ALEXITHYMIC TRAITS, MENTAL AND PHYSICAL HEALTH, AND EARLY-LIFE ADVERSITY –
FinnBrain Birth Cohort Study

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"That which besets me is indifference. I can't be bothered about people. Or rather, won't. For I avoid, carefully, all occasions for being bothered... Indifference is a form of sloth, and sloth in its turn is one of the symptoms of lovelessness. One isn't lazy about what one loves. The problem is: how to love?"

- Aldous Huxley, Eyeless in Gaza

ABSTRACT

Alexithymia is a personality construct first identified in hospitalized psychosomatic patients. It is characterized by difficulties in identifying (DIF) and describing (DDF) feelings, an externally oriented, or concrete and pragmatic thinking style (EOT), as well as a scarcity of fantasy and imagination. Alexithymia has been associated with increased psychiatric and somatic morbidity across diagnostic categories, as well as increased markers of physiological stress. The etiology of alexithymia is unclear although childhood environmental influences are likely to play a role in it. Several studies imply that alexithymia is a heterogeneous phenomenon with possible subtypes that have differential associations with mental health and emotion regulation.

This dissertation is part of the FinnBrain Birth Cohort Study, in which we analyzed a large sample of fathers and mothers and compared their alexithymic traits with mental and physical health outcomes, as well as self-reported early-life adversities in childhood.

Our results support the hypotheses of the existence of two alexithymia subtypes: One characterized by high levels of DIF, as well as increased depressive and anxiety symptoms; and another characterized by high levels of EOT, exhibiting lower psychiatric symptomatology. However, EOT, even while not increasing the risk for mood or anxiety symptoms, was associated with increased substance use in men, and a higher BMI and higher prevalence of gestational diabetes in women. In pregnant women, alexithymic traits, and especially the dimension of DIF, was additionally associated with higher hair cortisol concentrations during late pregnancy, indicating heightened levels of chronic stress. Regarding early-life adversity, we showed that alexithymia was specifically related to childhood experiences of emotional neglect and was associated with adult attachment insecurity.

These findings show that alexithymic traits have differential associations with psychiatric symptomatology, substance use and metabolic health. Importantly, they show that many of these associations are independent of mood and anxiety. Findings on early-life adversity in alexithymia imply that depression with concurrent alexithymia may represent a specific subtype of depression, treatment of which may benefit from a focus on childhood emotional neglect and attachment insecurity.

KEYWORDS: Alexithymia, Psychosomatic, Early-life adversity, Depression, Anxiety, Childhood Maltreatment, Chronic Stress, Cortisol

TIIVISTELMÄ

Aleksitymia kuvaa moniulotteista persoonallisuuden piirteistöä, jonka tunnusmerkkejä ovat vaikeudet tunteiden tunnistamisessa ja ilmaisussa, mielikuvituksen köyhyys sekä ulkokohtainen ajattelutyyli, jossa kiinnostus sisäiseen maailmaan ja tunteisiin on vähäistä. Aleksitymia on liitetty moniin somaattisiin ja psyykkisiin terveysongelmiin, sekä fysiologiseen stressiin. Useat tutkimukset viittaavat siihen, että aleksitymiaa ei voida pitää yksiulotteisena ilmiönä, vaan sillä on useita alatyyppejä, joilla saattaa olla erilaisia vaikutuksia terveyteen ja tunnesäätelyyn.

Aleksitymian syntymekanismit ovat edelleen epäselviä, mutta lapsuuden ympäristöllä ja vastoinkäymisillä ajatellaan olevan merkittävä rooli sen kehittymisessä.

Tämä tutkimus on osa FinnBrain syntymäkohorttitutkimusta. Tutkimusaineisto koostuu suuresta otoksesta isiä ja äitejä. Tutkimme tässä populaatiossa aleksityymisten piirteiden yhteyttä fyysiseen terveyteen, mielenterveyteen sekä lapsuuden vastoinkäymisiin.

Löydöksemme tukevat hypoteeseja aleksitymian kahdesta alatyypistä: Ensimmäistä alatyyppiä luonnehtivat subjektiivinen vaikeus tunnistaa ja ilmaista tunteita, sekä lisääntynyt masennus- ja ahdistuneisuusoireisto. Toisessa alatyypissä korostuneempana on ulkokohtainen ajattelutyyli, eikä siihen liity lisääntynyttä psykiatrista oireilua. Ulkokohtainen ajattelutyyli kuitenkin lisäsi alkoholin ja tupakan kulutusta miehillä, sekä oli yhteydessä ylipainoon ja raskausdiabetekseen naisilla, riippumatta samanaikaisista masennus- ja ahdistusoireista. Raskaana olevilla naisilla aleksitymia oli lisäksi yhteydessä korkeampiin hiusten kortisolitasoihin, mikä viittaa krooniseen stressiin. Lapsuuden vastoinkäymisten osalta löydöksemme viittaavat siihen, että aleksitymia on yhteydessä lapsuuden emotionaaliseen vaille jäämiseen sekä kiintymyssuhdeongelmiin.

Löydökset korostavat aleksitymian monimuotoisuutta, ja osoittavat, että aleksitymian eri ulottuvuudet ovat yhteydessä erilaisiin terveysongelmiin sekä päihteidenkäyttöön. Nämä yhteydet ovat lisäksi riippumattomia samanaikaisista masennus- ja ahdistuneisuusoireista. Löydökset liittyen lapsuuden vastoinkäymisiin aleksitymian taustalla korostavat emotionaalisen vaille jäämisen ja kiintymyssuhdeongelmien tärkeyttä, ja voivat auttaa uusien hoitomuotojen kehittämisessä psykiatrisille potilaille, joilla on aleksityymisiä piirteitä.

AVAINSANAT: Aleksitymia, psykosomatiikka, lapsuuden vastoinkäymiset, masennus, ahdistuneisuus, lapsuuden kaltoinkohtelu, krooninen stressi, kortisoli

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Abbreviations

DIF   Difficulty Identifying Feelings
DDF   Difficulty Describing Feelings
EOT   Externally Oriented Thinking Style
HCC   Hair Cortisol Concentration
EA   Early-Life Adversity
CM   Childhood Maltreatment
TAS-20   Toronto Alexithymia Scale 20
EPDS   Edinburgh Postnatal Depression Scale
SCL-90   Symptom Checklist 90
BMI   Body Mass Index

List of Original Publications

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I.   Kajanoja, J., Scheinin, N., Karlsson, L., Karlsson, H. and Karukivi, M. (2017). Illuminating the clinical significance of alexithymia subtypes: A cluster analysis of alexithymic traits and psychiatric symptoms. *Journal of Psychosomatic Research*, 97, pp.111-117.
II.   Kajanoja, J., Scheinin, N., Karukivi, M., Karlsson, L. and Karlsson, H. (2018). Alcohol and tobacco use in men: the role of alexithymia and externally oriented thinking style. *The American Journal of Drug and Alcohol Abuse*, 2018 Nov 14:1-9.
III.   Kajanoja J., Karukivi M., Scheinin N.M., Tuulari JJ., Ahrnberg H., Karlsson L., Karlsson H., (2019) Alexithymia, Body Mass Index and Gestatinal Diabetes in Pregnant Women -FinnBrain Birth Cohort Study. *Journal of Psychosomatic Research*, Vol 124.
IV.   Kajanoja J., Karukivi M., Mustonen P., Scheinin NM., Kortesluoma S., Karlsson H., Karlsson L., (2019) Alexithymic traits and hair cortisol concentrations in pregnant women (Submitted)
V.   Kajanoja J., Karukivi M., Scheinin NM., Ahrnberg H., Karlsson, L., Karlsson, H. (2019) Differential impacts of early-life adversities and adult attachment on depression and alexithymia. (Submitted)

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1   Introduction

Alexithymia is a personality construct characterized by difficulties in identifying and verbalizing emotions, a restricted capacity for imagination and fantasy, as well as an externally oriented thinking style, referring to a pragmatic way of thinking, lacking interest in emotional experience and introspection (Sifneos 1973). Individuals high in alexithymic traits exhibit deficiencies in emotional awareness, emotion regulation and interpersonal communication and thus, lack the capacity to reflect on their inner experience (Lumley, Neely & Burger 2007). For this reason, alexithymia has been seen as a hindrance to psychoanalytic and psychotherapeutic treatment (Bagby & Taylor 1997a). Indeed, alexithymia has been associated with poorer treatment responses not only to psychotherapy, but also to psychopharmacological treatment of mental health disorders (Ozsahin et al. 2003; Lumley, Neely & Burger 2007).

Alexithymia has been linked to a myriad of mental and physical health problems such as Major Depression, anxiety disorders, eating disorders, somatization, substance abuse, pain disorders, autoimmune disease and cardiovascular disease (Fernandez et al. 1989; Honkalampi et al. 2000a; Marchesi et al. 2005; Mattila et al. 2008; Thorberg et al. 2009; Grabe et al. 2010; Tolmunen et al. 2010; Nowakowski et al. 2013; Montoro et al. 2016; Chalah & Ayache 2017). It is commonly believed that alexithymia is a fixed personality trait that constitutes a risk factor for mental and physical illness (e.g. Karukivi et al. 2014a). However, empirical evidence regarding this view is not established, and other researchers have proposed that the alexithymia construct may simply be a marker of negative affect in depressed or anxious individuals, not a vulnerability factor in itself (e.g. Marchesi et al. 2014). As most alexithymia studies have been cross-sectional, this question of causality is still not fully resolved, but research seems to support the view that alexithymia is a relatively stable trait that can be slightly affected by changes in mood (Picardi et al. 2005; Saarijärvi et al. 2006; Hiirola et al. 2017).

The link between alexithymia and mental/physical illness could be explained by several factors. Alexithymic individuals are more often unmarried, and have a lower education level and income, all representing risk factors for impaired health outcomes (Mattila 2008). Some evidence suggests that alexithymia is related to impaired emotional awareness and emotion regulation (da Silva et al. 2017; Swart et

al. 2009), as well as problems in the interpersonal domain (Spitzer et al. 2005). These in turn could lead to chronically heightened levels of physiological stress, and thus, ultimately, to many stress-related mental and somatic health problems. This is known as the alexithymia-stress -hypothesis (Martin & Pihl 1985). Another possible pathway for impaired health in alexithymia lies in lifestyle factors and unhealthy behaviors. Alexithymic individuals seem to differ both in dietary and substance use patterns compared to non-alexithymic controls. Specifically, they are more prone to emotional eating and using substances to regulate stressful emotions (Lumley et al. 1996; Thorberg et al. 2009; Honkalampi et al. 2017; Lyvers et al. 2019; Pink et al. 2019). All of these risk factors ─ Low socioeconomic status, interpersonal problems, chronic stress and unhealthy behaviors ─ commonly overlap, and likely causally affect each other.

The etiology of alexithymia is largely unclear. Childhood experiences and quality of parenting are likely to play a significant role in the development of alexithymic features (Karukivi & Saarijärvi 2014). Alexithymia has been associated with childhood emotional neglect and inadequate maternal care (Aust et al. 2013; Thorberg et al. 2011). Genetic and twin studies indicate that alexithymia also has a heritable component (Jørgensen et al. 2007; Terock et al. 2018). Regarding the etiology of alexithymia, it is important to understand that alexithymic individuals are a heterogenous group, and the individual dimensions of alexithymia are differentially associated with mental health and emotional processing (Grabe et al. 2004). Therefore, some researchers have proposed the existence of alexithymia subtypes (Bagby et al. 2009; Chen et al. 2011) that could also differ in terms of etiology.

The nature of alexithymia as a distinct phenomenon or personality trait is still under debate, and so is its relevance as a risk factor for mental health problems. Therefore, it is important to carefully characterize alexithymic individuals and their health status, also using biological markers, controlling for concurrent psychopathology. The aims of this thesis were three-fold: Firstly, to characterize possible subtypes of alexithymia, and examine how the individual dimensions of alexithymia relate to mental and physical health status, as well as substance use. Secondly, to study the association of alexithymia and physiological stress, using hair cortisol concentrations as a biological marker of chronic stress. Thirdly, to elucidate the etiology of alexithymia by examining its associations with early-life adversity and adult attachment security.

2 Review of the Literature

2.1 On Psyche and Soma

As this dissertation concerns problems in emotional awareness and emotional processing, it seems appropriate to begin by attempting to define emotion. Despite millennia of philosophical inquiry and empirical research, we still lack a definitive description of what an emotion actually is and what its relationship is with other cognitive faculties. The Greeks and Romans saw emotions as "pertubationes animi", as disturbances hindering reason. If science has yet to elucidate the nature of emotion, what we do know nowadays is that they serve much more vital functions and cannot be regarded as simply inferior to cognition and rationality: The experience of emotion is central to human life and interpersonal functioning. In order to survive we need to steer attention towards both pleasurable/appetitive, as well as dangerous/threatening stimuli. We also derive our quality of life and sense of meaning and fulfillment from emotions. Moreover, negative affect and anhedonia — the inability to feel pleasure — are core features of most psychiatric disorders. One comprehensive definition of emotion describes it as a feeling state/process that motivates and organizes cognition and action (Izard 2010). In other words, emotion could be considered as a mental process that coordinates approach and avoidance behavior as a response to environmental stimuli. However, even this description is not exhaustive, and many researchers have questioned whether the term emotion actually represents any 'real' biological category (Feldman Barrett 2006; Kringelbach & Phillips 2014).

The idea that the psyche (mind) could affect the soma (body) and its health has been around for a long time. In ancient Greece, Socrates deemed physicians too somatically oriented, and emphasized that the body cannot be cured without addressing the mind (Raginsky 1948). Galen was one of the first physicians to advocate the view that 'passions' could both cause and cure diseases. Many medieval physicians and philosophers subscribed to this view and further developed them (Ackerknecht 1982). However, until the 19th century, the link between emotions and physical health was mostly based on opinions and anecdotes. In the 19th and early 20th centuries, the works of William James, Ivan Pavlov and Walter Cannon among others initiated empirical investigations into the physiological basis of emotions.

Interest in the psyche as an etiological factor in physical disease was further ignited by the rise of psychoanalysis (Lipowski 1982). Franz Alexander, an early psychoanalyst considered one of the founders of modern psychosomatic medicine, formulated a more detailed account of mental conflicts inducing physical disease (Lipowski 1982). He suggested that conflicts between unconscious drives and the ego or superego could create chronic tension, ultimately manifesting as dysfunction in specific organs (Lipowski 1982). These ideas set the stage for the emergence of psychosomatic medicine, which became a separate medical field in the 20th century, founded on the presumption that personality features and emotions can affect the onset and development of physical disease.

2.2 History of the Alexithymia Construct

Alexithymia, literally translating 'no words for mood', is defined as a difficulty in identifying and verbalizing feelings in the self, an externally oriented thinking style, as well as a scarcity of imagination and fantasy. Alexithymia was first conceptualized by Peter Sifneos in 1973 (Sifneos 1973). Psychoanalysts in the 1940s and 1950s had noticed that many patients with unexplained somatic symptoms, were unimaginative, lacking introspection and showing remarkable difficulties in verbalizing their emotions (Taylor 1984). These patients were considered difficult to treat by psychoanalytic methods, as they lacked introspective tendencies, showed disinterest in dreams and fantasies, and showed a pragmatic, externalizing cognitive style. They also engaged in substance abuse, aberrant eating behaviors and compulsions, seemingly to avoid negative emotions (Taylor 1984). Early psychoanalysts emphasized the role of intrapsychic conflict in psychosomatic diseases. Unconscious conflicts were seen to cause chronic emotional arousal, leading to physiological changes and disease (Lesser 1981). Subsequently, this conflict-based theory started to lose support as it was apparent that psychoanalytic treatment did not produce expected results (Lesser 1981; Taylor 1991).

The physician and neuroscientist Paul MacLean, who put forward the concept of the triune brain, had also noticed this tendency of diminished emotional expression in psychosomatic patients. He speculated that in these patients, the neocortex fails to symbolically process emotional information, and instead it finds an outlet through the autonomic nervous system, resulting in harmful physiological changes and possibly leading to disease (MacLean 1949). Nemiah and Sifneos were the first to conduct a systematic study of the personality features and cognitive style of psychosomatic patients, and their results seemed to confirm psychoanalysts' intuitions. Sifneos reported that psychosomatic patients were characterized by difficulties in identifying and verbalizing emotions, an externally oriented, pragmatic thinking style, as well as a paucity in imagination and fantasy. He termed

this constellation of features 'alexithymia' and developed the Beth Israel Hospital Psychosomatic Questionnaire to assess them (Sifneos 1973). At the same time, similar features were being described by other researchers in patient populations suffering from post-traumatic stress-disorder and substance abuse (Bagby & Taylor 1997a).

Instead of intrapsychic conflicts, theories of alexithymia focused on the differentiation of emotional experience, and emotion regulation. The lack of ability to accurately identify emotions, is thought to obstruct their expression and therefore also the regulation of emotion by interpersonal communication. Furthermore, lacking imagination and insight into their own emotional world, alexithymic individuals have difficulties in putting themselves in other people's situation and mental states, thus hindering their empathic abilities (Bagby & Taylor 1997a). Martin and Pihl (1985) later refined the theory on alexithymia and stress, suggesting that the link between alexithymic features and somatic symptoms would arise from an inability to consciously process emotional information. This inability was thought to lead to an excessive focus on physical sensations accompanying emotion. This was thought to explain the tendencies for hypochondria and somatization, as well as emotion regulation strategies through compulsive behaviors. This failure to process and regulate emotion consciously, was also hypothesized to amplify the physiological responses to stressful events and negative emotions, ultimately leading to physical illness (Martin & Pihl 1985; Taylor 1991).

Alexithymia was the main theme in the 1976 European Conference of Psychosomatic Research in Heidelberg. Here, a consensus on the concept of alexithymia was achieved, and agreed that further research validating the construct, and development of reliable measures were needed (Bagby & Taylor 1997a). Subsequently, alexithymia research gradually moved from concerning only the field of psychosomatics, to more broadly studying the effects of affects, emotion regulation and personality in health and sickness (Mattila 2008).

2.3   Measuring Alexithymia

In a clinical setting, the most common approach to assess alexithymia is clinical judgement based on interviews. However, as this approach is not psychometrically reliable, other ways of measuring alexithymia had to be developed for the purposes of advancing research (Lumley et al 2007). Sifneos (1973) in his original article where he coined the term alexithymia, introduced the Beth-Israel Hospital Psychosomatic Questionnaire. It is a 17-item, forced choice questionnaire that the interviewer fills after an unstructured conversation with the patient. The purpose of the unstructured conversation is to probe the patient's ability to describe emotions, fantasy and dreams. Some support for the validity and factor structure of this

questionnaire has been obtained, but its inter-rater reliability has been shown to be questionable (Bagby & Taylor 1997b). Since the release of the Beth-Israel Hospital Psychosomatic Questionnaire, several validated measures have been developed to assess alexithymia. These include questionnaires and structured interviews, as well as projective tests and speech content analyses (Taylor 1984).

The Schalling-Sifneos Personality Scale (SSPS) (Apfel & Sifneos 1979) was the first attempt to create a standardized self-report questionnaire to assess alexithymia. It was used in the Beth-Israel Hospital. Around the same time, Kleiger & Kinsman (1980) created the MMPI alexithymia scale, based on correlations between the Beth-Israel Hospital Psychosomatic Questionnaire and items in the Minnesota Multiphasic Personality Inventory. The MMPI alexithymia scale was widely used for a period of time, but its validity was later questioned (Federman & Mohns 1984; Bagby et al. 1988). Bagby et al. (1988), in their validity study comparing the MMPI and SSPS with the Toronto Alexithymia Scale (introduced below), found that both the SSPS and MMPI showed "response and/or gender biases, poor internal reliabilities, and no systematic relationship with somatic symptoms".

A few years later, Taylor et al. (1985) developed the Toronto Alexithymia Scale (TAS). This self-report questionnaire initially contained 26 items measured on a 5-point Likert scale. They included four dimensions: Difficulty Identifying Feelings (DIF), Difficulty Describing Feelings (DDF), reduced daydreaming, and an Externally Oriented Thinking style (EOT). The TAS-26 was later refined, and the dimension of reduced daydreaming was dropped out. In 1994, the authors introduced the 20-item TAS with three dimensions measuring DIF, DDF and EOT (TAS-20). The TAS-20 has been by far the most widely used self-report questionnaire in alexithymia studies and has repeatedly shown good validity and reliability (Bagby et al. 1994a; Joukamaa et al. 2001; Taylor et al. 2003). However, it does have some drawbacks. The TAS-20 does not measure lack of imagination, an essential part of the original alexithymia construct. Furthermore, the EOT dimension of the TAS has been found in some studies to have poor internal consistency (Kooiman et al. 2002, Müller et al. 2003).

The Bermond-Vorst Alexithymia Questionnaire (BVAQ) was developed later in the 1990s (Vorst & Bermond 2001). This questionnaire is divided into affective and cognitive components, measuring emotionalizing and fantasizing (affective), and identifying, describing, and analyzing feelings (cognitive). Emotionalizing here refers to the capacity to be emotionally aroused by emotion-evoking stimuli. The BVAQ has shown good psychometric quality in several studies (Vorst & Bermond 2001; Deborde et al. 2008; Vroege et al. 2018). However, emotionalizing was not part of the original alexithymia construct, and recent studies using both network analysis and factor analysis, do not support the inclusion of emotionalizing and

fantasizing as salient features of the alexithymia construct (Watters et al. 2016; Preece et al. 2017).

Recently, Preece et al. (2017) examined the theoretical components of the alexithymia construct via confirmatory factor analysis, using both TAS-20 and BVAQ as alexithymia measures. They concluded that previous literature, as well as their own findings, support the view that alexithymia consists of only three dimensions: DIF, DDF and EOT. Furthermore, they made an attempt to integrate the alexithymia construct into the wider theory of emotion regulation by James Gross (Gross 2015) and argued that DIF and DDF could be considered deficits in the accurate appraisal of emotional information, while EOT depicts inattention or disinterest concerning emotions and the inner world. They called this the attention-appraisal -model of alexithymia and developed the Perth Alexithymia Questionnaire, which focuses on the subjective capacity to accurately differentiate emotions across valences, and the tendency to pay attention to and be interested in emotions (Preece et al. 2018).

Structured interviews for assessing alexithymia include the modified version of the BIQ described above (Bagby et al. 1994b), the Alexithymia Provoked Response Questionnaire (APQR) (Krystal et al. 1986), and the Observer Alexithymia Scale (Haviland et al. 2000). However, these have received little attention in the research literature, and therefore will not be discussed further. Likely the most widely used interview is the Toronto Structured Interview of Alexithymia (TSIA) created by the developers of the TAS-20 questionnaire (Bagby et al. 2006). This measure seems to correlate well with the TAS-20 and has shown good psychometric quality (Bagby et al. 2006; Grabe et al. 2009). The authors suggested that the validity of alexithymia research could be enhanced by employing multiple measurement types simultaneously. However, as structured interviews are significantly more time-consuming compared to self-report questionnaires, their use has been limited, especially in studies with larger populations.

In addition to structured interviews and self-report questionnaires, some projective techniques for measuring alexithymia have been developed. These include the Rorschach alexithymia indices, and the Scored Archetypal Test, but these have also received little attention in alexithymia research (Taylor et al. 1997).

2.4 Validity of the Alexithymia Construct and its Measurement

The construct of alexithymia has been somewhat controversial from the beginning, and some researchers have questioned both its validity, as well as reliable measurement (Lane et al. 2015). Apfel & Sifneos (1979) already acknowledged that the question of whether alexithymia was best measured by self-report or interview

was unresolved. Lane et al. (1997) were the first to argue that the TAS-20, or self-report questionnaires in general, may be unsuitable for assessing the capacity to identify feelings, especially among those who putatively lack such a capacity. Despite of this valid and important criticism, available evidence supports the convergent and discriminant validity of self-report measures of alexithymia. For example, individuals scoring high in alexithymia or its dimensions, use less emotional words and show diminished physiological responses to emotion-eliciting stimuli (Roedema & Simons 1999; Davydov et al. 2013). TAS-20 scores are also negatively associated with empathy (Grynberg et al. 2010), emotional intelligence (Parker et al. 2001), and an observer-rated measure of emotional awareness (Levels of Emotional Awareness -Scale, LEAS) (Maroti et al. 2018). Importantly, alexithymia has been consistently associated with deficits in processing emotional facial expressions, regardless of their valence (Grynberg et al. 2012). Together these findings support the validity of self-report questionnaires in assessing alexithymia and imply that even alexithymic individuals are at least to some extent conscious of their own deficits in emotional processing. However, it is plausible that many individuals with alexithymic features may not perceive their lack of emotional awareness as a problem or deficit, and thus self-report questionnaires such as the TAS-20 may not identify them.

It seems that empirical research on alexithymia faces an insurmountable problem: Emotional experience and awareness of it, are among the most intimate aspects of the human psyche. Therefore, all attempts to measure them depend at least to some extent either on the subjects own, or the interviewer's personal judgement. This problem is of course not unique to alexithymia research, but to different degrees concern most areas of psychology and psychiatry, where researchers are interested in the characterization of subjective experience.

Another relevant critique concerns the discriminant validity and stability of the alexithymia construct. Several authors have argued that the TAS-20 has overlap with negative affectivity and could therefore more accurately depict general distress or negative affect in psychiatric patients, instead of measuring true alexithymia. More specifically, individual studies have observed that the differences in alexithymia levels between patient populations and healthy controls, as well as the relationship between alexithymia and somatoform symptoms disappear after controlling for current psychiatric symptomatology (Rief et al. 1996; Marchesi et al. 2014; Marchesi 2015). Furthermore, alexithymic traits in patients suffering from substance abuse might be at least partially a state-dependent phenomenon that is relieved following withdrawal (de Haan et al. 2012), although findings are mixed (de Timary et al 2008b).

As a response to the abovementioned critique, several studies have investigated the independent contribution of alexithymia to other traits and states, while

controlling for current depressive and anxiety symptoms. This line of research largely supports the validity of alexithymia as an independent construct. For example, alexithymia correlated with somatization even after controlling for the effects of somatic diseases, depression, anxiety and sociodemographic confounders (Mattila et al. 2008). Furthermore, the association of alexithymia with deficits in emotional processing are at least partially independent from concurrent psychiatric symptomatology (Swart et al. 2009; Grynberg et al. 2012).

Finally, the temporal stability of alexithymia has been examined in several follow-up studies (Honkalampi et al. 2000b; Luminet et al. 2001; Saarijärvi et al. 2006; Tolmunen et al. 2011; Hiirola et al. 2017). Earlier studies focusing on different psychiatric patient populations, have reported a lack of stability in alexithymic features. Particularly, they have reported that alexithymia levels and especially its DIF dimension are, to some degree, affected by changes in mood and anxiety (Fukunishi et al. 1997; Marchesi et al. 2008). For example, Honkalampi et al. (2000b) observed that alexithymia scores lack absolute stability in depressed patients, and that reductions in depressive symptoms associate with concurrent reductions in TAS-20 scores. However, subsequent studies have distinguished between absolute (absolute change in alexithymia scores over time) and relative (relative differences in alexithymia scores between individuals) measures of stability of alexithymia. A large 11-year follow-up study by Tolmunen et al. (2011) observed slight reductions in alexithymia scores over the follow-up period but nonetheless found high absolute and relative stability over time. Saarijärvi et al. (2006) followed a sample of patients suffering from major depression for a period of 5 years. In their study, alexithymia failed to show absolute stability, but changes in alexithymia scores were very small compared to reductions in depressive symptoms. Therefore, they concluded that alexithymia is a relatively stable trait that is at least partially independent from depressive symptoms. A recent Finnish study also followed a large population sample for 11 years, and they reported both high absolute as well as relative stability (Hiirola et al. 2017).

These findings indicate that alexithymia is likely to have both state-dependent as well as trait components. This seems to be in line with theories dividing alexithymia into primary and secondary forms. Specifically, alexithymia could primarily arise from genetic influences and early childhood experiences and manifest as a stable trait. However, in other cases, alexithymia could represent a transitory defense mechanism following psychic trauma, depression and/or anxiety (Parker et al. 1991).

A relevant point worth considering in this context, is that personality traits in general show only modest stability over the life course (Hampson & Goldberg 2006; Edmonds et al. 2013). Furthermore, changes in the 'Big 5' -personality traits (Norman 1963) such as neuroticism and openness to experience, have been observed following use of selective serotonin reuptake inhibitors (SSRIs) (Tang et al. 2009),

psychotherapy (Roberts et al. 2017), and psychedelic experience (MacLean et al. 2011). Therefore, changes in alexithymia levels following improvements in mood or abstinence from substance abuse, does not implicate that alexithymia should not be considered a personality trait.

2.5 Prevalence and Sociodemographic Correlates of Alexithymia

Two large population-based studies in Finland and Germany have examined the prevalence of alexithymia in the general population, as defined by a TAS-20 score of higher than 60 (Bagby & Taylor 1997b). In both studies, the prevalence of high alexithymia was 10% (Mattila et al. 2006; Franz et al. 2008). Alexithymia seems to represent a dimensional trait that is normally distributed in the population (Salminen et al. 1998; Franz et al. 2008), and slightly more prevalent in men (Mattila et al. 2006; Levant et al. 2009). As comprehensive population-based studies on the prevalence of alexithymia have mostly been conducted in modern Western cultures, there may be cultural differences in prevalence yet to be discovered. For example, some studies suggest that in the Chinese population, alexithymic traits may be generally higher (Zhu et al. 2007; Chen et al. 2011).

Sociodemographic factors associating with alexithymia are low education, income and socioeconomic status, being unmarried, as well as poor subjective health status (Kauhanen et al. 1993; Joukamaa et al. 1996; Salminen et al. 1996; Mattila et al. 2006). Mattila et al. (2006) further observed, in the Finnish general populations, that age was strongly associated with alexithymia levels. Specifically, elderly people had a higher prevalence of alexithymia. The reason for this finding is not known, nor is its generalizability to other countries and ethnicities. In the German population, age was not associated with alexithymia (Franz et al. 2008). It seems unlikely that alexithymia levels would markedly increase with age, as Hiirola et al. (2017) showed robust stability of alexithymia levels in an 11-year follow up, including in older individuals. However, different life circumstances and upbringing could explain the differences in alexithymia levels between Finnish generations. Fewer people in Finland lived in cities in the early 1900s, and rural living has been associated with alexithymia (Joukamaa et al. 2007). The elderly generation in Finland has also experienced major wars, and thus has likely been more exposed to chronic stress, uncertainty and traumatic events. However, this remains speculative, as no specific reason has been found for the associations between alexithymia and age.

Regarding children and adolescents, it is commonly thought that children naturally lack the cognitive capacity to accurately identify, differentiate and verbalize feelings, and that this ability gradually develops during early adolescence (Säkkinen et al. 2007). In existing studies, alexithymia has been measured in

adolescents ranging from 12 to 16 years of age, and its prevalence in youth has been shown to be comparable to adult prevalence (Horton et al. 1992; Säkkinen et al. 2007: Joukamaa et al. 2007; Karukivi et al. 2014b). A few studies have examined alexithymia levels in children/adolescents ranging from 8 to 14 years of age using a questionnaire specifically designed to assess alexithymia in children (Rieffe et al. 2006; Griffin et al. 2016). However, the exact meaning, stability and clinical relevance of alexithymic traits in children and youth is not clear (Säkkinen et al 2007).

2.6   Etiology of Alexithymia

Early theoretical explanations of the etiology of alexithymia ranged from psychoanalytic to genetic foundations as well as social learning. Most of these studies lacked methodological rigor and thus remained speculative (Lesser 1981). However, it was acknowledged from early on that many etiological factors are likely to be important in explaining a multifaceted construct such as alexithymia (Lesser 1981; Taylor 1984). Decades later, several factors increasing the risk for alexithymia have been identified, but full understanding of the development of alexithymic features is still lacking, as is the state of affairs with most psychiatric problems. Studies imply that alexithymia is transmitted intergenerationally, i.e. both parents' alexithymia levels correlate with their children's (Fukunishi & Paris 2001; Grabe et al. 2008). However, this intergenerational transmission can be attributable to both genetic and/or environmental (e.g. socioeconomic status, parenting style) factors.

2.6.1   Twin studies assessing heritability

Heiberg & Heiberg (1978) were the first to conduct a twin study of alexithymia in 33 pairs of twins. They concluded that alexithymia is possibly influenced by genetic factors. However, this study was limited by a small sample size and an unvalidated measurement of alexithymia. Valera & Berenbaum (2001) analyzed 77 twin pairs using the TAS-20 questionnaire. Their results suggested that the EOT dimension of alexithymia was most influenced by genetic factors, compared to DIF and DDF that were more influenced by shared environmental factors. The sample size also in this study limits any firm conclusions. Jørgensen et al. (2007) were first to conduct a large study on a sample of 8785 Danish twins with an age range of 20-71 years. They also used the TAS-20 to assess alexithymia levels. The results indicated that genetic effects were significant across all dimensions of alexithymia (DIF, DDF and EOT), as well as high alexithymia (TAS-20 score > 60 points). They estimated a heritability rate of 30-33%, with shared environmental factors accounting for 15-20% of the variance in alexithymia scores, and nonshared environment for the rest (47-55%).

Lastly, Picardi et al. 2011 analyzed a sample of 729 twins from the Italian Twin Register, whilst controlling for the effects of concurrent depression. The age range of their sample was limited to 23-24 years. This study also used the TAS-20 to assess alexithymia. Similarly to Jørgensen et al. (2007), they estimated a heritability rate of 28-35% for different alexithymia dimensions, with unshared environmental effects explaining the majority of variance in alexithymia levels.

It should be mentioned here that twin studies, although considered the gold standard of measuring heritability, have been subject to criticism (Rose 1995; Joseph 2002; Horwitz et al. 2003; Sapolsky 2017). They rest on the assumption that monozygotic and dizygotic twins share equally similar environments and are treated similarly by parents, peers and teachers. However, it is likely that compared to dizygotic twins, monozygotic twins are treated more similarly, spend more time together, share a closer emotional bond, and more often also the same social networks (Joseph 2002; Horwitz et al. 2003). These factors together may lead to a higher similarity between monozygotic twins that are due to other factors than genetic makeup. Therefore, even though twin studies do not support the view of alexithymia arising primarily from dysfunctional family environment and quality of parenting, this possibility should not be ruled out based on twin studies alone.

2.6.2 Candidate genes and gene-environment -interactions

Few studies exist linking specific genes to alexithymic features. Variants in the serotonin transporter-linked promoter region (5-HTTLPR) gene are widely studied in psychiatry (Kenna et al. 2012). Kano et al. (2012) were the first to show a positive association of the LL-allele of the 5-HTTLPR gene with alexithymia total scores and DIF. However, a recent study based on a large population sample reported an opposite result, linking the S-allele of 5-HTTLPR with alexithymia. However, the effect size was small, especially in comparison to the effect of childhood maltreatment (Terock et al. 2018). Individual studies have linked alexithymia to genes coding for the brain-derived neurotrophic factor (BDNF), dopamine-receptor D2 (Walter et al. 2011), as well as the cathecol-O-methyltransferase (COMT) genes (Ham et al. 2005). However, the results have been inconclusive and remain unreplicated (Karukivi & Saarijärvi 2014).

Gene-environment -interactions have become a target of increasing research interest as an explanatory model for psychiatric disorders (Caspi & Moffitt 2006; Klengel & Binder 2015; Assary et al. 2018). Influential theories such as the diasthesis-stress- and differential susceptibility models propose that certain individuals are genetically more vulnerable to a given illness such as depression, but environmental factors like stressful life-events are needed to trigger this underlying vulnerability into an actual disease phenotype (Kendler 2005; Belsky & Pluess

2009). Interestingly, evidence of potential gene-environment interactions on the development of alexithymia is completely lacking. Terock et al (2018) did examine potential interactions between childhood maltreatment and the functional variants of the 5-HTTLPR gene, but instead found that both genotype and maltreatment independently affected alexithymia levels.

2.6.3 Adverse childhood experiences and family environment

Sifneos, in his original paper on alexithymia in psychosomatic patients, did not make any speculations about possible etiology. Some years later, Joyce McDougall described her frustration and difficulty with alexithymic patients "who seemed superficially to have few psychological problems; at the same time they showed a rather robot-like adaptation to external reality and little contact with their own psychic reality; that is to say they had little identification with others and endlessly recounted external events that seemed to have no emotional significance for them" (McDougall 1982). Based on clinical observations, she remarked that alexithymic patients often depicted caregivers that were emotionally absent due to mental illness, or who invalidated, restricted, and/or were disinterested in their child's emotional experience. She argued that parents' attempts to control the child's affective expression, if repeated and sustained, may cause the child to end up feeling confused about emotions, and whether it is allowed to have emotions at all (McDougall 1982).

In later decades, the association of alexithymia with familial factors has been extensively studied. This body of research has provided empirical support for the association of alexithymia with parenting styles and parent-child interaction. A meta-analysis examining the impact of parental bonding in alexithymia, found moderate to strong negative correlations between maternal care, and overall alexithymia levels, as well as DIF and DDF, but not EOT. Both maternal and paternal overprotection also positively associated with alexithymia levels. They described this parenting style as 'affectionless control', characterized by a lack of adequate care, emotional neglect, overprotection and intrusiveness (Thorberg et al. 2011). Moreover, retrospective reports of low expressiveness in the childhood family have also been associated with higher alexithymia scores (Berenbaum & James 1994; Kench & Irwin 2000). Even if based on subjective and retrospective accounts, these findings support the early hypotheses on the influence of parenting on alexithymia. Other family environmental factors that increase the likelihood of alexithymia include low socioeconomic status and low education level (Kokkonen et al. 2001). However, it is unclear whether these correlations are direct, or mediated by genetics and/or parenting style.

Different forms of childhood maltreatment (CM) have been identified as strong risk factors for a myriad of psychological and psychiatric problems (Green et al. 2010; Nemeroff 2016). CM is usually divided into 5 types: Physical abuse and neglect, emotional abuse and neglect, and sexual abuse (Mandelli et al. 2015; Infurna et al. 2016). Of these, physical and sexual abuse are historically the most extensively studied (Infurna et al. 2016), while the different forms of childhood neglect have received less attention in the research literature (Stoltenborgh et al. 2013). Experience of CM broadly affects both cognitive and affective development and later functioning (Pechtel & Pizzagalli 2011). For example, children with a history of maltreatment show difficulties in identifying facial expressions, attentional biases to negative emotional stimuli, as well as aberrant brain limbic system structure and function (Pechtel & Pizzagalli 2011; Teicher & Samson 2013). In light of these findings, it is plausible that CM plays some etiological role also in alexithymia. Disturbances in parent-child interaction, especially in the form of abuse and neglect, could provide inadequate models and lack of positive reinforcement for emotional expression, thus leading to deficits in the domains of emotional awareness and regulation (Brown et al. 2016).

Many studies have examined the association between different forms of CM and alexithymic features. Kooiman et al. (2004) found no association between physical or sexual abuse and alexithymia. However, they did not examine emotional abuse or either form of childhood neglect. Joukamaa et al. (2008), in a Finnish study of patients attending primary care and psychiatric clinics, found that all forms of CM were associated with alexithymia, although only physical abuse in men remained significant after adjustments for concurrent psychopathology.

Emotional maltreatment (either abuse or neglect) may have specific harmful effects for the development of affective functioning, such as emotional clarity (Jessar et al. 2017). Aust et al. (2013) analyzed a sample of alexithymic individuals and a non-alexithymic control group and found that emotional neglect was the only form of CM associated with high levels of alexithymia, explaining 13% of the variance in alexithymia levels. Emotional abuse, physical abuse or neglect, or sexual abuse had no effect on alexithymia levels. In contrast, a recent study found positive associations between alexithymia, emotional neglect, emotional abuse, as well as physical neglect. However, alexithymia was a mediator between emotional neglect and internalizing symptoms, but not between other types of CM, suggesting that emotional neglect may be the most important form of CM in the development of alexithymia (Brown et al. 2016). These findings are consistent with early observations and speculations about the etiology of alexithymia. That is, children whose emotional needs are repeatedly and habitually unmet or ignored, may develop deficient emotional awareness and emotion regulation skills, manifesting as an alexithymic phenotype in some individuals.

Taken together, the evidence is inconclusive about which specific type of CM may lead to later alexithymia, although emotional types of maltreatment show more consistent positive associations. One crucial problem with studies linking specific types of CM to mental health outcomes is that different forms of CM are highly intercorrelated and co-occurring in the same families (Green et al. 2010; Vachon et al. 2015). For example, physical or sexual abuse in the absence of emotional maltreatment may be rare. Therefore, attempts to differentiate between effects of individual CM types by statistical methods are likely to be limited, and could even produce false results (Vachon et al. 2015). Therefore, no strong evidence exists on the differential impacts of CM types on alexithymic features.

It may seem contradictory that childhood experiences are strongly associated with alexithymia, while twin studies have shown that shared environment accounts for only a small proportion of alexithymia levels. However, as discussed above, the methodology and assumptions in twin studies are not scientifically undisputed. Furthermore, gene-environment effects could also play a role in explaining this discrepancy. Genes are unlikely to act alone in determining complex cognitions, affects and behaviors; rather, their expression and effects are in most cases dependent on environmental effects and life experiences (Ottman 1996; Kendler 2005; Belsky & Pluess 2009). Moreover, genes and nonshared environment could also confer resilience, protecting some individuals from the harmful effects of adverse childhood experiences (Davydov et al. 2010).

2.6.4 Parent-child attachment

Considering the mechanisms of how CM leads to psychopathology, attachment theory, first outlined by Bowlby (1958), is an extensively researched field (Mikulincer & Shaver 2012; Widom et al. 2018). Attachment theories hold that children are born with an innate tendency to seek proximity to caregivers in times of need. If parents fail to adequately respond to their child's emotional needs, they may develop a sense of insecurity in human interaction and form negative representations of self and others. This is referred to as insecure attachment, which in infants can take the form of anxious, avoidant, or disorganized attachment style. (Mikulincer & Shaver 2012, Fearon & Roisman 2017). An insecure attachment formation in childhood may interfere with the child's cognitive and affective development, increasing the risk for mental health problems in later life (Belsky 2000; Mikulincer & Shaver 2012; Moutsiana et al. 2014). The framework of attachment was later extended and applied for adult close relationships (Hazan & Shaver 1987). Attachment patterns are relatively stable from infancy to adulthood, and thus adult attachment style is thought to largely reflect attachment experiences in infancy and childhood (Waters et al. 2000; Fraley 2002).

Alexithymia has been consistently associated with both deficits in parental bonding, and insecure attachment styles, particularly avoidant attachment. Thus, several researchers have argued that alexithymia could arise from childhood neglect and/or inadequate parental bonding, leading to an insecure attachment formation and harmfully affecting the development of emotional differentiation and regulation. (Troisi et al. 2001; Montebarocci et al. 2004; Taylor & Bagby 2004; O'Loughlin et al. 2018; Lyvers et al. 2019) More specifically, in an emotionally unsafe environment children may learn to suppress unwanted emotions. When the identification, naming and expression of emotions are not encouraged, emotion regulation skills may cease to develop adequately (Taylor & Bagby 2004; O'Loughlin et al. 2018). However, studies linking alexithymia with parental bonding and attachment insecurity have been retrospective, and therefore no firm conclusions can be made concerning the role of attachment formation in the etiology of alexithymia.

2.6.5   Sociocultural factors

Growing evidence shows that the perception and expression of emotions are likely to be shaped (among other factors) by cultural influences (Feldman Barrett et al. 2011). Lesser (1981) remarked that alexithymia is a product of Western philosophy and the psychodynamic framework, which makes the implicit "value judgement that verbal expression of emotion is healthy and mature". He argues that this is not necessarily the case in many other cultures and traditions. Dion (1996) examined cultural factors in alexithymia prevalence and reported that native Chinese-language speakers scored higher in alexithymia scores compared to the native English and native European language speakers. He proposed that the Chinese culture encourages a more 'somatic' form of expressing emotions, compared to verbal expression that is the norm in Western countries. Furthermore, he warned against applying the alexithymia construct and directly translating Western self-report questionnaires to cultures where emotional expression may be conceived of differently. Le et al. (2002) compared Asian and Malaysian Americans to European Americans and found that Asian and Malaysian Americans had higher levels of alexithymia. Asian Americans also reported that their childhood families displayed less physical affection and positive expression of feelings. Dere et al. (2012) specifically studied the role of cultural values in alexithymic traits, and found that Chinese Canadians, compared to Euro-Canadians scored higher in the EOT dimension of alexithymia, and that EOT was negatively predicted by modernization and Euro-American values.

In addition to cultural influences, gender differences have been observed in the prevalence of alexithymia: Men typically score higher in alexithymia levels, although this has not been the case in all studies (Reviewed in Mattila 2008). Several theorists argue that men and women are culturally treated differently by their parents,

peers, and other adults, possibly affecting the perception and expression of emotion. For example, crying and displays of sadness are discouraged in boys, and politeness more encouraged in girls (Garner et al. 1997; Le et al. 2002; Chaplin et al. 2005). Le et al. (2002), in the study focusing on cultural differences in alexithymia, also observed that men in both cultures have experienced less physical affection compared to women, and European American men experienced less difficulties in expressing emotions compared to Asian American men. However, gender differences alone in alexithymia were not significant in this study. Levant has argued that cultural socialization of gender roles could enforce alexithymic traits in males. He called this notion 'normative male alexithymia' (Levant 1992). More recently, Levant et al. (2009) conducted a meta-analysis to examine gender differences in alexithymia, and found that men generally score higher in alexithymia, although the effect size was small. Research has so far remained scarce on the cultural influences and gender socialization as etiological factors in alexithymia.

2.6.6 Neural correlates of alexithymia

A clearer understanding of the underlying neurobiological basis of alexithymia is likely to help in illuminating its nature and etiology. However, to avoid simplistic biological reductionism, it should be noted that even well-established neurobiological correlates are not etiological explanations in themselves (Kendler 2008; Maj 2013; Borsboom et al. 2019). Neural structure and function are determined by a complex interplay of genes, early environment and experiences during the life course (Kendler 2005; Belsky & Pluess 2009). Therefore, psychological, social, genetic and neurobiological explanations are not mutually exclusive, but represent different levels of explanation (Kendler 2012).

Paul McLean, based on the concept of the triune brain, hypothesized that psychosomatic phenomena could be explained by a failure of communication between the more evolutionarily ancient rhinencephalon (visceral brain) and the neocortex. This disconnection, he postulated, would block intellectual evaluation and symbolic representation of emotional information, and it would instead find an outlet through the autonomic nervous system. This theory was later applied to the alexithymia concept particularly (Lesser 1981). A similar early theory on the neurobiology of alexithymia involved deficits in interhemispheric transmission and inadequate left-hemisphere dominance. This theory was based on the idea that the brain's right hemisphere is specialized in the perception and processing of emotional information, whereas the left hemisphere was thought to specialize in processing linguistic information (Silberman & Weingartner 1986; Tabibnia & Zaidel 2005). It had been observed that patients who had undergone surgical commissurotomies ('split-brain' patients) for epilepsy, exhibited similar features compared to

alexithymia (Hoppe 1977). Some empirical evidence supports these theories, showing that alexithymia may be associated with a left-hemisphere dominance in tasks involving the processing of emotional information (Jessimer & Markham 1997; Bermond et al. 2005; Tabibnia & Zaidel 2005; Kano & Fukudo 2013), as well as a deficit in interhemispheric transmission (Romei et al. 2008). Furthermore, alexithymia may occur more frequently following a stroke in the right hemisphere compared to the left (Spalletta et al. 2001).

In later decades, the line of research examining the neurobiology of emotion regulation has also informed the contemporary search for the neural basis of alexithymia. Circuits comprising numerous brain areas are implicated in the perception and regulation of emotion in humans. These include prefrontal cortical areas such as the orbitofrontal cortex (OFC), ventromedial prefrontal cortex and the anterior cingulate cortex. Other areas include the amygdala, hippocampus, hypothalamus, insula and ventral striatum (Davidson et al. 2000; Taylor & Liberzon 2007). Indeed, a recent meta-analysis of structural brain imaging studies in alexithymia found consistently smaller brain volumes in alexithymic individuals in the insula, amygdala, OFC and striatum (Xu et al. 2018).

In functional neuroimaging studies, using emotion tasks involving emotion processing, alexithymia has been associated with increased activity of the anterior (ACC) and middle cingulate cortex, as well as decreased activities in the amygdala, fusiform gyrus, premotor areas, dorsomedial PFC as well as the right insula (van der Velde et al. 2013). Most of these associations were specific to emotional valence, but the increased activity in the anterior and middle cingulate cortex was independent of valence (van der Velde et al. 2013). This finding is in line with the 'blindfeel' hypothesis of Lane et al. (1997), arguing that alexithymia results from a dysfunctional ACC, leading to reduced conscious experience of emotion. Therefore, increased activity of the ACC could possibly reflect increased cognitive demand in alexithymic individuals when presented with an emotional processing task (van der Velde et al. 2013). However, also discrepant findings with decreased ACC activity in alexithymic individuals have been reported (Kano et al. 2003; Karlsson et al. 2008).

The insula is another region of interest in functional neuroimaging studies of alexithymia. The anterior insula (AI) is thought to receive interoceptive signals from the body and integrate them into emotional experience (Graig 2009; Gu et al. 2013; Namkung et al. 2017). Indeed, decreased empathic responses in the AI have been reported to correlate with higher TAS-20 scores (Bird et al. 2010). Furthermore, a case-control study of combat veterans with traumatic brain injury showed that damage to the AI was associated with alexithymia (Hogeveen et al. 2016). Importantly, Ernst et al. (2014) showed that alexithymia was related to both decreased interoceptive awareness, and deviant neurotransmitter concentrations in

the AI and ACC. Interestingly, there is also evidence that both childhood maltreament and traumatic events in adulthood can affect the structure and function of both the insula and ACC (Baker et al. 2013; Heeringa et al. 2013; Teicher et al. 2014).

In conclusion, on a whole-brain level, differences in hemispheric specialization and transmission could play some role in the deficient cognitive processing of emotion in alexithymia. More recent studies, however, have focused on specific brain regions, most notably the ACC and AI. Consistent evidence seems to imply that the AI, with a key role in emotional awareness and interoceptive processing, could be a potential neurobiological mechanism mediating the diminished conscious experience of emotion in alexithymic individuals. In line with the theories on primary and secondary alexithymia, dysfunction of the AI could in theory result from traumatic brain injury or psychologically traumatic event (secondary alexithymia), or from chronic early-life stress such as maltreatment.

2.7   Alexithymia and Physical Health

As discussed in section 2.2, alexithymia research started with a primary focus on psychosomatic diseases. From there on, research interest on alexithymia has spanned many medical fields including psychiatry, gastroenterology, cardiology, immunology, neurology and dermatology (Guilbaud et al. 2003; Willemsen et al. 2008; Grabe et al. 2010; Porcelli et al. 2013; Samur et al. 2013; Ricciardi et al. 2015; Carrozzino & Porcelli 2018). Health status in alexithymia seems to be broadly affected in a harmful way, and increased rates of mortality in alexithymic individuals have been observed in two large Finnish studies (Kauhanen et al. 1996; Tolmunen et al. 2010). Current theories of alexithymia and health assume that emotion regulation deficits in alexithymia may lead to alterations in physiological stress regulation and immune system functioning, increasing the risk for both impaired psychiatric and somatic health (Guilbaud et al. 2003; Lumley et al. 2007; mattilan väikkäristä; Alkan Härtwig et al. 2013).

2.7.1   Alexithymia and stress physiology

A potential underlying mechanism that might explain the increased prevalences of both somatic and psychiatric morbidity in alexithymic individuals is chronic stress. The hypothalamic-pituitary-adrenal (HPA) -axis is considered one of the main components of the human stress response system along with the sympathetic adrenal medullary (SAM) -axis (Sapolsky et al. 2000; Kozlov & Kozlova 2014). The SAM response is quick, occurring within seconds following stressful stimuli, and results in the secretion of catecholamines (adrenaline and noradrenaline) leading to

increased heart rate, blood pressure, faster breathing, and glucose release into the bloodstream (Sapolsky et al. 2000; Kozlov & Kozlova 2014). The HPA axis responds more slowly compared to SAM, and initiates a cascade of hormonal release, the end product of which is cortisol. Cortisol is a glucocorticoid steroid hormone that is a crucial component in stress responses, inducing a number of adaptive physiological changes (Sapolsky et al. 2000). Different methods of measuring peripheral cortisol levels have been widely used to assess both acute and chronic stress (Russell et al. 2012; Kozlov & Kozlova 2014).

As briefly discussed in section 2.2, Martin & Pihl (1985) were first to propose a link between alexithymia and physiological stress, arguing that the decreased ability to process emotional information would lead to prolonging of stress responses. For example, alexithymic individuals display higher resting heart rate and blood pressure, which has been interpreted as a sign of heightened SAM activity (Papciak et al. 1985; Wehmer et al. 1995). However, discrepant results have also been reported where no differences in resting cardiovascular parameters were observed between alexithymic and non-alexithymic older individuals (Waldstein et al. 2002). Later findings imply that instead of simply being related to increased hyperarousal and stress-responses, alexithymia may lead to a dissociation of subjective and objective measures of arousal and stress. This is known as the 'decoupling hypothesis' (Papciak et al 1985). However, evidence concerning this hypothesis is somewhat contradictory, some studies showing differences only in subjective ratings, and others in physiological measures of stress (Papciak et al. 1985; Stone & Nielson 2001; Bermond et al. 2010; Pollatos et al. 2011; McIntosh et al. 2014; Kleiman et al. 2016).

Recent studies regarding alexithymia and stress have focused more on cortisol-related measures, an early study examining the link between alexithymia and reactivity in the dexamethasone suppression test, found that alexithymia, but not clinical depression was related to a positive result in the dexamethasone suppression test, reflecting an abnormal cortisol-related stress response (Lindholm et al. 1990). The association was independent of age, as well as socioeconomic and marital status. Alkan Härtwig et al. (2013) studied a sample of healthy alexithymic individuals with a non-alexithymic control group. They showed a lower cortisol awakening response in the alexithymic group, possibly reflecting effects of chronic stress exposure. Two studies have examined the association of alexithymia and cortisol responses during a social stress test. The first study showed higher salivary cortisol concentrations in alexithymic individuals only when anticipating the stressor (De Timary et al. 2008a). Similarly, the second study showed higher overall cortisols concentrations before, during and after the stress-test in alexithymic individuals (Hua et al. 2014).

One limitation of existing studies on alexithymia and stress is a predominant focus on acute stress markers in experimental settings. In other words, biomarkers

reflecting chronic levels of stress have been less explored. Furthermore, the associations between individual alexithymia dimensions and stress markers remain unclear. As the affective (DIF & DDF) and cognitive (EOT) components of alexithymia are differentially associated with psychopathology, they may also show differences in terms of physiological stress.

2.7.2   Alexithymia and metabolic health

In addition to psychiatric and psychosomatic disease, later research has implicated alexithymia in many somatic health problems that inflict the most disease burden in Western developed countries. These include obesity, hypertension, type II diabetes and cardiovascular disease (Elfhag & Lundh 2007; Grabe et al. 2010; Tolmunen et al. 2010; Lemche et al. 2014). Several mechanisms could possibly link alexithymia to impaired physical health. Alexithymia may associate with an unhealthier diet (Honkalampi et al. 2017), increasing the risk for lifestyle diseases. Other lifestyle factors are also likely involved such as lack of exercise (Helmers & Mente 1999). Chronic stress in alexithymia (discussed further in section 2.8.6) could also have a synergistic effect with lifestyle factors in promoting weight gain (Sinha & Jastreboff 2013). However, the direction of causality could also be reverse with physical illness affecting emotion processing and alexithymia levels; or alternatively, alexithymia and physical disease could be linked via a shared risk factor (Lumley et al. 1996).

Alexithymic individuals consistently show higher body weight and an increased prevalence of obesity compared to controls. However, findings concerning the link between alexithymia dimensions and body weight are inconclusive: Fukunishi & Kaji (1997) found that obese individuals scored higher in EOT compared to normal weight controls, but not in DIF or DDF. A later study reported opposite findings, showing that obese individuals compared to controls scored higher in DIF and DDF, but not EOT (Pinna et al. 2011). Elfhag & Lundh (2007) reported higher scores in all alexithymia dimensions in obese women, but only higher DIF and EOT in obese men, compared to a normal-weight community sample.

Regarding cardiovascular health, alexithymia has been consistently linked to hypertension in both men and women (Nordby et al. 1995; Todarello et al. 1995; Jula et al. 1999). In a sample of 1168 individuals under 65 years of age, and representative of the general population, Grabe et al. (2010) showed an association of alexithymia with hypertension and atherosclerotic plaques in carotid arteries, even after controlling for sociodemographic factors, known CVD risk factors and psychiatric symptoms. A Finnish population study published in the same year, reported that alexithymia is associated with higher cardiovascular mortality in middle-aged Finnish men (Tolmunen et al. 2010). In their study, each one-point

increase in the TAS-26 increased the risk of death due to cardiovascular cause by 2.3%. Mean follow-up time was 20 years.

2.7.3   Alexithymia and somatoform/functional disorders

Somatoform disorders and somatization (redefined in the DSM-5 as Somatic Symptom Disorder) refer to persistent physical symptoms where an underlying organic disease mechanism cannot be identified (Fink et al. 2005; Mattila et al. 2008). Somatization is a common problem in primary care, causing a remarkable burden due to increased healthcare utilization (Barsky et al. 2005; Fink et al. 2005) The term somatization implies that underlying the physical symptoms is a psychiatric disorder or mental distress (Fink et al. 2005). Many theories have attempted to explain the phenomenon of somatization (Fink et al. 2005; Mattila 2008). Psychodynamic theories conceive of somatization as a defense mechanism where subconscious drives and conflicts are only partially allowed to manifest via bodily symptoms (Taylor et al. 1997; Mattila 2008). More recent theories view somatization as abnormal illness behavior, where mental distress is communicated in the form of bodily symptoms (Taylor et al. 1997).

As alexithymia is thought to involve an inability to translate bodily feelings into conscious emotional states, it makes theoretical sense that alexithymia would predispose individuals to somatization. For example, Krystal (1990) hypothesized that alexithymic individuals fail to understand emotions as signals of information processing, and instead focus on the physical sensations alone. Several studies have indeed shown that alexithymia associates with somatization and physical symptom reporting, although some negative findings have also been reported. Furthermore, studies have often been conducted in students or clinical populations, and concurrent psychiatric symptoms have not been controlled for (reviewed in Mattila 2008). Mattila et al. (2008) conducted a study on a large population-based sample (N>5000), whilst controlling for the effects of socioeconomic variables, somatic disease and psychiatric symptoms. They showed a positive independent association of alexithymia with somatization, particularly driven by the DIF dimension.

In addition to somatization, alexithymia has been associated with other disorders considered to have a functional and/or stress-related component, such as irritable bowel syndrome (IBS) (Kano et al. 2018) and fibromyalgia (Montoro et al. 2016). Functional disorders share a similar definition with somatization, regarded as those somatic conditions "which involve disturbance of function without physical abnormality." (Berry 2000). In IBS, alexithymia has been identified as a strong predictor of symptom severity and associated with gastrointestinal-specific anxiety (Porcelli et al. 2014). It has been hypothesized that the increased symptom severity in alexithymic individuals could be due to their tendency to excessively focus on,

and amplify physiological sensations accompanying emotional arousal, and misinterpret them as signs of disease (Surdea-Blaga et al. 2012). Similarly, fibromyalgia patients exhibit higher rates of alexithymia compared to healthy controls, although the association of alexithymia and pain severity in fibromyalgia may be mediated by symptoms of psychological distress (Montoro et al. 2016; Di Tella et al. 2017)

2.8   Alexithymia and Mental Health

Alexithymia appears to be a transdiagnostic trait associating with many common psychiatric disorders. These include depression (Honkalampi et al. 2000a), anxiety disorders including generalized anxiety (Onur et al. 2013), panic disorder (Marchesi et al. 2005) and obsessive-compulsive disorder (Grabe et al. 2006), several types of substance abuse (Haviland et al. 1988; Michael 1990; Thorberg et al. 2009; Dorard et al. 2017), psychotic disorders (van Rijn et al. 2011; Kubota et al. 2012), post-traumatic stress disorder (Yehuda et al. 1997), as well as eating disorders (Nowakowski et al. 2013). Because of this transdiagnostic nature of alexithymia in psychiatry, it is tentative to conceive of it as a general vulnerability factor increasing the risk for psychiatric morbidity. However, as almost all studies have been cross-sectional, this conclusion is premature. It can also be argued that alexithymia may represent a state caused by the disorders themselves, or general distress associated with them, as has been discussed in section 2.4.

Some longitudinal studies have attempted to examine alexithymia as a vulnerability factor for mental health disorders, but results have been inconclusive (Kojima 2012; Karukivi et al. 2014a). A review of prospective studies of alexithymia by Kojima (2012) concluded that evidence of alexithymia as a prognostic risk factor for disease is not established. However, studies were few and sample sizes mostly small. Karukivi et al. (2014a) did find that the DIF dimension of alexithymia increased the risk for future anxiety symptoms in adolescents. Adolescence may be a fruitful age to study this issue, as alexithymia can already be measured, but psychiatric disorders have often not yet emerged.

2.8.1   Alexithymia, depression and anxiety

The association of alexithymia and depression has been studied in the Finnish general population. While the prevalence of alexithymia was only 4.3% among non-depressed individuals, it was 32.1% in those scoring above 9 points in the Beck Depression Inventory (Honkalampi et al. 2000a). Furthermore, depressive symptoms explained 29.2% of the variability in alexithymia scores. Because of this large overlap, the authors emphasized the need to treat depression as a confounding factor

in alexithymia research. Still, many studies imply that despite the strong association between depression and alexithymia, they represent at least partly distinct constructs (Lipsanen et al. 2004), with alexithymia levels showing more temporal stability compared to depressive symptoms (Saarijärvi et al. 2006).

In addition to depression, elevated rates of alexithymia have been observed in many anxiety disorders. In panic disorder, the prevalence of alexithymia seems especially high, ranging from 34% to 67% in different studies. Furthermore, high alexithymic traits in those suffering from panic disorder, predict worse symptom severity (De Berardis et al. 2008). Regarding obsessive-compulsive disorder (OCD), Grabe et al. (2006) showed that OCD patients had higher alexithymia levels compared to healthy controls, but the first-degree relatives of these groups did not differ in alexithymia levels. They thereby concluded that alexithymia is elevated in OCD but does not pose a familial risk factor for OCD. A recent review concluded that OCD patients show higher alexithymia scores compared to controls, but alexithymia levels are not higher in OCD compared to other clinical populations (Robinson & Freeston 2014). In anxious adolescents, alexithymia seems to be a common trait: Paniccia et al. (2018) studied adolescents with generalized anxiety disorder (GAD) and healthy controls, as well as their parents. They showed that adolescents suffering from GAD, as well as their mothers, had higher alexithymia levels compared to the control group and their mothers. Similarly, a Finnish study in a large population-based sample of adolescents showed that alexithymia was associated with anxiety, and that the majority of alexithymic adolescents were highly anxious (Karukivi et al. 2010).

Most studies have examined alexithymia as a unidimensional construct, studying associations of overall alexithymia scores with mental or physical health outcomes. However, it is likely that the individual alexithymia dimensions have differential associations with symptomatology and disorders (Bankier et al. 2001). The affective dimension (DIF and DDF) of alexithymia is consistently linked to increased depression and anxiety, whereas the EOT dimension seems unrelated to them (Grabe et al. 2004; Alkan Härtwig et al. 2014). This idea of alexithymia subtypes is further explored in section 2.9.1.

2.8.2   Alexithymia and psychosis

An impaired capacity to regulate emotion may be a core component of psychotic disorders such as schizophrenia (O'Driscoll et al. 2014; Chapman et al. 2019). Thus, alexithymia is also assumed to represent a vulnerability factor for psychosis (Fogley et al. 2014; O'Driscoll et al. 2014). A recent study compared patients with schizophrenia, their siblings, as well as individuals at ultra-high risk for psychosis with healthy controls (van der Velde et al. 2015b). They concluded that all three

groups scored higher in cognitive alexithymia compared to controls. Cognitive alexithymia was defined here as a subtype with difficulties in identifying and describing emotions, but normal levels of fantasizing and emotional arousal. Alexithymia has also been associated with poorer neurocognition in schizophrenia (Fogley et al. 2014), the authors suggest that self-reflective functions such as the awareness and regulation of emotion, may require a certain degree of neurocognitive competence.

2.8.3 Alexithymia and Autism Spectrum Disorders

The Autism Spectrum Disorders (ASD) are considered neurodevelopmental disorders characterized by pervasive deficits in interpersonal communication, as well as repetitive, stereotypic and restricted behaviors (APA 2013). Alexithymia is thought to be more prevalent in populations with ASD compared to healthy controls, but representative studies with adequate sample sizes are lacking (Kinnaird et al. 2019). In existing studies, approximately 50% of individuals with ASD seem to have co-occurring alexithymia.

The core characteristics of alexithymia and ASD show some conceptual overlap (Fitzgerald & Bellgrove 2006; Poquérusse et al. 2018), which has generated interesting research in recent years regarding their differences and similarities. Specifically, some researchers consider deficits in emotional processing such as lower empathy to represents core characteristics of ASD. Alexithymia and ASD also show similar patterns of deficits in emotion recognition and social communication (Poquérusse et al. 2018). Recent evidence shows that many of the deficits in emotion processing previously considered core components of ASD, may actually be more adequately explained by co-occurring alexithymia (Bird & Cook 2013; Kinnaird et al. 2019). For example, one study showed that empathic brain responses to other peoples' pain is moderated not by autism, but by alexithymia (Bird et al. 2010). Similarly, deficits in emotion recognition from faces may be better predicted by alexithymia levels than diagnosis of ASD (Cook et al. 2013). This is not simply a conceptual distinction as most, but not all individuals with ASD show moderate to high levels of alexithymia (Hill et al. 2004; Bird & Cook 2013). Further studies are needed to clarify the prevalence and meaning of alexithymia in ASD, as well as whether individuals with co-occurring ASD and alexithymia could benefit from individualized treatment.

2.8.4 Alexithymia and eating disorders

Eating disorders comprise a group of disorders related to problematic eating behaviors. These include Anorexia Nervosa, Bulimia Nervosa and Binge Eating

Disorder. Alexithymic traits have been widely studied in the context of eating disorders (Nowakowski et al. 2013; Westwood et al. 2017). A recent systematic review and meta-analysis concluded that across the spectrum of eating disorders, all diagnostic groups scored higher in alexithymia levels than healthy controls, with medium to large effect sizes (Westwood et al. 2017). However, many studies had not controlled for concurrent depression and/or anxiety.

Theories on the etiology of eating disorders share some similarities with the assumed origins of alexithymia. It has been suggested that eating disorders develop in a childhood family environment which discourages and invalidates emotional expression, and that disordered eating behaviors are maladaptive strategies to regulate negative affect (Corstorphine 2006; Nowakowski et al. 2013). As supportive evidence, some studies have shown that the link between childhood maltreatment and eating disorders is at least partially mediated by alexithymia (reviewed in Nowakowski et al. 2013).

2.8.5   Alexithymia, substance use and addictive disorders

Problems in emotion regulation have been widely implicated in the etiology of substance abuse (Aldao et al. 2010; Morie et al. 2016). Therefore, it is not surprising that alexithymia is linked to problematic use of many addictive substances (Haviland et al. 1988; Michael 1990; Dorard et al. 2017). An especially high prevalence (30-49%) of alexithymia has been repeatedly observed in patient populations suffering from alcohol dependence (for a review, see Cruise & Becerra 2018).

The association of alexithymia with substance use in healthier, non-clinical populations is less studied (Cruise & Becerra 2018). A Finnish large population-based study of middle-aged men found that alexithymia was associated with heavier alcohol use per occasion, more frequent use as well as binge drinking (Kauhanen et al. 1992). They also used biomarkers of alcohol use to validate the self-report data. A more recent study also associated alexithymia with heavier drinking patterns in a sample of college students (Lyvers et al. 2014).

The role of alexithymia in tobacco use is also an understudied area. One study found that during acute abstinence from tobacco, alexithymia predicted increased craving in regular smokers (Sutherland et al. 2013). However, an earlier study found no relationship between alexithymia, tobacco use or nicotine dependence in regularly smoking adults (Lumley et al. 1994). No studies have so far compared alexithymia levels between regular smokers and non-smokers in population-based samples.

Regarding the use and abuse of other substances and illicit drugs, existing research is very scarce. A recent study found a higher prevalence of alexithymia in adolescents with cannabis abuse or dependence, compared to healthy controls (Dorard et al. 2017). A few studies have observed high alexithymia levels in patients

seeking treatment for problematic use of psychoactive substances, but these studies have not differentiated between specific substances (Haviland et al. 1988; Michael 1990).

In addition to addictive substances, alexithymia could also be associated with behavioral addictions. However, this field of research is relatively new, and existing studies are few in number. Gambling disorder, currently the only behavioral addiction acknowledged by the DSM-5, has been associated with alexithymia (Parker et al. 2005; Gori et al. 2016). Other problematic behaviors often conceptualized as behavioral addictions such as internet gaming disorder and problematic mobile phone use have also been positively associated with alexithymia levels in young adults (Mei et al. 2018; Bonnaire & Baptista 2019).

Different mechanisms have been proposed to explain the link between alexithymia and addiction. Lyvers et al. (2019) have studied the role of parental bonding and attachment in alexithymic individuals with alcohol abuse. They have hypothesized that substance abuse in alexithymia may be a result of an inadequate parental bonding, harmfully affecting the development of emotional awareness and regulation, thereby promoting substance use as a means to cope with stressful life-events and difficult emotions.

Another possible pathway to increased substance use in alexithymia could be the increased levels of physiological stress described in detail in section 2.8.1. Chronic stress is an important factor in both the onset and relapse in addictive disorders (Sinha 2008). For many, substance use can be a coping strategy to alleviate stress, particularly social stress (Morris et al. 2005). A study by Kauhanen, however, did not find evidence of stress contributing to the increased alcohol use in alexithymic men (Kauhanen et al. 1992). They measured job stress and autonomic reactivity to physical stress but lacked measures of cortisol reactivity and social stress that may be important in alexithymia (de Timary et al. 2008a).

Preliminary results by Morie et al. (2016) have linked alexithymia to aberrant brain responses in the processing of rewards, which could mediate the association with substance abuse. Furthermore, individuals with high alexithymia often suffer from social anhedonia (Prince & Berenbaum 1993), also reflecting altered reward processing in the social domain. Anhedonia is an important phenomenon in addiction, possibly increasing the risk for substance abuse, but also resulting from neurochemical changes associated with addiction itself (Volkow et al. 2011; Garfield et al. 2014).

While each of these possible mechanisms behind alexithymia and addiction represent a different viewpoint, they are not mutually exclusive. For example, difficulties in emotion regulation, interpersonal problems and social anhedonia could result from inadequate parental bonding and attachment insecurity, and further lead to chronic physiological stress and aberrant reward processing (Spitzer et al. 2005; Quirin et al. 2008)

2.9   Heterogeneity of Alexithymia

2.9.1   Alexithymia subtypes and differences between alexithymia dimensions

It has been pointed out that individuals scoring high on alexithymia scores are not a homogenous population, and therefore many researchers have proposed the existence of alexithymia subtypes (Bermond et al. 2007; Alkan Härtwig et al. 2014; Ueno et al. 2014). Bermond et al. (2007) were the first to hypothesize the existence of alexithymia subtypes, based on the division of alexithymia into cognitive (identifying, describing and analyzing emotions) and affective (emotionalizing, fantasizing) components in the BVAQ questionnaire. According to their model, type I alexithymia is characterized by reductions in both cognitive and affective domains, while type II alexithymia is a deficit in only the cognitive domain. However, they pointed out that theoretically there are 4 extremes (one of which is non-alexithymic) depending on which domain is affected (Bermond et al. 2007). They showed evidence of these subtypes in several samples using confirmatory factor analysis (Bermond et al. 2007). Several studies have later used the distinction of cognitive and affective alexithymia in studying differences in emotion regulation and associated brain activity (van der Velde et al. 2015a; Goerlich-Dobre et al. 2015). However, only one cluster analytical study has been conducted using the BVAQ, and this study failed to show evidence of a cognitive and affective subtype (Bagby et al. 2009).

Previous evidence indicates that the individual dimensions of the TAS-20 differ in their effects on emotion regulation and mental health, supporting the idea of possible alexithymia subtypes also based on the TAS-20 (Grabe et al. 2004; Davydov et al. 2013; Wiebe et al. 2017). For example, DIF and DDF seem to be more consistently associated with psychopathology, compared to EOT (Grabe et al. 2004; Conrad et al. 2009). Interestingly, although EOT does not seem to increase the risk for psychiatric symptoms, it may be associated with other negative traits such as social detachment and impaired cognitive processing (Vanheule et al. 2011), a general deficit in empathy (Grynberg et al. 2010), and even psychopathic traits (Lander et al. 2012). Furthermore, EOT seems to be associated with reduced physiological responses, as well as attention allocation to negative (sad or dysphoric) stimuli (Davydov et al. 2013; Wiebe et al. 2017). Together, these results suggest that EOT may indeed have different origins and consequences as an emotion processing trait, as Preece et al. (2017) hypothesized based on the broader theory of emotion regulation. Whereas individuals high in DIF and DDF could be more prone to chronic negative affect, and therefore at an increased risk for disorders such as anxiety and depression; those high in EOT could instead downregulate negative

emotions, leading to detached social behavior and deficits in empathy. It has therefore been hypothesized that EOT could be conceptualized as a coping mechanism and a possible resilience factor, protecting the mind from extremely traumatic events and circumstances (Davydov 2017).

Some studies have examined possible alexithymia subtypes based on the TAS-20. However, as the TAS-20 does not acknowledge the purported affective dimension of alexithymia, these subtypes are conceptualized differently. Cluster analytical studies seem to support the conceptual distinction between DIF/DDF and EOT. For example, Chen et al. (2011) examined differences in emotional expression and emotion regulation in alexithymics, using cluster analysis. They found three subtypes, which they called introvert-high (high in DIF and DDF), extrovert-high (high in EOT), and general-high alexithymia (high in all dimensions). Introvert-high and general-high alexithymia was associated with suppressive emotion regulation and increased psychiatric symptomatology, compared to the extrovert-high group and individuals low in alexithymia. Similarly, Ueno et al. (2014) conducted a cluster analysis based on the TAS-20 and the Big-5 personality features. They found two alexithymia clusters, one scoring high in DIF and neuroticism, and the other high in EOT and low in openness to experience. They hypothesized that individuals with high DIF/DDF, may not be truly alexithymic, as they are aware of their disposition to chronic negative affect, and actively avoid situations where negative affect might arise. In contrast, EOT and low openness could represent a 'truer' form of alexithymia, as EOT is not clearly associated with depression or anxiety, and low openness to experience relates to blunted and constricted affect. Finally, Alkan Härtwig et al. (2014) used a latent-profile analysis, an found similar subgroups compared to previous studies. Their findings implied that individuals scoring high specifically in DIF experienced most psychological distress, compared to those scoring high on every dimension of alexithymia. These findings seem consistent with Davydov's (2017) argument that EOT could serve as a protective factor in alexithymia. Those high in EOT, could be less distressed by reduced emotional awareness, as they may be less interested in emotional content to begin with; whereas individuals high only in DIF are more aware of their inability to process emotions, and suffer more from this trait (Alkan Härtwig et al. 2014).

2.9.2 Primary and secondary alexithymia

The distinction between primary and secondary alexithymia was made soon after the conception of the alexithymia construct (Freyberger 1977; Lesser 1981). Primary alexithymia is hypothesized to represent a stable, developmental trait that acts as a risk factor for disease. In contrast, secondary alexithymia could result for example from organic disease or brain injury that compromises emotion regulation abilities;

Or alternatively, a major traumatic event, causing the individual to dissociate from the painful experience (Lesser 1981). In other words, primary alexithymia is regarded as a developmental risk factor for illness, whereas secondary alexithymia is thought to be caused by an illness or some other traumatic event.

Some empirical support for the distinction of primary and secondary alexithymia has been obtained. Zeitlin et al. (1989) showed that a sample of Vietnam combat veterans had markedly higher alexithymia levels compared to controls. However, in a sample of holocaust survivors, PTSD was associated with alexithymia, but traumatic events were not. This implies that alexithymia in holocaust survivors could be a predisposing factor, or a consequence of chronic PTSD, but does not support secondary alexithymia simply due to psychological trauma (Yehuda et al. 1997). A later study on victims of sexual assault found that rape victims were more alexithymic that controls without sexual trauma history. The effect was independent of PTSD, and alexithymia was even higher in individuals with repeated trauma, compared to those with a single traumatic event (Zeitlin et al. 1993).

A study by Spalletta et al. (2001) provided interesting evidence for the existence of secondary alexithymia due to stroke. They observed a remarkably high prevalence of alexithymia in patients that had suffered a right-hemisphere stroke (48%), compared to control patients with a left-hemisphere stroke (22%). Similarly, a Finnish study found that patients suffering from traumatic brain injury had higher scores on alexithymia measures, compared to a control group matched for age, gender and depressive symptoms. However, severity of the injury, MRI findings or laterality of injury was not associated with alexithymia in this sample (Koponen et al. 2005). Regarding organic disease, several studies have observed high rates of alexithymia in cancer patients, although results are inconclusive and lack methodological rigor (De Vries et al. 2012). The direction of causality is also unclear and could plausibly be bidirectional. A study by Messina et al. (2011) analyzed a sample of oncological patients and showed that although psychological factors explained the majority of variance in alexithymia, anemia and the degree of cancer invasion were independent predictors of alexithymia levels. This suggests that the severity of cancer *per se* could disturb affective functioning and lead to alexithymia.

Taken together, these studies support the existence of secondary alexithymia due to organic disease, brain injury or traumatic events. However, more studies applying a longitudinal setting are needed to adequately address this question.

2.10   Conclusions based on the Literature Review

High levels of alexithymia are broadly related to impaired physical and mental health. However, the nature of this association remains unclear, as alexithymia has not been established as a prospective risk factor for any somatic or psychiatric

disease. The nature of alexithymia as a distinct phenomenon from depression or anxiety is still also under debate. Regardless, alexithymia associates with aberrant processing of emotional information, interpersonal difficulties, as well as increased measures of physiological stress (Spitzer et al. 2005; Grynberg et al. 2012; Alkan Härtwig et al. 2013). Therefore, it is plausible that alexithymia itself could increase the risk for stress-related health conditions. The etiology of alexithymia remains unclear. Twin studies suggest a relatively low heritability rate, leaving room for a substantial environmental influence. Early-life adversity such as low parental socioeconomic status or different forms of childhood maltreatment have been associated with alexithymia (Kokkonen et al. 2001; Joukamaa et al. 2008; Aust et al. 2013). However, the specificity of these associations is unclear as virtually no studies have controlled for the effects of other types of early-life adversity such as divorce, financial difficulties or mental illness in the childhood family. Most studies have examined alexithymia as a unidimensional construct. However, more recent results imply that subtypes of alexithymia may lead to very different phenotypes between alexithymic individuals (Chen et al. 2011; Alkan Härtwig et al. 2014). While the affective dimension (DIF & DDF) of alexithymia has been consistently associated with increased psychiatric symptomatology, the cognitive dimension (EOT) has not (Grabe et al. 2004). Therefore, studies analyzing alexithymia as a multidimensional construct and from a subtype perspective are needed, using diverse health outcomes.

3   Aims

The aims of this thesis were to further characterize the structure, nature and etiology of the alexithymia construct, and to illuminate the significance of individual alexithymia dimensions for mental and physical health as well as physiological stress measures. Specific aims were:

1.   To investigate the existence of alexithymia subtypes in the FinnBrain study sample, and to compare these subtypes in terms of psychiatric symptomatology, diagnoses of depression and anxiety disorders, and childhood maltreatment history.
2.   To examine how different alexithymia dimensions associate with substance use (alcohol and tobacco) patterns in men.
3.   To investigate associations between alexithymia dimensions, overweight and gestational diabetes in pregnant women.
4.   To examine how alexithymia dimensions relate to chronic stress (as measured by hair cortisol concentrations) in pregnant women.
5.   To clarify the etiology of alexithymia by examining its associations with self-reported early-life adversity.
6.   To illuminate the relationship between depression and alexithymia, by comparing their associations with early-life adversity and adult attachment style.

4 Materials and Methods

4.1 Study Design – FinnBrain Birth Cohort Study

The present study is based on the FinnBrain Birth Cohort study (www.finnbrain.fi), a prospective cohort established to study the effects of prenatal and early life stress exposure on child brain development and health outcomes (Karlsson et al. 2017). Participants were recruited between December 2011 and April 2015 from maternal welfare clinics in the South-Western Hospital District and the Åland Islands in Finland. The study population (N for the whole cohort=3808 families) consists of consecutive women attending the free-of-charge ultrasound in a public healthcare facility [coverage close to 100% in the population (www. thl.fi)] at gestational week 12, their children-to-be-born, as well as fathers of the children/partners of the mothers. After recruitment, the participants filled in a set of self-report questionnaires three times during pregnancy, at gestational weeks 14, 24, and 34. After birth, the families are followed up at three- to six-month intervals (the first 30 months) or 12-to 36-month intervals (from 36 months onwards) and the study is planned to continue for decades. The focus of the FinnBrain project is primarily neurodevelopmental and aims to identify biomarkers for prenatal- and early-life stress exposures, as well as trajectories for psychiatric and somatic morbidity.

4.2 Subjects in studies I-V

In the present study, the focus was exclusively in adults (parents participating in the FinnBrain Birth Cohort). In studies I-III and V, we included all subjects who had filled in the relevant questionnaires. In study IV, we included those mothers who had their hair samples collected and cortisol levels successfully analyzed. Study I included 994 fathers and 1992 mothers. Study II focused on men only and included 994 fathers. Study III focused on women only and included 1660 mothers. Study IV included 130 mothers. Study V included 1713 mothers and 882 fathers.

4.3   Sociodemographic variables

4.3.1   Age

Subjects reported their age when entering the FinnBrain Study at the first maternal ultrasound at gestational week 12. Age was applied as a control variable in all studies and was used as a continuous variable.

4.3.2   Parity

Information on parity was asked in the first trimester and was coded dichotomously as 1. Primiparous and 2. Multiparous. Parity was used as a control variable in study III.

4.3.3   Education

Education was either divided into three classes: 1. High school or lower; 2. Vocational / upper secondary school degree; 3. Applied sciences / University degree (Studies I and V); Or into five classes (studies II-IV): 1. High school or lower; 2. Vocational degree; 3. Upper secondary school; 4. Applied sciences or bachelor's degree; 5. Graduate school or PhD degree.

4.3.4   Income

Individual income of both mothers and their partners was asked on recruitment into the study and was divided into four categories: 1. < 1000€/month, 2. 1000–2000€/month, 3. 2000–3000€/month and 4. > 3000€/month.

4.4   Questionnaires

4.4.1   Alexithymia

For measuring alexithymia, we applied the Toronto Alexithymia Scale (TAS-20) (Bagby et al. 1994; Joukamaa et al. 2001; Taylor et al. 2003): The TAS- 20 is one of the most commonly used self-report scales used to measure alexithymic features, it has been validated in several languages including Finnish (Joukamaa et al. 2001; Taylor et al. 2003). It consists of 20 items divided into three subscales: difficulty identifying feelings (DIF), difficulty describing feelings (DDF) and externally oriented thinking (EOT). Items are rated with a 5- point Likert-scale (1=Strongly disagree, 5=Strongly agree). Thus, the total score ranges from 20 to 100. An

individual is considered "high" in the alexithymia scale if the TAS-20 total score exceeds 60 points, and "moderate" if the total score is between 52 and 60 points (Taylor et al. 1997). The TAS-20 was sent to the study participants when their baby was 6 months old.

4.4.2 Depressive symptoms

The Edinburgh Postnatal Depression Scale (EPDS) (Cox et al. 1987) is a widely used questionnaire for screening pre- and postnatal depression, but the questionnaire has also been validated in men (Edmondson et al. 2010). It is a 10-item self-report scale asking respondents to rate their mood and other symptoms related to depression during the previous week. Questions are scored from 0 to 3 and thus, the total score ranges from 0 to 30 points. Cut-off points for "possible" and "probable" depression have been suggested at 9/10 and 12/13 points, respectively (Gibson et al. 2009). The EPDS has also shown good psychometric properties in Finnish mothers (Tamminen 1990). The EPDS was sent to the study participants in the 1st, 2nd and 3rd trimesters, and when the baby was 3 and 6 months old.

4.4.3 Anxiety symptoms

The Symptom Checklist-90 (SCL-90) (Derogatis et al. 1973; Holi et al. 1998) is a self-report questionnaire to assess intensity of symptoms on many domains of psychopathology. In the present studies, only the anxiety subscale was used. This subscale asks the respondent to report anxiety symptoms experienced during the previous month. The items are rated on a 5-point scale ranging from 0 (not at all) to 4 (extremely). The total score of the anxiety subscale ranges from 0 to 40 points. The SCL-90 anxiety scale was sent to the study participants in the 1st, 2nd and 3rd trimesters, and when the baby was 3 and 6 months old.

4.4.4 Adult Attachment

Adult Attachment Style was assessed in study V using the Experiences in Close Relationships -questionnaire (ECR-R, Fraley et al. 2000). The ECR-R is a 36-item questionnaire divided into two dimensions of attachment anxiety and avoidance. It measures adult attachment security in romantic relationships. Items are scored on a seven-point scale from 1 (strongly disagree) to 7 (strongly agree). Higher scores indicate attachment insecurity. The dimension of attachment anxiety reflects preoccupation and worry concerning the relationship and the partner's emotional availability. Attachment avoidance reflects distrust and avoidance of emotional closeness, as well as repeated attempts to maintain independence, emotional distance

and self-reliance (Miculincer & Shaver 2012). The ECR-R was administered to study participants in mid-pregnancy

4.4.5 Prescription drug use

Prescription drug use during pregnancy was asked in the second and third trimesters and was used as a control variable in study III. We included use of antidepressant (SSRI or SNRI) and glucocorticoid medications.

4.4.6 Substance Use

Questionnaires sent in the first trimester (T1) and 3 months after the baby was born (T2) asked about current alcohol, tobacco, and illicit drug use. Regarding alcohol, frequency of use was divided into six categories: 1. Never; 2. Less than monthly; 3. Once or twice per month; 4. Weekly; 5. Several times a week, and 6. Daily. Quantity of alcohol use per occasion was asked in standard doses of 12 g of ethanol. It was further clarified that a standard dose of alcohol is equivalent to a bottle (0,33 litres) of beer or a glass (12 cl) of wine. Similarly, quantity and frequency of tobacco use was asked. Alcohol and tobacco use were the main outcome variables in study II. In study III and IV, alcohol and tobacco use in women during pregnancy was initially used as a control variable but dropped out of final analyses as reported consumption in women was negligible.

4.4.7 Body Mass Index

Body Mass Index was used as an outcome variable in study III. The information was obtained from the Finnish Medical Birth Register kept by the National Institute of Health and Welfare (THL; www.thl.fi). Data on weight was based on self-reported weight before pregnancy, and BMI was calculated in the maternal welfare clinic at gestational week 12.

4.4.8 Gestational Diabetes

Screening for gestational diabetes was conducted in gestational weeks 14-16 or 24-26, depending on the mother's potential risk factors (Current Care Guidelines 2013). Diagnosis of gestational diabetes was confirmed if fasting glucose was > 5.3 mmol/l, if the 1-hour value of the glucose tolerance test was > 10.0 mmol/l, or if the 2-hour value was > 8.6 mmol/l (Current Care Guidelines 2013). This data was also drawn from the Finnish Medical Birth Register. We only had access to diagnoses of gestational diabetes, not the actual measurement values.

4.4.9   Hair Cortisol Assessment (Study IV)

Hair samples were collected from a random population of mothers participating in the FinnBrain Cohort at the hospital maternity ward 1 – 3 days after delivery. A strand of hair was cut from a standardized area of the posterior vertex region of the head as close to the scalp as possible. Hair samples were stored in foil in a dry place protected from light according to good research practice, Finnish legislation and data protection until the analyses. The analyses were performed at Life and Health Sciences Research Institute (ICVS), University of Minho, Portugal. For the analysis, a 5 cm segment was cut from the samples and 5 - 15 mg of each sample was analysed. As hair grows approximately 1 cm per month, a 5 cm segment was estimated to reflect the cortisol concentrations of the previous five months.

The hair segments were washed in isopropanol three times for three minutes and finely minced using surgical scissors. For extraction of cortisol, 1.5 ml of methanol was added to each sample and the samples were incubated at 55°C for 24h. After centrifuging at 10000 rpm for 2 minutes, the supernatant was transferred to a new vial. Methanol was evaporated at 60°C under a constant stream of nitrogen until the samples were dried completely. Finally, 0,15 mL of phosphate buffer was added and 50 μL of each sample was analysed with ELISA (IBL International Cortisol Saliva ELISA) following the manufacturer's procedure. All samples were analyzed in duplicates with coefficients of variation below 13%. Values above 3 standard deviations (SD) above the mean were considered as outliers and excluded from the final analyses (HCC > 190.5 pg/mg, N=5) (Stalder et al. 2017). Hair samples weighting under 5 mg (N=0) or more than 15 mg (N=7) were also excluded.

4.4.10   Early-life Adversity

The Trauma and Distress Scale (TADS) (Salokangas et al. 2016) was used to assess childhood maltreatment (CM). The TADS is a 43-item self-report questionnaire developed to assess childhood maltreatment retrospectively. It includes five categories of maltreatment: emotional and physical abuse, sexual abuse, emotional neglect, and physical neglect. Frequency of maltreatment exposure is assessed using a five-point scale (0 = never, 4= almost always). Other types of EA were assessed using the Health 2000 -questionnaire (Heistaro 2008). Parental common psychiatric disorders (Major Depression, anxiety disorders, eating disorders, psychotic disorders, bipolar disorder or ADHD), substance abuse, as well as parental divorce during childhood, were asked as single yes/no questions. Financial problems in the childhood family were also assessed by a single item: "There were long-term financial difficulties in my childhood family", using a five-point scale (0 = never, 4= almost always). This measure was dichotomized in the same way as the TADS

maltreatment domains. The TADS and Health 2000 questionnaires were administered in the first trimester of pregnancy.

4.5 Statistical analysis

All statistical analyses in all the studies were conducted using the IBM SPSS software (version 22 or 24). In all studies, the limit for statistical significance was deemed at $p<0.005$ (two-tailed).

4.5.1 Study I

Normality of distribution within the continuous variables was tested using the Shapiro-Wilk test. As TAS-20, SCL-90 and EPDS scores were all non-normally distributed, Mann-Whitney U test was used to analyze group differences for these variables and Spearman's rho (ρ) was used in the correlation analyses. Chi square test was used to assess group differences between categorical variables (high alexithymia, sex and education level). The Bonferroni method was used to correct the p-value in multiple comparisons. Cohen's d was used to describe effect sizes between alexithymia subtypes. Internal consistencies (Crohnbach's alpha) were calculated for the TAS-20 as a whole, and for individual subscales (DIF, DDF and EOT). Sex, educational level and income were controlled for when analyzing associations with alexithymia levels, depression and anxiety symptoms, using hierarchical regression analysis. General Linear Model (GLM) was used for group comparisons to control for the same covariates. To uncover possible subtypes in alexithymia groups, a cluster analysis was conducted using the Ward's method. The cluster analysis was conducted separately for high, moderate and low alexithymia groups.

4.5.2 Study II

Normality of distribution was tested visually and with the Shapiro-Wilk test. TAS-20, EPDS and SCL-90 scores were all non-normally distributed. Therefore, Mann-Whitney U test was used to examine group differences in continuous outcome variables. Chi square test was used for categorical variables. In the intercorrelations between alexithymia scores and continuous outcome variables Spearman's rho (ρ) was used to illustrate the strength of the association. Alcohol use was assessed at two different timepoints: In the first trimester of spouse's pregnancy (T1), and 3 months after the baby was born (T2). Wilcoxon signed-rank test was used to assess changes in alcohol use from T1 to T2. Bonferroni method was used to correct for multiple comparisons. Hierarchical regression (alcohol use) and binomial logistic regression

(smoking status) analyses were conducted to examine associations between alexithymia dimensions and substance use, whilst controlling for age, educations level and concurrent anxiety symptoms. We chose anxiety symptoms as a covariate because it showed a slightly stronger association with alcohol use compared to depressive symptoms. To avoid multicollinearity, we did not include both as covariates.

To better illustrate the relationship of EOT on substance abuse, we also used a categorical approach. As there is no established cut-off for high EOT scores, we compared the highest and lowest EOT quartile. To this end, we matched individuals in the highest ('High EOT group' N=173) and lowest ('Low EOT group' N=173) EOT quartile, using age, education level and anxiety scores as matching variables. Criteria for match was <4 years difference in age, <2 points difference in anxiety scores, and an exact match in education level. Case-control matching was conducted with the 'Fuzzy' extension of the SPSS. Cohen's d was used to illustrate the effect sizes between groups.

4.5.3   Study III

Normality of distribution was tested visually and using the Shapiro-Wilk test. TAS-20, BMI and EPDS scores were all non-normally distributed. Thus, chi-square test was used to analyze categorical variables and Mann-Whitney U test for continuous variables. Kruskal-Wallis test was used for multiple group comparisons. Spearman's rho (ρ) was used to quantify the strength of intercorrelations between variables. Bonferroni method was used to correct for multiple comparisons. Separate hierarchical regression analyses were conducted to examine associations between alexithymic traits and outcome variables, whilst controlling for the effects of age, education and current depressive symptoms at gestational week 34. Control variables were chosen based on the correlation analyses. Depressive symptoms were controlled for because depression commonly co-occurs with alexithymia and involves changes in appetite and weight. Control variables were entered in the hierarchical regression analysis in step 1, and alexithymia dimensions or overall TAS-20 score at step 2. For gestational diabetes, a binomial regression analysis was conducted using the same approach and covariates. For the regression analysis, BMI was transformed to its natural logarithm, after which residuals were normally distributed. As EOT explained the associations between alexithymia, BMI and gestational diabetes, we focused on this dimension in the subsequent group comparisons. As there is no established cut-off score for high EOT scores, we divided participants into quartiles by their EOT score.

4.5.4   Study IV

Normality of distribution within variables was tested visually and using the Shapiro-Wilk test. Differences between categorical variables were analyzed with Chi Square test. Differences in hair cortisol concentrations (HCC) between alexithymia groups were analyzed using the Student's t test. As BMI had a skewed distribution, Mann Whitney U test was used when analyzing group differences. An analysis of covariance (ANCOVA) was conducted to examine group differences between highly alexithymic individuals and controls, while controlling for potential confounders. Multiple regression analyses were conducted to examine the associations between alexithymia dimensions, overall alexithymia scores, and HCC, controlling for the effects of educational level, BMI and current depressive symptoms (EPDS) at gestational week 40. Natural logarithmic transformations were performed on the HCC data to reduce skewness. After transformation, HCC was normally distributed (Shapiro-Wilk test p>0.4 for both alexithymia groups).

4.5.5   Study V

Normality of distribution within variables was tested visually and using the cut-off values of larger than 7 for kurtosis and larger than 2 for skewedness, indicating a non-normal distribution (Kim 2013). We did not use the Shapiro-Wilk test because it is overly sensitive to non-normality in large samples of data. All continuous predictor and outcome variables (TAS-20, EPDS, TADS dimensions and ECR-R) were non-normally distributed. TAS-20 scores and ECR-R scores were log-transformed, after which they were normally distributed. Non-parametric tests were used when analyzing EPDS and SCL-90 scores because of high skewedness. Chi-square test was used to assess group differences between categorical variables, and Student's t test (for normally distributed data) or Mann-Whitney U test (for non-normally distributed) between continuous variables. In the intercorrelations between maltreatment types, Spearman's rho (ρ) (non-parametric) or Pearson's r (parametric) was used to quantify the strength of the association. Analysis of Variance (ANOVA) was used to examine the association between education level and attachment security. When analyzing attachment insecurity in depression and alexithymia, General Linear Model (GLM) was used to control for sex, age and education level. GLM was additionally used when examining associations between non-maltreatment types of EA, and alexithymia levels and depressive symptoms.

    To disentangle the specific impacts of CM types, individuals who reported a history of only one type of CM were compared to those who reported no maltreatment. As sexual abuse very rarely occurred alone, controlling for other types of CM was not possible, and therefore sexual abuse was left out of the final analyses. Binary logistic regression analysis was used to assess the impacts of non-

maltreatment types of EA, whilst controlling for the effects of concurrent CM. Here, raw TADS total scores were used as a continuous control variable. As high alexithymia was rarer compared to current depression, the associations between CM types and alexithymia had wider confidence intervals. We therefore also analyzed associations of EA types, overall alexithymia scores, an scores of each alexithymia dimension separately, in order to avoid false negative conclusions concerning the relationship between EA types and alexithymia.

4.6 Ethical Considerations

The parents gave written informed consent on their own and on their child's behalf. The children will be asked for personal consent at an appropriate age. The ethics Committee of the Hospital District of Southwest Finland has approved the study protocol.

5 Results

5.1 Study I

5.1.1 Characteristics of the study sample

Basic information and characteristics of the study sample is displayed in Table 1. Level of education and income were negatively associated with all outcome measures (EPDS, SCL-90 and TADS, p<0.01 for all comparisons). Women scored higher than men in depressive symptoms, but no differences between men and women were observed in SCL-90 anxiety score or TADS scores. Overall prevalence of high alexithymia was 2.8% in women and 6.0% in men. Mean ages in the low, moderate and high alexithymia groups were 32.0, 31.3 and 31.2 years respectively. Alexithymia scores had a weak negative association with age (ρ= −0.054, p=0.004). Moderate and high alexithymia groups had a lower education compared to the low alexithymia group (p<0.001, see Table 1), however, they did not differ in income level (p=0.131).

Table 1:   Comparisons of low, moderate and high alexithymia groups

		Low alexithymia (N=2471)		Moderate alexithymia (N=290)		High alexithymia (N=113)		All (N=2876)	
		N	%	N	%	N	%	N	%
Gender	Female	1662	67.3%	167	57.6%	52	46.4%	1881	65.5%
	Male	809	32.7%	123	42.4%	60	53.6%	992	34.5%
Education	Low	773	32.7%	142*	51.1%	59*	54.6%	974	35.4%
	Mid	721	30.5%	67*	24.1%	27*	25.0%	815	29.6%
	High	871	36.8%	69*	24.8%	22*	20.4%	962	35.0%
Income level	<1000€/mo	382	16.2%	52	18.7%	24	22.4%	458	16.7%
	1000-2000€/mo	1052	44.6%	130	46.8%	43	40.2%	1225	44.6%
	2000-3000€/mo	777	32.9%	83	29.9%	36	33.6%	896	32.6%
	>3000€/mo	150	6.4%	13	4.7%	4	3.7%	167	6.1%
MDD diagnosis		209	8.5%	42*	14.5%	21*	18.8%	272	9.5%
Anxiety diagnosis		91	3.7%	19	6.6%	12*	10.7 %	122	4.2%
		Median (IQR)		Median (IQR)		Median (IQR)		Median (IQR)	
EPDS		3.0 (4.0)		6.0 (6.0) *		8.0 (8.0) *		3.0 (5.0)	
SCL-90		1.0 (3.0)		3.0 (7.8) *		5.3 (10.0) *		1.0 (4.0)	
TADS		6.0 (10.0)		11.0 (14.0) *		12.0 (14.3) *		7.0 (10.0)	

EPDS=depressive symptoms, SCL-90=anxiety symptoms, TADS =self-reported early life adversity, MDD diagnosis=lifetime diagnosed major depressive disorder, Anxiety diagnosis =lifetime diagnosed anxiety disorder. TAS-20 score under 52=low alexithymia, TAS-20 score 52–60=moderate alexithymia, TAS-20 score over 60= high alexithymia. Education level: Low=high school or lower, Mid=applied sciences degree, High=university degree. Moderate alexithymia was compared to low alexithymia group, high alexithymia was compared to low/moderate group. * p-value<0.01.

5.1.2   Intercorrelations Between Alexithymia Dimensions

DIF/DDF (ρ=0.563, p < 0.001) and DDF/EOT (ρ=0.394, p < 0.001) showed a moderate to strong positive correlation in the whole sample, whereas DIF/EOT (ρ=0.150, p<0.001) showed a mild positive correlation. However, analyzing moderate and high alexithymia groups separately, DIF and EOT had strong negative correlations (ρ= −0.701, p < 0.001 for moderate, and ρ= −0.513, p<0.001 for high alexithymia, see Fig. 1). In the low alexithymia group, DIF and EOT were not significantly correlated (ρ=0.020, p =0.311).
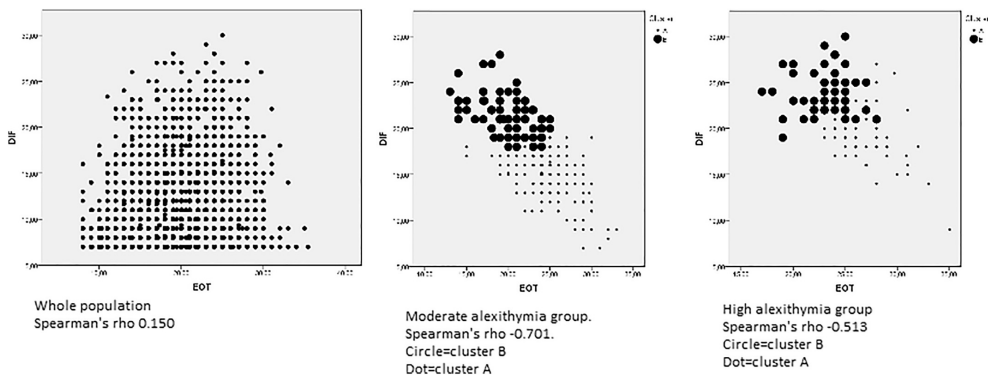
Figure 1: Correlation between difficulty identifying feelings (DIF) (y-axis) and externally oriented thinking style (EOT) (x-axis) in different alexithymia groups.

5.1.3 The Relationship of Alexithymia and Psychopathology

TAS-20 total scores were significantly associated with depressive symptoms (ρ=0.370, p < 0.001), anxiety symptoms (ρ=0.308, p<0.001), and self-reported early life adversity (ρ=0.203, p < 0.001). DIF showed the strongest, and EOT the weakest correlation with psychiatric symptoms. EOT also showed a mild negative correlation with early-life adversity (ρ= −0.069, p<0.001). Individuals with high alexithymia more frequently reported having been diagnosed with MDD (18.6% vs. 9.1%; p=0.003) and anxiety disorder (10.6% vs. 4.0%; p =0.003) compared to those with low or moderate levels of alexithymia.

5.1.4 Cluster Analyses

To uncover possible subtypes of alexithymia, we first conducted a cluster analysis in the high alexithymia group. A two-cluster solution showed the best fit, as indicated by the largest change in the agglomeration coefficient in the last step of the cluster analysis. We will call these clusters Type A (TA) and Type B (TB) alexithymia. TA was characterized by significantly higher scores in DDF and EOT, while TB scored higher in the subscale DIF. The most distinct differences between TA and TB were seen in DIF and EOT (Table 2). Importantly, there were no significant differences in alexithymia total scores between the two subtypes (median scores 64.0 in both clusters; p=0.639).

We replicated the cluster analyses in the moderate- and low alexithymia groups separately. In both cases, a similar two-cluster model emerged. Specifically, in both groups there was one cluster with higher DIF scores, and another cluster with higher EOT scores. As there were differences in the gender distribution among the clusters, we also replicated the cluster analyses in men and women separately. These analyses

also produced two clusters with similar patterns of alexithymia levels and psychiatric symptoms.

Table 2:   Differences Between Alexithymia Clusters

		Type A alexithymia (N=60)	Type B alexithymia (N=53)	All (N=2876)
Gender	Female	36.7%	58.5%	65.4%
	Male	63.3%	41.5%	34.6%
TAS-20 total	Item mean (SD)	3.3 (0.2)	3.2 (0.2)	2.0 (0.5)
DIF	Item mean (SD)	2.7 (0.4)	3.4 (0.3) *	1.6 (0.6)
DDF	Item mean (SD)	3.8 (0.5)	3.5 (0.5) *	1.9 (0.7)
EOT	Item mean (SD)	3.4 (0.3)	2.9 (0.3) *	2.4 (0.5)

TAS-20=Alexithymia total score, DIF=Difficulty identifying feelings, DDF=Difficulty describing feelings, EOT=Externally oriented thinking style.TAS-20 score under 52=Low alexithymia, TAS-20 score 52-60=Moderate alexithymia, TAS-20 score over 60=High alexithymia. * $p<0.01$ (cluster A vs. B)

Comparing the two alexithymia subtypes showed that TB scored higher in EPDS (effect size comparing TA and TB alexithymia d=0.77), SCL-90 anxiety scale (d=0.82) and TADS (d=0.42) compared to TA (Table 3). The TB group also reported a higher prevalence of MDD and anxiety disorders (Table 3). Similarly, both in the moderate- and low alexithymia groups, cluster B scored higher in EPDS, SCL-90 anxiety scale, and TADS scores. As education, income and sex were significant predictors of psychiatric outcomes, we tested whether differences in these variables explained the group differences between alexithymia subtypes. However, the general linear model showed that group differences remained significant after controlling for these factors ($p < 0.001$ for EPDS and SCL-90, p=0.030 for TADS).

Table 3:   Alexithymia Subtypes: Differences in Psychopathology and Early-life Adversity

		Type A alexithymia (A) (N=60)	Type B alexithymia (B) (N=53)	p (A vs. B)	Low/moderate alexithymia (C) (N=2763)
EPDS	Median (IQR)	6.0 (7.0)	11.0 (8.0)	<0.001[1]	3.0 (5.0)
SCL-90	Median (IQR)	3.75 (8.0)	8.0 (13.0)	<0.001[1]	1.0 (4.0)
TADS	Median (IQR)	10.0 (12.25)	15.0 (17.0)	<0.05[1]	6.0 (11.0)
MDD diagnosis	N (%)	5 (8.3%)	16 (30.2%)	<0.01[2]	251 (9.1%)
Anxiety diagnosis	N (%)	2 (3.3%)	10 (18.9%)	<0.01[2]	110 (4.0%)

EPDS=Depressive symptoms, SCL-90=Anxiety symptoms, TADS=Self-reported early life adversity, MDD diagnosis=Lifetime diagnosed major depressive disorder, Anxiety diagnosis=Lifetime diagnosed anxiety disorder. TAS-20 score under 52=Low alexithymia, TAS-20 score 52-60=Moderate alexithymia, TAS-20 score over 60=High alexithymia. [1]=Mann-Whitney U test, [2]=Chi square test

5.2 Study II

5.2.1 Study Population and Correlations Between Variables

Demographic information, substance use and alexithymia levels of the study sample are displayed in Table 4. Age and education were both positively associated with frequency of alcohol use ($\rho=0.088$, $p=0.008$ and $\rho=0.071$, $p < 0.033$ respectively), but lower quantity per occasion ($\rho= -0.146$, $p < 0.001$ and $\rho=0.136$, $p < 0.001$ respectively). Both SCL-90 anxiety scale and EPDS showed positive associations with frequency of alcohol use in T2 ($\rho=0.070$, $p=0.035$ for EPDS and $\rho=0.094$, $p=0.005$ for SCL-90), but not in T1. Neither SCL-90 anxiety scale nor EPDS were associated with quantity of alcohol per occasion. DIF, DDF or TAS-20 overall scores were not associated with any measure of alcohol use ($p>0.2$ for all comparisons). EOT showed a weak correlation with alcohol quantity both in T1 ($\rho=0.103$, $p=0.008$) and T2 ($\rho=0.095$, $p=0.020$), but was not related to frequency of alcohol use ($p>0.2$ in both timepoints).

Prevalence of daily smoking was 13.9%. Smoking status was associated with lower age, lower education and higher EOT ($p<0.001$ for all comparisons), as well as higher TAS-20 overall scores ($p=0.004$), but not DIF or DDF ($p>0.1$ for both comparisons). Daily smoking was also related to higher depression and anxiety scores in T1 ($p<0.01$ for both comparisons) but not T2 ($p>0.1$ for both comparisons). Both the frequency and quantity of alcohol use declined from T1 to T2.

Table 4: Demographic information on the total sample, and group differences between matched individuals with high vs. low EOT scores.

	Whole sample	Lower quartile EOT	Upper quartile EOT	p (lower vs. upper quartile)
Education				
1.	36 (3.6%)	4 (2.3%)	4 (2.3%)	
2.	256 (25.8%)	34 (19.7%)	34 (19.7%)	
3.	103 (10.4%)	20 (11.6)	20 (11.6)	N/A
4.	310 (31.2%)	74 (42.8%)	74 (42.8%)	
5.	237 (23.8%)	41 (23.7%)	41 (23.7%)	
Age (SD)	33.1 (5.4)	33.3 (4.6)	33.1 (4.7)	0.381[a]
EPDS mean (SD)	3.5 (3.3)	3.4 (3.5)	3.7 (3.2)	0.201 [a]
SCL-90 mean (SD)	2.3 (3.3)	2.3 (2.8)	2.1 (3.2)	0.055[a]
DIF mean (SD)	1.6 (0.6)	1.4 (0.5)	1.7 (0.7)	<0.001[a]
DDF mean (SD)	2.2 (0.8)	1.8 (0.7)	2.5 (0.8)	<0.001[a]
EOT mean (SD)	2.6 (0.6)	1.9 (0.3)	3.3 (0.3)	<0.001[a]
TAS-20 mean (SD)	2.2 (0.5)	1.7 (0.3)	2.5 (0.4)	<0.001[a]
Alcohol quantity* mean T1 (SD)	3.6 (3.7)	2.9 (2.7)	4.8 (5.6)	<0.001[a]
Alcohol quantity* mean T2 (SD)	2.7 (2.6)	2.3 (2.4)	3.1 (2.9)	0.012[a]
Alcohol frequency T1				
Never	70 (7.0%)	19 (11.4%)	11 (6.7%)	
Less than monthly	113 (11.4%)	17 (10.2%)	31 (19.0%)	0.495 [a]
1-2 times per month	339 (34.1%)	44 (26.3%)	44 (27.0%)	
Weekly	339 (34.1%)	65 (38.9%)	57 (35.0%)	
Many times a week	106 (10.7%)	22 (13.2%)	20 (12.3%)	
Daily	5 (0.5%)	0 (0.0%)	0 (0.0%)	
Alcohol frequency T2				
Never	75 (8.3%)	16 (9.3%)	15 (8.8%)	
Less than monthly	142 (15.7%)	26 (15.1%)	39 (22.8%)	0.152 [a]
1-2 times per month	305 (33.8%)	62 (36.0%)	59 (34.5%)	
Weekly	326 (26.1%)	57 (33.1%)	52 (30.4%)	
Many times a week	52 (5.8%)	11 (6.4%)	6 (3.5%)	
Daily	3 (0.3%)	0 (0.0%)	0 (0.0%)	
Cigarettes smoked per day (SD)	11.1 (6.4)	9.7 (7.2)	13.0 (6.2)	0.051 [a]

Education: 1. High school or lower 2. Vocational degree 3. Upper secondary school degree 4. Applied sciences or bachelor's degree 5. University degree. DIF=Difficulty Identifying Feelings. DDF = Difficulty Describing Feelings. EOT=Externally Oriented Thinking Style. TAS-20=alexithymia total scores. EPDS = depressive symptoms. SCL-90=anxiety symptoms. *Alcohol quantity=Amount of alcohol consumed per occasion in standard doses of 12g of ethanol. T1=gestational week 14, T2=3 months after participant's baby was born. [a]=Mann-Whitney U test.

5.2.2 Regression analyses

After controlling for the effects of age, education level and current anxiety symptoms, EOT remained significantly associated with alcohol quantity both at T1 (B=0.011, F change=4.330, p=0.038) and at T2 (B=0.009, F change=3.992, p=0.046). DIF, DDF or TAS-20 total scores did not explain any variance in alcohol quantity (p > 0.05 for all tests). Frequency of alcohol use was not related to any alexithymia dimension, or total alexithymia level. In the binomial regression

analysis, smoking status was not associated with alexithymia levels or individual dimensions (p > 0.05 for all tests).

5.2.3   Group Comparisons

Group comparisons between matched individuals from the high and low EOT groups are shown in Table 4. The high EOT group consumed more alcohol per occasion at T1 (Cohen's d 0.43, p<0.001) and T2 (Cohen's d 0.30, p<0.012), and were more often daily smokers (8.7% vs. 17.3%, p=0.023, Figure 2) compared to the low EOT group. The high EOT group also reported more binge drinking (drinking five or more doses of alcohol per occasion, 23.7% vs 41.6%, p=0.001) compared to the low EOT group. The groups did not differ in frequency of alcohol use in either timepoint.
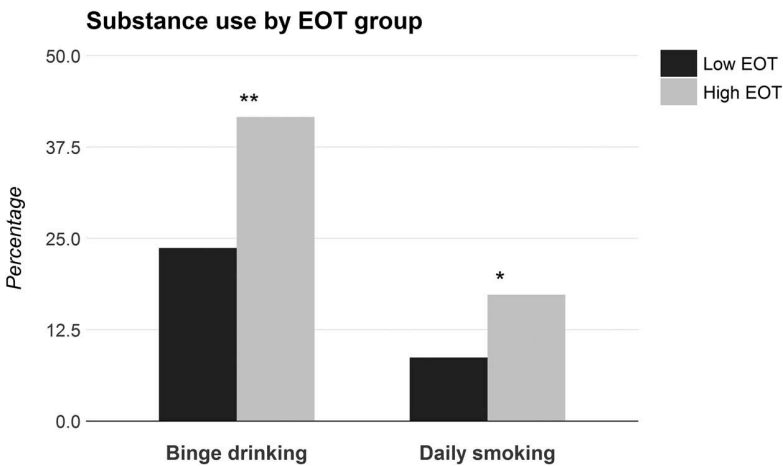
Figure 2:   Prevalence of binge drinking (either timepoint T1 or T2) and daily smoking between high and low EOT groups. Binge drinking: 5 or more doses of alcohol consumed per occasion.

5.3   Study III

5.3.1   Study Population and Correlations Between Variables

Characteristics of the study sample and differences between alexithymia groups are shown in Table 5. 35.6% (N=591) of participants were overweight and 16.7% (N=278) fulfilled the criteria for gestational diabetes. 2.8% (N=46) of the participants scored high, and 9.1% (N=151) moderately high in alexithymia. EPDS total scores (ρ=0.01, p=0.62) in gestational week 34, as well as DIF (ρ= -0.003, p=0.88) and DDF (ρ=0.027, p=0.243), were unrelated to BMI in the correlation analyses. TAS-20 total scores showed a weak positive correlation with BMI

(ρ=0.058, p=0.01), but the association was entirely explained by the EOT subscale (ρ=0.103, p<0.001).

Those fulfilling the criteria for gestational diabetes had a higher BMI (24.0 vs. 27.9, p<0.001) as well as higher scores in EOT (18.5 vs. 19.2, p=0.006) compared to those with normal glucose levels. Gestational diabetes was not associated with EPDS scores (4.7 vs. 4.7, p=0.74), DIF (11.6 vs. 11.7, p=0.97), DDF (9.6 vs. 9.6, p=0.93) or TAS-20 total scores (39.6 vs. 40.5, p=0.16).

Table 5: Demographic information on the total sample, and group differences between alexithymia groups

	Low alexithymia (N=1462)	Moderate alexithymia (N=151)	High alexithymia (N=46)	Whole sample (N=1660)	p (difference between groups)
Education					
Low	4.9%	8.6%	6.4%	5.3%	
Mid	28.9%	43.0%	48.9%	30.8%	<0.001 [a]
High	66.1%	48.3%	44.7%	63.9%	
Mean (SD)					
Age in years	31.2 (4.3)	30.2 (4.6)	30.3 (4.3)	31.1 (4.4)	0.02 [b]
BMI	24.6 (4.7)	25.0 (5.5)	26.7 (5.2)	24.7 (4.8)	0.006 [b]
EPDS	4.3 (3.7)	6.7 (4.3)	8.8 (5.1)	4.7 (4.0)	<0.001 [b]
TAS-20	37.5 (6.7)	55.2 (2.5)	64.7 (4.3)	39.9 (9.3)	<0.001 [b]
Prevalence (%)					
Primiparous	55.1%	42.5%	52.3%	53.9%	0.014 [a]
Overweight	34.8%	34.7%	66.0%	35.7%	<0.001 [a]
Gestational diabetes	16.6%	15.9%	25.5%	16.7%	0.26 [a]

Education: Low=High school or lower. Mid=Vocational / upper secondary school degree. High=Applied sciences or university degree. BMI=Body Mass Index. Overweight = BMI ≥25 EPDS = Edinburgh Postnatal Depression Scale. TAS-20=Alexithymia total score. [a]=Chi square test, [b]=Kruskal Wallis test.

5.3.2   Regression analyses

After controlling for the selected confounders (age, education, EPDS scores), the overall level of alexithymia (β=0.080, p=0.002, R^2=0.006) as well as the EOT dimension (β=0.085, p=0.001, R^2=0.007) remained significantly associated with BMI. Binomial logistic regression showed that the overall level of alexithymia (Exp(B) 1.015, CI95% 1.001-1.030, p=0.041), as well as EOT (Exp(B) 1.041, CI95% 1.009-1.073, p=0.011) were also independently associated with gestational diabetes. DIF and DDF had no relationship to either outcome variable (p>0.1 for all tests).

5.3.3   Group Comparisons

High alexithymia (TAS-20 total score > 60) was associated with a higher BMI (26.7 vs. 24.7, p=0.001) and a higher prevalence of overweight [(66.0% vs. 34.8%, OR (unadjusted)=3.6 , OR (adjusted)=3.6, CI95% 1.9-6.8, p<0.001)] compared to low/moderate levels of alexithymia. Differences in the prevalence of gestational diabetes was not significant (25.5% in high alexithymia group, 16.5% in controls, p=0.102).

To better illustrate the impact of EOT on overweight and gestational diabetes, we divided participants into quartiles by EOT scores, and compared the highest and lowest quartiles. Between the lowest and highest EOT quartile, the adjusted odds ratio for overweight was 1.94 [CI95% 1.43-2.62, p<0.001]; and for gestational diabetes 1.75 [CI95% 1.19-2.58, p=0.005]. (Figure 3).
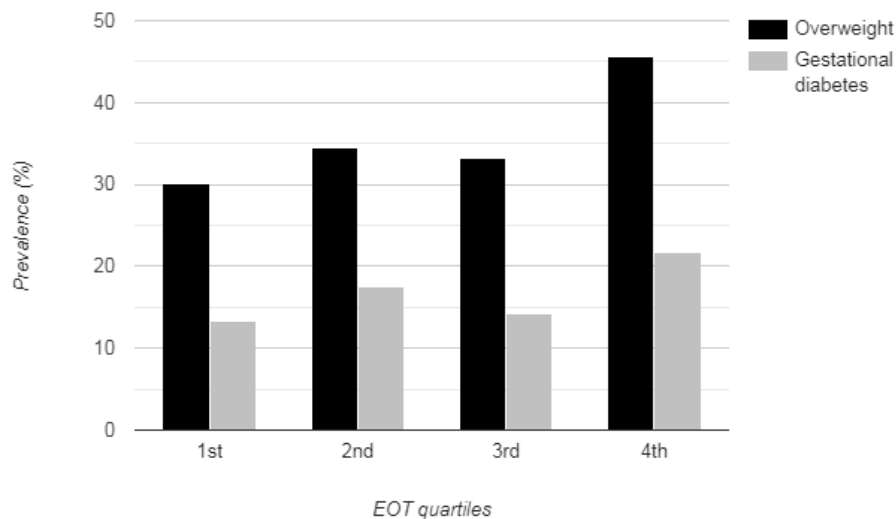
Figure 3: Prevalence of overweight and gestational diabetes by EOT quartile. EOT=Externally Oriented Thinking Style.

5.4   Study IV

Demographic information of the study sample, as well as differences between alexithymia groups are shown in Table 6. Reported substance use among the participants was negligible: Only one participant in each group reported tobacco use after the first trimester of pregnancy. There was no significant difference in alcohol use between alexithymia groups (7.7% vs 8.3%). Frequency of alcohol use in all cases was less than once a month, and ≤ 1 standard dose of alcohol per occasion. No participants reported current illegal drug use.

Table 6: Basic information and comparison of hair cortisol concentrations between alexithymia groups

	No alexithymia (N=118)	Moderate to high alexithymia (N=12)	test statistic	p
Level of education*				
1.	0%	16.7%		
2.	9.6%	25.0%		
3.	9.6%	8.3%	-2.257[b]	**0.024**
4.	37.4%	25.0%		
5.	43.5%	25.0%		
	Mean (SD)	Mean (SD)		
Age	31.6 (3.7)	30.2 (4.6)	1.24[a]	0.217
Depressive symptoms	4.3 (3.9)	7.3 (3.9)	-2.55[b]	**0.011**
BMI	24.2 (27.6)	27.6 (7.2)	-1.68[b]	0.094
HCC (pg/ml)	17.8 (19.3)	35.1 (31.5)	-2.73[a]	**0.007**
DIF	11.2 (3.6)	20.8 (4.3)	-5.22[b]	**<0.001**
DDF	9.2 (3.0)	16.4 (3.4)	-5.12[b]	**<0.001**
EOT	17.7 (4.3)	22.0 (3.4)	-3.21[b]	**<0.001**
TAS-20 total	38.0 (7.2)	59.2 (5.8)	-5.67[b]	**<0.001**

[a] Student's t test, [b] Mann Whitney U test. HCC=Hair cortisol concentrations. BMI=Body mass index DIF=Difficulty Identifying Feelings, DDF=Difficulty Describing Feelings, EOT=Externally Oriented Thinking. *Level of education: 1. High school or lower; 2. Vocational degree; 3. Upper secondary school; 4. Applied sciences or bachelor's degree; 5. Graduate school or PhD degree.

As shown in Table 6, the moderate/high alexithymia group had higher levels of HCC. This difference stayed significant after controlling for the potential confounders (F=5.11, partial η^2 0.040, p=0.026). Removing two participants who reported current SSRI/SNRI use during pregnancy slightly strengthened the group difference (F=6.12, partial η^2 0.049, p=0.015). Additionally removing one participant who reported SSRI/SNRI only in the first trimester, and five participants who reported glucocorticoid use during pregnancy, did not affect the results.

As most participants had low levels of alexithymia, we also analyzed the linear association of alexithymia levels and HCC in the whole sample. As EPDS scores were not associated with HCC, they were removed from covariates at this stage. In the regression analysis, DIF remained significantly associated with HCC (Table 7). Other alexithymia dimensions or overall scores were not significantly associated with HCC (p>0.1 for all tests). Additionally, education level and BMI were negatively associated with HCC (Table 7).

Table 7: Summary of multiple regression analysis of variables predicting hair cortisol concentration

	B	Standard error	β	t	p
Body mass index	-.045	.017	-.243	-2.668	.009
Level of education	-.213	.080	-.234	-2.667	.009
DIF	.039	.019	.187	2.064	.041

DIF=Difficulty Identifying Feelings

5.5 Study V

5.5.1 Study Sample

Demographic information on the study sample, as well as prevalences of EA types are shown in Table 8. All types of CM were associated with lower education (p<0.02 for all). Raw scores of CM types were highly intercorrelated (ρ=0.489 – 0.641, p<0.001 for all). The strongest associations were between emotional abuse and emotional neglect (ρ=0.641, p<0.001), and as well as emotional neglect and physical neglect (ρ=0.637, p<0.001). Non-maltreatment types of EA were also all associated with every type of CM (p<0.005 for all).

43.5% (N=1128) of participants reported no history of childhood maltreatment. 5.7% (N=148) reported only emotional neglect. 9.1% (N=236) only physical neglect, 2.8% (N=72) only emotional abuse, 2.1% (N=55) only physical abuse, and 0.6% (N=16) only sexual abuse.

Table 8: Demographic information and prevalence of different types of early-life adversity
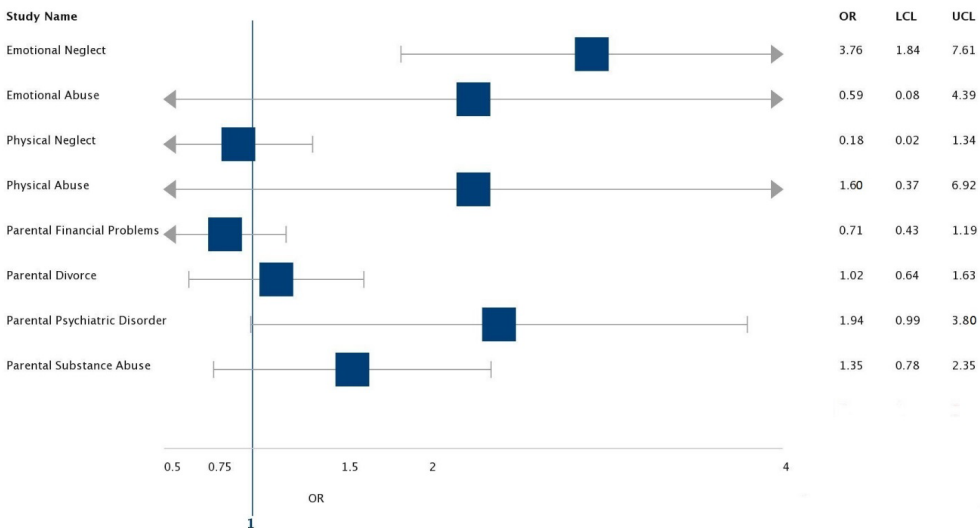
	Men (N=882)	Women (N=1713)	Whole sample (N=2595)
Level of education	1. 4.1%	1. 2.0%	1. 2.7% *
	2. 39.2%	2. 30.6%	2. 33.5%
	3. 56.7%	3. 67.4%	3. 63.8%
	Mean (SD)		
Age	32.8 (5.3)	31.2 (4.3)	31.8 (4.8) *
TAS-20 score	43.0 (9.7)	39.7 (9.3)	40.9 (9.5) *
ECR-R anxiety	2.2 (0.8)	2.4 (0.9)	2.3 (0.9) *
ECR-R avoidance	2.5 (0.8)	2.3 (0.8)	2.4 (0.8) *
	Median [IQR]		
EPDS score	2.0 [4.0]	4.0 [6.0]	3.0 [5.0] *
	Prevalence (%)		
Current depression	7.8%	15.9%	13.2% *
High alexithymia	6.2%	2.7%	5.4% *
Emotional neglect	34.7%	34.9%	34.8%
Emotional abuse	22.7%	31.1%	28.2% *
Physical abuse	21.1%	22.2%	21.8%
Physical neglect	38.7%	36.9%	37.5%
Sexual abuse	1.7%	4.6%	3.6% *
Parental separation	22.6%	25.2%	24.3%
Parental financial problems	10.9%	16.1%	14.3% *
Parental psychiatric disorder	9.2%	15.2%	13.2% *
Parental substance abuse	13.4%	19.7%	17.5% *

Level of education: 1. High school or lower; 2. Vocational / upper secondary school degree; 3. Applied sciences / University degree. TAS-20=Toronto Alexithymia Scale, EPDS=Edinburgh Postnatal Depression Scale, ECR-R=Experiences in Close Relationships. * Significant difference between men and women (p<0.05).

5.5.2 Impacts of specific types of EA on depression and alexithymia

Figure 4 shows the specific contributions of each EA type on current depression and alexithymia. 65.3% of participants scoring high in alexithymia reported a history of emotional neglect compared to 33.6% of those with low or moderate alexithymia levels (p<0.001).

Prevalence of Alexithymia by Type of Early Adversity

Study Name		OR	LCL	UCL
Emotional Neglect		3.76	1.84	7.61
Emotional Abuse		0.59	0.08	4.39
Physical Neglect		0.18	0.02	1.34
Physical Abuse		1.60	0.37	6.92
Parental Financial Problems		0.71	0.43	1.19
Parental Divorce		1.02	0.64	1.63
Parental Psychiatric Disorder		1.94	0.99	3.80
Parental Substance Abuse		1.35	0.78	2.35

Prevalence of Current Depression by Type of Early Adversity

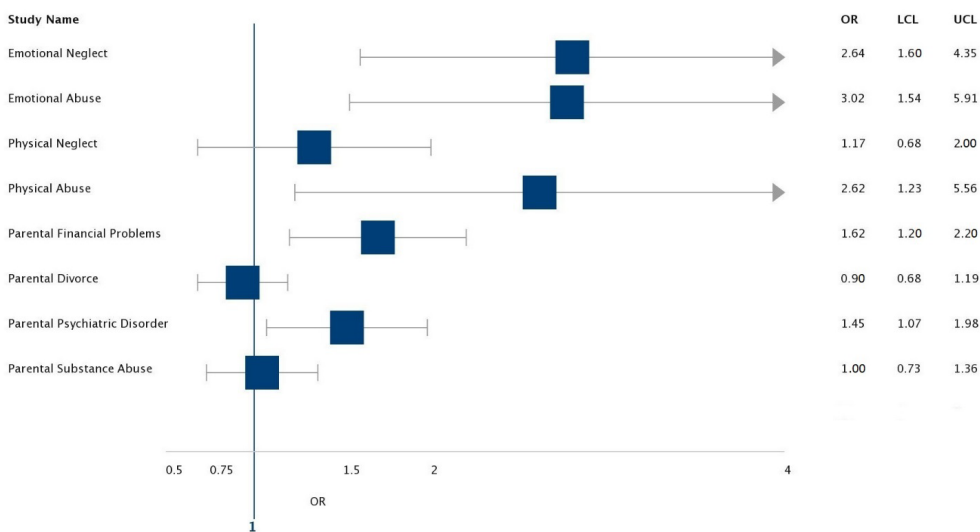| Study Name		OR	LCL	UCL
Emotional Neglect		2.64	1.60	4.35
Emotional Abuse		3.02	1.54	5.91
Physical Neglect		1.17	0.68	2.00
Physical Abuse		2.62	1.23	5.56
Parental Financial Problems		1.62	1.20	2.20
Parental Divorce		0.90	0.68	1.19
Parental Psychiatric Disorder		1.45	1.07	1.98
Parental Substance Abuse		1.00	0.73	1.36

Figure 4: Associations of specific types of early-life adversity (EA) with depression and alexithymia. OR=Odds Ratio, LCL=Lower limit for 95% confidence interval UCL=Upper limit for 95% confidence interval. For each type of childhood maltreatment (CM), history of other types of CM has been excluded. For non-maltreatment types of EA, adjusted ORs are displayed, after controlling for the effects of concurrent CM. Graph created by Forest Plot Generator by Evidence Partners.

Analyzing alexithymia levels as continuous variables showed that emotional neglect was the strongest predictor of all alexithymia dimensions and overall scores (t=3.237

for DIF, t=4.328 for DDF, t=4.915 for EOT, t=5.9 for total scores, p<0.001 for all comparisons). Additionally, emotional abuse was weakly related to DIF (t=2.307, p=0.021) and physical neglect was weakly related to EOT (t=2.2, p=0.029).

All non-maltreatment types of EA were unrelated to overall alexithymia levels after controlling for the effects of CM. Regarding individual alexithymia dimensions, after controlling for CM, parental substance abuse was positively associated with DIF, whereas parental psychiatric disorders and substance use were both negatively associated with EOT, but the effect sizes were small (F=7.45, p=0.006, partial η^2=0.003 for substance abuse and DIF), (F=23.70, p<0.001, partial η^2=0.009 for psychiatric disorder and EOT), (F=4.69, p=0.03, partial η^2=0.002 for substance abuse and EOT)

As alexithymia, depression and some types of EA where unevenly distributed among men and women, we also investigated if the associations between EA and outcome variables were gender-specific. Emotional neglect was significantly associated with overall alexithymia levels in both men and women (t=3.1, p=0.002 for men, t=4.5, p<0.001 for women). Parental financial problems (F=7.5, partial η^2=0.004, p=0.006) and substance abuse (F=6.1, partial η^2=0.004, p=0.014) showed a positive association with overall alexithymia levels in women, but not in men. Other types of EA had no gender-specific effects on alexithymia levels. However, for women several types of EA were associated with depressive symptoms (parental psychiatric disorders, financial problems, emotional neglect and emotional abuse), whereas in men emotional neglect was the only predictor of depressive symptoms.

5.5.3   Adult Attachment

Women scored higher in attachment anxiety (2.41 vs. 2.23, t=4.81, p<0.001), whereas men scored higher in attachment avoidance (2.34 vs. 2.49, t=4.33, p<0.001). Depressive symptoms and alexithymia levels were both positively correlated with attachment anxiety (ρ=0.343, p<0.001 for EPDS; ρ=0.329, p<0.001 for TAS-20) and avoidance (ρ=0.179, p<0.001 for EPDS; ρ=0.379, p<0.001 for TAS-20). After controlling for potential confounders, attachment anxiety was most strongly related to depressive symptoms, while attachment avoidance was more strongly related to alexithymia levels (Table 9).

Table 9: Results of the General Linear Model Predicting Depressive Symptoms and Alexithymia Levels

	EPDS			TAS-20		
	F	p	Partial η^2	F	p	Partial η^2
Sex	35.74	<0.001	0.014	82.09	<0.001	0.031
Age	2.44	0.118	0.001	31.99	<0.001	0.012
Education	4.05	0.044	0.002	34.45	<0.001	0.013
ECR-R anx	214.72	<0.001	0.077	116.20	<0.001	0.043
ECR-R av	4.28	0.039	0.002	194.77	<0.001	0.070
Full model	78.32	<0.001	0.131	151.66	<0.001	0.227

EPDS=Edinburgh Postnatal Depression Scale; TAS-20=Toronto Alexithymia Scale; ECR-R anx=Attachment Anxiety; ECR-R av=Attachment Avoidance

5.5.4 Depression with and Without Alexithymia

Depressive symptoms and alexithymia levels were moderately correlated (ρ=0.367, p<0.001). 14% (N=48) of depressed participants had high levels of alexithymia. 30.4% of depressed men were highly alexithymic compared to 9.9% of depressed women (p<0.001). Of depressed individuals with high alexithymia, 81.3% reported a history of childhood emotional neglect, compared to 54.4% of those with low or moderate levels of alexithymia (p<0.001). Depression with alexithymia associated with higher levels of attachment anxiety (mean scores 3.20 vs. 2.84, t=2.38, p=0.018) and attachment avoidance (mean scores 3.03 vs. 2.52, t=4.03, p<0.001) compared to depression without alexithymia.

6 Discussion

6.1 Alexithymia subtypes (Study I)

In light of previous research, this study aimed to confirm the existence of alexithymia subtypes, and to illuminate their differences in terms of psychiatric symptoms using a cluster analytical approach. We identified two clusters (subtypes) of alexithymia: Type A alexithymia (TA) was characterized by high scores in externally oriented thinking and was more prevalent in men compared to women. Type B alexithymia (TB) was in turn characterized by high scores in DIF, was more equally distributed among genders, associated with increased depressive and anxiety symptoms, and those with it more frequently reported a history of diagnosed Major Depression and anxiety disorders. Replicating the cluster analysis in the moderate- and low alexithymia groups produced similar clusters. Specifically, higher DIF, but not EOT, was related to higher levels of psychiatric symptoms, regardless of the overall alexithymia score. This supports the view of alexithymia as a heterogeneous and dimensional construct. Therefore, it may be problematic that many studies examine alexithymia as a unidimensional and categorical outcome.

Our results are partially similar to a cluster analytical study by Chen et al. (2011) in a Chinese sample of students. This study also found separate alexithymia groups scoring high in DIF and EOT. Furthermore, those with high DIF scored higher in depressive and anxiety symptoms and used more suppressive emotion regulation strategies compared to those with only high EOT. However, the results may not be directly comparable as most participants in this study showed high levels of EOT.

When analyzing intercorrelations between alexithymia dimensions in the whole sample, DIF, DDF and EOT showed moderately positive correlations. Interestingly, when examining their correlations in the moderate- and high alexithymia groups separately, DIF and EOT showed moderate to strong negative correlations. This is a new finding and supports the results of our cluster analyses, implying that individuals with higher alexithymia levels tend to divide into two groups, scoring high either in DIF or EOT. In other words, individuals who score high in EOT do not report subjective difficulties in identifying feelings. This is somewhat puzzling, as EOT has been found to negatively associate with e.g. emotional intelligence (Parker et al. 2001). Alkan Härtwig et al. (2014) have previously reported similar findings,

showing that individuals with high alexithymia who score high in DIF but not in EOT, exhibit more psychological distress compared to those with high scores in both DIF and EOT. They hypothesized that EOT may serve as a protective trait in alexithymia, buffering the effects of psychological distress. Our results support this hypothesis. It could be that some alexithymic individuals (TA) may develop a disinterest in emotions, perhaps protecting them from depression and anxiety. Interestingly, this phenotype was more common in men. However, it is unclear whether EOT offers any 'real' protective value, as it could be that the type A alexithymia group is simply less prone to reporting psychiatric symptoms. EOT is characterized by a lower tendency and interest in introspection, fantasy, and emotional content. Therefore, it is possible that individuals scoring high in EOT also have a deficit in emotional processing, but they may not easily recognize or admit this as a problem.

Ueno et al. (2014) also analyzed alexithymia subtypes based on the Big-5 personality features. They identified two subtypes: The first was characterized by high scores in DIF and neuroticism, the other by high scores in EOT and low scores in openness to experience. The authors hypothesized that high scores in DIF may not represent 'true' alexithymia, as these individuals are at least to some extent aware of their difficulties in identifying feelings and exhibit negative affect. EOT on the other hand, as it associates with low openness to experience, may instead characterize the construct alexithymia more accurately. Indeed, some evidence has shown that particularly the EOT dimension of alexithymia may modulate attention allocation and physiological responses to affective stimuli (Davydov et al. 2013; Wiebe et al. 2017). Therefore, future studies should address these subtypes of alexithymia, and examine how individual alexithymia dimensions contribute to objective markers of stress, affective functioning, and more diverse outcomes of psychopathology, including externalizing behaviors and addictive disorders.

6.2 The impact of alexithymia on men's alcohol and tobacco use (Study II)

Previous studies have reported a consistently high prevalence of alexithymia in patient populations with alcohol and substance abuse (see section 2.7.4). However, fewer studies have focused on the relationship of alexithymia and substance use in healthier populations. We examined the role of alexithymia dimensions in men's alcohol and tobacco use. Previous research implies that individuals with substance abuse disorders show high levels of alexithymia. Our results suggest that at least in men, the EOT dimension of alexithymia may be of particular importance associating with patterns of substance use. High levels of EOT independently associated with quantity of alcohol use per occasions, as well as daily smoking. Overall alexithymia

levels, as well as DIF and DDF were unrelated to substance use levels. Comparing the matched groups of high and low EOT showed that individuals with high EOT were nearly twice as likely to report binge drinking and daily smoking compared to the low EOT group.

Our findings add knowledge into the role of individual alexithymia dimensions in mental health. Previous research consistently shows that while DIF and DDF strongly associate with depressive and anxiety symptoms, EOT does not (Grabe et al. 2004; Chen et al. 2011; Kajanoja et al. 2017). It has even been speculated that EOT could serve as a protective factor in alexithymic individuals. However, we argue that the issue is likely to be more complex than that. Recently, Preece et al. have suggested that DIF/DDF and EOT may represent problems in different phases of emotion regulation. Their attention-appraisal model of alexithymia holds that DIF/DDF may constitute a difficulty in the conscious appraisal of emotional information (distinguishing the meaning and significance of emotional information), whereas EOT could arise from a deficit in the attentional phase (less attention allocated to emotional content and stimuli) (Preece et al. 2017). Our findings, as well as previous research on alexithymia subtypes may support the attention-appraisal model, as DIF/DDF and EOT seem to be associated with different risk profiles in terms of mental health (Chen et al. 2011; Alkan Härtwig et al. 2013; Ueno et al. 2014; Kajanoja et al. 2017). Specifically, inattention and disinterest in emotional information as characterized by EOT, may protect those with alexithymia from depression and anxiety, but instead predispose them to regulate emotions by substance use, and perhaps other externalizing behaviors.

6.3 Alexithymia, Overweight and Gestational Diabetes in Pregnant Women (Study III)

We examined associations between alexithymia levels, BMI and gestational diabetes in pregnant women. The main finding of this study was that expecting mothers with high levels of alexithymia had a markedly higher BMI, and an increased prevalence of overweight (66% vs. 34.8%) compared to those with low or moderate levels of alexithymia. Several previous studies have similarly associated alexithymia with overweight, obesity and metabolic problems (see section 2.7.5). However, most have not differentiated between alexithymia dimensions. We found that the alexithymia dimension EOT accounted for the associations between alexithymia and BMI. EOT was also the only dimension of alexithymia that was associated with an increased prevalence of gestational diabetes. This is an important finding because EOT, as opposed to the affective component of alexithymia (DIF & DDF) is usually unrelated to depressive and anxiety symptoms, as was the case in our study. Therefore, the

association between EOT, BMI and gestational diabetes seems to be independent of mood and anxiety.

The results are partially in line with previous studies. In the study by Fukunishi & Kaji (1997), EOT was also the only alexithymia factor related to obesity. In contrast, other studies have reported that all alexithymia dimensions, or only DIF and DDF have been associated with obesity (Elfhag & Lundh 2007; Pinna et al. 2011). One explanation for this discrepancy might be that our study sample was relatively healthy, and we measured overweight instead of obesity, as only few individuals in our sample met the criteria for obesity. For example, in the study sample of Elfhag & Lundh (2007), the average BMI was higher than in our study, and a number of participants fulfilled the criteria for binge-eating disorder, which was most strongly correlated with the alexithymia dimension DIF.

Several possible mechanisms could explain the link between alexithymia, overweight and gestational diabetes. As reviewed in section 2.7.5, alexithymia associates with an unhealthier diet and emotional eating which both promote weight gain. For example, Pink et al. (2019) recently found that DIF and DDF were associated with a higher BMI, and the relationship was largely mediated by negative affect and emotional eating. There was also an association between EOT and higher BMI, but instead of emotional eating, it was mediated by negative urgency. This is logical given that EOT is not associated with negative affect. Chronic stress could also contribute to the dietary habits and metabolic problems in alexithymia. Chronic stress is an important risk factor for several addictive behaviors and is associated with unhealthier and more energy-dense food choices leading to weight gain (Dallman 2010; Sinha 2018).

Our results are especially interesting because they share parallels with the concepts of internalizing and externalizing problems: The alexithymia dimensions DIF and DDF are strongly correlated with negative affect and an increased prevalence of depression and anxiety disorders, suggesting that DIF and DDF could be conceptualized as internalizing traits. EOT on the other hand seems to have no effects on mood or anxiety, but instead seems to associate with lower empathy (Grynberg et al. 2010), increased substance use (Kajanoja et al. 2018) and primary psychopathic traits (Lander et al. 2012), reflecting an externalizing trait. Therefore, it could be that the individual alexithymia dimensions may contribute to overweight by different pathways. As implied by the results of Pink et al. (2019), individuals with difficulties in the affective dimension of alexithymia (DIF & DDF) may be more prone to emotional eating due to negative affect. The positive association between EOT and negative urgency on the other hand implies that EOT may predispose to externalizing behaviors such as addictive use of substances and possibly food.

6.4 Alexithymia and hair cortisol concentrations in pregnant women (Study IV)

We found that pregnant women with moderate to high alexithymia levels had higher hair cortisol concentrations compared to those with low levels of alexithymia. Additionally, in the whole sample, DIF was positively associated with HCC. Importantly, the association between alexithymia and HCC was independent from depressive symptoms. This is in line with the 'alexithymia-stress -hypothesis' (Martin & Pihl 1985), arguing that the decreased emotional awareness in alexithymics may in itself contribute to chronic physiological stress. In previous studies alexithymia has been associated with altered HPA-axis activity in the context of acute social stress (de Timary et al. 2008; Hua et al. 2014). Other studies have shown altered immune activity and increased inflammation in alexithymia (Honkalampi et al. 2011; Honkalampi et al. 2014), possibly also indicating physiological consequences of chronic stress.

As discussed in section 2.7 and 2.8, alexithymia is transdiagnostically associated with impaired physical and mental health. Many of the diseases and disorders that are more common in those with alexithymia are considered at least partially related to chronic stress, such as depression, substance abuse, obesity and cardiovascular disease (Hammen 2005; Dimsdale 2008; Sinha & Jastreboff 2013). Therefore, chronic stress due to impaired emotional processing is a plausible candidate explaining the associations between alexithymia and health problems. However, as our study sample consisted exclusively of pregnant women, and pregnancy itself likely affects cortisol levels (Mustonen et al. 2018), the results need to be replicated in more diverse populations.

Our previous findings show that alexithymia dimensions differentially affect mental health outcomes. We have hypothesized that DIF/DDF may predispose to internalizing problems such as depression and anxiety, whereas EOT may predispose to externalizing problems such as substance abuse and overeating. Therefore, we expected all alexithymia dimensions to be related to increased HCC, despite of their differential associations with health outcomes. Interestingly, only the DIF dimension showed an association with HCC. This might be explained by the fact highly alexithymic women tend to generally score higher in DIF, whereas men score higher in EOT. Another explanation is that if EOT is associated with chronic stress, it may be mediated by substance use, which in our sample was negligible due to pregnancy. This is another reason why it is important to replicate the findings in more diverse samples including men.

The association between HCC levels and alexithymia specifically in pregnant women is important because it may have transgenerational effects for offspring health. Circulating maternal glucocorticoids can at least partially pass the placenta and they play crucial roles in normal fetal development. However, excessive

exposure to glucocorticoids, e.g. due to maternal stress or external glucocorticoid treatment, may harmfully affect the fetus and have long-term adverse effects for brain development (Seckl & Holmes 2007; Charil et al. 2010). Animal models suggest that prenatal stress or glucocorticoid treatment induces permanent changes in the offspring, increasing the risk for neurodevelopmental disorders (Seckl & Holmes 2007). Human studies similarly show that both prenatal stress and glucocorticoid levels in pregnant mothers can affect later socioemotional functioning and brain structure of the child (Buss et al. 2012; Madigan et al. 2018). Therefore, theoretically, alexithymia could be transferred intergenerationally via maternal prenatal stress. However, this possibility remains speculative, and future research will need to address possible effects of maternal alexithymia for fetal and child development.

6.5 Alexithymia, Depression, Adult Attachment and Early-life Adversities (Study V)

We found that alexithymia was specifically associated with childhood experiences of emotional neglect, whereas depression was more broadly connected to several types of early-life adversity. Our findings clarify the overlap and differences between depression and alexithymia and suggest partly different recollections of childhood experiences underlying these two conditions. Experience of childhood emotional neglect increased the prevalence of alexithymia nearly fourfold, and the majority of participants with high alexithymia reported experience of emotional neglect. Previous studies have consistently found an association between alexithymia and CM, particularly emotional neglect (Aust et al. 2013; Brown et al. 2016). Our findings add support to this evidence, and further show that the relationship between alexithymia and CM may be specifically explained by emotional neglect, as no other type of CM increased the prevalence of alexithymia. Brown et al. (2016) recently reported similar findings, showing that all forms of CM were associated with alexithymia, but in the path analyses, emotional neglect was the only form of CM uniquely contributing to alexithymia. They argued that emotional forms of CM may particularly disturb the development of affect regulation.

Lyvers et al. (2019) have studied alexithymia in the context of alcohol abuse and have proposed that alexithymia may result from problematic parental bonding in childhood, leading to an insecure attachment style and deficient emotion regulation in adulthood. Our findings suggest that both attachment anxiety and avoidance are related to alexithymia, but attachment avoidance was more closely associated with it. Attachment theories hold that children may develop an avoidant style of attachment if caregivers habitually dismiss their emotional needs (Miculincer & Shaver 2012; O'Loughlin et al. 2018). Avoidantly attached individuals rely on self-

sufficiency and independence and show a decreased tendency to seek social support in distressing situations (Mikulincer & Shaver 2019). Our results on the specificity of emotional neglect in predicting alexithymia fit this theory well, supporting the view that emotional neglect in childhood may lead to attachment problems and alexithymia. However, as we only measured attachment style in adulthood, and could not directly assess childhood attachment, reverse causality cannot be ruled out. It is also possible that alexithymia itself may predispose to interpersonal problems and attachment insecurity.

Regarding the overlap and differences between alexithymia and depression, we found that only a minority of depressed individuals were highly alexithymic. Depression with concurrent alexithymia was associated with remarkably high levels of emotional neglect and attachment avoidance. This suggests that alexithymic depression may a specific subtype, arising from certain types of childhood experiences and attachment problems. Recently, the idea of ecophenotypes of depression has been put forward (Teicher et al. 2013). Evidence implies that depression with a history of self-reported CM may be by nature different compared to depression without adverse childhood experiences. The maltreated ecophenotype of depression has been associated with aberrant brain structure and function in limbic areas, as well as diminished responses to antidepressant treatment (Teicher et al. 2013; Williams et al. 2016; Opel et al. 2019). We hypothesize that depression with concurrent alexithymia may similarly represent a subtype of depression that is more closely related to adverse childhood experiences and attachment insecurity. Interestingly and similarly to depression with childhood maltreatment, alexithymic depression may also be associated with poorer responses to antidepressants (Ozsahin et al. 2003). Therefore, patients suffering from depression with concurrent alexithymia may benefit more from psychosocial treatments focusing specifically on early emotional neglect and attachment insecurity.

Some gender differences were observed in terms of CM prevalence and psychopathology. Women reported more emotional and sexual abuse compared to men. Prevalences of other types of CM showed no gender differences. Emotional and physical neglect were the most common types of CM, and emotional neglect was strongly associated with both depression and alexithymia. This is an important finding as many studies exploring the effects of CM have not included childhood neglect (Stoltenborgh et al. 2013). Regarding gender differences in depression, depressed men had higher levels of alexithymia and attachment avoidance compared to depressed women. Furthermore, emotional neglect was a unique predictor of both depression and alexithymia in men. This implies that emotional neglect and alexithymia may be particularly relevant in men's depression. This difference may be explained by cultural factors, as several researchers have argued that the higher prevalence of alexithymia in men could be due to cultural influences that discourage

the expression of emotion in boys and young men (Le et al. 2002; Levant et al. 2009). Therefore, an emotionally distant family environment may enhance these cultural influences and hinder the development of emotional awareness and expression in men particularly.

6.6   Limitations

This study has several limitations that should be addressed. Firstly, the prevalence of alexithymia in our sample was relatively low compared to estimates from the general population. We conducted attrition analyses for study I and found that the low prevalence of alexithymia is likely due to non-random attrition. That is, participants who dropped out of the study before the 6-month timepoint where we administered the alexithymia questionnaire, had lower education, were more likely to be men, and had higher depressive scores, all of which are also associated with alexithymia levels. Sample selection bias may also partly explain the low prevalence of alexithymia in our cohort. As alexithymia is associated with interpersonal problems especially in intimate relationships, it might be that this trait is underrepresented in a population having a baby.

Secondly, even though many outcomes were assessed during the women's pregnancy (hair-cortisol concentrations, substance use, BMI and gestational diabetes), alexithymia levels in our sample were assessed 6 months after giving birth. In theory, this might distort some associations between alexithymia levels and outcomes. However, even though alexithymia seems to have both state and trait components, it has been shown to be a highly stable across time (Saarijärvi et al. 2006; Hiirola et al. 2017). One study has also shown high stability in alexithymia levels across the perinatal period (Le et al. 2007).

Another potential limitation is our use of self-report questionnaires. The problems of measuring alexithymia by self-report questionnaires are discussed in section 2.3. However, the TAS-20 is considered to have good validity and reliability in measuring alexithymia and is widely used. Self-report measures early-life adversity have also been recently criticized (Colman et al. 2016; Baldwin et al. 2019), as they are subject to recall bias and correlate poorly with objective measures. Nonetheless, they are widely used in childhood maltreatment research, and recent studies have shown that self-report measures of CM predict abnormalities in brain structure and functions in the limbic areas, independent of psychiatric symptomatology (e.g. Teicher & Samson 2013; Opel et al. 2019). This strongly supports their value in psychopathology research. Self-report measures of substance abuse are also likely subject to underreporting, especially during pregnancy (Ernhart et al. 1988). Despite of this, they are considered sufficiently reliable and are widely used (Poikolainen et al. 2002). Information on pre-pregnancy weight was also based

on self-report, although drawn from the National Birth Registers. However, height was measured, and pre-pregnancy weight inquired at a doctor's visit in gestational week 12. Therefore, significant errors concerning information on BMI are unlikely.

7   Conclusions

As expected from previous research on alexithymia subtypes, we found that different dimensions of alexithymia showed differential associations with mental and physical health, physiological stress as well as early-life adversity. These findings underscore the need to treat alexithymia as a multidimensional phenomenon, with its individual facets having unique impacts on mental and physical health. The findings also imply that although many alexithymic individuals may not suffer from depressive or anxiety symptoms, they may still be at an increased risk for other medical problems such as substance abuse, metabolic problems or chronic physiological stress. This vulnerability may be due to problems in emotion regulation that are at least partially independent of psychiatric symptoms, but this remains a topic for future studies to address. The specificity of self-reported emotional neglect in predicting alexithymic traits illuminates the possible origins of this condition and its relationship with depression. Psychosocial treatment efforts directly addressing childhood experiences of emotional neglect and attachment insecurity should be investigated in the context of alexithymia.

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