5 (1.0)	<.05
AS[a]	3.4 (1.1)	2.6 (1.1)	<.001	2.5 (1.0)	2.5 (1.0)	.958
NP[a]	3.5 (1.1)	2.0 (1.0)	<.001	3.0 (1.2)	2.2 (1.1)	<.05
EI[a]	2.9 (1.0)	1.9 (1.0)	<.001	2.6 (1.5)	1.5 (0.7)	<.01
US[a]	3.7 (1.1)	2.8 (1.1)	<.001	2.6 (1.1)	2.7 (1.1)	.838
PU[a]	3.2 (1.0)	2.2 (1.0)	<.001	2.4 (1.1)	2.1 (1.1)	.186
Schema total	52.5 (14.2)	33.1 (10.5)	<.001	41.6 (14.5)	32.7 (9.3)	<.01
Schema mean	2.9 (0.8)	1.8 (0.6)	<.001	2.3 (0.8)	1.8 (0.5)	<.01

Note: [a] Early Maladaptive Schema abbreviations are presented in Table 9, [b] Mann-Whitney U-test

Figure 1. Schema profiles: mean scores of Early Maladaptive Schemas[a] of alexithymic men and women and nonalexithymic men and women.



Note: Early Maladaptive Schema abbreviations are presented in Table 9

6 DISCUSSION

The study was intended to explore the complex nature of the chronic pain phenomenon by exploring its relations to alexithymia, depression, Early Maladaptive Schemas (EMSs) and by assessing the outcome of treatment interventions. The literature review showed that alexithymic patients are more prone to have concomitant factors exacerbating the pain experience and distress such as negative affectivity, depression, catastrophizing, lower self-efficacy, anxiety, fear of pain and unfavourable childhood circumstances. In the present study depression and EMSs represented the psychological factors which are connected to cognitive distortions and maladaptive coping styles. Furthermore, all the phenomena studied (chronic pain, alexithymia, depression, EMSs) have associations with early life adversities and also with traumatic incidences occurring later in life.

The special interest of the study was in the subgroup of alexithymic chronic pain patients and how they might differ from nonalexithymic patients. Chronic pain research currently places more emphasis on differences between chronic pain patients, not only according to the biomedical diagnoses but the biopsychosocial entity of the patient in question. Individual assessments of the overall situation and accordingly planned tailored interventions are in the focus of pain researchers. This study supported the concept of different subgroups among chronic pain patients. The psychological factors explored; alexithymia, depression and EMSs, contributed to the pain experience. This co-occurrence suggested their possible common origin in adverse childhood experiences.

The participants of the study represented a selected pain patient group referred for their first consultation to the pain clinic because of their unresolved pain problems. In the Finnish health care context consultation in the pain clinic usually means the final trial to find a treatment option for the patient's pain situation after other biomedical interventions have failed to achieve a satisfactory outcome. Patients did not represent any particular disease group or pain syndrome, their common characteristic was specially their complaint of severe, persistent pain.

6.1 Sociodemographic features of the study population and prevalence of alexithymia

The prevalence of alexithymia estimated by the standard dichotomization (total score of TAS-20 >60) showed that approximately one in five patients was alexithymic. The prevalence was higher than in Finnish general population studies: 13.0% (Salminen et al. 1999), 10.3% (Honkalampi et al. 2000) and 9.9% (Mattila et al. 2006). The control sample of the present study clearly had a low prevalence of alexithymia (4.3%). The prevalence rates of earlier studies among chronic pain patients have yielded mixed results. In somatoform pain syndromes the occurrence of alexithymia was reportedly as high as 53.0% (Cox et al. 1994) or 59.0% (Burba et al. 2006). Fibromyalgia has repeatedly been the target in alexithymia research and reported prevalence rates vary from 15.0% (Pedrosa et al. 2008) to 44.0% (Steinweg et al. 2011). Among migraine repeaters the prevalence of alexithymia was 53.6% (Villani et al. 2010).

The variety of prevalence rates of alexithymia among chronic pain patients is likely caused by disparities in study populations and designs. Unfortunately, in only few of the studies (see 2.5) were the prevalence rates of alexithymia calculated, probably due to exploring alexithymia as a dimensional variable without dichotomization. The impression (of the author) from the studies reviewed was that the pain syndromes without a clear biomedical pathology were more associated with alexithymia (Cox et. al 1994, Sipilä et al. 2001, Miranda et al. 2005, Sayar et al. 2004, Burba et al. 2006, Steinweg et al. 2011), especially fibromyalgia and somatoform pain, but not unanimously (Pedrosa et al. 2008). In the present study design, pain syndromes or pain types were not classified nor were specific diagnoses available, thus the impression cannot be confirmed by this data. The results supported the higher prevalence of alexithymia among chronic pain patients than in general population.

The low prevalence of alexithymia among controls may be explained by the absence of depressiveness. A general population study reported an equal prevalence rate (4.3%) of alexithymia among nondepressive participants (Honkalampi et al. 2000). The control sample and the participants of the present study also included sociodemographic differences; the control group consisted mainly of women; they all were employed and more educated than the patients. Male gender and low level of education have been found to be characteristic sociodemographic features in alexithymic populations (Salminen et al. 1999, Mattila et al. 2006). The mean age was similar in the alexithymic and nonalexithymic

patient groups, which made the groups more comparable and removed the impact of the age factor from the prevalence rates. In this study, alexithymic and nonalexithymic patients were also comparable in terms of education. This finding may reflect common psychosocial factors such as low education in chronic pain (Klijs et al. 2014, Shmagel et al. 2016). Low level of education combined with childhood adversities predicted health problems while attainment of a high level of education enhanced health status (Montez and Hayward 2014).

There was no significant difference in the number of males and females in the total pain patient sample but the alexithymic group included a preponderance of males. The overrepresentation of males among alexithymic subjects has also been found in general population (Salminen et al. 1999, Mattila et al. 2006) as well as in clinical samples (Honkalampi et al. 1999). The higher prevalence of alexithymia among men has been explained by social and cultural differences in bringing up males to adapt to the restricted emotionality belonging to the male role (Carpenter and Addis 2000). The term "normative alexithymia" has been used to refer to traditional masculine ideology and fear of intimacy (Sullivan et al. 2015). However, the majority of men are not alexithymic, thus the upbringing does not give a sufficient answer. Furthermore, the prevalence of alexithymia in adolescents was found to be higher among girls than among boys, although boys had a higher mean value on the TAS-20 score (Joukamaa et al. 2007). Another study among adolescents found no gender differences in the prevalence of alexithymia (Karukivi et al. 2010).

6.2 Pain duration

Pain duration before the first visit in the pain clinic was decidedly long, the mean value being almost ten years (median six years). This fact describes an ethical and economic side of chronic pain. According to Breivik et al. (2006), a minimal proportion of chronic pain patients are referred to specific pain care, mainly due to a lack of facilities or knowledge. One can imagine how much suffering and disappointing interventions patients have faced before their referral for pain consultation. The costs of examinations and treatment trials were not calculated in this study, but the statistics published elsewhere reveal that chronic pain is one of the most resource-consuming disorders in health care (Breivik et al. 2013).

Long duration of an untreated pain condition has been supposed to strengthen the neurological and psychological learning of the central nervous system thereby

maintaining chronicity (Fine 2011). A neuroimaging study showed that pain duration was associated with an increase of pain related changes in the brain (Baliki et al. 2011). Alexithymic and nonalexithymic patients had similar pain durations but in the alexithymic group pain duration correlated with depression. Sullivan et al. (2002) found that chronic pain patients having longer pain duration also had more associations between catastrophizing and pain disability than did patients with shorter pain duration.

6.3 Pain intensity

Pain intensity in chronic pain is the most used and the most criticized measure. The critique is directed towards its ability to reflect "real pain intensity" and towards its use in treatment solutions. It is likely that the patient complaining of high pain intensity will more easily get examinations, intervention trials and strong medication such as opioids. It is preferable to regard pain intensity in chronic pain as a subjective assessment of individual overall distress or suffering which is not necessarily related to the severity of noxious processes and tissue pathology, but rather to depression and anxiety (Sullivan and Ballantyne 2016). Pain intensity may also reflect pain beliefs; an experimental study revealed that the tissue-damaging meaning of pain increased scoring on pain intensity (Arntz and Claassens 2004).

In the present study, alexithymic patients showed higher pain intensity values at all measurement points (baseline and both follow-ups) than did nonalexithymic patients. In spite of these results, pain intensity at baseline did not correlate highly or even moderately with alexithymia or its factors. Furthermore, pain intensity in the alexithymic group did not correlate with any other pain variables or depressiveness. In the nonalexithymic group, pain intensity correlated only with pain disability, which lost its significance when depression was controlled for. In the one-year follow-up study, "no improvement" in pain intensity was associated with higher pain intensity at baseline and alexithymia factor DIF (difficulties identifying feelings). After eight years, "no improvement" in pain intensity was associated with male gender, baseline total alexithymia score and alexithymia factor DDF (difficulties describing feelings). The association between male gender and pain intensity was explained by higher occurrence of alexithymia among males.

Earlier research has yielded variable results on relations between pain intensity and alexithymia. Hosoi et al. (2010) found that pain intensity correlated with alexithymia, but the correlation diminished when negative affect was controlled for.

In a sample of CRPS patients pain severity correlated significantly with alexithymia factor DIF, even when psychological distress was controlled for (Margalit et al. 2014). Stronger visceral pain severity was found to be related to alexithymia factor DIF (Kano et al. 2007) while in somatoform pain patients alexithymia did not correlate with pain intensity (Celikel and Saatcioglu 2006). Comparison of studies is difficult due to varying study designs; the other psychological factors than alexithymia contributing to pain intensity were different and statistical analyses varied. However, the present study, like earlier research, reflects the influence of alexithymia factors DIF and DDF on experienced pain intensity. These factors may contribute to pain intensity by several mechanisms, such as hypersensitivity, misunderstanding the bodily felt emotional states and somatosensory amplification. It has also been observed that severity of pain reflected a positive correlation between anger inhibition and depression (Estlander et al. 2008). Anger suppression has been found to be associated with alexithymia and chronic pain (Castelli et al. 2013) as well as depression.

In the present study pain intensity seemed to behave independently and to be more a personal expression of the patient unrelated to other measures. In an earlier study with the same materials (Saariaho et al. 2011), the path analysis revealed that pain intensity in those controls, who had reported some kind of pain condition, was related to pain disability, but among chronic pain patients pain intensity had a minimal effect on pain disability while depression had a remarkable impact on pain disability and also some influence on pain intensity. When pain duration increased, pain intensity was no longer related to pain disability, which in turn, was connected significantly with depression. When regarding pain intensity in chronic pain as a measure linked to overall distress, it is more understandable that its subjective estimation fluctuates randomly with the individual experience. In the study by Kojima et al. (2014), alexithymic rheumatoid arthritis patients reported greater pain severity, were more disabled and depressive (74% from alexithymic sample) than nonalexithymic patients. The study showed that nonalexithymic patients reported pain severity according to the CRP-level, i.e. the state of inflammation was related to pain severity, but this linear association was not found among alexithymic patients, thus supporting the notion that pain intensity does not follow the tissue pathology.

However, the reason for assessing pain intensity is its prognostic value. Among the factors predicting persistence of pain syndrome high pain intensity has been shown to predict problems in recovery (Kindler et al. 2010, Dunn et al. 2012, Verkerk et al. 2013, Mehta et al. 2015). A large cross-sectional study showed that

those chronic pain patients who reporting a history of abuse had more severe pain, more severe depression, greater anxiety, poorer physical functioning, worse pain interference and higher catastrophizing than non abused patients (Nicol et al. 2016). Thus high pain intensity may mirror other underlying important factors such as (early) traumatic experiences. Pain intensity in the present study did not correlate with EMSs, but regression analysis performed to explore EMS domains, alexithymia and depression in relation to pain intensity, showed that the domain "Impaired autonomy and performance" with depression predicted pain intensity to some extent. The results of the present study supported the assumption that pain intensity is a valuable measure when used as a predictive indicator. High level of reported pain intensity may mask important factors related to pain experience and is associated with poorer prognosis.

6.4 Pain sites

There was no difference in the number of pain sites between alexithymic and nonalexithymic patients, which was unexpected as alexithymia is associated with somatosensory amplification and somatic complaints and alexithymic patients had more severe depression, which is also connected with somatic symptoms. Both groups had medium-sized correlations between pain disability and the number of pain sites but these correlations diminished when depression was controlled for.

At baseline alexithymic patients reported significantly more abdominal and low back pain than nonalexithymic patients. Porcelli et al. (1999) compared inflammatory bowel disease patients, functional gastrointestinal disorder patients and healthy controls. The results showed that both patient groups were more alexithymic than the controls and the prevalence of alexithymia was highest (66.0%) among patients with functional gastrointestinal symptoms, even after controlling for depression and anxiety. Abdominal pains are common symptoms of distress in children (Korterink et al. 2015) and one might speculate that alexithymic individuals may express their emotional states like anxiety through uncomfortable visceral sensations. Abdomen and low back are common sites of vague, transient pain symptoms. It is possible that alexithymic individuals interpret their symptoms to be more threatening than nonalexithymics and via negative affectivity and catastrophizing focus on their "harmless" symptoms and thus unintentionally magnify them. Somatization and somatosensory amplification as a part of alexithymic characteristics give these symptoms more power. Bodily felt emotions

and stress may also produce symptoms which alexithymic people fail to understand as a part of their emotional processes.

6.5 Pain disability

Pain disability describes the patient's conception of how much and in which aspects he/she claims pain to be responsible for limitations and restrictions. In the present study, pain disability was related to depressiveness in both alexithymic and nonalexithymic patients but alexithymic patients reported significantly more pain disability at all measuring points when compared with nonalexithymic patients. Depression was also the mediator between alexithymia and pain disability. Chronic pain patients usually regard their pain disability as a consequence of pain severity ("*I am in such pain that I cannot exercise*") but the results of the present study confirmed the importance of depression in pain disability.

Earlier studies have shown that depressiveness is an important factor in pain disability. Postoperative disability and pain symptoms in a follow-up study of lumbar spinal stenosis patients were predicted by preoperative depressiveness (Sinikallio et al. 2009). Kinesiophobia and depression with anxiety were associated with significant pain disability (Bean et al. 2014). A review of prospective studies stated that chronicity and disability in low back pain were connected to somatization, depressive mood, catastrophizing and major distress (Pincus et al. 2002). In a path-analysis depression predicted significantly more pain disability than pain intensity (Saariaho et al. 2011). The higher scores of alexithymic patients on pain disability are at least partly explained by their more severe depression when compared with nonalexithymic patients.

In earlier studies on alexithymia and chronic pain, pain disability as itself was not regularly assessed, but analogous findings have been reported. A study on fibromyalgia patients reported that factor DIF predicted hypocondrial illness behaviour (Huber et al. 2009). Alexithymia was related to less perceived physical presentation among low back pain patients (Pecukonis 2009). A study on chronic pain patients found that pain interference was related to alexithymia but the association became insignificant when negative affect was controlled for (Makino et al. 2013).

Pain disability also inversely mirrors the ability to cope with experienced pain. Self-efficacy beliefs explained the variance of Pain Disability Index (PDI) better than pain intensity or pain duration in a sample of subacute and chronic

musculoskeletal pain patients (Denison et al. 2004). A path-analytic model tested in three different chronic pain patient groups found that self-efficacy was a mediator between pain disability and pain intensity, also among nondepressive patients (Arnstein 2000). Pain disability has been found to be influenced and exacerbated by pain catastrophizing (Severeijins et al. 2001, Arnow et al 2011). It has been suggested that pain catastrophizing is a dysfunctional way to cope (avoidant coping strategy) with negative emotions raised by the pain situation/life situation (Flink et al. 2013). Fear-avoidance beliefs (Grotle et al. 2004), poor self-efficacy (Costa Lda et al. 2011) and pain related anxiety and fear (Keefe et al. 2004) exacerbate pain disability. Depression was found to be partially mediating the relations between fear-avoidance model factors (Seekatz et al. 2016). Alexithymia has been shown to be associated with low physical self-efficacy (Pecukonis 2009). Catastrophizing and diminished self-efficacy were connected with alexithymia in a sample of chronic myofascial pain patients (Lumley et al. 2002). Fibromyalgia patients had high correlations between catastrophizing and alexithymia factors DIF and DDF, additionally fear of pain correlated with DIF (Martínez et al. 2015).

In the present study, the pain disability related factors above mentioned were not explored, but EMSs, which include similar concepts, were explored. There were significant correlations between pain disability and following EMS: Dependence /Incompetence (DI), Social Isolation (SI), Subjugation (SB) and Negativity/Pessimism (NP). DI schema represents maladaptive beliefs about one's ability to perform and cope independently. SB schema also describes one's poor capacity to take account of one's own needs. In this context, SI schema may reflect psychosocial difficulties found also in alexithymia and depression and lack of social support and communication with others. NP schema points to catastrophizing, negative affect and in case of chronic pain, possibly promotes fear-avoidance behaviour. Pain disability, depressiveness and mean scores on EMSs showed linear increasing suggesting that pain disability was strongly related to psychological factors. Furthermore, alexithymic patients scored generally higher on EMSs.

6.6 Early Maladaptive Schemas

Early maladaptive schemas (EMSs) reflect adverse childhood circumstances. They represent negative core beliefs and distortive cognitions and their impact manifests in schema driven behaviour styles and life choices. In the present study, alexithymic patients scored significantly higher on all schema domains and on all

individual schemas (except on Self-Sacrifice Schema). The comparisons between women and men showed that alexithymic men had the highest schema scores and nonalexithymic women the lowest, otherwise the schema profiles were roughly similar in shape. EMSs were also strongly associated with depressiveness.

6.6.1 Early Maladaptive Schemas and connections with alexithymia

EMSs have been shown to be associated with several health disorders. Studies on EMSs have mainly used psychiatric samples and their unfavourable contribution or predisposing effects have been found in depression (Halvorsen et al. 2009), posttraumatic stress disorder (Cockram et al. 2010), personality disorders (Nordahl et al. 2005), eating disorders (Unoka et al. 2010) and substance abuse (Shorey et al. 2013). Alexithymia has also been connected with the above-mentioned health disorders such as eating disorders (Nowakowski et al. 2013), depression (Honkalampi et al. 2000, Bamonti et al. 2010), substance dependence (Morie et al. 2016), personality disorders (Nicolò et al. 2011, Coolidge et al. 2013) and posttraumatic stress disorder (Frewen et al. 2008, Declercq et al. 2010).

Associations between EMSs and alexithymia were reported in studies on eating disorders (Lawson et al. 2008), suicidal adolescents (Hirsch et al. 2001), posttraumatic stress disorder after sexual abuse (Zlotnick et al.1996) and in irritable bowel syndrome (Phillips et al. 2013). Studies on relations between EMSs and chronic pain showed that EMSs contributed to the pain experience (Saariaho 2012). A recent study on migraine patients found that EMSs were connected with anxiety, pain intensity and pain disability on migraine patients (Tavallaii et al. 2015). No studies on EMSs with chronic pain and alexithymia could be found by the present author.

6.6.2 Disconnection and Rejection schema domain

In the present study both alexithymia and depression showed notable correlations with EMSs in the schema domain Disconnection and Rejection. This consists of five unconditional schemas (AB, MA, ED, DS and SI) reflecting abuse, insecurity, neglect and feelings of social inferiority and defectiveness. According to Young et al. (2003), individuals with these schemas "*are often most damaged*" as a consequence of a traumatic childhood. The child has remained without safe attachment, nurture, protection and empathy and has been physically and/or emotionally abused and

hurt. In adulthood, the victim of these adversities has problems in commitment and is at risk of being abused. The self-esteem is weak and the self is felt to be inadequate and worthless.

In an earlier study, the most disabled chronic pain patients had pronounced values on EMSs in the Disconnection and Rejection schema domain reflecting childhood adversities (Saariaho et al. 2011). There is substantial research evidence of associations between alexithymia and childhood adversities and neglect (Joukamaa et al. 2008, Honkalampi et al. 2004, Joukamaa et al. 2008, Carpenter and Chung 2011, Aust et al. 2013). In a sample of chronic pain patients, maternal abuse was connected with alexithymia (Pedrosa et al. 2008). Alexithymic individuals also have interpersonal problems and paucity of close relationships (Spitzer et al. 2005, Vanheule et al. 2007b, Mattila et al. 2010).

Psychosocial support from a network of close relationships protects from depression. Low self-esteem and difficulties in interpersonal relationships associated with these schemas together with alexithymia probably predispose to depression and also in this way exacerbate the pain experience. These EMSs, alexithymia and depression may also disrupt commitment to treatment interventions and trustful relationships with health care personnel, thus exerting a negative influence on treatment outcome.

6.6.3 Emotional Inhibition schema

Emotional Inhibition schema (EI) belonging to the Overvigilance and Inhibition schema domain correlated strongly with alexithymia (total score and DDF). The schema describes unemotional style and repression of emotions. Its origin has been considered to be in childhood circumstances where rules have been strict, rationality and self-control overemphasized and emotions not expressed spontaneously (Young et al. 2003). EI schema has been regarded as one schema which causes anger suppression and inhibition of positive impulses. Young describes people with EI schema as "*flat, constricted, withdrawn or cold*". EI schema has been regarded as a conditional schema, developed later as a coping schema to avoid feelings of shame encountered in childhood when expressing emotions spontaneously.

EI schema and alexithymia share similar characteristics and may overlap each other as psychological phenomena developed together from the same developmental circumstances. Both reflect adverse childhood experiences with

unfavourable circumstances for emotional maturation. Dysregulation of emotions, especially inhibition and suppression, has been proposed to have a predisposing and exacerbating influence on health disorders, among them chronic pain and depression (Keefe et al. 2001, Lumley et al. 2011). Alexithymia has been found to be associated with anger suppression in chronic pain patient samples (Sayar et al. 2003, Castelli et al. 2013). EI schema has been found to be common in obsessive-compulsive disorder which has been shown also to have associations with alexithymia (Roh et al. 2011).

6.6.4 Other important schemas

Negativity/ Pessimism (NP) schema, which was also a noticeable schema among alexithymic patients, belongs to the Overvigilance and inhibition schema domain. NP schema provides a negative view of life events and resembles catastrophizing style of conceptualization; one expects that at any moment a personal disaster will occur. Vulnerability to Harm (VH) and Failure (FA) schemas correlated notably with alexithymia. They both belong to the Impaired Autonomy and Performance schema domain reflecting childhood circumstances where the child was brought up without reinforcement of self-confidence, the parents have been overprotective or alternatively the very opposite – the child has been left alone to manage without any guidance. VH schema represents fear of catastrophe (any kind) without trusting one's own coping skills. A person with FA schema believes that he/she will fail in all endeavours and is inadequate compared with others. NP, FA and VH schemas are unconditional, therefore their "download" in the network of the mind has early been installed and will be automatically triggered to interpret life events accordingly. NP schema is closely linked to depression and its presence with alexithymia and VH schema may serve to increase catastrophizing and add a degree of experienced pain while FA schema guided coping style probably impairs self-efficacy.

6.6.5 The relation of Early Maladaptive Schemas to experienced pain

EMSs have not been a popular subject of detailed analysis, so studies for purposes of comparison are rare. EMSs consist of several known elements familiar in pain research as factors associated with the development and maintenance of chronic pain: adverse childhood experiences, low self-esteem, low self-efficacy,

catastrophizing, emotion avoidance and suppression, workaholism, interpersonal and commitment problems, all of which all have been found to be associated with alexithymia and depression.

EMSs and their related coping styles have been regarded as consequences and attempts to survive and adapt in early emotionally painful situations. It has been suggested that in the case of chronic pain, one uses similar processes to cope with pain and painful (negative) emotions – avoidance, catastrophic worry (= catastrophizing and recurring negative thinking) and suppression - in order to alleviate the stress and maintain homeostasis. Unfortunately these regulation styles sensitize to focus on pain as one must to be alert to the situation for possible cues to predispose to pain or painful emotions (Linton 2013).

EMSs remained stable during the eight-year follow-up period as also did alexithymia. The comparisons of EMSs between chronic pain patients and controls showed that borderline/high alexithymic patients and controls did not differ from each other. The theoretical background combined with the study results give reason to speculate that childhood adversities create circumstances which predispose to EMSs and alexithymia which through unfavourable life events are conducive to depression and chronic pain.

6.7 Alexithymia and depressiveness

6.7.1 Depression

The present results highlighted the impact of depression on chronic pain. This relation has been found in several earlier studies (see 2.4.7). Depressiveness is like a shadow hanging over (or a glue holding together) all factors which have been shown to be associated with phenomena predisposing to, maintaining and exacerbating pain such as emotional dysregulation, catastrophizing, fear-avoidance behaviour, low self-esteem, psychosocial and interpersonal problems. Depression is closely connected with early adversities, alexithymia and EMSs. One can really ask if in the context of chronic pain depression is just other name for chronic pain or better, its "operative model". From another point of view, it is possible to define chronic pain as a special depressive disorder manifesting in bodily felt pain symptoms. Similar suggestions have been made earlier by Engel (1959), Hudson and Pope (1989) and Goldenberg (2010).

6.7.2 Alexithymia

The most striking difference between alexithymic and nonalexithymic patients was the magnitude and the degree of depression. Almost all alexithymic patients were depressive and the proportion of severe depression was significantly higher among alexithymics than among nonalexithymics. Depression was also the mediator between alexithymia and pain disability in cross-sectional and longitudinal study path models. The course of chronic pain patients in this study showed that alexithymic patients remained depressive, reporting more pain interference but nonalexithymic patients recovered, depression was relieved and the pain situation rendered tolerable.

At one-year follow-up there was an increase in the proportion of alexithymic patients which was associated with increasing depressiveness. The parallel fluctuation of depression and alexithymia has been reported in earlier depression studies (Honkalampi et al. 2001), notably both factors DIF and DDF varied in concordance with depressiveness (Saarijärvi et al. 2001). During eight years the correlation between alexithymia and depression remained significant and large, even increased to some extent. Contrary to expectations, depression no longer predicted pain intensity and pain disability at eight-year follow-up. This result may be explained by changes in the whole group – the total depressiveness decreased as the nonalexithymic patients recovered while alexithymia and its effect on experienced pain remained more stabile.

Alexithymic individuals having problems describing and identifying their emotional states may interpret their bodily felt feelings as threatening signs of a health disorder. Somatization (Mattila et al. 2008a), somatosensory amplification (Nakao et al. 2002) and tendency to psychosomatic manifestations of emotions (Lindqvist and Feldman Barret 2008) are symptomatic of alexithymia. In case of experienced pain or other sensations resembling pain, alexithymic people may be prone to overestimate or misinterpret the meaning of their symptoms. Furthermore, when focusing on bodily sensations and pain symptoms with negative affect (fear) and cognition (catastrophizing), the magnitude and importance of those symptoms will increase with the help of automatic learning mechanisms of the central nervous system (Ingvar 2015). Unfortunately, this learning mechanism is connected to brain neuroplastic changes which in turn may maintain the symptoms and exacerbate them. Thus alexithymic people concentrating on their somatic symptoms unwittingly provide "learning material" for their brains and add to and maintain their symptoms. In this way, for example,

bodily felt anxiety or an innocent transient low back pain (people feel often tiredness in their backs when they are doing too many working hours) may transform into chronic pain.

6.7.3 "Alexithymic depression"

Depression contributes to negative assumptions concerning the meaning and consequences of somatic symptoms. Depression itself produces different somatic symptoms including bodily felt pain. A study exploring the effects of childhood trauma on somatization in major depressive patients showed that alexithymia was associated with childhood trauma and current somatic complaints, and contributes to the occurrence of somatic symptoms in depressive patients (Güleç et al. 2013). It has been proposed that depression with alexithymia is different from "normal" depression. "Alexithymic depression" was found to be characterized by more somatic-affective symptoms and distant interpersonal functioning (Vanheule et al. 2007a). Earlier studies have found that alexithymic depressive individuals complain of more somatic symptoms (Sayar et al. 2003) and they are more prone to suicidal ideation (Hintikka et al. 2004). As alexithymia is associated with somatization, somatosensory amplification and tendency for psychosomatic symptoms and depression itself also produce somatic symptoms, it is reasonable to assume that alexithymia together with depressiveness may multiply bodily felt symptoms. Cognitive distortions of depression help interpret these symptoms as a physical, painful illness. Furthermore, in this study both alexithymia and depression correlated to a large extent with EMSs which are associated with several maladaptive beliefs and coping styles and which may feed and modulate negatively the pain experience or other bodily felt sensations. It was found that emotional maltreatment correlated with alexithymia and somatic complaints in a study among undergraduates and alexithymia mediated the relation between maltreatment and somatic symptoms (Smith and Flannery-Schroeder 2013).

Alexithymic people have been found to have interpersonal difficulties (Vanheule et al. 2007b) as well as insecure attachment styles (Carpenter and Chung 2011). A recent study showed that alexithymia factors DIF and DDF mediated the association between avoidant attachment and interpersonal problems (independently of negative affect) in somatoform disorder patients (Koelen et al. 2016). In the present study depression and alexithymia showed significant correlations with EMSs suggesting poor interpersonal functioning guided by EI

and SI schemas. Lack of support through healthy relationships in "alexithymic depression" may be seen a one factor more to maintain the problem. Both alexithymia and depression are characterized by emotional processing problems, which may be the underlying basic problem.

6.8 Treatment interventions and outcome

Chronic pain is difficult to treat. Interventions intended to alleviate suffering are usually based on biomedical approaches, thus multidisciplinary and more patient-specific methods are recommended. In the present study the patients received multiple types of treatment choices and according to their reports the treatment interventions were regarded as "treatment as usual". The treatment provided followed well accepted and approved treatment guidelines of biomedicine. Patients having group therapy (pain groups) or psychotherapy were rarities.

None of the treatment interventions proved superior achieving an acceptable level in pain intensity or pain disability. The results confirmed those of several earlier studies; treatment of chronic pain is challenging and pain is really persistent (Elliott et al. 2002, Andersson 2004). Nonetheless, a proportion of the patients recovered and the results suggested that nondepressive and nonalexithymic patients may benefit from treatment provided. It is possible that the characteristics of the patients were crucial for recovery. Improved patients probably had more adaptive coping styles and capacities and different pain conditions/pain disorders.

Negative expectations (pain beliefs) and severe pain intensity were prognostic indicators among low back pain patients (Campbell et al. 2013). An earlier study among low back patients found that baseline characteristics such as age, work status, belief system, quality of life, pain and disability had an influence on outcome but not on treatment response (Underwood et al. 2007). A systematic review of prospective studies on low back pain stated that persistence of symptoms and disability were associated with psychological distress, depressive mood and somatization and to some extent with catastrophizing (Pincus et al. 2002). A more recent study noted that recovery in low back pain after a multidisciplinary rehabilitation programme was predicted by absence of psychological and physical dysfunction at baseline (Verkerk et al. 2013). Pain-related beliefs (self-efficacy, fear-avoidance) have been shown to predict outcome in physiotherapy (Denison et al. 2004).

Compliance with and adherence to treatment are connected with the personal psychological characteristics of the patient, and also the health care provider. An earlier study confirmed that adherence to pain self-management strategies and reductions in catastrophizing and fear-avoidance beliefs alleviated pain intensity, pain disability and depressive symptoms (Nicholas et al. 2012). The outcome of the chronic pain rehabilitation programme was predicted by the patient-physician relationship (Farin et al. 2013). A medication compliance study (Kipping et al. 2014) assessing pain patients and pre-surgical control patients showed that high depression scores predicted non-compliance. A meta-analysis of non-compliance with medical treatment (Di Matteo et al. 2000) found a substantial and significant relation between depression and patient non-compliance. Interpersonal problems and unsafe attachment styles associated with alexithymia and depression may predispose to impaired treatment compliance and adherence and thus to affect on outcome.

In the present study the baseline situation characterized by alexithymia, depression and severe pain situation was predictive of persistence of symptoms and poor recovery. EMSs were not explored in relation to outcome but one can speculate that they also helped to maintain the problems. Poor recovery in the pain situation associated with alexithymia and depression reflected several intertwined factors. First, both have been shown to contribute to a more severe pain experience and both *per se* may produce somatic symptoms which may be interpreted as pain disorder or pain disease. These symptoms are severe enough to mask depression and emotional dysregulation and lead to misdiagnosis and untreated depression. Secondly, both include factors exacerbating and predisposing to pain experience (see 6.7), which may impede recovery. Finally, alexithymia and depression may inhibit compliance with and adherence to proposed treatment interventions.

The severity of pain situation did not cause variation in treatment variables describing activity and diversity in treatment interventions. Medication comparisons between "improvement" and "no improvement" groups showed that higher pain intensity at follow-up was associated with heavier use of opioids and antidepressants and higher pain disability at follow-up was related to heavier use of sleeping pills and antidepressants. More detailed calculations revealed that over half of the patients took opioids (53%) but not so heavily antidepressants (27%). It is obvious that high pain intensity reported by patients was treated by prescriptions for opioids. It is difficult to know if antidepressants were used on purpose to treat depression or pain intensity as antidepressants are commonly used to elevate the

pain threshold. Baseline alexithymia was connected with heavier use of opioids and antiepileptic drugs. Depression at baseline was associated with higher use of opioids, sleeping pills and antidepressants.

The opioid medication may be an understandable response to pain severity but it has been observed that opioid therapy (prescribed and/or demanded) is a warning sign of mental problems in a chronic pain situation. It was found that depressive non-cancer patients were more likely to receive a higher dose and a longer term in opioid therapy than non-depressive pain patients (Braden et al. 2009). A high rate of opioid therapy has been suggested to be a response to psychological distress manifesting in reported pain intensity (Howe and Sullivan 2014) or "comfort care" for overall suffering (Ballantyne and Sullivan 2012). Alexithymia and depression with their somatic symptoms may lead to misdiagnosis, and ineffective and unnecessary use of opioids, thus "alexithymic depression" has been treated by opioids.

6.9 Limitations, concerns and strengths of the study

6.9.1 Theory and measures

The fundamental scientific demand is objectivity, by which "the truth" will be reached. However, every study inevitably contains errors and respondent, researcher and survey bias. The study design with theoretical assumptions has an important role in creating reliability and scientifically convincing results. The theoretical base of the present study was the results of earlier studies on childhood adversities, chronic pain, alexithymia, depression and Early Maladaptive Schemas (EMSs) and on a hypothesis of their joint function in a health disorder defined as chronic pain.

The results of the study were based on self-report questionnaires measuring VAS, PDS, TAS-20, BDI-II and EMSs. The critique against self-report questionnaires is usually respondent bias defined as inability or unwillingness to give "proper" answers. This type of bias can possibly be avoided by using multiple questions of the same kind to expose incoherence. The comparisons of the different measures suggested that the patients answered honestly enough as the results followed linear expectations (based on earlier studies), for example pain disability and depressiveness correlated accordingly as well alexithymia and

depressiveness. Only pain intensity lacked this linearity although it appeared in general to be equally related to the other measures. All except pain disability measurement instruments were internationally and nationally validated and tested, thus their psychometric properties and comparability with other studies were sufficient. The Pain Disability Scale (PDS) was tested and compared with the previously validated Pain Disability Index (PDI) and the PDS was proved to be equal to the PDI. In the study questionnaire the patients were asked to draw their pain intensity on the Visual Analogue Scale (VAS) but throughout the study the values were not expressed in millimeters but in numbers. However, the numbers did correspond to the values on the VAS scale (Jensen et al. 2003).

Alexithymia and depression have been claimed to be overlapping phenomena because of their notable correlations and co-occurrence. There are studies supporting and rejecting this notion, mainly tending to see them as discrete structures (Parker et al. 1991, Wiebking and Northoff 2015). In this study, alexithymia and depressiveness were indeed closely connected but a clear proportion of the patients were depressive but not alexithymic. Furthermore, alexithymic depressive patients seemed to comprise a special subgroup with more pain problems, and depressiveness had a mediating role between pain variables and alexithymia. It is possible that "alexithymic depression" is one special feature among a subgroup of more seriously disabled chronic pain patients.

There is also criticism of the scoring values of BDI-II both in chronic pain (Poole et al. 2009) and in alexithymia (Mattila et al. 2008b); higher cut-off points for grades of depressiveness have been recommended for chronic pain patients/alexithymic individuals. Among the alexithymic chronic pain patients in this study study, even at higher cut-off points they would have shown more severe depression than nonalexithymic participants.

6.9.2 Multidisciplinarity

Multidisciplinarity has been recommended in health research (Coen et al. 2010). Combined multidisciplinary measures such as interview based semi-structural assessments, neuroimaging explorations, clinical diagnoses or perhaps immunological/hormonal research methods would have complemented the self-report questionnaires for more accurate and objective results. Unfortunately these supplementary methods were beyond the resources of the author. However, pain is a subjective experience and still impossible to measure in an empiric, "objective"

way (the same applies also to most psychological assessments about the self). "Subjective" self-report data (pain intensity and mood) and "objective" neuroimaging (machine classification algorithms) were compared in their ability to discriminate between individuals with and without chronic pain. Classification by self-report data yielded better performance than the neuroimaging model (Robinson et al. 2015).

6.9.3 Statistics

Statistical methods as an explorative instrument have their flaws and benefits. The advantage is the objective and uncompromising nature of mathematics, which Bertrand Russell described as "*a beauty cold and austere*". This study used dimensional and categorical quantitative measures with statistical tools. So the results mainly reflect "the mean truth" calculated by statistical methods. This is of course the most used study protocol and rendered the results comparable with other studies in the scientific world. The statistical methods were mainly basic procedures by which means of study variables were calculated and compared and completed by path and regression analyses. The results obtained by different methods were linear and mutually supportive. The same tendency in the differences between alexithymic and nonalexithymic patients continued from baseline until eight-year follow-up. The statistical power estimated by the number of participants was good enough, especially at baseline. The number of participants at eight-year follow-up remained low, which limited the value of results. Fortunately, there were no differences in baseline variables between baseline and follow-up study participants. That also rendered reliable the results of the eight-year follow–up. The number of alexithymic women was too low for reliable comparisons between nonalexithymic and alexithymic women. The study used dichotomization and standard cut-off points in creating groups for comparisons. This system is of course artificial and theoretical and may have had a notable influence on results and their interpretation. The purpose of dichotomization was to bring clearly into view the differences between the patients seeking treatment for chronic pain and thus to highlight some factors which have prognostic value and may need special attention.

6.9.4 Other possible biases

The statistical "truth" consists of only those variables which the researcher has selected to describe the phenomenon in question = researcher bias. In the present study, the intention was to collect indirect proof of the effect of childhood adversities on the phenomenon of chronic pain. Alexithymia, depression and EMSs were selected as there was evidence available to connect them with childhood adversities. Thus the researcher bias was guided by prior knowledge. Furthermore, the clinical practice with chronic pain patients has given the present author an impression that chronic pain patients have these characteristics and the aim was to demonstrate and explore their presence and relations. The lack of "positive variables" limited the analysis of factors associated with "improvement" outcome. Also, including assessment for anxiety would have given more information and a broader understanding of the psychological phenomena underlying the pain experience.

The survey bias contained the data collecting arrangement. The data for baseline was controlled as the study questionnaire was sent to the patients with the letter confirming their appointment and probably the patients felt it appropriate/obligatory to participate in the study. Follow-up questionnaires were sent directly to home addresses without any contact with pain clinics, which had an influence on drop out and postal losses. There is also unofficial information that patients who at baseline declined to participate felt offended due to the psychological questions in the study questionnaire, so those missing patients could have made an interesting contribution to the study results but the study protocol failed to reach them.

6.9.5 Strengths

The study had its strengths. The number of study participants was sufficient for statistical calculations, especially at baseline and at one-year follow-up. The variables used in the study represented factors (pain variables and psychological variables) which are recommended to assess in chronic pain research (Dworkin et al. 2005). The measures were widely used, accepted and validated in scientific research and clinical practice and thus the results are comparable with those of other studies. Statistical methods were reliable and their interpretation adhered to normal scientific principles.

The theoretical background was wide and included sufficient evidence for analytical interpretations. The pain phenomenon was explored using measurements which reflect both biopsychosocial and developmental aspects in chronic pain. To our knowledge, co-occurrence of chronic pain, alexithymia, depression and EMSs in a clinical sample has not previously been investigated. Evaluation of relations between alexithymia and EMSs yielded new knowledge. Assessment of the stability of EMSs and alexithymia in chronic pain patients gave indirect evidence of early adversities as a predisposing factor to chronic pain. Longitudinal studies on chronic pain with alexithymia and depression are rare. Clinical studies on chronic pain assessing value of treatment interventions and the effect of psychological variables on outcome are necessary for evaluating and developing treatment choices.

7 CONCLUSIONS AND IMPLICATIONS FOR THE FUTURE

7.1 Conclusions

1. The chronic pain patients in this study suffered from severe pain which had lasted approximately six years (median). Prevalence of alexithymia among the chronic pain patients in the study was 19.2%. The alexithymic patient group was characterized by more severe pain intensity, pain disability and depressiveness both at baseline and follow-ups. Depressiveness mediated the effect of alexithymia on pain disability at baseline and at one-year follow-up.

2. At one-year follow-up, the majority of the patients still reported disruptive pain intensity and pain disability. However, during follow-up there was a clear polarization among the patients: nonalexithymic, nondepressive patients recovered better than alexithymic patients. Higher pain intensity and pain disability with alexithymia and depression at baseline were connected to poorer outcome at one-year follow-up. Alexithymia and male gender at baseline were associated with poorer pain situation at eight-year follow-up.

3. No treatment intervention proved superior to others. The better recovery of nonalexithymic patients suggested a different type or state of pain disorder and benefit from the treatment. Alexithymic patients represented pain disorder with psychological problems beyond the treatment provided. Furthermore, alexithymia and depressiveness were associated with heavier consumption of opioids reflecting possible mental problems masked by experienced pain and eased with narcotics.

4. The relationship between alexithymia and depression was close and intensified during follow-up, suggesting untreated depressiveness among alexithymic chronic pain patients and supporting the idea of "alexithymic depression" with bodily felt pain symptoms.

5. In general, the "EMSs profiles" were similar in both alexithymic and nonalexithymic groups but alexithymic patients scored higher on Early Maladaptive Schemas (EMSs) than nonalexithymic patients. Alexithymia and depression correlated strongly with EMSs. Their co-occurrence was related to more severe pain disability. The co-existence of alexithymia, depression and EMSs refers to the presence of several psychological factors such as low self-esteem and self-efficacy, catastrophizing and interpersonal problems exacerbating coping with the pain situation.

6. Alexithymia and EMSs remained stable throughout the eight-year follow-up. This is explained by their common early origin and the fact that treatment interventions were not targeted at psychological factors.

7. The stability of alexithymia and EMSs with more severe pain situation and depressiveness in the present study highlight their common connecting factors – childhood adversities. With the existing theoretical background in the literature the results support the concept of early maltreatment as a predisposing factor to chronic pain in the subsample of alexithymic chronic pain patients.

7.2 Future implications for practice and research

7.2.1 Clinical recommendations

Health care personnel should be better educated to encounter chronic pain patients:

1. The biopsychosocial approach to understand the entity of chronic pain needs more attention in training health professionals. As the number of chronic pain patients is high, primary health care personnel should be better prepared to address patients' problems.

2. Health care professionals should not by their own behaviour strengthen patients' pain beliefs and maladaptive coping. If the suffering of the patient is received with firm empathy and acceptance, it is possible to model how to cope with the pain situation and create a safe base for therapeutic co-operation. The evaluation of the

status of the chronic pain patient in health care should be done according to the biopsychosocial approach:

a. A comprehensive status including physical examination and evaluation of psychosocial status using self-report questionnaires as additional tools creates the basis to understand the individual situation of the patient.

b. Assessing depression, alexithymia and coping abilities (for example catastrophizing, pain disability, EMSs) will be helpful in evaluating prognosis and in planning treatment interventions.

c. Initial pain conditions (severe pain, noted pain disability, depressed mood, alexithymic features) should be identified as prognostic warning signs of the persistence of the pain problem and a possible need for multidisciplinary interventions. Opioids should not be prescribed according to pain severity but pain severity should be regarded as a prognostic sign of the total suffering of the patient.

d. Treatment interventions should be based on current knowledge of chronic pain and on the individual situation of the patient and planned in co-operation with the patient. As chronic pain syndrome is considered an outcome of lifelong learning in the central nervous system, it is reasonable to support re-learning strategies using the knowledge available in current research.

7.2.2 Implications for future research

1. The salient problem in pain research is the low level of multidisciplinarity and interdisciplinarity. Combining research results and co-operation between different disciplines may help to put the pieces of multifaceted chronic pain into a more comprehensible and proper form.

2. The gap between researchers and clinical practitioners is still great. Translational medicine is a trial to diminish the "from bench to bed" time and promote collaboration between researchers and clinicians. Chronic pain research should seek for means to get the results in practical use.

3. Psychological factors seem to have a great impact in chronic pain. Cognitive-behavioural therapy has been used for decades as a tool to help with pain. It would be also appropriate to develop therapeutic approaches to be adjusted according to assessments of patients' individual problems (expressed as pain experience). There

are several possibilities to be considered such as trauma therapy, emotion focused therapy, schematherapy, psychodynamic therapy and art therapy among others. Re-learning strategies need more focus in research and may be combined with both physical and psychological interventions.

4. More research exploring alexithymia and its factors in different clinical settings with comparisons between clinical groups and health controls would be useful in understanding the role of emotion dysregulation problems. A combination of qualitative and quantitative methods may be fruitful.

7.2.3 Closing words

These observations among chronic pain patients indirectly point out the long-lasting effects of possible childhood adversities. In a clinical situation the background factors of the suffering patient are often hidden, and instead of empathy and support, the patient is a target of endless interventions, examinations and drug prescriptions. In a trustful relationship the patient will tell the real story as a result of the psychosomatic medicine tradition by the "*gentle art of listening*".

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APPENDIX

TAS-20

Ympyröi seuraavien toteamusten kohdalla jokin numeroista yhdestä viiteen sen mukaan, miten hyvin kukin toteamus sopii kuvaamaan sinua.

	Ei lainkaan pidä paikkaansa	Ei juuri pidä paikkaansa	En osaa sanoa	Pitää melko lailla paikkansa	Pitää täysin paikkansa
1. Olen usein epävarma siitä, mitä milloinkin tunnen.	1	2	3	4	5
2. Minun on vaikea löytää oikeita sanoja kuvatakseni tunteitani.	1	2	3	4	5
3. Minulla on fyysisiä tuntemuksia, joita lääkäritkään eivät ymmärrä.	1	2	3	4	5
4. Minun on helppo kuvailla tunteitani.	1	2	3	4	5
5. Mieluummin erittelen ja tutkin ongelmia kuin vain kuvailen niitä.	1	2	3	4	5
6. Kun olen poissa tolaltani, en tiedä olenko surullinen, peloissani vai vihainen.	1	2	3	4	5
7. Olen usein ymmälläni kehoni tuntemuksista.	1	2	3	4	5
8. Annan mieluummin asioiden mennä omalla painollaan kuin mietin mistä ne oikein johtuvat.	1	2	3	4	5
9. Minulla on tunteita, joita en täysin pysty tunnistamaan.	1	2	3	4	5
10. On erityisen tärkeää olla kosketuksissa tunteisiinsa.	1	2	3	4	5
11. Minun on vaikea kuvailla tunteita, joita toiset ihmiset minussa herättävät.	1	2	3	4	5
12. Ihmiset ovat kehottaneet minua kertomaan enemmän tunteistani.	1	2	3	4	5
13. En tiedä, mitä sisimmässäni oikein tapahtuu.	1	2	3	4	5
14. En aina tiedä, miksi olen vihainen.	1	2	3	4	5
15. Mieluummin puhun ihmisten kanssa heidän päivittäisistä puuhistaan kuin heidän tunteistaan.	1	2	3	4	5
16. Katselen mieluummin kevyttä viihdettä kuin psykologisia näytelmiä.	1	2	3	4	5
17. Minun on vaikea paljastaa sisimpiä tuntojani edes läheisille ystäville.	1	2	3	4	5
18. Voin tuntea läheisyyttä toiseen ihmiseen, vaikka oltaisiin hiljaa.	1	2	3	4	5
19. Olen huomannut, että omien tunteiden kuunteleminen ja pohtiminen auttaa henkilökohtaisten ongelmien ratkaisemisessa.	1	2	3	4	5
20. Elokuvista tai näytelmistä häviää nautinto, jos niistä yrittää etsiä syvällisiä merkityksiä.	1	2	3	4	5

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Alexithymia and depression in a chronic pain patient sample

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ABSTRACT

Objective: The aim of the present study was to assess the prevalence of alexithymia in a sample of general chronic pain patients, to explore possible differences in depression and pain variables between alexithymic and nonalexithymic chronic pain patients and to analyze if depression is a mediator between alexithymia and pain disability.

Methods: Two hundred and seventy-one patients making their first visit to a pain clinic completed the study questionnaire including various pain measures, the Beck Depression Inventory-II (BDI-II) and the 20-item Toronto Alexithymia Scale (TAS-20). The sample was dichotomized to alexithymic and nonalexithymic groups. The means of the study variables were compared between the groups. The correlation analysis of the variables was carried out separately in both groups. Path analysis was done to ascertain the mediation effect of BDI-II between the TAS-20 and pain disability.

Results: Every fifth chronic pain patient was alexithymic. The BDI-II and pain variable scores were significantly higher in the alexithymic group than in the nonalexithymic group. Pain variables were not associated with alexithymia when BDI-II was controlled for. BDI-II worked as a full mediator between TAS-20 and pain disability.

Conclusion: The alexithymic patient group was more morbid than the nonalexithymic group. The results suggest that depression is the main factor in pain conditions of alexithymic chronic pain patients. The authors recommend screening and treatment of depression in alexithymic chronic pain patients.

1. Introduction

Alexithymia [1] is a personality trait characterized by impaired emotion and affect regulation which is regarded as "a deficit in the cognitive–experiential domain of emotion response system" [2,3]. The typical features of alexithymia include difficulties in identifying and describing feelings, externally oriented thinking-style, and lack of imagination and fantasies. The prevalence of alexithymia in general population is approximately 7%–10% [4–6]. It has been hypothesized that the origin of alexithymia is in early childhood, when the cognitive processing of emotions is disturbed by adverse environmental factors such as neglect and abuse [7] or an unfavorable social situation [8]. Genetic predisposition may also be involved [9]. Alexithymia has been considered a personality trait, but it has also been suggested that later life events, such as traumatic experiences or disease, may predispose to the development of alexithymic features [10]. A deficiency in affect regulation is considered to be a background factor in many diseases [11]. It has been suggested that disturbed affect regulation produces a pathological stress response which through neuroimmunological mechanisms predisposes to illnesses. Altered or impaired immune responses have been found in alexithymic populations [10,12]. Elevated prevalence rates of alexithymia have been shown, for example, in rheumatoid arthritis, essential hypertension, peptic ulcer, inflammatory bowel syndrome, cardiac disease, breast cancer, diabetes, morbid obesity, eating disorders, substance dependence, posttraumatic disorder and chronic pain [10].

The International Association for the Study of Pain [13] defines chronic pain as pain that has persisted beyond the normal tissue healing time (usually 3 months). This definition has been widely used in research and clinical work but has also been considered to be too narrow, and assessments consisting of functional and psychobiological factors are recommended [14,15]. The advanced neurobiological knowledge of the involvement of the central nervous system in chronic pain has changed the focus from the painful body region to the brain. Several studies have shown that the development and persistence of chronic pain are complex phenomena where lifelong experiences, stress responses, learning, memory and emotions modify the perceived pain [16–19]. It has also been shown that adverse experiences in childhood, such as neglect and stress, can produce

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changes in the sensitive phase of the developing brain, which later in life may predispose to somatic illnesses and mental disorders [20–22]. Engel [23] stated that chronic pain patients have negative childhood experiences. This assumption has subsequently been corroborated in numerous studies [22,24–31], but contrary findings have also been reported [32].

The prevalence of alexithymia in chronic pain patient samples varies according to the study design and the chosen chronic pain subgroup; prevalence rates of 19%–53% have been reported [33,34]. Higher levels of alexithymia have been found in a heterogeneous chronic pain sample [35], low back pain [36], orofacial pain [37], chronic myofascial pain [33], somatoform pain disorder [38], fibromyalgia [34], chronic pain with neuromuscular disease [39] and chronic migraine [40,41]. In chronic pain patient samples, alexithymia is also associated with less self-efficacy and greater catastrophizing [33], maladaptive illness behavior [34] and depression [41,42]. In several studies, chronic pain and depression have been shown to coincide [43–45]. The adversities in childhood have been found to be a predisposing factor for depression [46,47]. Thus, according to the literature, it seems that chronic pain, alexithymia and depression share the same potentially predisposing factor, adverse experiences in childhood, with many patients having all of these. However, later traumatic events, such as the pain disease itself or other stressful life situations producing posttraumatic stress disorder, may also predispose to both depression [48] and alexithymia [10], both of which are connected to maladaptive emotion processing modifying the pain experience [49]. The coincidence of alexithymia, depression and chronic pain leads to a theoretical question of a specific patient group with bodily felt pains, low mood and restricted emotion regulation.

Chronic pain and depression as well as many other clinical disorders have been found to be related to alexithymia; however, in clinical work, the assessment of alexithymia is not yet common practice. In spite of mounting evidence that alexithymia is an important part of chronic pain problems, studies with large groups of clinical chronic pain patients are rare. Our goal in this study was to ascertain the importance of alexithymia and its relations to chronic pain and depression in a clinical sample. Thus, the aim of this study was to measure the prevalence of alexithymia in a general chronic pain patient sample, to assess whether the duration of painful condition was associated with the prevalence of alexithymia, to ascertain whether alexithymic and nonalexithymic patients have significant differences in pain variables and depression and to analyze the mediating effect of depression between alexithymia and pain disability. We hypothesized that alexithymic chronic pain patients would differ in pain variables and depression from nonalexithymic patients.

2. Material and methods

2.1. Participants

Consecutive 18–64-year-old first-visit pain patients were recruited for this study from six pain clinics in Central and Northern Finland during a period of 1 year (from January 2004 to January 2005). Sources of referral included primary health care and various medical specialists. Patients having a psychotic disorder or malignant disease were excluded from the study. The patients were informed in advance about the study protocol by letter. Every patient attending the pain clinic was given the questionnaire by which the data were gathered. The patients completed the questionnaire before the consultation. From 318 eligible patients, 47 (15%) refused to take part in the study, so the final sample comprised 271 participants (127 men, 144 women). All these patients were suffering from nonmalignant, daily chronic pain lasting for 3 months or longer [13]. The patients completed the study questionnaire before their first visit, so no medical diagnosis was set at that point.

The study protocol was approved by the ethical committee of the Northern Ostrobothnia Hospital District. Written informed consent was obtained from all participants.

2.2. Pain variables

The pain questionnaire was developed for this study to collect information on sociodemographic data (age, gender and occupation), pain localization (body map), the duration of pain disease, current pain intensity and pain disability. The pain intensity was measured with two 10-cm visual analogue scales (VAS) where 0 represents *no pain* and 10 represents *the worst pain one can imagine*. On the first VAS scale, the participants were asked to rate their current maximal experienced pain and, on the second VAS scale, their current minimal pain at the time of the study. The pain intensity was calculated to be the mean of these two measures. The Pain Disability Scale (PDS) was developed for this study. It is a nine-item self-report scale consisting of seven direct statements: "My pain is disturbing my sleep," "…my hobbies," "…my sex life," "…my work," "…my ability to move," "…my economy," and "…my social contacts" and two inverted statements: "I can enjoy life despite my pain" and "I can control my pain." All the items were self-reported on a Likert-type 0–3 scale: 0=not at all, 1=to some extent, 2=significantly and 3=very much. The total score (range 0–27) reflects the severity of pain disability. A score of 0–4 indicates "no disability," a score of 5–13 "mild disability," a score of 14–22 "remarkable disability" and a score of 23–27 "severe disability." Cronbach's alpha for the PDS was 0.83. The reliability and validity of the PDS were estimated in a pilot study of 103 chronic pain patients by comparing the correlation between the PDS and the Pain Disability Index (PDI) [50]. The correlation between the PDS and the PDI was .81, and their associations with the Beck Depression Inventory-II (BDI-II) (r=.56 and r=.58, respectively) and with the VAS (r=.62 and r=.62, respectively) were similar. The pilot study results supported the use of PDS in this study.

2.3. Alexithymia

Alexithymia was measured with the 20-item Toronto Alexithymia Scale (TAS-20). Its internal consistency, test–retest reliability, as well as convergent, discriminant and concurrent validity have been demonstrated to be good [51–54]. The Finnish Version of TAS-20 has proven to be reliable [55]. TAS-20 consists of 20 items (five inverted) scored from 1 to 5 and then added up. The recommended cutoff point to indicate alexithymia is >60 [56]. The items of TAS-20 are divided into three subscales (factors) each assessing the different features of the alexithymia concept: difficulties with identifying feelings (DIF=factor 1, seven items), difficulties with describing feelings (DDF=factor 2, five items) and externally oriented thinking (EOT=factor 3, eight items).

2.4. Depression

Depression was assessed with the revised 21-item version of the BDI-II [57]. All the items were self- rated from 0 to 3 and added up to obtain a total score ranging from 0 to 63, with higher values indicating more severe depressive symptoms. The questionnaire is widely used and has been proven to be suitable for measuring depression in chronic pain patients [58]. It has also been validated in Finnish [59]. A score of 0–13 indicates minimal depressive symptoms (the individual faces normal "ups and downs"), a score of 14–19 indicates mild, a score of 20–28 moderate and a score of 29–63 severe depressive symptoms [57].

Table 1
The comparisons of pain variables, TAS-20 and BDI-II between alexithymic and nonalexithymic groups

	All patients$n=271$		Alexithymic group$n=52$		Nonalexithymic group$n=219$		Significance	Effect size
	Mean	S.D.	Mean	S.D.	Mean	S.D.	*P* value	
TAS-20 score	47.4	12.5	66.8	5.5	42.8	8.7	$P<.001$[a]	2.92[b]
BDI-II score	15.7	10.2	25.0	9.3	13.5	9.1	$P<.001$[a]	1.26[b]
Pain disability (PDS)	16.5	5.1	19.0	3.8	15.9	5.1	$P<.001$[a]	0.63[b]
Pain intensity (VAS)	5.9	1.2	6.3	1.3	5.8	1.2	$P<.010$[a]	0.43[b]
Pain duration (years)	9.3	8.8	10.2	9.5	9.1	8.6	.436[a]	0.12[b]
Number of pain sites	2.1	1.3	2.3	1.4	2.1	1.2	.262[a]	0.17[b]

[a] Student's *t* test.
[b] Cohen's *d*.

2.5. Statistics

The sample was dichotomized according to the cutoff point of TAS-20 >60 to the alexithymic and nonalexithymic pain patient groups. Baseline characteristics, pain variables, alexithymia and depression data were compared between the study groups. The means of the study variables were also compared in both groups between women and men. χ^2 test was used with categorical data and Student's *t* test with normally distributed data to make group comparisons. Pearson correlation (*r*) was used, and the association was regarded as small if *r* was ±0.1–±0.29, moderate if ±0.30–±0.49 and large if ±0.50–±1.0 [60]. Level of significance was set at $P<.01$ in this study. In order to calculate effect sizes for the categorical variables, the φ coefficients were calculated; the interpretation for φ is equal to that of Pearson correlation coefficient. For continuous data, Cohen's *d* values were calculated; Cohen's $d=0.2$ is considered a small effect size, and $d=0.5$ and $d=0.8$ are considered medium and large, respectively [60]. The statistical analyses were conducted with SPSS (version 16.0. for Windows; SPSS Inc., Chicago, IL, USA). In order to ascertain if the effect of TAS-20 on pain disability (PDS) was mediated through BDI-II, the normal scores were calculated with Prelis 2.80, and the mediation analysis was conducted with Lisrel 8.80. Mediation was indicated if there was a lower or nonsignificant path coefficient between two variables after the mediating variable was entered into the model. The level of significance in the Lisrel path analysis was a path's *t* value >1.96.

3. Results

The total sample comprised 271 chronic pain patients. The overall prevalence of alexithymia was 19.2 % ($n=52$). There was a significant difference in the TAS-20 scores between men and women (50.9, S.D. 12.3, versus 44.4, S.D. 11.8; $P<.001$). The prevalence of alexithymia in men was 27.6% and in women was 11.8% ($P<.001$). Men were significantly overrepresented in the alexithymic patient group (male/female ratio: alexithymic group, 35/17 and nonalexithymic group, 92/127; $P<.001$). The alexithymic and nonalexithymic groups were similar in terms of age [46.8 and 47.1 years, respectively ($P=.853$)] and education [10.8 and 11.2 years, respectively ($P=.121$)] and did not differ in terms of pain duration and number of pain sites. The alexithymic pain patients had significantly higher BDI-II, PDS and VAS scores than the nonalexithymic group (confirmed by Student's *t* test and Cohen's *d* values). Pain variables, depression and alexithymic data of the total study group, the alexithymic group and the nonalexithymic group are presented in Table 1.

In the alexithymic pain patient group, men had a higher VAS score ($P=.003$) than women, whereas in the nonalexithymic group, men had a higher TAS-20 composite score ($P=.004$) and women had a lower EOT score ($P<.001$). In both groups, no other differences between the women and men were found.

The pain sites were categorized into six regions according to the pain map drawings: face, neck–shoulder region, low back, abdominal region, limbs and thorax. The alexithymic group had significantly more commonly abdominal pain ($P=.009$) and almost significantly more commonly low back pain ($P=.031$). However, effect size values did not support the difference between the groups (Table 2).

In the total sample, BDI-II scores were as follows: 48.3% scored 0–13, 20.3% scored 14–19, 18.1% scored 20–28 and 13.3% scored 29–63. The distribution of BDI-II scores in the alexithymic and nonalexithymic pain patient samples is shown in Fig. 1. According to the χ^2 test, the alexithymic pain patient sample was overrepresented among the groups with moderate or severe depressive symptoms (χ^2 56.9, $P<.001$).

The correlations between pain variables (pain disability, pain intensity, pain duration and the number of pain sites), TAS-20 scores, TAS-20 factor scores and BDI-II scores were measured separately in the alexithymic and nonalexithymic pain patient groups (Table 3). Because the results of these correlations suggested the notable role of BDI-II, the partial correlation controlling for the BDI-II was performed between all the foregoing variables.

In both groups, there was a large correlation between the BDI-II and PDS scores. In the alexithymic group, there were also a large correlation between the TAS-20 and BDI-II scores and a moderate correlation between the TAS-20 and PDS which, however, vanished

Table 2
Percentages of different pain sites in alexithymic and nonalexithymic pain patients

	Alexithymic group($n=52$)	Nonalexithymic group($n=219$)	χ^2	Effect size[a]
Face	17.3%	11.4%	0.249	0.070
Neck/shoulder/upper back	42.3%	54.8%	0.105	−0.098
Thorax	13.5%	13.2%	0.967	0.003
Abdomen	36.5%	19.6%	0.009	0.158
Low back	80.8%	65.3%	0.031	0.131
Limb	40.4%	43.8%	0.652	−0.027

[a] The φ coefficient.

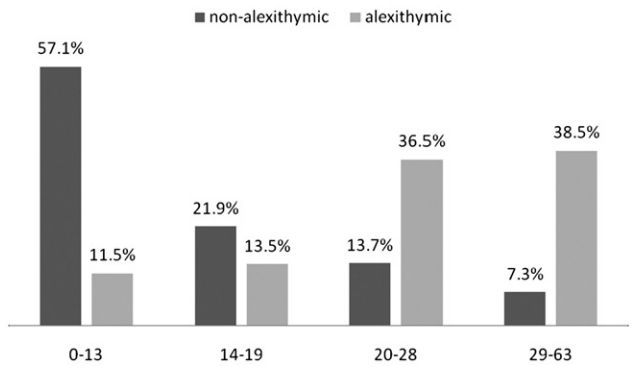

Fig. 1. Percentages of BDI-II scores in alexithymic and nonalexithymic pain patient groups (0–13=no depression, 14–19=mild depression, 20–28=moderate depression and 29–63=severe depression).

Table 3
Pearson correlations between pain variables, depressiveness and alexithymia data in the alexithymic and nonalexithymic pain patient groups

		TAS-20	Factor 1 DIF	Factor 2 DDF	Factor 3 EOT	BDI-II	PDS	VAS	Pain duration
Alexithymic pain patient group($n=52$)	BDI-II	0.510[a]	0.450[a]	0.464[a]	−0.055				
	PDS	0.331[b]	0.323[b]	0.195	0.013	0.526[a]			
	VAS	0.167	−0.035	0.186	0.161	0.168	0.206		
	Pain duration	0.111	0.176	0.087	−0.089	0.344[b]	0.174	0.104	
	Number of pain sites	0.103	0.188	0.115	−0.138	0.255	0.357[a]	−0.013	0.193
Nonalexithymic pain patient group($n=219$)	BDI-II	0.325[a]	0.382[a]	0.355[a]	−0.034				
	PDS	0.154[b]	0.154[b]	0.259[a]	−0.055	0.522[a]			
	VAS	0.095	0.145[b]	0.133	−0.065	0.239[a]	0.318[a]		
	Pain duration	−0.043	−0.024	0.085	−0.120	0.030	0.187[a]	0.118	
	Number of pain sites	0.032	0.192[b]	0.091	−0.20[a]	0.256[a]	0.396[a]	0,171[b]	0.159[b]

[a] Correlation is significant at the 0.01 level (two-tailed).
[b] Correlation is significant at the 0.05 level (two-tailed).

when the BDI-II was controlled for. In both groups, TAS-20 factors DIF and DDF were moderately correlated with the BDI-II (Table 3). In the nonalexithymic group, the moderate correlations of PDS with VAS and number of pain sites were no longer statistically significant when BDI-II was controlled for.

In the total sample, testing of the mediator effect of the BDI-II score was done as follows: the TAS-20 score was used as a predictor of pain disability, and the path coefficient was significant ($\beta=0.27$, $t=4.65$). Then, BDI-II was entered as a mediator in the model. The aforementioned path became nonsignificant ($\beta=-0.02$, $t=-0.36$). The path from TAS-20 to BDI-II was significant ($\beta=0.52$, $t=9.87$), and the path from BDI-II to disability was also significant ($\beta=0.57$, $t=9.69$). BDI-II can be seen as a full mediator between TAS-20 and pain disability.

4. Discussion

The present study included 271 clinical chronic pain patients. The main results of the present study are as follows: Every fifth chronic pain patient was alexithymic, and men were overrepresented in the alexithymic group. The alexithymic group was more depressive and disabled than the nonalexithymic group. Depression worked as a full mediator between alexithymia and pain disability. Pain duration was not associated with alexithymia. As far as the authors know, there is no similar study with such a large number of pain clinic patients with heterogeneous pain disorders.

The prevalence of alexithymia in this sample (19.2%) was lower than that in several other studies [33], but it was higher than that in the general population. In these earlier studies, the patient groups represented one special subgroup of chronic pain such as fibromyalgia [61], migraine [41] or chronic back pain [62], or the study group consisted of chronic pain patients attending a psychiatric clinic [63]. In the present study, the patient group was a heterogeneous group of different pain disorders. In the study by Lumley et al. [35], the patients were suffering from of multiple pain disorders, but the group was smaller ($n=30$), and the researchers used a different alexithymia scale, which makes comparison difficult. According to these earlier studies, the common concept that alexithymia is a part of a chronic pain problem seems to be based on study designs with limited numbers of participants and special medical diagnoses.

Male gender was overrepresented in the alexithymic pain patient group. This finding is consistent with a Finnish prevalence study of alexithymia in general population [5]. The male alexithymic patients reported more pain than alexithymic females or nonalexithymic patients. It is unclear why men are more prone to alexithymia, but one might speculate that, in the upbringing of boys, emotional subjects are given lesser importance, and furthermore, pain is a more accepted "emotion" than, for example, grief. Gender differences in alexithymia have been proposed to be related to "restrictive emotionality," which possible is a consequence of male gender role in the society [64].

Pain duration was not associated with alexithymia, but it was moderately correlated with the BDI-II score. Consequently, this may suggest that alexithymia is a constant trait and not attributable to the pain disease. Even though the direction of causality cannot be ascertained in a cross-sectional study, this may suggest that the traumatic effect of chronic pain did not cause any secondary alexithymia. The increasing depression when pain persists may indicate a depressive effect of the chronic pain disorder or that the untreated depression is masked by pain disease. Pain is a common reason for seeking medical help [65], and it has been shown that the majority of depressive patients complain of bodily felt pain [66]. Thus, the depression disguised by the pain disorder may not be easily diagnosed. It was also notable that, at the first pain clinic visit, patients had a mean pain duration of 9.3 years. This means that the patients had been suffering from physically felt pain for an extended period of time without sufficient care. The prolonged pain works as a learning experience in the central nervous system and by neuroplasticity mechanisms becomes more persistent [19].

The alexithymic patients relatively more commonly had abdominal and low back pain than the nonalexithymic patients. This result may be merely a coincidental finding, but may also refer to the psychosomatic aspects of alexithymia. The patients may interpret their bodily felt emotional states as physical symptoms or disorders. The abdomen and low back are common sites of transient, innocent pains, but somatization and somatosensory amplification may increase the personal significance and magnitude of experienced pain. According to several earlier studies, alexithymia has been shown to be associated with somatization [67,68] and somatosensory amplification [69]. Pain catastrophizing also exacerbates the pain experience [70], and alexithymia has been found to be connected with greater pain catastrophizing [33], which may lead to a tendency to overestimate the somatic symptoms.

In several studies, alexithymia has been found to be associated with chronic pain problems [35]. In this study, the alexithymic patients reported significantly more pain and pain disability than the nonalexithymic patients, but no remarkable associations between pain intensity and disability with alexithymia were found. The severity of pain disease measured by pain disability in alexithymic patients appeared to be mediated by higher scores on depression scale. As the emotional factors DIF and DDF of TAS-20 were responsible for significant correlations between PDS, TAS-20 and BDI-II, but the correlations between the cognitive factor EOT and all these three variables were negligible, it seems plausible that the mediational effect of alexithymia on pain disability through depression was mainly attributable to the emotional factors of alexithymia.

Adverse experiences in early childhood have an effect on the development of stress response system, and later coping with different illnesses and disorders is impaired [71]. The same adversities may also produce the deficits in the emotion regulation system. Alexithymic individuals have been reported to have diminished immune-mediated cellular response with oversecretion of glucocorticoids, which may increase the risk for stress-related disorders [72]. The evidence of early neurobiological developmental disturbance of

the hypothalamus–pituitary–adrenal axis induced by adverse environmental factors may provide a basis to understand the complex relations between chronic pain, depression and alexithymia [73]. More research is needed to elucidate the possible shared neurobiological basis of alexithymia, chronic pain and depression.

The role of depression among the chronic pain patients was highlighted in this study. In alexithymic and nonalexithymic patients alike, pain disability and the BDI score had the strongest correlation. The association of number of pain sites (in both groups) and pain intensity (in the nonalexithymic group) with pain disability was no longer statistically significant when the BDI score was controlled for. Depression has been shown to be the main predictor of pain disability in a sample of chronic pain patients [45]. In a previous study, depression was shown to be associated with pain disability, and the effect increased as the duration of pain extended. At the same time, the effect of pain intensity became insignificant [74]. Measuring depression by a questionnaire in individuals with alexithymic features has been criticized, and it has been suggested that the cut points to estimate the level of depressiveness should be higher in alexithymic individuals [75]. In this study, the alexithymic patients scored notably higher on the BDI-II than did the nonalexithymic patients, so that even if higher cut points had been used, the results would have remained the same. Furthermore, depression has been suggested to be a mediator between alexithymia and affective pain [33]. In this study, the TAS-20 score and pain disability were moderately correlated, but the correlation was no longer significant when the BDI score was controlled for. The further mediation analysis showed that the BDI score was a full mediator between the TAS-20 score and pain disability.

According to earlier literature, a developmental deficit in emotion regulation (alexithymia) may predispose one to depression. However, the cross-sectional design of our study does not allow for such causal interpretations. It is noteworthy that the circumstances which may expose to alexithymia may also predispose to depression. The grade of alexithymia has been found to be associated with the severity of depressive symptoms measured by BDI-II [76]. Depression may be seen as a maintaining factor for alexithymia. It has been shown that difficulties in identifying and describing feelings (DIF and DDF) are associated with changes of mood [77], and in the study by Honkalampi et al. [78], it was found that a decrease in TAS-20 scores was associated with a concurrent decrease in BDI scores. The same finding was repeated in their recent paper [79]. The concurrence of alexithymia and depression has led to an assumption that they are overlapping constructs. Some study results support this view [80], but other studies suggest that alexithymia and depression are distinct and separate constructs [81,82].

The results also highlight the existing problems in the treatment of pain. The time of the first visit to the pain clinic tells about the delayed and probably futile earlier treatment attempts. The later the treatment of the prolonged pain problem begins, the more there are central nervous system alterations, and thus the more difficult it is to find an adequate cure. The high percentage of depression, especially among the alexithymic patients, refers to the underestimated and unnoticed area in clinical practice of chronic pain management. The chronic pain problem is unsolvable without taking depression into account. The findings of the present study combined with the results of several earlier studies on chronic pain and depression adduce the need for special treatment protocols for depression in chronic pain patients. One can suggest that the treatment of depression in chronic pain patients may relieve pain disability and possibly has a positive effect on the alexithymia grade. Traditionally, alexithymia has been considered to be a factor making patient–health care personnel relationships and especially psychotherapeutic ones challenging. The promising study [83] on the Affect School therapy for alexithymic chronic pain patients introduces one treatment protocol to manage this problem.

The present study explored the relation of alexithymia to pain variables and depression in a clinical chronic pain patient group. The study design, where the pain patients were dichotomized by TAS-20 scores to alexithymic and nonalexithymic groups, produced two distinct groups. The alexithymic patient group was clearly more morbid than the nonalexithymic group. In both groups, depression was significantly associated with pain disability. According to the results in the present study, the estimation of depression and alexithymia as a part of the comprehensive evaluation of chronic pain patients is important for understanding the special features and problems of the patients and for the planning their treatment protocol. Earlier intervention in the pain problem is also favorable for both depression and pain and theoretically for alexithymia, too.

The limitation of this study is the self-report method of data collection. The measuring of subjective assessments by questionnaire is controversial, and the study design did not allow us to draw causal conclusions. One limitation of the study was the method used for pain intensity measurement. The variable was calculated by using the mean of the current experienced maximum and minimum pain intensity, which may not reflect the usual average pain intensity of the patient.

There is earlier evidence that chronic pain, depression and alexithymia are all associated with negative childhood experiences. According to current knowledge, these experiences affect the developing brain and predispose the individual to cope with any stressful situations by inadequate and deficient means. The concurrent occurrence of these three phenomena — chronic pain, depression and alexithymia — needs more research work. It is common knowledge that each of them complicates patient's treatment; however, when concomitant, the situation is often even more difficult.

In the future, research analyzing specific psychological factors connected with alexithymia in chronic pain patient samples is needed in order to find more effective and accurate treatment practices. The authors recommend the cognitive–behavioral and schema therapeutic approaches in this area.

Our study encourages the recommended practice of assessing alexithymia [10] and depression in pain clinic patients.

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Personality and Social Psychology

Alexithymia and Early Maladaptive Schemas in chronic pain patients

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Psychological factors have an impact on subjective pain experience. The aim of this study was to explore the occurrence of alexithymia and Early Maladaptive Schemas in a sample of 271 first visit chronic pain patients of six pain clinics. The patients completed the study questionnaire consisting of the Toronto Alexithymia Scale-20, the Finnish version of the Young Schema Questionnaire short form-extended, the Beck Depression Inventory-II, and pain variables. Alexithymic patients scored higher on Early Maladaptive Schemas and had more pain intensity, pain disability and depression than nonalexithymic patients. Both alexithymia and depression correlated significantly with most Early Maladaptive Schemas. The co-occurrence of alexithymia, Early Maladaptive Schemas and depression seems to worsen the pain experience. Screening of alexithymia, depression and Early Maladaptive Schemas may help to plan psychological treatment interventions for chronic pain patients.

Key words: Chronic pain, alexithymia, Early Maladaptive Schema, depression.

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INTRODUCTION

The chronic pain problem affects millions of people. In spite of enormous amounts of research work and emergent neurobiological knowledge about pain mechanisms, the suffering of this patient group cannot yet be alleviated. The Cartesian theory that tissue damage alone is responsible for the pain experience has been replaced by more complex neurobiological approaches focusing on the brain as a pain learning, modifying, and maintaining organ (Apkarian, Hashmi & Baliki, 2011).

During the first years of life, the brain is most receptive to various factors, which may modify the brain and its ability to cope with challenges during the lifespan (Sullivan, Wilson, Feldon *et al*., 2006). Early adversities and maltreatment serve as epigenetic factors impinging on genetic expression and producing morphological and functional outcomes with a heightened response to stress and an increased risk of different disorders (Gudsnuk & Champagne, 2011). Research has shown that lifetime pain exposures ("pain memory"), stress responses, cognitions, and emotions modify the individual experience of perceived pain (Apkarian, Baliki & Geha, 2009; Apkarian *et al*., 2011; Hirsh, George, Bialosky & Robinson, 2008; Lumley, Cohen, Borszcz *et al*., 2011; McLean, Clauw, Abelson & Liberzon, 2005). In several studies, chronic pain has been associated with early adversities, abuse, neglect and emotional deprivation (Imbierowicz & Egle, 2003; Jones, Power & Macfarlane, 2009; Lampe, Doering, Rumpold *et al*., 2003; Sachs-Ericsson, Kendall-Tackett & Hernandez, 2007; Scott, Von Korff, Angermeyer *et al*., 2011; Teicher, Andersen, Polcari, Anderson, Navalta & Kim, 2003). Based on current knowledge, the biomedical approach to chronic pain has turned to a search for a biopsychosocial model of chronic pain (Gatchel, Peng, Peters, Fuchs & Turk, 2007).

The characteristics of alexithymia were first observed in patients with a tendency to somatization and psychosomatic disorders, and the term was coined by Sifneos (1973). Alexithymia, "no words for feelings," describes a personality trait or construct characterized by difficulties in identifying and describing feelings or emotions, externally oriented thinking style, and limited imaginary capacity. The combination of alexithymic features reflects defects in emotion-processing and emotion-regulating systems (Bagby & Taylor, 1997a). Early childhood adversities, such as neglect and abuse or an unfavorable social situation may predispose to alexithymia (Bagby & Taylor, 1997b; Joukamaa, Kokkonen, Veijola *et al*., 2003; Joukamaa, Luutonen, von Reventlow, Patterson & Karlsson, 2008). Alexithymia has been shown to be associated with a variety of disorders or diseases such as depression, substance abuse, eating disorders, inflammatory bowel disease, hypertension, and chronic pain among others (Lumley, Smith & Longo, 2002; Taylor, 2000). In general population the prevalence of alexithymia on average is 10% (Mattila, Salminen, Nummi & Joukamaa, 2006), but in different chronic pain subgroups the prevalence rates of alexithymia vary from 15% (Pedrosa, Weigl, Wessels, Irnich, Baumüller & Winkelmann, 2008) to 53% (Lumley *et al*., 2002). Alexithymia has been shown to be involved in several chronic pain disorders such as chronic myofascial pain (Lumley *et al*., 2002), migraine (Vieira, Vieira, Gomes & Gauer, 2013), low back pain (Mehling & Krause, 2005), orofacial pain (Sipilä, Veijola, Jokelainen *et al*., 2001), somatoform pain disorder (Burba, Oswald, Grigaliunien *et al*., 2006), somatization (Mattila, Kronholm, Jula *et al*., 2008), fibromyalgia (Di Tella & Castelli,

2013) and complex regional pain syndrome (Margalit, Ben Har, Brill & Vatine, 2014). In chronic pain samples alexithymic features have been found to be associated with depressiveness, low self-efficacy and high catastrophizing, and with sensitivity to affective pain.

Young (1990) developed the concept of Early Maladaptive Schemas (EMSs) and schema therapy. According to the theory of schema therapy, early life experiences form the patterns and models of the self, others, and the world. If the innate needs of the child for nurturing, safety, love, understanding, and acceptance are not adequately met, the child will develop adaptive patterns for that life situation. EMS is defined as "a broad, pervasive theme or pattern; comprised of memories, emotions, cognitions, and bodily sensations; regarding oneself and one's relationships with others; developed during childhood or adolescence; elaborated throughout one's lifetime; dysfunctional to a significant degree" (Young, Klosko & Weishaar, 2003, p. 7). EMSs have been found in various disorders, such as depression (Renner, Lobbestael, Peeters, Arntz & Huibers, 2012), eating disorders (Anderson, Rieger & Caterson, 2006; Unoka, Tölgyes, Czobor & Simon, 2010), personality disorders (Carr & Francis, 2010), posttraumatic stress disorder (Cockram, Drummond & Lee, 2010), and substance abuse (Shorey, Stuart & Anderson, 2013). In a study comparing chronic pain patients with a control sample the results showed that chronic pain patients had more EMSs than the control group (Saariaho, Saariaho, Karila & Joukamaa, 2011) and in an another study the second-order factor structure of EMSs in chronic pain patients was different from that of the control sample (Saariaho, Saariaho, Karila & Joukamaa, 2012).

Both alexithymia and EMSs have been found to be connected to interpersonal problems (Thimm, 2013; Vanheule, Desmet & Meganck, 2007) and unfavorable attachment styles (Carpenter & Chung, 2011; Simard, Moss & Pascuzzo, 2011). Interpersonal problems reflect problems in attachment style and thus, reflect early childhood adversities such as neglect or abuse. As chronic pain patients have been shown to have negative childhood experiences, it is reasonable to explore if alexithymia and EMSs (which both are connected with early adversities) are associated in a sample of chronic pain patients and estimate their possible effect on pain experience. Alexithymia, characterized by emotional "blindness" and EMSs, representing dysfunctional cognitions and emotional states, describe different concepts and psychological facets. Their joint effect in the clinical situation is difficult to predict.

According to several studies depression co-occurs with chronic pain (Arnow, Hunkeler, Blasey *et al*., 2006; Ericsson, Poston, Linder, Taylor, Haddock & Foreyt, 2002), alexithymia and EMSs. The relation of depression to these phenomena is contradictory; it is assumed to be a consequence or a predisposing or a mediating factor.

The aim of this study was to explore the composition of pain experience in a sample of chronic pain patients by defining the relations of alexithymia and Early Maladaptive Schemas. We hypothesized that alexithymic chronic pain patients would have more EMSs than nonalexithymic patients. Our goal was to identify the possible typical schemas/schema domains of alexithymic chronic pain patients. The relations of depression to alexithymia and EMSs are discussed according to the results.

METHOD

Participants

The participants of the study were recruited from six pain clinics in Central and Northern Finland during a period of one year (from January 2004 to January 2005). The study inclusion criteria were: first visit to the pain clinic, age between 18-64, daily chronic pain lasting for three months or longer, no psychotic disorder or malignant disease. The patients received the information letter about study protocol and the study questionnaire to be completed before the consultation. From 318 eligible patients 47 (15%) refused to take part in the study, so the final sample comprised 271 participants (127 men, 144 women). The mean age of participants was 47 (SD 9.3) years. The mean duration of education was 11 (SD 1.6) years and was estimated from the occupation. There was no difference in age or duration of education between male and female participants.

The study protocol was approved by the ethics committee of the Northern Ostrobothnia Hospital District. Written informed consent was obtained from all participants.

Measures

A questionnaire was designed for the study to collect data on basic characteristics (age, gender, occupation), pain variables, alexithymia, Early Maladaptive Schemas, and depression.

Pain variables. The pain questionnaire contained questions about current pain intensity, the duration of pain disease, pain localization (body map) and pain disability. The pain intensity was measured with two 10-cm Visual Analogue Scales (VAS) where 0 represents no pain and 10 represents the worst pain one can imagine. On the first VAS scale the participants were asked to rate their current maximal experienced pain, and on the second VAS scale their current minimal pain at the time of the study. The pain intensity was calculated to be the mean of these two measures. The Pain Disability Scale (PDS) was developed for studying chronic pain. It is a nine-item self-report scale consisting of seven direct statements: "My pain is disturbing my sleep," "... my hobbies," "... my sex life," "... my work," "... my ability to move," "... my economy," "... my social contacts" and two inverted statements: "I can enjoy life despite my pain" and "I can control my pain." All the items were self-reported on a four-point Likert-type scale ranging from "not at all" to "very much." The total score (range 0–27) reflects the severity of pain disability. A score of 0–4 indicates 'no disability', a score of 5–13 'mild disability', a score of 14–22 'considerable disability' and a score of 23–27 'severe disability'. Cronbach's alpha for the PDS was 0.83. The psychometric properties of the PDS were tested in a pilot study of 103 chronic pain patients by comparing the correlation between the PDS and the Pain Disability Index (PDI), which is a widely used and validated method to measure disability caused by pain (Tait, Pollard, Margolis, Duckro & Krause, 1987). The correlation between the PDS and the PDI was 0.81 and their associations with BDI-II were similar ($r = 0.56$ and $r = 0.58$, respectively) likewise with VAS ($r = 0.62$ and $r = 0.62$, respectively). The pilot study results supported the use of PDS in this study.

Table 1. *Schema domains and descriptions, Early Maladaptive Schemas and abbreviations (Young et al., 2003)*

Schema domain	Description	Early Maladaptive Schema	Abbreviation
Disconnection and rejection	The belief that one's needs for security, safety, stability, nurturance, empathy, sharing of feelings, acceptance or respect will not be met.	Abandonment/Instability[a]	AB
		Mistrust/Abuse[a]	MA
		Emotional Deprivation[a]	ED
		Defectiveness/Shame[a]	DS
		Social Isolation/Alienation[a]	SI
Impaired autonomy and performance	The belief that one's ability and capacity to separate, survive, cope independently or perform successfully is impaired.	Dependence/Incompetence[a]	DI
		Vulnerability to Harm or Illness[a]	VH
		Enmeshment/Underdeveloped Self[a]	EM
		Failure[a]	FA
Impaired limits	Difficulties in setting internal limits, feel responsibility or set long-term goals.	Entitlement/Grandiosity[a]	ET
		Insufficient Self-Control/Self-Discipline[a]	IS
Other-directedness	The needs, desires or responses of others are over respected and taken into account at the expense of own needs.	Subjugation[b]	SB
		Self-Sacrifice[b]	SS
		Approval-Seeking/ Recognition-Seeking[b]	AS
Overvigilance and inhibition	The spontaneous feelings and impulses are suppressed and replaced by rigid, internalized rules about performance and behavior.	Negativity/Pessimism[a]	NP
		Emotional Inhibition[b]	EI
		Unrelenting -Standards/ Hypercriticalness[b]	US
		Punitiveness[a]	PU

Notes: [a] Unconditional schema, [b] Conditional schema.

Alexithymia. Alexithymia was measured with the twenty-item Toronto Alexithymia Scale (TAS-20). Its internal consistency, test-retest reliability, as well as convergent, discriminant, and concurrent validity have been demonstrated to be good (Bagby, Parker & Taylor, 1994; Bagby, Taylor & Parker, 1994; Parker, Taylor & Bagby, 2003; Taylor, Bagby & Parker, 2003). The Finnish version of TAS-20 has proven to be reliable (Joukamaa, Miettunen, Kokkonen *et al*., 2001). TAS-20 consists of 20 items (five inverted) scored from 1 to 5 and then added up. The recommended cut-off point to indicate alexithymia is >60 (Bagby &Taylor, 1997c). The TAS-20 cutpoint is originally based on the study of Bagby, Taylor and Parker (1994) and has become a generally accepted cutpoint among the alexithymia researchers. The items of TAS-20 are divided into three factors, each assessing the different dimensions of the alexithymia concept: difficulties in identifying feelings (DIF = factor 1, 7 items), difficulties in describing feelings (DDF = factor 2, 5 items) and externally oriented thinking style (EOT = factor 3, 8 items).

Early Maladaptive Schemas. Early Maladaptive Schemas (EMSs) were assessed by the Finnish version of the Young Schema Questionnaire short form-extended (= YSQ-S2-extended), which consists of 18 current EMSs, each reflecting a different type of schema pattern. The reliability and 18-factor structure of YSQ-S2-extended in Finnish language have been established (Saariaho, Saariaho, Karila & Joukamaa, 2009). The YSQ-S2-extended is a self-report, Likert-type questionnaire, where each EMS is described by five statements (items), which can be rated from one (completely untrue of me) to 6 (describes me perfectly). The 18 EMSs are grouped into five domains, each of them representing one part of the core needs of the child. The EMSs are divided into unconditional and conditional schemas. Unconditional schemas are developed earlier in life and represent unconditional beliefs about the self and others. Conditional schemas are consequences of patterns of unconditional schemas and may be seen as attempts to cope with the unconditional schema (Table 1). The higher the patient scores in a particular EMS, the greater the importance of the schema in the patient's life and the more often it is triggered by life events (Young *et al*., 2003). In this study, the value of the schema was calculated as a mean of five schema items.

Depressiveness. Depressiveness was assessed with the revised twenty-one-item version of the Beck Depression Inventory (BDI-II) (Beck, Steer & Brown, 1996). All the items were self-rated from 0 to 3 and added up to obtain a total score ranging from 0 to 63, with higher values indicating more severe symptoms of depression. The questionnaire is widely used and has been proven to be suitable for measuring depression in chronic pain patients (Harris & D'Eon, 2008). It has also been validated in Finnish (Beck, Steer & Brown, 2004). A score of 0–13 indicates minimal depressiveness (the individual faces normal 'ups and downs'), a score of 14–19 indicates mild, a score of 20–28 moderate and a score of 29–63 severe depressive symptoms (Beck *et al*., 1996).

Statistical methods. The sample was dichotomized to alexithymic and nonalexithymic pain patient groups according to the TAS-20 cutoff point > 60. The means and standard deviations of basic characteristics, pain variables, and BDI-II scores were calculated in the total pain patient group and separately in the alexithymic and nonalexithymic patient groups. Student's *t*-test was used with normally distributed data to make group comparisons and Chi-square test was used with categorical data. The means of individual EMSs were calculated for the total sample, the alexithymic and nonalexithymic groups. As the distribution of Early Maladaptive Schema data was skewed, Mann-Whitney U-test was used to compare the differences in EMSs between the alexithymic and nonalexithymic pain patient groups. The level of significance was set at $p < 0.01$ to improve the reliability of the results. In order to calculate effect sizes, phi coefficient was calculated for categorical data, Cohen's *d* values were calculated for continuous data when comparisons were made by Student's

t-test. Effect size is considered small if $d = 0.2$, medium if $d = 0.5$ and large if $d = 0.8$. When Mann-Whitney U-test was used, the r value was calculated to determine effect sizes. Effect size is regarded as small if $r = 0.1$, medium if $r = 0.3$ and large if $r = 0.5$. In the whole sample, as the distribution of the scores of EMSs was not normal but skewed Spearman's correlation coefficients were used to measure the associations between the alexithymia variables (TAS-20 total score, DIF, DDF, EOT), pain variables and BDI-II score with the EMS data. Post hoc, a partial correlation test between alexithymia variables and the EMSs was performed to control for depression. The correlation was regarded as small if r was +/–0.1 – +/–0.29, moderate if +/–0.30 – +/–0.49 and large if +/–0.50 – +/–1. A series of regression analyses was performed as pain intensity (VAS) as the dependent factor and TAS-20 and its factors (DIF, DDF, EOT), BDI-II and Early Maladaptive Schema domains (Table 1) as independent factors.

The alexithymic and nonalexithymic patients were divided into four groups according to the severity of depressiveness indicated by BDI-II scores: BDI-scores <14, 14–19, 20–28 and >28. The means of EMSs, VAS and PDS were calculated in each group separately to explore the effect of alexithymia and depression on EMSs and pain variables.

The statistical analyses were conducted with SPSS (version 19.0. for Windows [SPSS Inc., Chicago, IL, USA]).

RESULTS

For the whole sample, the mean duration of pain was 9.3 years, mean pain intensity (VAS) 5.9, mean number of pain sites 2.1, the mean pain disability (PDS) score was 16.5, the mean BDI-II score was 15.7, and the mean TAS-20 score was 47.4. The prevalence of alexithymia was 27.6% among men and 11.8% among women ($p < 0.001$). The alexithymic and nonalexithymic groups were similar in terms of age and education and did not differ in pain duration or number of pain sites. The alexithymic patients scored significantly higher on BDI-II score ($p < 0.001$), pain disability ($p < 0.001$) and pain intensity $p < 0.01$). The baseline characteristics and the means of variables for the whole group, and also the alexithymic and nonalexithymic groups are presented in Table 2. The alexithymic group scored significantly higher on all Early Maladaptive Schemas (EMSs) than the non-alexithymic group, except on the Self-Sacrifice schema (SS) (Table 3).

In the whole group, Spearman's correlation showed large correlations between the TAS-20 total score and Emotional Inhibition (EI) schema, between DIF and Vulnerability to Harm or Illness (VH), and between DDF and the Mistrust/Abuse (MA), Emotional Deprivation (ED) and EI schemas. The TAS-20 total score, DIF and DDF correlated largely with BDI-II. All the EMSs except SS schema correlated largely or moderately with BDI-II. The EMSs and alexithymia variables correlated only to a small extent with pain variables. All the correlations between study variables are presented in Table 4. After controlling for BDI-II there were moderate sized correlations between the TAS-20 total score and EI schema (0.349, $p < 0.001$), between DDF and EI schema (0.434, $p < 0.001$) and between DIF and VH (0.322, $p < 0.001$) schema. Most of the correlations between TAS-20 and EMSs diminished by size but the association remained significant ($p < 0.001$). The results of regression analyses showed that TAS-20 predicted 3.6%, BDI-II predicted 7% and EMSs domains 6% of the variance of the pain intensity. Among EMSs domains only the domain "Impaired Autonomy and Performance" was significant. When only BDI-II and Impaired Autonomy and Performance" were entered to the regression analyses, they both were significant predictors of pain intensity and the variance explained was the highest, 8% (Table 5).

The inspection of EMS scores compartmentalized on the basis of the grade of depressiveness and alexithymia/nonalexithymia indicated that both depression and alexithymia were associated with higher EMSs scores, pain intensity and pain disability (Table 6). The prevalences of the BDI-II scores >14 were as follows: 88.5% for the alexithymic group and 43.0% for the nonalexithymic group.

DISCUSSION

The main findings in the present study were as follows. The alexithymic chronic pain patients had higher scores on all Early Maladaptive Schemas (EMSs) than did the nonalexithymic patients. The alexithymic patients reported more pain intensity and pain disability and had higher BDI-II scores. Pain intensity was not connected with alexithymia factors and only slightly with depression or Impaired Autonomy and Performance schema

Table 2. *Means (and standard deviations) of baseline characteristics, pain variables, alexithymia (TAS-20) and depressiveness (BDI-II) in the total sample and in the alexithymic and nonalexithymic pain patient groups with comparison of alexithymic and nonalexithymic groups*

	All patients n = 271	Alexithymic group n = 52	Nonalexithymic group n = 219	Significance *p* value	Effect size
Male/female	127/144	35/17	92/127	0.001[a]	−0.20[c]
Age	47.0 (9.3)	46.8 (9.3)	47.1 (9.3)	0.853[b]	−0.03[d]
Education in years	11.1 (1.6)	10.8 (1.5)	11.2 (1.6)	0.121[b]	−0.24[d]
TAS-20 score	47.4 (12.5)	66.8 (5.5)	42.8 (8.7)	<0.001[b]	2.92[d]
BDI-II score	15.7 (10.2)	25.0 (9.3)	13.5 (9.1)	<0.001[b]	1.26[d]
Pain disability (PDS)	16.5 (5.1)	19.0 (3.8)	15.9 (5.1)	<0.001[b]	0.63[d]
Pain intensity (VAS)	5.9 (1.2)	6.3 (1.3)	5.8 (1.2)	<0.01[b]	0.42[d]
Pain duration in years	9.3 (8.8)	10.2 (9.5)	9.1 (8.6)	0.436[b]	0.12[d]
Number of pain sites	2.1 (1.3)	2.3 (1.4)	2.1 (1.2)	0.262[b]	0.17[d]

Notes: [a] Chi-square test, [b] Student's *t*-test, [c] Phi coefficient, [d] Cohen's *d*.

Table 3. *Means (and standard deviations) of Early Maladaptive Schemas in the total pain patient sample and in the alexithymic and nonalexithymic pain patient groups and the comparison of the differences between the groups*

	All patients n = 271	Alexithymic patients n = 52	Non-alexithymic patients n = 219	Significance *p*-value[a]	Effect size[b]
Abandonment/Instability	1.8 (1.0)	2.7 (1.4)	1.6 (0.8)	<0.001	0.35
Mistrust/Abuse	1.7 (0.9)	2.5 (1.3)	1.5 (0.7)	<0.001	0.34
Emotional Deprivation	2.0 (1.6)	3.0 (1.4)	1.7 (0.9)	<0.001	0.39
Defectiveness/Shame	1.6 (1.0)	2.5 (1.4)	1.4 (0.7)	<0.001	0.38
Social Isolation/Alienation	1.9 (1.2)	3.0 (1.5)	1.6 (0.9)	<0.001	0.37
Dependence/Incompetence	1.6 (0.8)	2.3 (1.2)	1.4 (0.6)	<0.001	0.39
Vulnerability to Harm or Illness	1.8 (1.0)	2.7 (1.4)	1.6 (0.8)	<0.001	0.37
Enmeshment/Undeveloped Self	1.3 (0.7)	1.7 (1.1)	1.2 (0.5)	0.003	0.18
Failure	1.8 (1.1)	2.6 (1.5)	1.6 (0.8)	<0.001	0.34
Entitlement/Grandiosity	1.7 (0.8)	2.2 (1.1)	1.5 (0.7)	<0.001	0.29
Insufficient Self-Control/Self-Disclipine	1.9 (1.0)	2.5 (1.2)	1.8 (0.8)	<0.001	0.26
Subjugation	1.5 (0.8)	2.1 (1.1)	1.4 (0.7)	<0.001	0.33
Self-Sacriface	3.4 (1.1)	3.6 (1.2)	3.3 (1.1)	0.076	0.10
Approval-Seeking/Recognition-Seeking	2.6 (1.1)	3.1 (1.2)	2.5 (1.0)	<0.001	0.21
Negativity/Pessimism	2.4 (1.2)	3.3. (1.2)	2.1 (1.0)	<0.001	0.40
Emotional Inhibition	1.9 (1.0)	2.8 (1.5)	1.7 (0.8)	<0.001	0.40
Unrelenting Standards/Hypercriticalness	2.9 (1.2)	3.3 (1.2)	2.7 (1.1)	0.001	0.19
Punitiveness	2.3 (1.1)	3.0 (1.1)	2.1 (1.0)	<0.001	0.29
Schema total	36 (12.7)	49.0 (15.1)	32.8 (9.8)	<0.001	0.43
Schema mean	2.0 (0.7)	2.7 (0.8)	1.8 (0.5)	<0.001	0.43

Notes: [a] Mann-Whitney U Test, [b] Effect size = r value.

domain. The most notable correlations between alexithymia variables and EMSs were in the Disconnection and Rejection schema domain. Alexithymia also had considerable correlations with the Emotional Inhibition (EI) and the Vulnerability to Harm or Illness (VH) schemas. However, when controlling for BDI-II, the correlations between the EMSs and alexithymia variables diminished. Higher EMS scores were associated with higher BDI-II scores in both the alexithymic and nonalexithymic groups, the alexithymic group generally scoring higher on EMSs. As far as the authors know, this is the first study to explore the relations of alexithymia, EMSs and depressiveness in a sample of chronic pain patients.

Table 4. *Spearman's correlations (rho-values) between Early Maladaptive Schemas (EMSs), alexithymia (TAS-20), alexithymia factors (DIF, DDF, EOT), depressiveness (BDI-II) and pain variables in the total sample*

EMSs[a]	TAS-20[b]	DIF[c]	DDF[d]	EOT[e]	VAS[f]	Pain duration	Pain sites	PDS[g]	BDI-II[h]
AB	0.410*	0.458*	0.430*	0.065	0.163	0.041	0.087	0.270*	0.504*
MA	0.453*	0.475*	0.517*	0.074	0.226*	0.069	0.152	0.290*	0.498*
ED	0.488*	0.488*	0.517*	0.137	0.134	0.135	0.166	0.270*	0.533*
DS	0.468*	0.488*	0.442*	0.169	0.110	0.015	0.109	0.255*	0.560*
SI	0.428*	0.477*	0.464*	0.056	0.153	0.145	0.162	0.344*	0.628*
DI	0.485*	0.490*	0.431*	0.205*	0.245*	0.011	0.123	0.369*	0.635*
VH	0.462*	0.512*	0.444*	0.107	0.186*	−0.002	0.081	0.298*	0.580*
EM	0.246*	0.264*	0.262*	0.080	0.128	−0.064	0.064	0.170	0.379*
FA	0.454*	0.462*	0.432*	0.169	0.162	0.029	0.083	0.225*	0.453*
ET	0.322*	0.370*	0.324*	0.069	0.130	0.025	0.006	0.095	0.336*
IS	0.365*	0.369*	0.376*	0.113	0.106	0.052	0.077	0.204*	0.479*
SB	0.418*	0.407*	0.416*	0.148	0.167	0.074	0.162	0.300*	0.534*
SS	0.150	0.162	0.167	0.040	0.054	0.036	–0.034	0.129	0.172*
AS	0.278*	0.265*	0.258*	0.115	0.096	0.041	–0.054	0.065	0.347*
NP	0.480*	0.487*	0.463*	0.165	0.157	0.043	0.118	0.318*	0.671*
EI	0.552*	0.460*	0.612*	0.246*	0.122	0.131	0.018	0.212*	0.479*
US	0.150	0.181	0.199*	–0.004	0.078	0.019	0.017	0.060	0.334*
PU	0.389*	0.394*	0.405*	0.122	0.156	0.080	0.034	0.292*	0.542*
VAS	0.164	0.171	0.174	0.025	–	0.160	0.147	0.334*	0.251*
PDS	0.265*	0.277*	0.310*	0.034	0.334*	0.186*	0.283*	–	0.574*
BDI-II	0.521*	0.546*	0.524*	0.136	0.251*	0.077	0.244*	0.574*	–

Notes: [a] Early Maladaptive Schema (abbreviations explained in Table 1), [b] Toronto Alexithymia Scale, [c] Difficulties in Identifying Feelings, [d] Difficulties in Describing Feelings, [e] Externally Oriented Thinking Style, [f] Visual Analogous Scale (pain intensity), [g] Pain Disability Scale, [h] Beck Depression Inventory-II. *Correlation is significant at the 0.0025 level (2-tailed).

Table 5. *Linear regression analysis (enter method) of schema domains (1a), TAS-20 (1b), TAS-20 factors (1c), BDI-II (1d) predicting mean pain intensity (dependent variable); Impaired Autonomy & Performance schema domain, TAS-20 and BDI-II (2a) predicting together mean pain intensity (dependent variable); Impaired Autonomy & Performance schema domain and BDI-II (2b) predicting together mean pain intensity (dependent variable)*

								CI 95	
	Independent variable(s)	β (stand.)	R2	F	t	Sig.	df	Upper	Lower
1a	Schema domains		0.060	4.44		0.001	5, 264		
	DisRej	−0.122			−1.136	0.257		−0.473	0.127
	ImpAPe	0.335			3.219	0.001		0.223	0.928
	ImpLi	−0.028			−0.310	0.756		−0.319	0.232
	OthDi	0.008			0.094	0.925		−0.262	0.288
	OVInh	0.066			0.654	0.514		−0.190	0.379
1b	TAS-20	0.189	0.036	9.97	3.16	0.002	1, 269	0.007	0.031
1c	TAS-20 factors		0.040	4.75			3, 267		
	DIF	0.086			1.002	0.317		−0.016	0.050
	DDF	0.170			1.901	0.058		−0.002	0.096
	EOT	−0.049			−0.764	0.446		−0.046	0.020
1d	BDI-II	0.271	0.073	21.3	4.61	<0.001	1, 269	0.019	0.047
2a			0.077	8.47		<0.001	3, 267		
	ImpAPe	0.150			1.79	0.074		−0.025	0.542
	TAS-20	0.022			0.303	0.76		−0.012	0.016
	BDI-II	0.156			1.88	0.061		−0.001	0.039
2b			0.080	12.7		<0.001	2, 268		
	ImpAPe	0.158			1.976	0.049		0.001	0.541
	BDI-II	0.163			2.041	0.042		0.001	0.039

Notes: BDI-II = Beck Depression Inventory (sec. edit.), TAS-20 = Toronto alexithymia scale; OVInh = Overvigilance and Inhibition, ImpLi = Impaired Limits, OthDi = Other-Directedness, ImpAPe= Impaired Autonomy and Performance and DisRej = Disconnection and Rejection schema domains. DIF = Difficulty Identifying Feelings, DDF = Difficulty Describing Feelings and EOT = Externally Oriented Thinking are TAS-20 factors. β (stand.) = standardized regression coefficient; R2 = coefficient of determination; CI95 = confidence interval of 95% for an independent factor; F = F-value; t = Student's t-value; df = degrees of freedom.

Table 6. *Means (and standard deviations) of Early Maladaptive Schemas (EMS), pain intensity (VAS) and pain disability (PDS) in alexithymic and nonalexithymic pain patient groups according to the Beck Depression Inventory-II (BDI-II) scores*

	BDI-II<14		BDI-II14–19		BDI-II20–28		BDI-II>28	
	Non-alexithymic (n = 125)	Alexithymic (n = 6)	Non-alexithymic (n = 48)	Alexithymic (n = 7)	Non-alexithymic (n = 30)	Alexithymic (n = 19)	Non-alexithymic (n = 16)	Alexithymic (n = 20)
AB[a]	1.4 (0.5)	2.4 (2.1)	1.8 (0.8)	1.5 (0.7)	2.1 (1.0)	2.9 (1.3)	2.4 (1.6)	3.1 (1.3)
MA[a]	1.4 (0.6)	1.7 (0.9)	1.5 (0.5)	1.4 (0.5)	1.7 (0.6)	2.5 (1.0)	2.4 (1.4)	3.2 (1.5)
ED[a]	1.5 (0.7)	1.9 (0.9)	1.9 (0.9)	2.1 (1.0)	1.9 (1.0)	2.8 (1.3)	2.9 (1.6)	3.8 (1.2)
DS[a]	1.2 (0.3)	1.7 (1.0)	1.3 (0.4)	1.2 (0.4)	1.6 (0.7)	2.3 (1.2)	2.6 (1.7)	3.3 (1.4)
SI[a]	1.3 (0.6)	1.8 (1.5)	1.7 (0.7)	1.7 (0.8)	2.0 (1.0)	2.9 (1.2)	3.1 (1.4)	3.8 (1.5)
DI[a]	1.2 (0.3)	1.6 (0.9)	1.5 (0.6)	1.6 (0.5)	1.7 (0.6)	2.1 (0.9)	2.4 (1.2)	2.9 (1.4)
VH[a]	1.3 (0.5)	1.9 (1.1)	1.6 (0.7)	1.9 (0.8)	2.0 (1.0)	2.6 (1.2)	2.6 (1.2)	3.3 (1.5)
EM[a]	1.1 (0.3)	1.6 (0.9)	1.3 (0.5)	1.2 (0.4)	1.3 (0.5)	1.7 (0.9)	2.0 (1.0)	2.0 (1.4)
FA[a]	1.4 (0.5)	2.6 (1.1)	1.6 (0.7)	2.0 (0.8)	1.9 (0.9)	2.1 (1.2)	2.9 (1.6)	3.3 (1.6)
ET[a]	1.4 (0.5)	1.8 (0.6)	1.6 (0.6)	1.7 (0.5)	1.7 (0.8)	2.0 (0.9)	2.0 (1.3)	2.8 (1.3)
IS[a]	1.5 (0.5)	2.1 (1.3)	1.8 (0.8)	1.8 (0.9)	2.2 (1.0)	2.4 (1.1)	2.6 (1.3)	3.0 (1.3)
SB[a]	1.2 (0.4)	1.4 (0.6)	1.3 (0.5)	1.3 (0.4)	1.7 (1.0)	1.9 (0.9)	2.5 (1.3)	2.7 (1.2)
SS[a]	3.2 (1.1)	2.0 (1.1)	3.3 (1.1)	3.7 (0.9)	3.7 (1.1)	3.5 (0.9)	3.6 (1.1)	4.0 (1.5)
AS[a]	2.3 (1.0)	3.1 (1.6)	2.5 (0.9)	2.5 (0.9)	3.2 (1.0)	2.9 (0.8)	3.1 (1.2)	3.5 (1.3)
NP[a]	1.7 (0.7)	2.7 (1.0)	2.3 (0.8)	2.4 (1.2)	2.7 (1.0)	3.3 (1.0)	4.0 (1.2)	3.9 (1.2)
EI[a]	1.5 (0.6)	1.5 (0.4)	1.8 (0.8)	2.1 (0.8)	1.9 (0.9)	2.9 (1.1)	2.5 (1.3)	3.4 (1.1)
US[a]	2.6 (1.1)	2.1 (1.2)	2.8 (1.0)	2.3 (1.0)	3.2 (1.2)	3.6 (0.9)	3.2 (1.3)	3.8 (1.2)
PU[a]	1.8 (0.9)	2.3 (0.9)	2.1 (0.8)	1.9 (0.8)	2.8 (1.0)	2.9 (1.0)	3.3 (1.1)	3.6 (1.1)
EMS total	28.6 (6.4)	37.2 (11.4)	33.7 (6.8)	34.3 (5.4)	39.0 (8.9)	47.3 (10.1)	50.2 (15.1)	59.2 (15.4)
EMSmean	1.6 (0.4)	2.1 (0.6)	1.9 (0.4)	1.9 (0.3)	2.1 (0.5)	2.6 (0.6)	2.8 (0.8)	3.3 (0.9)
VAS	5.5 (1.1)	5.9 (2.1)	6.1 (1.3)	6.0 (0.8)	6.2 (1.2)	6.4 (1.2)	5.8 (1.5)	6.4 (1.2)
PDS	13.9 (4.7)	15.0 (2.8)	17.1 (5.1)	17.9 (2.6)	19.7 (3.8)	18.8 (3.9)	20.4 (3.1)	20.8 (3.4)

Note: [a] Early Maladaptive Schema (abbreviations explained in Table 1).

In earlier studies, relations between alexithymia and EMSs have been assessed in some psychiatric patient groups: in a study on female eating disorder patients, alexithymia factor DIF was associated with the Entitlement/Grandiosity schema (ET) and factor DDF was associated with the Abandonment/Instability (AB) and the EI schemas (Lawson, Emanuelli, Sines & Waller, 2008). In another study, the researchers concluded that vulnerability to an attempted suicide in adolescences was influenced by EMSs and the interactive set of factors consisting of depression, alexithymia, hopelessness and an episode of major depression (Hirsch, Hautekeete & Kochman, 2001). In a study on the consequences of sexual abuse in a psychiatric sample, alexithymia and EMSs were found to be a part of the complex posttraumatic stress disorder (Zlotnick, Zakriski, Shea *et al*., 1996). A recent study showed that alexithymia factors DIF and DDF and Defectiveness/Shame (DS) and ET schemas predicted irritable bowel syndrome and its severity (Phillips, Wright & Kent, 2013). None of these studies estimated how alexithymia or EMSs were influenced by depression in their study context.

There are numerous studies which separately connect alexithymia or EMSs to health related disorders, such as personality disorders (Coolidge, Estey & Segal, 2013; Nordahl, Holthe & Haugum, 2005), eating disorders (Berthoz, Perdereau, Godart, Corcos & Haviland, 2007; Unoka *et al*., 2010), substance abuse (Coriale, Bilotta, Leone *et al*., 2012; Shorey *et al*., 2013), posttraumatic stress disorder (Cockram *et al*., 2010; Declercq, Vanheule & Deheegher, 2010), and depression (Halvorsen, Wang, Richter *et al*., 2009; Honkalampi, Hintikka, Tanskanen, Lehtonen & Viinamäki, 2000). EMSs have been proposed to be associated with psychosomatic symptoms (Young *et al*., 2003), as well as alexithymia (Taylor, 1997).

The Disconnection and Rejection schema domain reflects abuse, being abandoned, lack of empathy, neglect, insecurity, instability, and feelings of social inferiority in early reciprocal relations and environment (Young *et al*., 2003). In the present study, all the schemas in the Disconnection and Rejection schema domain were largely or moderately correlated with TAS-20 total score, DIF, and DDF. The consequences of the schemas belonging to the Disconnection and Rejection schema domain include difficulties in close relationships, social relations, and emotional life. Alexithymia has also been shown to be related to interpersonal problems (Mattila, Luutonen, Ylinen, Salokangas & Joukamaa, 2010; Vanheule *et al*., 2007). In clinical practice, the health care personnel- chronic pain patient-relationship is often felt demanding and frustrating (Matthias, Papart, Nyland *et al*., 2010). This well known reality may account for interpersonal problems in patients. Cecero, Beitel and Prout (2008) studied the relations of EMSs belonging to the Disconnection and Rejection schema domain with psychological mindedness and college adjustment, and found a significant negative effect of EMSs on both variables. The psychological mindedness scale (PMS) measures the cognitive-emotional skills, and has been found to be negatively correlated with TAS-20 total score (Shill & Lumley, 2002). Emotional neglect was found to be associated with TAS-20 total score in a study exploring the relationship of alexithymia and early life stress (Aust, Härtwig, Heuser & Bajbouj, 2013). In a study assessing parental bonding in fibromyalgia patients, higher TAS-20 scores were associated with maternal abuse and higher scores on the alexithymia factor DIF were associated with paternal indifference (Pedrosa *et al*., 2008).

In the Impaired Autonomy and Performance schema domain there was a large correlation between DIF and the Vulnerability to Harm or Illness schema (VH), which also correlated moderately with the TAS-20 total score and with DDF. Anxiety and beliefs, that sudden, uncontrollable catastrophes like medical illness or other disasters may happen at any moment, are typical of this schema. In an earlier study alexithymic chronic pain patients were shown to have catastrophic beliefs (Lumley *et al*., 2002), and anxiety has been connected to alexithymia (Karukivi, Hautala, Kaleva *et al*., 2010). Alexithymia may increase the interpretation of bodily felt emotional states as symptoms of diseases and with the VH schema, their joint effect may intensify the physical symptoms and perceived pain. The Dependence/Incompetence (DI) schema correlated moderately with the TAS-20 total score, as well as, the DIF and DDF factors, and also slightly with EOT. The schema can be described in terms of passivity and helplessness. Alexithymia together with the DI schema may increase schema driven coping difficulties, and in case of chronic pain, restrict the abilities to control the pain situation. The Failure schema (FA) also correlated moderately with TAS-20, DIF and DDF. The schema contains negative, almost depressive beliefs about one's own abilities, and often drives individuals to under- or over-achieve, which may impair coping with pain disorder.

The Emotional Inhibition (EI) schema (the Overvigilance and Inhibition schema domain) showed large correlations with DDF and TAS-20 total score, moderate correlation with DIF, and even a small correlation with EOT. As the items of TAS-20 reflect the difficulties in identifying and describing emotional states, the items of the EI schema clearly reflect the conscious control of feelings. Theoretically, it is possible to assume that the problems in the cognitive awareness of emotions, as an unpredictable and confusing state, may lead to their control. Alexithymic individuals may have uncontrolled emotional outbursts of rage or grief (Bagby & Taylor, 1997a) and thus, fearing embarrassing behavior they may control the expression of any feelings. The EI schema has been suggested to develop in such childhood circumstances, where spontaneous expressions of feelings are subdued with shame and considered "bad behavior" (Young *et al*., 2003).

In this study we replicated the results of numerous earlier studies on the role of depression as a co-occurent factor in chronic pain, alexithymia and EMSs. In earlier studies depression occurred as a mediator between pain disability and alexithymia (Saariaho, Saariaho, Mattila, Karukivi & Joukamaa, 2013) and between second-order EMSs factors and pain disability (Saariaho *et al*., 2012). Our exploration of scores on EMSs in different states of depression in alexithymic and nonalexithymic patients showed that higher EMSs scores are related to the severity of depression and also to alexithymia.

The results of the partial correlation analyses brought out the connection between depression and alexithymia together with EMSs.Their concurrent presence reflect the possible shared origin in early adversities. The plausible conclusions based on the literature available concerning the relative stability of alexithymia (Luminet, Bagby & Taylor, 2001) and EMSs (Renner *et al*., 2012) suggest that both alexithymia and EMSs may predispose to depression. In the case of chronic pain, one possible theoretical

model of the relations between alexithymia, EMSs and depression may be as follows: Early adversities predispose to EMSs and alexithymia, which exert a negative influence on self-image, self-efficacy and coping abilities and thus on the individual's capacity to conceptualize and manage with different problems. The inability to adapt leads to depression, which exacerbates the outcome, and in chronic pain patients, increases the pain disability. It is also possible that early adversities predispose individuals into different grades of EMSs, alexithymia, depression and chronic pain, and these four phenomena interact together intensifying each other.

The limitation of this study is the cross-sectional design, which makes estimating causalities indirect, while the interpretation depends on background theories. The data collected by self-report questionnaires may have been affected by response bias. Qualitative and structural interview methods would have yielded more detailed and objective data. However, the validated questionnaires with a satisfactory number of participants can provide reliable results on the study questions and provide an opportunity to compare the results with those of other studies. Furthermore, patients attending pain clinics have a tendency to underreport their psychological symptoms, therefore we evaluate that at any rate the scores of the TAS-20 and EMSs were not overestimated. The used cutpoint of TAS-20 is based on one research (Bagby *et al*., 1994) with a small number of participants, but its use is justified because then the results of the current study can be comparable with other alexithymia studies. Descriptive results presented in the Table 6 concerning the values of EMSs compartmentalized by BDI-II scores and alexithymia do not allow any conclusions to be made but they give an impression that both alexithymia and EMSs add on depression. The lack of similar studies and a control group makes our conclusions tentative.

The pain experience is commonly rated by pain intensity and pain disability. The usual treatment target is to diminish the pain intensity and decrease pain disability. However, experienced pain and how to cope with it is a highly individual and subjective state influenced by a myriad of factors. In this study we examined alexithymia and Early Maladaptive Schemas as factors which have an effect on the subjective pain situation. We noticed that the alexithymic chronic pain patients reported greater pain intensity, pain disability and depressiveness than the nonalexithymic patients. The reported pain intensity remained an unanswered phenomenon, as it was not influenced by alexithymia factors and very slightly by depressiveness or EMSs explored in this study. We found that alexithymic patients scored significantly higher on almost all EMSs. The Disconnection and Rejection schema domain, where the chronic pain patients of the present study had the largest correlations between alexithymia and EMSs, reflects the emotionally or otherwise abusive childhood. The schemas in this domain are all unconditional, that is, early developmental in origin. The correlation between the EI schema and alexithymia reflects the difficulties in emotional coping and may predispose to bodily felt symptoms. We assume that our findings suggest that there is a special group among chronic pain patients reporting more pain intensity and pain disability and having psychological factors referring to remarkable negative childhood experiences. These factors, alexithymia, EMSs and depression, in the case of chronic pain, modify the pain experience in a complex and individually different manner.

Our study highlights the importance of screening for psychological factors in chronic pain patients. We suggest that screening for alexithymia, EMSs and depression may help clinicians to understand their patients' problems more profoundly and to detect subgroups needing more psychological intervention in their pain situation. Schema therapy has been shown to afford symptom relief in the treatment of personality disorders (Giesen-Bloo, van Dyck, Spinhoven *et al*., 2006; Masley, Gillanders, Simpson & Taylor, 2012). The treatment strategies adopted from personality disorder therapies may offer an alternative method with conventional cognitive-behavioral therapy for chronic pain. However, more studies are needed to develop effective therapeutic tools for chronic pain patients bearing a psychological burden, and longitudinal studies are needed to explain the complex interactions between chronic pain, alexithymia, EMSs and depression.

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ALEXITHYMIA AND DEPRESSION IN THE RECOVERY OF CHRONIC PAIN PATIENTS: A FOLLOW-UP STUDY

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ABSTRACT

Background: Childhood adversities and emotional dysregulation are connected with chronic pain, alexithymia and depression. Longitudinal studies exploring the impact of their co-occurrence on the pain situation are rare.

Aims: The influence of alexithymia, depression, baseline pain situation and treatment options on the course of chronic pain in a clinical sample was studied.

Methods*:* The baseline data was collected from chronic pain patients (n=154) before their first pain clinic visit, and the follow-up data after one year by self-report questionnaires. Study variables consisted of pain intensity, pain disability, alexithymia (TAS-20), depression (BDI-II) and treatment interventions. Statistical analyses were performed to find out differences between baseline and follow-up, as well as between alexithymic and nonalexithymic patients, and to estimate the effect of the treatment provided.

Results*:* At-follow up, the majority of the patients had pain intensity and disability severe enough to disrupt with their daily living. None of treatment interventions was related to better outcome. Alexithymic patients reported more pain disability and depression at both baseline and at follow-up. The effect of alexithymia on pain disability was mediated by depression. The use of opioids was connected to alexithymia and depressiveness. Alexithymia and depression made a substantial contribution to poorer outcome.

Conclusions*:* Severe pain intensity and disability with depression and alexithymia predicted difficulties in achieving improvement. Depression and alexithymia probably impair compliance with treatment and adherence to interventions. Their co-occurrence with a more severe pain situation and with the use of opioids indicates psychological problems underlying the pain experience.

Keywords**:** Alexithymia, Depression, Chronic Pain, Treatment Interventions, Follow-Up Study

1. INTRODUCTION

Chronic pain is a major health problem worldwide causing individual suffering, impaired quality of life and an enormous burden on health care systems. Chronic pain is a persistent problem; in spite of the large number of treatment intervention methods and trials, the number of patients who are cured or who recover has remained low. The modern conception perceives chronic pain as an outcome of complex learning by the nervous system influenced by lifelong neurophysiological and psychological events and experiences (1-3). Several studies have shown that early stress predisposes to health disorders in adulthood. Childhood adversities have been found in the backgrounds of chronic pain patients (4). Emotional dysregulation, negative mood and inhibition of negative emotions may predispose to chronic pain (1, 5). Chronic pain is often accompanied by alexithymia and depression (6, 7), both of which have been connected with underlying early adversities (8, 9) and emotion processing problems.

Alexithymia, meaning literally "no words for feelings", is considered a personality characteristic with "a deficit in the cognitive-experiential domain of emotion response systems" (10), possibly originating from the disturbed cognitive processing of emotions in early childhood (11). Typical features of alexithymia include difficulties in describing and identifying emotional states and having restricted imaginary capacity. Alexithymic individuals have been shown to have had adverse childhood experiences (8, 12), insecure attachment styles (13), and problems in interpersonal relationships (14). Studies have detected higher than average levels of alexithymia in various health related problems such as chronic pain, depression, personality disorders, inflammatory bowel diseases, eating disorders, substance abuse and chronic fatigue syndrome (15).

Depression is regarded as a predisposing factor to or as a consequence of chronic pain (16, 17). Furthermore, it has been suggested that suppression or lack of awareness of primary, adaptive emotions (such as anger and sadness) may contribute to the pain experience and provoke secondary, maladaptive emotional states manifesting in depressiveness and anxiety (5) and that emotional dysregulation links depression and physical illness (18). Depression frequently co-

occurs with alexithymia (19). Alexithymic depressive patients have been observed to differ from nonalexithymic depressive patients in presenting with more suicidal ideation and more somatic symptoms (20). In a chronic pain patient sample alexithymic patients reported more depressiveness, pain intensity and disability than nonalexithymic patients (21). Early maladaptive schemas reflect childhood adversities and alexithymic depressive chronic pain patients had them more than did nonalexithymic, nondepressive patients (22).

The aims of the present study were as follows: 1.to explore the course of chronic pain in a longitudinal study design and to assess the differences between alexithymic and nonalexithymic patients 2. to assess the effect of alexithymia and depression on choice of treatment preference, 3. to assess the influence of baseline situation and treatment interventions on outcome in pain disease. We hypothesized that alexithymic chronic pain patients differ from nonalexithymic patients by being more depressive and by having a poorer baseline pain situation as well as a poorer prognosis compared with nonalexithymic patients.

2.METHODS

2.1. Participants

Chronic pain patients referred to six pain clinics during a period of one year (from January 2004 to January 2005) in Central and Northern Finland were recruited for the study. The inclusion criteria were: nonmalignant, chronic pain lasting for three months or more, no psychotic disorder or cognitive impairment, age 18-65 years, and that the patient was referred to the pain clinic for the first time. The referral sources were primary health care and various medical specialists. The information letter with the study questionnaire was sent to all eligible patients (n=318) to be completed at home before the consultation. The final sample consisted of 271 participants as 47 patients refused to take part. The follow-up data was collected one year after the first visit to the pain clinic (January 2005-January 2006). The

original study questionnaire with additional treatment variables was sent to all the 271 patients who participated in the study at baseline. Of these, 154 (56.8%, male/female 68/86) returned the one-year follow-up questionnaire and comprised the sample for the present study. The baseline data of the study variables were compared between respondents and non-respondents and no significant differences were found in any of the study variables (Table 1).

Table 1. Comparisons of basic characteristics and baseline study variables between at follow-up responding and nonresponding patients. Values presented in means (SD).

	respondents (n=154)	non-respondents (n=117)	sig.	effect size
age (years)	47.9 (9.0)	46.0 (9.5)	.084*	.205%
gender M/F	68/86	59/58	.305§	.062§
education (years)	11.1 (1.8)	11.0 (1.4)	.426*	.062%
pain duration (years)	9.4 (9.0)	9.3 (8.6)	.918*	.011%
VAS	5.9 (1.3)	5.8 (1.1)	.296*	.083%
PDS	16.3 (4.9)	16.7 (5.2)	.573*	.079%
TAS-20	47.6 (12.2)	47.2 (13.0)	.800*	.031&
DIF	15.7 (6.3)	15.4 (6.4)	.696*	.047%
DDF	11.1 (4.4)	11.3 (4.6)	.836*	.044%
EOT	20.7 (4.6)	20.5 (5.1)	.735*	.041%
BDI-II	15.7 (10.8)	15.7 (9.4)	.968*	.000%

Note: VAS = Visual Analogue Scale, PDS = Pain Disability Scale, TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II= Beck Depression Inventory, *Student's t-test, §Chi-Square, % Cohen's d, & φ coefficient

The study protocol was approved by the ethics committee of the Northern Ostrobothnia Hospital District. Written informed consent was obtained from all participants at both baseline and follow-up.

2.2. Measures

2.2.1. Baseline study questionnaire

The baseline pain questionnaire was developed for the chronic pain study to collect information on basic characteristics (age, gender and occupation/education), pain variables (pain intensity, pain disability, pain duration), alexithymia and depression.

Pain intensity was measured with two 10-cm Visual Analogue Scales (VAS) where 0 represents no pain and 10 represents the worst pain one can imagine. The interpretation of the VAS values was changed to follow the interpretation of the numerical scale: 0 =no pain, 1-4 = mild pain, 5-6 = moderate pain and 7-10 = severe pain (23).

The Pain Disability Scale (PDS) was developed for the study of chronic pain (24). It is a 9-item self-report Likert-type scale consisting of nine statements covering sleep, work, hobbies, mobility, economy, social contacts, life enjoyment and pain control. The total score (range 0 – 27) reflects the severity of pain disability. A score of 0-4 indicates 'no disability', a score of 5-13 'mild disability', a score of 14-22 'remarkable disability' and a score of 23-27 'severe disability'.

In this study, VAS and PDS at follow-up were used as outcome measures and cut-off points VAS $\leq$ 4 and PDS $\leq$ 13 at follow-up were used to dichotomize the patients to the better/poorer outcome groups.

Alexithymia was measured with the 20-item Toronto Alexithymia Scale (TAS-20). The Finnish version of TAS-20 has been proven to be reliable (25). The items of TAS-20 are divided into three subscales each assessing the different features of the alexithymia concept: difficulties identifying feelings (DIF), difficulties describing feelings (DDF) and externally oriented thinking style (EOT). In the present study, the cut-off point of the TAS-20 score > 60 (26) was used to dichotomize alexithymic and nonalexithymic patients.

Depressiveness was assessed with the revised 21-item version of the Beck Depression Inventory (BDI-II). The questionnaire has been proven to measure depressiveness in chronic pain patients (27) and it has also been validated in Finnish (28). In the present study, a cut-off point of BDI-II $\leq$ 13 was used to dichotomize nondepressive and depressive patients (28).

2.2.2. The follow-up study questionnaire

The follow-up questionnaire consisted of the same items as the aforementioned baseline questionnaire with the addition of treatment intervention variables: pain treatment methods, the number of different treatment methods, the number of pain clinic visits and drug therapy.

Pain treatment methods were divided into two groups: invasive methods (such as surgery, anaesthesiological procedures, acupuncture) and noninvasive methods (such as drug therapy, physiotherapy, psychotherapy, pain groups). The number of different pain treatment methods was calculated according to the patient's report. The number of visits to the pain clinic was divided into two categories: one or two visits and three or more visits. The drug therapy used was divided as follows: anti-inflammatory analgesics (NSAID), opioids, antiepileptic drugs, sleeping pills, low-dose antidepressants and depression treatment dose antidepressants.

The treatment interventions covered the current generally recommended biomedical methods and were considered to be "the treatment as usual". The patients did not report any participation in multidisciplinary rehabilitation interventions.

2.3. Analyses

McNemar test was used to explore the changes between baseline and follow-up in the groups dichotomized according to the following levels of pain intensity (VAS≤4), pain disability (PDS≤13), alexithymia (TAS-20≤60) and depression (BDI-II≤13).

Paired samples t-test was used to measure the differences between baseline and follow-up in pain variables, TAS-20 total score, TAS factors and BDI-II score among the total sample, and among alexithymic and nonalexithymic patients.

Student's t-test and Chi-Square test were used to compare basic characteristics and study variables both at baseline and at follow-up between alexithymic and nonalexithymic patients,

The influence of baseline alexithymia and depressiveness on treatment interventions was analysed by comparing treatment variables between alexithymic and nonalexithymic patients, and similarly between depressive and nondepressive patients (Chi-Square test, Student's t-test).

The variables associated with the follow-up outcome estimated by pain intensity (VAS) and pain disability (PDS) were explored by comparing baseline pain variables, TAS-20, DIF, DDF and EOT cores, BDI-II score and the treatment intervention variables between poorer and better outcome groups (Chi-Square test, Student's t-test).

In order to calculate effect sizes for the categorical variables, the φ coefficients were calculated and the effect size was regarded as small if r was ±0.1–±0.29, moderate if ±0.30–±0.49 and large if ±0.50–±1.0. For continuous data, Cohen's d values were calculated; Cohen's d=0.2 is considered a small effect size, and d=0.5 and d=0.8 are considered to be respectively medium and large.

Post hoc, two additional analyses were performed:

As the results showed that the number of alexithymic patients had increased, the data was dichotomized to alexithymic and nonalexithymic groups according to the TAS-20 total score (≤60) at follow-up. The changes in study variables were explored separately in alexithymic (n=36) and nonalexithymic patients (n=118) by paired samples t-test.

A mediation analysis was performed to ascertain if the effect of TAS-20 on pain disability (PDS) was mediated through BDI-II, the normal scores were calculated with Prelis 2.80, and the mediation analysis was conducted with Lisrel 8.80 (Student edition). Mediation was indicated if there was a lower or nonsignificant path coefficient between two variables after the mediating variable was entered into the model. The level of significance in the Lisrel path analysis was a path's t-value >1.96.

3. RESULTS

The changes of study variables after one year showed that the percentage of the patients having an acceptable situation regarding pain intensity (=VAS ≤ 4) and pain disability (=PDS ≤ 13) increased. There was no significant change in depressiveness. The percentage of nonalexithymic patients decreased (Table 2).

Table 2. Proportions of dichotomized pain intensity, pain disability, TAS-20 and BDI-II scores at baseline and follow-up in the total sample.

	baseline	follow-up*	sig.*
Pain intensity ≤ 4	7.2%	26.1%	p <.001
Pain disability ≤ 13	28.9%	44.7%	p <.001
TAS-20 ≤ 60	85.0%	76.5%	p=.015
BDI-II ≤ 13	51.3%	56.6%	p=.24

Note: TAS-20 = Toronto Alexithymia Scale, BDI-II= Beck Depression Inventory, *McNemar test

Pain intensity and pain disability decreased in the whole sample and in alexithymic (at baseline) and nonalexithymic (at baseline) groups. The scores on TAS-20, DDF and DIF increased significantly during the follow-up period in the whole sample and in the nonalexithymic group (Table 3).

Alexithymic (at baseline) and nonalexithymic (at baseline) patients were similar regarding age, education and pain duration. The alexithymic group had clear preponderance of males. Alexithymic patients had significantly more pain disability and depressiveness than nonalexithymic patients at both baseline and follow-up (Table 4). Almost all alexithymic patients were depressive both at baseline (91.2%) and at follow-up (88.9%) and the proportion of severely depressive patients (=BDI-II > 28) was significantly higher (p<.001) in the alexithymic group than in the nonalexithymic group both at baseline and at follow-up.

Table 3. Comparisons of means (SD) of pain variables, alexithymia and depression between baseline and 1-year follow-up in the whole group (n=154), in the alexithymic (at baseline) group (n=24) and in the nonalexithymic (at baseline) group (n=130).

	baseline	follow-up	sig.*	effect size§
Pain intensity (VAS)				
all	5.9 (1.3)	5.1 (1.9)	<.001	.491
nonalexithymic	5.9 (1.3)	4.9 (1.9)	<.001	.614
alexithymic	6.3 (1.4)	5.7 (1.8)	.006	.372
Pain disability (PDS)				
all	16.3 (4.9)	14.3 (6.0)	<.001	.365
nonalexithymic	15.8 (5.0)	13.7 (6.0)	<.001	.362
alexithymic	19.1 (3.2)	17.4 (5.3)	.034	.388
TAS-20				
all	47.6 (12.2)	49.7 (13.1)	.005	.166
nonalexithymic	43.8 (8.7)	46.7 (11.3)	.001	.288
alexithymic	68.0 (6.3)	66.6 (9.7)	.34	.171
DIF				
all	15.7 (6.3)	16.7 (7.0)	.017	.150
nonalexithymic	13.9 (4.7)	15.2 (6.1)	.010	.239
alexithymic	25.5 (4.7)	25.3 (5.5)	>.9	.039
DDF				
all	11.1 (4.4)	12.1 (4.3)	<.001	.230
nonalexithymic	10.0 (3.5)	11.3 (3.8)	<.001	.356
alexithymic	17.6 (3.3)	16.9 (3.9)	.28	.194
EOT				

all	20.7 (4.6)	20.9 (4.4)	.63	.044
nonalexithymic	20.0 (4.4)	20.3 (4.4)	.35	.068
alexithymic	24.9 (3.5)	24.3 (2.7)	.22	.192
BDI-II				
all	15.7 (10.8)	15.4 (11.6)	.58	.027
nonalexithymic	13.6 (9.5)	13.1 (9.6)	.39	.052
alexithymic	27.3 (9.8)	28.7 (12.9)	.46	.122

Note: TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II = Beck Depression Inventory, * paired samples t-test, § Cohen's d

The influence of baseline alexithymia on treatment interventions was estimated by comparing alexithymic and nonalexithymic patients. The results showed that baseline alexithymia was connected with more use of opioids (p=.007) and epilepsy drugs (p=.033) but not with other treatment variables. Depressiveness at baseline was connected with more use of opioids (p=.002), sleeping pills (p=.003) and antidepressants (p=.018). There were no significant differences between baseline depressive and nondepressive patients in other treatment variables.

Table 4. Comparisons between means (SD) of study variables of patients alexithymic (at baseline) patients (n=24) nonalexithymic (at baseline) patients (n=130).

	alexithymic	nonalexithymic	sig.	effect size
age (years)	46.8 (8.5)	48.1 (9.2)	.51*	.147%
gender M/F	17/7	51/79	.004$	.231§
education (years)	11.1 (2.0)	11.2 (1.7)	.84*	.054%
pain duration (years)	11.3 (10.6)	9.0 (8.6)	.25*	.238%
VAS baseline	6.3 (1.4)	5.9 (1.3)	.12*	.296%
VAS follow-up	5.7 (1.8)	4.9 (1.9)	.086*	.432%
PDS baseline	19.1 (3.2)	15.8 (5.0)	.002*	.786%
PDS follow-up	17.4 (5.3)	13.7 (5.9)	.006*	.660%
BDI-II baseline	27.3 (9.8)	13.6 (9.5)	<.001*	1.420%
BDI-II follow-up	28.7 (12.9)	13.1 (9.6)	<.001*	1.372c%

Note: VAS = Visual Analogue Scales, PDS = Pain Disability Scale, BDI-II = Beck Depression Inventory, *Student's *t*-test, $Chi-Square, %Cohen's d, §φ coefficient

Table 5. Comparisons of baseline variables and treatment variables between pain intensity ≤ 4 (n=40) and pain intensity > 4 groups (n=113) at follow-up. Values presented in means (SD).

	pain intensity≤ 4	pain intensity > 4	sig.	effect size
gender (M/F)	18/22	50/63	.93*	.007%
age	47.4 (9.7)	48.1 (8.8)	.67$	.077§
education	11.1 (1.4)	11.2 (1.9)	.75 $	.056§
pain duration	7.4 (7.5)	10.1 (9.4)	.092 $	.302§
pain disability (PDS)	15.4 (4.9)	16.7 (4.9)	.15 $	.265§
pain intensity (VAS)	5.0 (1.1)	6.3 (1.2)	<.001 $	1.106§
TAS-20 total score	46.0 (9.7)	48.4 (12.8)	.23 $	.199§
DIF	14.0 (5.4)	16.4 (6.5)	.027 $	.385§
DDF	10.4 (3.4)	11.5 (4.7)	.16 $	.250§
EOT	21.6 (3.6)	20.5 (4.9)	.17 $	.239§
BDI-II	14.6 (9.9)	16.2 (11.1)	.40 $	.148§
invasive/noninvasive treatment	26/14	74/36	.79 $	.021%
number of treatment methods	2.5 (1.3)	2.4 (1.3)	.78 $	.077§

1-2 visits/ >2 visits	19/20	56 /54	.81 *	.019%
anti-inflammatory analgesic no/yes	19/21–	56/57–	.82*	.018%
opioid no/yes	24/16–	46/67–	.035*	.170%
antiepileptic no/yes	29/11–	70/43–	.23*	.097%
sleeping pill no/yes	33/7–	79/34–	.12*	.125%
low dose antidepressant no/yes	32/8–	85/28–	.54*	.050%
antidepressant no/yes	37/3–	74/39–	.001*	.266%

Note: TAS-20 = Toronto Alexithymia Scale, DIF = difficulties with identifying feelings, DDF = difficulties with describing feelings, EOT = externally oriented thinking style, BDI-II= Beck Depression Inventory, *Chi-Square test, §Students's *t*-test, %φ coefficient, § Cohen's d, _the number of patients not on (=no) or on (=yes) medication

Patients reporting pain intensity (VAS) > 4 at follow-up had higher pain intensity and higher scores on TAS factor DIF at baseline. This group took more opioids and treatment dose antidepressants (Table 5). Among patients reporting pain disability (PDS) > 13 at follow-up there was a preponderance of males, longer pain duration, more severe pain disability and greater pain intensity, likewise higher TAS-20 total, DIF and DDF scores and higher BDI-II scores at baseline. This group took more sleeping pills and treatment dose antidepressants (Table 6).

Table 6. Comparisons of baseline and treatment variables between pain disability ≤ 13 (n=68) and pain disability > 13 (n=84) groups at follow-up. Values presented in means (SD).

	pain disability≤13	pain disability>13	sig.	effect size
gender (M/F)	24/44	44/40	.035*	.171%
age	47.0 (9.4)	48.4 (8.8)	.35§	.154§
education	11.1 (1.4)	11.2 (2.0)	.70§	.057§
pain duration	7.4 (7.6)	10.8 (9.8)	.018§	.383§
pain disability (PDS)	13.4 (4.7)	18.6 (3.9)	<.001§	1.216§
pain intensity (VAS)	5.4 (1.1)	6.4 (1.3)	<.001§	.823§
TAS-20 total score	44.0 (10.4)	50.4 (12.7)	.001§	.546§
DIF	13.8 (5.3)	17.2 (6.6)	.001§	.562§
DDF	9.6 (3.4)	12.3 (4.7)	<.001§	.648§
EOT	20.6 (5.0)	20.8 (4.4)	.77§	.043§
BDI-II	11.1 (8.0)	19.6 (11.3)	<.001§	.853§
invasive/noninvasive treatment	45/22	55/27	>.90*	.001%
number of treatment methods	2.5 (1.3)	2.4 (1.3)	.52§	.077§
1-2 visits/ >2 visits	37/31	37/43	.32*	.081%
anti-inflammatory analgesic no/yes	32/36–	42/42–	.71*	.029%
opioid no/yes	37/31–	34/50–	.087*	.139%
antiepileptic no/yes	49/19–	50/34–	.10*	.131%
sleeping pill no/yes	61/7–	51/33–	<.001*	.327%
low dose antidepressant no/yes	51/17–	64/20–	.86*	.014%
antidepressant no/yes	58/10–	52/32–	.001*	.260%

Note: TAS-20 = Toronto Alexithymia Scale, DIF = difficulties with identifying feelings, DDF = difficulties with describing feelings, EOT = externally oriented thinking style, BDI-II= Beck Depression Inventory, *Chi-square test, §Student's *t*-test, %φ coefficient, §Cohen's d, _the number of patients not on (=no) or on (=yes) medication

Post hoc:

The paired samples t-test showed a significant increase in BDI-II score in the alexithymic group Pain disability decreased statistically significantly only in the nonalexithymic group. Moreover, the means of theTAS-20 total score in the

alexithymic group increased and did not change in the nonalexithymic group (Table 7).

Table 7. Comparisons of means (SD) of pain variables, alexithymia and depression between baseline and 1-year follow-up in the alexithymic (at follow-up) group (n=36) and in the nonalexithymic (at follow-up) group (n=116).

	baseline	follow-up	sig.*	effect size§
Pain intensity (VAS)				
alexithymic	6.5 (1.3)	5.8 (1.6)	.002	.483
nonalexithymic	5.8 (1.3)	4.8 (1.9)	<.001	.614
Pain disability (PDS)				
alexithymic	18.9 (4.1)	17.8 (4.7)	.097	.249
nonalexithymic	15.5 (4.9)	13.2 (5.9)	<.001	.424
TAS-20				
alexithymic	59.6 (11.5)	68.7 (5.5)	<.001	1.009
nonalexithymic	43.8 (9.6)	43.9 (8.4)	.888	.011
DIF				
alexithymic	21.2 (6.3)	26.2 (4.0)	<.001	.947
nonalexithymic	13.9 (5.2)	13.8 (4.7)	.717	.020
DDF				
alexithymic	15.4 (4.5)	17.8 (3.0)	.001	.627
nonalexithymic	9.8 (3.4)	10.4 (3.0)	.019	.187
EOT				
alexithymic	22.0 (4.2)	24.7 (2.9)	.013	.748
nonalexithymic	20.1 (4.5)	19.7 (4.1)	.339	.092
BDI-II				
alexithymic	24.5 (12.3)	27.5 (12.3)	.026	.243
nonalexithymic	13.0 (8.7)	11.7 (8.4)	.046	.152

Note: TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II = Beck Depression Inventory, * paired samples t-test, § Cohen's d

As higher scores on pain disability at follow-up were connected with higher scores on alexithymia and depression at baseline and as alexithymia is known to be connected with depression, a post hoc mediation analysis was performed to explore their relation to pain disability. In the total sample, testing for the mediator effect was done as follows: the TAS-20 score (baseline) was used as a predictor of

pain disability (follow-up), and the path coefficient was significant (β=0.28, t=3.54). Then, BDI-II (baseline) was entered as a mediator into the model. The aforementioned path became nonsignificant (β=0.07, t=0.85). The path from TAS-20 (baseline) to BDI-II (baseline) was significant (β=0.50, t=7.00) and the path from BDI-II (baseline) to pain disability (follow-up) was also significant (β=0.42, t=4.96). Therefore, BDI-II (baseline) can be seen as a full mediator between TAS-20 (baseline) and pain disability (follow-up).

4. DISCUSSION

One year after their first visit to the pain clinic, a proportion of chronic pain patients reported a decrease in pain intensity and pain disability but the majority of the patients had pain intensity and pain disability severe enough to interfere with normal life to a considerable extent. Almost all alexithymic patients were depressive and they reported more pain disability both at baseline and at follow-up. Baseline alexithymia and depression were connected with heavier opioid consumption. None of the treatment interventions of the present study showed any statistically significant tendency towards better outcome. Greater pain intensity at follow-up was related to greater pain intensity and alexithymia factor DIF at baseline. Greater pain disability at follow-up was related to male gender, greater pain intensity and pain disability at baseline, but was also strongly related to alexithymia and depression. Alexithymia scores increased in parallel with depressiveness. Depression mediated the effect of baseline alexithymia on follow-up pain disability.

There are a few clinical follow-up studies of alexithymia and pain situation: poorer outcome after physiotherapy in low back pain patients was associated with alexithymic features (29) and alexithymia predicted post-surgical pain after one year in a sample of breast cancer patients (30). An intervention follow-up study showed that pain patients receiving psychodynamic body therapy gained increased affect consciousness which was related with a significant alleviation of pain (31). Clinical follow-up study designs including chronic pain, depression and alexithymia were not found by the authors of the present study.

The present study indicated that alexithymia and depression have an exacerbating influence on pain situation and a negative impact on outcome. The results may be explained as follows: Alexithymic individuals are prone to somatization (32), somatosensory amplification (33) and psychosomatic manifestations of their emotional states (34) and may interpret bodily felt emotional symptoms as threatening signs which in case of experienced pain and catastrophizing exacerbate the pain situation. Depression frequently co-occurs with various somatic symptoms (35), alexithymia has been shown to contribute to the somatic symptoms in major depressive patients (36) and in "alexithymic depression" somatic symptoms are more frequent than in "nonalexithymic depression" (20). Furthermore, alexithymia and depression have connections with several factors in the cognitive and emotional domains of pain experience (such as somatization, depressive mood, pain catastrophizing, self-efficacy, self-esteem and pain related fear), which have shown to present a crucial role in the development and persistence of and recovery from chronic pain (37- 43). Compliance with and adherence to treatment are also dependent on the patient's personal psychological characteristics (44, 45) and insecure attachment styles associated with alexithymia (14) and depression (46) may impair treatment compliance and adherence and hence the outcome

At baseline alexithymic patients reported consuming more opioids and antiepileptic drugs than did nonalexithymic patients. Baseline depression was associated with higher consumption of opioids, sleeping pills and antidepressants. A poorer outcome in pain intensity was also connected with the use of opioids and antidepressants. The drug therapy selected may reflect the severity of the pain situation and depressiveness, but there is also evidence that opioid therapy in a severe pain situation may be the only sign of mental problems associated with chronic pain (47) or used as "comfort care" for overall suffering (48). Depressiveness with somatic symptoms (35) and the emotional dysregulation of alexithymic patients manifesting in bodily processes (49) may lead to misdiagnosis and ineffective and unnecessary use of opioids and other drugs. The increase of alexithymia in the proportion of patients having more severe depression at follow-up may be a consequence of untreated and unnoticed depression. The corresponding fluctuation in the severity of alexithymia and depression has been observed in earlier studies (50).

The follow-up outcome suggested that nondepressive and nonalexithymic patients may benefit from 'treatment as usual'. They may also have more adaptive coping capacities and possibly a different state of chronic pain disease. In a recent

longitudinal study, recovery from low back pain was associated with no psychological or physiological dysfunction at baseline (51). It was also noteworthy that alexithymic patients, in spite of more severe pain and depressiveness at baseline, did not receive more specific attention in treatment interventions except for the medication choices, which were intended to treat pain but unfortunately not depression. The unemotional alexithymic style of emphasizing physical symptoms has probably influenced the treatment decisions and failure to detect depression.

The limitations of the study include the evaluation measures. The use of self-report questionnaires may produce a response bias. Alexithymia was measured only with TAS-20 although it has been recommended to improve the specification using other instruments such as semi-structured interview methods (52, 53). It has been suggested that in measuring depression in chronic pain patients with BDI-II a higher cut-off point should be used (54) and a higher cut-off point has also been proposed for measuring depression in alexithymic individuals (55). However, we used cut-off points established and widely accepted in the literature in order to make the results comparable with those of other studies. A proportion of the patients improved, but our results did not reveal any particular factor related to this better outcome as the study design did not include measures of the "positive" variables such as self-efficacy. Among the baseline study population, 43% did not take part in the follow-up study, which is a limitation. Fortunately there were no significant differences among the baseline study variables between respondents and nonrespondents.

The strengths of the study: Follow-up studies of alexithymia and chronic pain are rare, so the present study added to the knowledge concerning the connection of alexithymia (with depression) with chronic pain using a longitudinal study design. Both psychological and biomedical variables were used to evaluate the one-year outcome in the pain situation as is recommended in pain research (56). The questionnaires were internationally and nationally confirmed and validated. The number of patients in the clinical sample was sufficient to base our conclusions on statistical analyses.

Conclusions

Alexithymia was tightly associated with depression and their co-occurrence predicted difficulties in achieving improvement. It has been proposed that emotional dysregulation predisposes to chronic pain and alexithymic and depressive individuals have difficulties coping with their emotional states in adaptive styles. The present knowledge of chronic pain suggests that pain network

in the central nervous system is linked to emotional areas which may be sensitized by early negative experiences. Childhood adversities were not explored in this study, but the literature available (see Introduction) has shown that early trauma predisposes to chronic pain, alexithymia and depression, and their combined effect may be expressed in experienced pain. Alexithymia and depression are connected with several psychosocial factors maintaining and exacerbating the pain condition and there is a possibility of overtreating pain (as a biomedical disease) and of undertreat problems in processing emotions. The results draw attention to the possible misuse of opioids for psychological problems. We did not count the costs of the treatment given ('treatment as usual'), but a rough estimate of reported interventions compared to the benefits derived gives a picture of "sunk costs" without satisfied patients.

We recommend that chronic pain patients be screened for alexithymia, depression and traumatic life history in order to identify those individuals who may need more detailed evaluation of their psychological condition. The connection between alexithymia and chronic pain is well known in the academic world, but not sufficiently acknowledged in pain clinics. Patients presenting with complicating psychological features need more tailored and multidisciplinary treatment interventions. Structured cognitive-behavioural therapies, emotion focused therapies, trauma therapy and psychophysical methods may be helpful for depressive alexithymic chronic pain patients.

Disclosure of Interest

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The role of alexithymia: An 8-year follow-up study of chronic pain patients

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Abstract

Objective: The aim of this 8-year follow-up study was to ascertain changes in alexithymia, depressiveness and pain situation in a sample of chronic pain patients and to explore the impact of alexithymia and depression on the outcome.
Methods: Participants (n = 83) were chronic non-malignant pain patients who completed self-report study questionnaires before their first visit to the pain clinic and again 8 years later. Study variables consisted of pain intensity measured by the Visual Analogous Scale, the Pain Disability Scale, the Toronto Alexithymia Scale and the Beck Depression Inventory. The moderate improvement in the pain situation was estimated as a decrease of 30% or more in pain intensity or pain disability.
Results: In the whole sample there was a significant decrease in pain intensity, pain disability and depressiveness, but only some of the patients achieved moderate improvement in their pain situation. Alexithymia remained stable during the 8-year period. The alexithymic patients had poorer pain situation and more depressiveness both at baseline and at follow-up. Unfavorable outcome in the pain situation was connected with male gender and alexithymia at baseline but not with depressiveness. Alexithymia and depressiveness were closely related to each other and the connection strengthened during the follow-up period.
Conclusion: Alexithymic depressive chronic pain patients represent a special, more disabled subgroup among chronic pain patients. The authors recommend screening for and identifying alexithymia and depression in chronic pain patients. Structural treatment protocols such as cognitive–behavioral therapy may benefit these patients. More research is needed to develop treatment interventions for alexithymic patients.

1. Introduction

The concept of alexithymia, literally "no words for feelings", was coined by Sifneos [1] to describe psychosomatic patients having a restricted capacity to identify and describe their feelings, limited imagination and externally oriented thinking style. Its prevalence in Finnish general population is approximately 10%, and it is more common in males [2]. Alexithymia is a dimensional, not a categorical, construct, in most studies showing relative stability [3,4], and thus regarded as personal trait. The degree of severity may be influenced by and varies due to other psychological phenomena as depression or traumatic experiences [5,6].

Early stressful experiences and deficiency in the learning process of emotions have been proposed to be the origin of alexithymia [7]. Genetic and environmental factors are involved in the development of alexithymia, and functional changes have been found in the central nervous systems of alexithymic subjects [8]. Alexithymia has been shown to be associated with number of health-related disorders [9–14] including depression [15], anxiety [16] and chronic pain [17]. Several different chronic pain syndromes such as fibromyalgia [18], migraine [19], myofascial pain [20], chronic regional pain syndrome [21], orofacial pain [22] and chronic low back pain [23] are characterized by an elevated number of alexithymic individuals. The mechanism through which alexithymia contributes to the onset, course or exacerbation of health problems has been researched: the predisposing factors associated with alexithymia include altered immunological status, elevated resting sympathetic activity, unhealthy behavior, reluctance to participate in psychological interventions, problems comprehending the

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psychological side of disease and difficulties in committing to a therapeutic alliance [10].

The modern perception with regard to chronic pain as a complex multifaceted biopsychosocial syndrome typically characterized by persistency, sufferer's poor quality of life, a poor response to biomedical treatment interventions and a bundle of concomitant problems such as depression, anxiety, drug addiction, personality disorders, and huge costs to the health care system. Cognitive and emotional factors play an important role in the variance of chronic pain [24]. In addition to chronic pain disorders there are special features typical of alexithymia which contribute to the pain experience such as a tendency to susceptibility to psychosomatic symptoms [25], somatization [26], and somatic amplification [27]. The tendency of alexithymic individuals to somatic manifestations of emotions may lead to false interpretations of bodily felt symptoms and exacerbate their pain experience [28]. In an experimental study alexithymic students reported greater pain intensity to thermal stimulation than nonalexithymic students [29].

Early negative experiences have been found to underlie alexithymia [30], likewise chronic pain [31,32] and depression [33]. The neurobiological and neuropsychological consequences of maltreatment, abuse or neglect in childhood produce reactions which modify stress and emotion regulating systems in the developing central nervous system and increase vulnerability to later health problems [34–36]. The concepts of alexithymia, depression and chronic pain represent separate and distinct entities [37,38], but in the clinical situation they manifest as interwoven and overlapping interactive features. Alexithymic chronic pain patients have been found to be more depressed and experience greater pain intensity and pain disability than nonalexithymic patients [39]. A follow-up study of depression and chronic pain in a general population sample concluded that depression predicts chronic pain and vice versa [40] and it has been suggested that alexithymia increases the risk for depressiveness [4].

The prognostic value of alexithymia in health disorders varies. In earlier prospective studies alexithymia did not make a difference in the course of medical unexplained syndrome [41] or obsessive–compulsive disorder [42] while in a study of somatizing patients alexithymia predicted persistent symptoms [43]. In a review of prospective studies examining the effects of alexithymia on health outcomes most studies showed the adverse effects of alexithymia but some showed no or even positive influence [12]. In a study of general population alexithymia was associated with higher risk of having chronic pain [17].

The present study was intended to explore the effect of alexithymia and depressiveness on the outcome, and to ascertain the course of the pain situation, alexithymia and depressiveness in a sample of chronic pain patients. We hypothesized that alexithymia and depression at baseline are connected with poorer outcome of pain disease at follow-up.

2. Methods

2.1. Participants

The baseline study participants were 271 first visit pain clinic chronic pain patients referred to six pain clinics during a period of 1 year (from January 2004 to January 2005) in Central and Northern Finland. Sources of referral of participants were primary health care and various medical specialists. All these patients were suffering from nonmalignant, chronic pain lasting for 3 months or longer and their age was 18–65 years. Patients having a psychotic disorder or cognitive impairment were excluded from the study. The patients were informed in advance about the study protocol by letter and they completed the study questionnaire at home before the consultation. The follow-up data were collected 8 years after the first visit to the pain clinic. The study questionnaire was sent to all 271 patients to their home addresses and the patients were asked to return their completed questionnaires to the research team in the envelope provided. The pain clinics were not involved in the collection of the follow-up questionnaires, which probably explains the lower response rate. The postal services returned 23 study questionnaires which were wrongly addressed, and the relatives of four patients reported their deaths. Out of 244 eligible patients, 83 (34.0%, male/female 34/49) returned the 8-year follow-up questionnaire and so comprised the sample in the present study. The baseline data of the study variables were compared between respondents and nonrespondents and no significant differences were found in all other study variables (basic characteristics, pain variables, alexithymia and depression measures) except in age (the respondents being older, mean 49.5 years versus 46.0 years, $p = .003$, than the nonrespondents).

The treatment interventions were explored according to the patients' reports and the treatment choices were regarded to follow the normal treatment protocols based on the biomedical concept and recommendations. None of the choices were connected with better outcome. The treatment was approved to be "treatment as usual".

The study protocol was approved by the ethics committee of the Northern Ostrobothnia Hospital District. Written informed consent was obtained from all participants at both baseline and follow-up.

2.2. Measures

2.2.1. Study questionnaire

The study questionnaire was developed for a chronic pain study to collect information on basic characteristics (age, gender and education), pain variables, alexithymia and depression. Data concerning medical history, current health status and treatment interventions were collected.

2.2.1.1. Pain variables. Pain variables consisted of current pain intensity, pain disability and duration of pain condition.

Pain intensity was measured with two 10-cm Visual Analogue Scales (VAS) where 0 represents no pain and 10 represents the worst pain one can imagine. On the first VAS scale the participants were asked to rate their current maximal experienced pain and on the second VAS scale their current minimal pain. The pain intensity was calculated to be the mean of these two measures. In the present study, the interpretation of the VAS scale followed the interpretation of the numerical scale: 0 = no pain, 1–4 = mild pain, 5–6 = moderate pain and 7–10 = severe pain [44]. A 10–20% decrease in pain is regarded as minimal, a decrease of at least 30–33% as moderate [44,45]. In the present study, a decrease of 30% or more in pain intensity was taken to be a sufficient improvement.

The Pain Disability Scale (PDS) was developed for the study of chronic pain [46]. The psychometric properties of the PDS were tested in a pilot study and found to be satisfactory. Cronbach's alpha for the PDS was 0.83. This is a 9-item self-report scale consisting of seven direct statements: "My pain disturbs my sleep", "...my hobbies","...my sex life","...my work","...my ability to move","...my economy","...my social contacts" and two inverted statements: "I can enjoy life despite my pain" and "I can control my pain". All the items were self-reported on a Likert-type 0–3-scale: 0 = not at all, 1 = to some extent, 2 = significantly and 3 = very much. The total score (range 0–27) reflects the severity of pain disability. A score of 0–4 indicates 'no disability', a score of 5–13 'mild disability', a score of 14–22 'significant disability' and a score of 23–27 'severe disability'. In the present study, a sufficient improvement was estimated to be achieved by a decrease of 30% or more in pain disability score.

2.2.1.2. Alexithymia. Alexithymia was measured with the 20-item Toronto Alexithymia Scale (TAS-20). Its internal consistency, test–retest reliability, as well as convergent, discriminant and concurrent validity have been demonstrated to be good [47–50]. The Finnish Version of TAS-20 has proven to be reliable [51]. TAS-20 consists of 20 items (five inverted) scored from 1 to 5 and then summed. The recommended cut-off point to indicate alexithymia is >60 [52]. The items of TAS-20 are divided into three subscales (factors) each assessing the different features of the alexithymia concept: difficulties identifying feelings (DIF = factor 1, 7 items), difficulties describing feelings (DDF = factor 2, 5 items) and externally oriented thinking style (EOT = factor 3, 8 items).

2.2.1.3. Depression. Depressiveness was assessed with the revised 21-item version of the Beck Depression Inventory (BDI-II) [53]. All the items were self-rated from 0 to 3 and summed to obtain a total score ranging from 0 to 63, with higher values indicating more severe depressive symptoms. The questionnaire has been proven to measure depressiveness in chronic pain patients [54] and it has also been validated in Finnish [55]. A score of 0–13 indicates minimal depressiveness (the individual faces normal 'ups and downs'), a score of 14–19 indicates mild, a score of 20–28 moderate and a score of 29–63 severe depressive symptoms [53].

2.3. Statistics

Student's *t*-test and chi-square test were used to compare data at baseline between respondents and nonrespondents, and to compare baseline and follow-up study variables between alexithymic and nonalexithymic patients.

In the whole sample, paired samples *t*-test was conducted to compare scores of pain intensity, pain disability, TAS-20, DIF, DDF, EOT and BDI-II between values at baseline and at follow-up.

Effect size was calculated by phi coefficient for categorical data and regarded as small if ±0.1 to ±0.29, moderate if ±0.30 to ±0.49 and large if ±0.50 to ±1.0. For continuous data effect size was estimated by Cohen's *d* and this is considered small if $d = 0.2$, medium if $d = 0.5$ and large if $d = 0.8$.

The patients were dichotomized according to follow-up scores of pain intensity and pain disability to "improvement" (a score decrease of 30% or more) and "no improvement" groups. The comparisons of baseline variables between "improvement" and "no improvement" groups were performed by chi-square test and Student's *t*-test. The baseline variables predicting improvement (0)/no improvement (1) of pain intensity and pain disability at follow-up were explored using a series of binary logistic regression analyses. Three different models consisting of baseline variables were formed: 1. basic characteristics (gender, age, education), 2. pain variables (pain duration, pain intensity, pain disability) and 3. psychological variables (alexithymia and depression). The last model was completed by best predictor(s) of previous models.

The association between TAS-20 and BDI-II was estimated by Pearson's correlation (*r*). The association was regarded as small if *r* was ±0.1 to ±0.29, moderate if ±0.30 to ±0.49 and large if ±0.50 to ±1.0 [56]. The associations were calculated both at baseline and at follow-up and illustrated with a scatter plot containing a fitted regression line with a Lowess smoothing line [57].

As male gender showed a predictive effect on poorer outcome of pain intensity and pain disability, a post hoc analysis (Student's *t*-test) was conducted to compare the study variables between males and females.

3. Results

In the whole sample, pain intensity, pain disability and depressiveness decreased during the 8-year follow-up period, but there were no significant changes in the alexithymia scores (Table 1).

Alexithymic patients at baseline reported significantly more pain disability and depressiveness, and at follow-up

significantly more pain intensity, pain disability and depressiveness than nonalexithymic patients (Table 2).

In the whole sample, 23 patients (28.0%) had a 30% or greater decrease in the pain intensity score. Prevalence of male gender, baseline TAS-20 total score and DDF score were significantly higher in the "no improvement group" (Table 3). In the binary logistic regression analysis, after testing all models, the best model supported the relation of baseline TAS-20 total score with "no improvement" outcome in pain intensity (Table 4). The relation of male gender with "no improvement" outcome in pain intensity disappeared when baseline TAS-20 total score was added into the model (Table 4).

In the whole sample, 36 patients (43.4%) had a 30% or greater decrease in the pain disability score. The "no improvement" group contained significantly more males and had higher TAS-20 baseline scores (Table 5). The binary logistic regression analysis showed a significant relation of male gender to "no improvement" outcome (Table 6).

Pearson's correlation showed a large correlation between TAS-20 and BDI-II both at baseline ($r = 0.612$, $p < .001$, Fig. 1a) and at follow-up ($r = 0.743$, $p < .001$, Fig. 1b).

In the post hoc analysis between males and females there were significant differences at baseline in TAS-20 total score [50.5 (SD 11.8), 44.3 (SD 13.6) respectively, $p = .035$] and in EOT score [22.7 (SD 4.2), 18.9 (SD 5.1) respectively, $p = .001$]. At follow-up there was a significant difference between males and females in pain disability scores [13.6 (SD5.7), 10.6 (SD 6.3) respectively, $p = .033$] and almost significant differences in pain intensity [5.2 (SD 1.8), 4.3 (SD 2.1) respectively, $p = .051$] and in TAS-20 total score [49.6 (SD 11.1), 44.0 (SD 13.2) respectively, $p = .057$] and in EOT score [22.0 (SD 3.5), 19.7 (SD 6.0) respectively, $p = .057$].

4. Discussion

The main results are as follows: 8 years after their first consultation in the pain clinic the sample of chronic pain patients showed a significant decrease in pain intensity, pain disability and depressiveness. There was no significant change in alexithymia scores. The patients who had been alexithymic at baseline reported greater pain disability and depressiveness at baseline and greater pain intensity, pain disability and depressiveness at follow-up than did those patients who had been nonalexithymic at baseline. Unfavorable outcome in pain situations was connected to male gender and alexithymia at baseline. The association between alexithymia and depression was large sized both at baseline and at follow-up.

Table 1
Comparisons of means (SD) of pain variables, alexithymia and depression between baseline and follow-up data of chronic pain patients ($n = 83$).

	Baseline	Follow-up	Sig.[a]	Effect size[b]
Pain intensity (VAS)	5.7 (1.2)	4.6 (2.0)	<.001	.67
Pain disability (PDS)	16.3 (4.7)	11.2 (6.2)	<.001	.93
TAS-20	46.6 (13.1)	46.3 (12.6)	.84	.02
DIF	15.2 (6.7)	14.6 (6.6)	.20	.09
DDF	10.9 (4.6)	11.2 (4.1)	.40	.07
EOT	20.5 (5.2)	20.7 (5.1)	.70	.04
BDI-II	14.7 (11.0)	10.8 (9.1)	<.001	.36

TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II = Beck Depression Inventory.
[a] Paired samples *t*-test.
[b] Cohen's *d*.

Table 2
Comparisons of means (SD) of the study variables between alexithymic ($n = 17$) and nonalexithymic patients ($n = 66$).

	Baseline alexithymic	Baseline nonalexithymic	Sig.	Effect size
Gender (M/F)	9/8	25/41	.26[a]	.12[b]
Age	48.7 (5.4)	49.7 (7.6)	.60[c]	.15[d]
Education, years	11.1 (1.6)	11.4 (1.9)	.52[c]	.17[d]
Pain duration, years at baseline	9.0 (8.9)	10.3 (9.0)	.61[c]	.15[d]
Pain intensity at baseline	6.2 (1.5)	5.6 (1.1)	.089[c]	.46[d]
Pain disability at baseline	20.1 (3.3)	15.4 (4.5)	<.001[c]	1.19[d]
BDI-II at baseline	26.4 (11.3)	11.9 (8.5)	<.001[c]	1.45[d]
Pain intensity at follow-up	5.6 (1.2)	4.4 (2.1)	.034[c]	.70[d]
Pain disability at follow-up	15.2 (6.0)	11.1 (6.0)	.015[c]	.68[d]
BDI-II at follow-up	20.8 (11.2)	8.5 (6.8)	<.001[c]	1.33[d]

BDI-II = Beck Depression Inventory.
[a] Chi-square.
[b] Phi coefficient.
[c] Student's *t*-test.
[d] Cohen's *d*.

Table 3
Comparisons of baseline variables between "improvement" ($n = 23$) and "no improvement" ($n = 59$) patient groups in terms of pain intensity.

	Improvement	No improvement	Sig.	Effect size
Gender M/F	5/18	28/31	.033[a]	.24[b]
Age, years	51.9 (8.4)	48.7 (6.5)	.071[c]	.45[d]
Education, years	11.0 (1.6)	11.5 (1.9)	.30[c]	.29[d]
Pain duration, years	11.3 (9.7)	9.5 (8.8)	.42[c]	.19[d]
Pain intensity	5.5 (1.2)	5.8 (1.2)	.20[c]	.25[d]
Pain disability	14.9 (4.9)	16.9 (4.4)	.062[c]	.48[d]
TAS-20	41.1 (8.1)	48.8 (14.0)	.016[c]	.67[d]
DIF	13.0 (4.1)	16.2 (7.3)	.052[c]	.54[d]
DDF	9.2 (2.5)	11.6 (5.0)	.034[c]	.61[d]
EOT	18.9 (5.0)	21.0 (5.1)	.097[c]	.42[d]
BDI-II	13.3 (10.2)	15.1 (10.8)	.50[c]	.17[d]

Values presented in means (SD). TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II = Beck Depression Inventory.
[a] Chi-square.
[b] φ coefficient.
[c] *T*-test.
[d] Cohen's *d*.

Table 4
Binary logistic regression analysis predicting "no improvement" in pain intensity at follow-up.

Model 1: basic characteristics

Independent variable	*B*	SE	Wald	*df*	Sig.	Exp(*B*)	95% CI for EXP(*B*)	
							Lower	Upper
Gender (M/F)	−1.299	.591	4.838	1	.028	.273	.086	.868
Age	−.074	.041	3.346	1	.067	.929	.858	1.005
Education	.195	.167	1.377	1	.241	1.216	.877	1.685

Chi-square 10.114, Sig. = .018 and Nagelkerke R^2 = .167

Model 2: pain variables

Independent variable	*B*	SE	Wald	*df*	Sig.	Exp(*B*)	95% CI for EXP(*B*)	
							Lower	Upper
Pain duration	−.027	.027	1.005	1	.316	.974	.924	1.026
Pain intensity at baseline	−.014	.224	.004	1	.952	.986	.636	1.530
Pain disability at baseline	.082	.059	1.980	1	.159	1.086	.968	1.218

Chi-square 4.553, Sig. = .208, Nagelkerke R^2 = .078

Model 3: psychological variables and gender

Independent variable	*B*	SE	Wald	*df*	Sig.	Exp(*B*)	95% CI for EXP(*B*)	
							Lower	Upper
Gender (M/F)	−.951	.594	2.372	1	.124	.401	.125	1.283
TAS-20 total score at baseline	.055	.027	4.033	1	.045	1.057	1.001	1.115
BDI-II score at baseline	−.022	.031	.499	1	.480	.978	.920	1.040

Chi-square 9.666, Sig. = .022, Nagelkerke R^2 = .160.
TAS-20 = Toronto Alexithymia Scale, BDI-II = Beck Depression Inventory.

In spite of a general decrease in pain intensity and pain disability, the majority of the patients did not achieve moderate improvement in pain intensity or in pain disability. General population studies have confirmed the persistence and poor prognosis of chronic pain [58,59]. Pain experience in chronic pain is a multifaceted phenomenon influenced by cognitive and emotional factors, coping capacities and methods and individual life time experiences [60,61]. Research has shown that there are several different components having detrimental effects on current state and prognosis of experienced pain situation, such as low self-esteem, catastrophizing, fear avoidance beliefs, pain related negative beliefs, somatization, kinesiophobia, pain related fear, anxiety and distress, negative affectivity, depressed mood, reduced self-efficacy, limited coping capacity, unfavorable attachment styles, traumatic life history and early negative experiences [60–70]. Most of these components have also been found to be connected with alexithymia [6,10,15,30,71–73]. In the present study, the subsample of alexithymic chronic pain patients showed poorer pain situation than nonalexithymic patients, both at baseline and at follow-up. This result supports the concept of the negative impact of alexithymia in developing and coping with chronic pain.

In the present study, as the baseline pain situation, depressiveness (contrary to the study hypothesis) or level of education did not predict the outcome, in contrast to a number of earlier studies, where baseline higher pain intensity [74,75], higher degree of pain disability [75], depressiveness [65] and low level of education [75] have predicted poorer outcome of in pain situations. However, the studies differed in design and are difficult to compare as alexithymia was not included among the study variables.

Table 5
Comparisons of baseline variables between "improvement" (n = 36) and "no improvement" (n = 47) patient groups in terms of pain disability.

	Improvement	No improvement	Sig.	Effect size
Gender M/F	9/27	25/22	.010[a]	.28[b]
Education, years	11.0 (1.7)	11.6 (1.8)	.13[c]	.34[d]
Age, years	49.75 (7.4)	49.34 (7.1)	.80[c]	.06[d]
Pain duration, years	9.9 (9.0)	10.1(9.0)	.900[c]	.02[d]
Pain intensity	5.5 (1.2)	6.0 (1.2)	.074[c]	.42[d]
Pain disability	16.1 (4.4)	16.5 (4.8)	.68[c]	.09[d]
TAS-20	43.4 (12.0)	49.5 (13.5)	.035[c]	.48[d]
DIF	14.0 (6.0)	16.5 (7.2)	.097[c]	.38[d]
DDF	10.1 (4.4)	11.7 (4.7)	.13[c]	.35[d]
EOT	19.2 (5.5)	21.3 (4.6)	.063[c]	.41[d]
BDI-II	14.0 (10.5)	15.6 (11.1)	.53[c]	.15[d]

Values presented in means (SD). TAS-20 = Toronto Alexithymia Scale, DIF = difficulties identifying feelings, DDF = difficulties describing feelings, EOT = externally oriented thinking style, BDI-II = Beck Depression Inventory.
[a] Chi-square.
[b] φ coefficient.
[c] T-test.
[d] Cohen's d.

Table 6
Binary logistic regression analysis predicting "no improvement" in pain disability at follow-up.

Model 1: basic characteristics

Independent variable	*B*	SE	Wald	*df*	Sig.	Exp(*B*)	95% CI for EXP(*B*)	
							Lower	Upper
Gender (M/F)	−1.334	.498	7.160	1	.007	.263	.099	.700
Age	−.009	.033	.065	1	.799	.929	.929	1.059
Education	.263	.157	2.808	1	.094	1.301	.956	1.768

Chi-square 10.309, Sig. = .016, Nagelkerke R^2 = .157

Model 2: pain variables

Independent variable	*B*	SE	Wald	*df*	Sig.	Exp(*B*)	95% CI for EXP(*B*)	
							Lower	Upper
Pain duration	−.001	.025	.001	1	.979	.999	.951	1.050
Pain intensity at baseline	.389	.223	3.027	1	.082	1.475	.952	2.285
Pain disability at baseline	−.020	.055	.138	1	.710	.980	.880	1.091

Chi-square 3.472, Sig. = .324, Nagelkerke R^2 = .055

Model 3: psychological variables and gender

Independent variable	*B*	SE	Wald	*df*	Sig.	Exp(*B*)	95% CI for EXP(*B*)	
							Lower	Upper
Gender (M/F)	−1.056	.498	4.485	1	.034	.348	.131	.924
TAS-20 total score at baseline	.039	.023	2.790	1	.095	1.040	.993	1.089
BDI-II score at baseline	−.019	.028	.462	1	.497	.981	.929	1.036

Chi-square 9.979, Sig. = .019, Nagelkerke R^2 = .152.
TAS-20 = Toronto Alexithymia Scale, BDI-II= Beck Depression Inventory.

Most studies exploring the co-occurrence of alexithymia and chronic pain are presented in cross-sectional study design, the conclusions being that alexithymia is connected to some extent with chronic pain and may be related to its severity and other facets such as illness behavior, coping and catastrophizing. A few longitudinal studies have reported some evidence about the prospective value of alexithymia as a predictor of development of chronic pain in general population [17,22]. An earlier 1-year follow-up study of a treatment intervention in a sample of low back pain patients reported poorer outcome and increased disability in a group of patients with alexithymic features [76] and in a study of somatizing patients alexithymia predicted persistent symptoms [43]. In the present study, alexithymia was connected with insufficient improvement in pain intensity and pain disability. However, alexithymia explained the variance in these only to some extent.

Male gender had a negative influence on outcome. A similar result was reported in a study exploring the gender differences in outcomes of a multimodal pain management program [77]. In the present study there were no differences in pain situation or depressiveness at baseline but the males were more alexithymic than the females. Thus the result suggested that the gender effect on pain outcome is associated with alexithymia. In a general population study the prevalence of alexithymia was higher in male gender [78].

The finding that baseline depression did not predict outcome was unexpected and contrary to the study hypothesis. Major depression occurs in chronic pain syndromes with high prevalence when compared with pain-free individuals, and its rate has been reported to be in line with pain severity [79,80]. Depressive patients often seek treatment for somatic pains and may be misdiagnosed and overexamined with a delay in obtaining specific treatment for depression. A chronic pain patient with depression may receive pain treatment interventions without improvement because depression inhibits adherence to suggested treatment protocols. Alexithymia has been considered to disturb compliance with treatment choices provided [10]. An earlier study found that the effect of antidepressants in major depression is poorer in alexithymic patients than in nonalexithymic patients [81] and another study proposed that "alexithymic depression" retains more somatic symptoms than "nonalexithymic depression" [82].

In the present study, the whole sample at follow-up showed improvement in depression but the alexithymic patients remained depressive, and the relation between alexithymia and depression was close and constant. It is also possible that a proportion of high pain intensity and pain disability reported by alexithymic patients with depression describes the bodily felt emotional states. Depression and alexithymia in combination may produce numerous somatic symptoms, which are misunderstood, misdiagnosed and treated as somatic disorders leading to poor outcome because the underlying problem was alexithymia and depression, not the somatic pain.

The limitations of the present study include the small number of participants and the small number of alexithymic patients that made the statistics less reliable and warrant

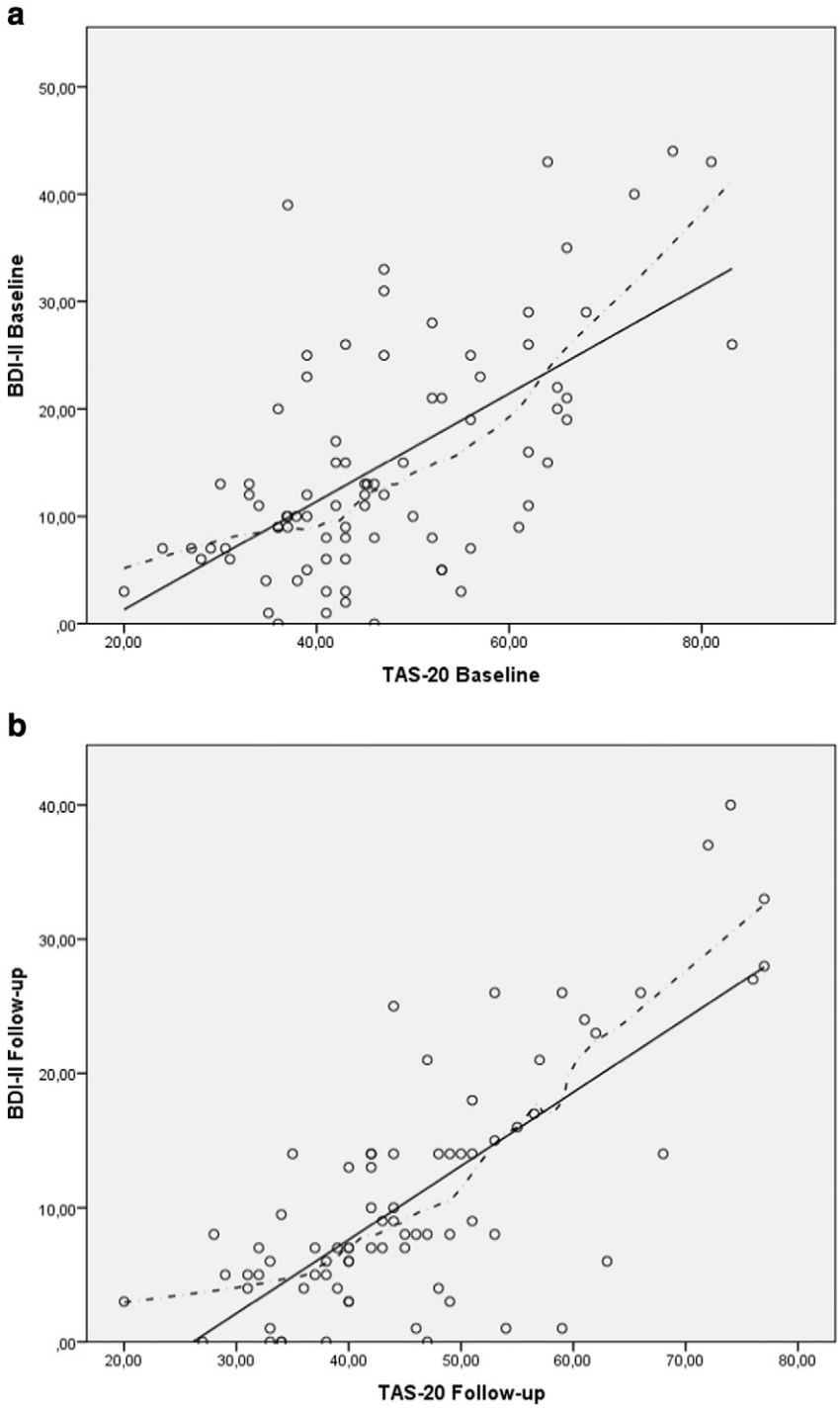

Fig. 1. a: The scatter plot of TAS-20 and BDI-II (baseline) with the fitted regression line (continuous line) and the Lowess smoothing line (dashed line). Pearson correlation $r = 0.612$, $p < 0.001$. b: The scatter plot of TAS-20 and BDI-II (follow-up) with the fitted regression line (continuous line) and the Lowess smoothing line (dashed line). Pearson correlation $r = 0.743$, $p < 0.001$.

interpreting the results with caution. However, we double-checked the results using two different statistical methods (t-test and logistic regression) and the results were parallel. The lack of positive variables such as self-efficacy to explain improvement would have yielded more information but was unfortunately beyond scope of the study design.

The use of BDI-II in measuring depression in alexithymic individuals [83] and in chronic pain [84] has been criticized for producing too high scores because of overlapping phenomena and higher cut-off points have been recommended. There was nevertheless a clear difference in BDI-II scores between alexithymic and nonalexithymic patients at

follow-up indicating real depressiveness among the alexithymic chronic pain patients. The results of the effects of treatment were not included in the design of the present study, which is a limitation. However, the exploration of treatment methods and outcome suggested that none of the methods was connected with better outcome. Thus, we cautiously suggest that the differences between outcomes were probably due to the characteristics of the patients, not the treatment. The connection of psychological factors with persistence of pain disorder has been confirmed in several studies [74,65].

The strengths of the study are a long follow-up period and the measures used to describe the outcome. The generally accepted recommendation for follow-up outcome measures includes at least two of following items: pain intensity, physical capacity, mood and life satisfaction [85]. In the present study the outcome was estimated by pain intensity, pain disability and depressiveness, which can be deemed to adequately describe the severity and the degree of the pain disease.

5. Conclusions

Alexithymia and male gender were connected with poor outcome in a sample of chronic pain patients. The poorer outcome may refer to difficulties in committing to the treatment provided as the compliance with the treatment as well the adherence to interventions may have been disturbed by depression and/or alexithymia [10,86] or the biomedical treatment given to the patients did not alleviate their psychological problems. Depression in alexithymic patients may lead to overestimation of somatic symptoms and underestimation of psychological factors as alexithymic patients prefer to concentrate on their somatic symptoms. Our results highlight the need to identify special subgroups among chronic pain patients and the need for more tailored treatment protocols. There is already evidence that structural cognitive–behavioral strategies or other kinds of structural treatment protocols may benefit alexithymic patients [10]. Emotion school for alexithymic chronic pain patients improved their quality of life [87]. The authors recommend screening for alexithymia and depression in chronic pain patients. We encourage the development of special treatment options for this problematic patient group to relieve their suffering.

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