Univerzita Karlova v Praze

1. lékařská fakulta

Studijní program: Psychologie

Studijní obor: Lékařská psychologie a psychopatologie

MUDr. Tomáš Uher

Psychoneuroimunologie alexithymie
Psychoneuroimmunology of alexithymia

Typ závěrečné práce

Disertační

Vedoucí závěrečné práce/Školitel: Doc. RNDr. Petr Bob, Ph.D.

Praha, 2012

Prohlášení:

Prohlašuji, že jsem závěrečnou práci zpracoval samostatně a že jsem řádně uvedl a citoval všechny použité prameny a literaturu. Současně prohlašuji, že práce nebyla využita k získání jiného nebo stejného titulu.

Souhlasím s trvalým uložením elektronické verze mé práce v databázi systému meziuniverzitního projektu Theses.cz za účelem soustavné kontroly podobnosti kvalifikačních prací.

V Praze, 07.03.2012

Jméno - Příjmení: Tomáš Uher

Podpis:

Identifikační záznam:

UHER, Tomáš. *Psychoneuroimunologie alexithymie. [Psychoneuroimmunology of alexithymia]*. Praha, 2012. Počet stran 110. Dizertační práce (Ph.D.). Univerzita Karlova v Praze, 1. lékařská fakulta, Psychiatrická klinika. Školitel: Doc. RNDr. Petr Bob, Ph.D.

CONTENT

1. Theoretical introduction and review of literature

1.1. INTRODUCTION

A core principle of current medicine is the „biopsychosocial“ model of human illness that implicates close connection among various ethiological factors in disease initiation and progession (Engel, 1977). Coexistence of those factors historically initiated the term „psychosomatic illness“, which denotes that medical disorders may be signicantly influenced by psychological factors (Levenson and James, 2006). Further development of this concept within the framework of psychosomatic medicine emphasized physiological interactions between psychological states, emotions, autonomic, neuroendocrine and immunological response and implicated its broader implications in biological sciences and medicine. Attempts to explain basic psychological characterists and pathophysiological processes in psychosomatic patiens generated several theories that have emerged in the recent decades. Hypothesis that aversive emotional states are associated with adverse health outcomes (Kiecolt-Glaser et al., 2002) and that interference with the experience or expression of emotions, particulary negative, can have negative affect on health belong among most important principles (Levenson, 1994; Lane, 2008). In this context, physiology of emotions represents important area in the field of psychosomatic research. Consecutive research has confirmed this assumption in numerous studies and emhasized evidence that dysregulation of an emotional experience and its expression has negative effects on health of the individual (Taylor, 1987; Kiecolt-Glaser et al., 2002; Guilbaud et al., 2003). Already Alexander (1943, 1950) has proposed that some specific changes of mental functions and typical alterations in cognitive and affective functioning may cause psychosomatic diseases. Alexander suggested that not only onset, but also a course of many somatic illnesses are influenced by repression of certain conflicting ideas and related emotional disturbances. Conceptualisation of psychosomatic disorders by Ruesch in 1948 has pressumed that a deficit or developmental arrest in the capacity of symbolic mental representations of emotions is a basic dysfunction in psychosomatic patients. Further research in this direction has led to development of a model connecting the psychosomatic diseases with functions of the „visceral brain“ (MacLean, 1949). This model suggested that when emotional feelings do not find expression and discharge in the symbolic use of words and behaviour, emotions may be „transformed“ into somatic states as an„organ language“. French psychoanalytic researchers Marty and M'Uzan (1963), coined the term „pensée opératoire“ which means, "operativ thinking“ and decribes characteristic signs of psychosomatic pacients mainly characterized as behavior without emotions as a consequence of stress-induced internal psychic arousal (Nemiah, 2000).

Nemiah and Sifneos in 1970s have observed that many patients with the so-called "psychosomatic" diseases have deficits in capacity of symbolization of emotions, verbal behavior, fantasies, and dreams and also failure to respond to dynamic

psychotherapy. The authors have proposed that these features can cause various symptoms including physiological dysfunctions that may result in various illnesses, dispositions to impulsive behavior, discomfort or avoidance of social relationships and decreased capacity for self-care and self- regulation. This hypothesis has afterwards evolved into the concept of alexithymia proposed by Sifneos in 1973. Alexithymia concept today represents one of the key concepts in psychosomatic medicine that links the influence of emotions and personality types and/or features on physical illnesses and health. Sifneos (1994, 1996) used the term „alexithymia" in order to describe one of the basic traits of psychosomatic patients that is characterised by diminution or absence of the ability to experience feelings which is one of the most strikikng human characteristics. From the beginning of the alexithymia research it was hypothesized that alexithymic features of the personality can influence and even contribute to the development or maintanence of psychosomatic illness (Bach and Bach, 1995; Ahlberg et al., 2004). Some authors also emphasized focus on alexithymia research in order to find appropriate procedures for treatment of psychosomatic patients. Further research has confirmed the hypothesis suggesting significant association between alexithymia and psychosomatic complaints (Sifneos 1973, 1975; Krystal 1979; Cooper and Holstrom, 1984).

Worthy of mentioning is also the fact that alexithymia concept has continuosly underwent its development. Originally alexithymia concept has evolved from the field of psychoanalysis, but consequently the wider scientific arena has taken an interest in alexithymia research (Bagby and Taylor, 1997; Lane et al., 1997, De Gucht and Heiser, 2003). Although the alexithymia concept origins in the area of psychosomatics (Nemiah and Sifneos, 1970; Sifneos, 1973), later focus on alexithymia significantly extended on general aspects of emotional influences on mental and somatic health (Taylor et al., 1991). Following this progress alexithymia developed into clinically relevant concept confirmed by a large body of empirical data (Taylor et al., 1997; Taylor, 2000, Taylor and Bagby, 2004) and currently the Pubmed database includes more than 1500 journal articles focused on alexithymia.

1.2. DEFINITION OF ALEXITHYMIA CONCEPT

Since the 1970s many researches have contributed to the development of alexithymic concept (Taylor et al., 1991, 1997). Today alexithymia represents multidimensional construct that generally reflects deficits in the cognitive processing and the regulation of emotions, which remain undifferentiated, poorly regulated and disrupted from conscious experience (Lane et al., 1996, 1997; Taylor et al., 1991; Larsen et al., 2003; Taylor and Bagby, 2004; Bermond et al., 2006). Some authors conceptualized alexithymia as a deficit in both cognitive and affective aspects of the mental emotional responses (Vorst and Bermond, 2001) and found that alexithymic features are distributed continuously in the general population (Bagby and Taylor, 1997). The term

alexithymia was coined by Sifneos in 1973 and in exact translation means „ no words for feelings "; „absence of words for emotions", or „without words for emotions". The Greek designation alexithymia is based on a few Greek words as follows: a = lack, lexis = word, thymos = emotion. The core features of alexithymia include a set of four basic cognitive-affective deficits characterised by a deficit in experience and identifying of various feelings, deficits in introspective ability to describe feelings, decreased fantasy and externaly oriented cognitive style (Nemiah and Sifneos, 1970; Sifneos, 1972; Nemiah et al., 1976; Taylor, 2000).

Typical characteristics of alexithymic persons are:
1. They report less emotional experiences and deficit in reaching the conscious awareness of emotions. Alexithymia also involves a marked deficit in identifying one's own emotional states, deficit in distinguishing between various feelings and little insight into his/her own feelings and psychosocial processes (Sifneos 1973; Nemiah et al., 1976). In addition, there is difficulty in distinguishing between emotions and verbally communicating feelings (Nemiah and Sifneos, 1970; Sifneos, 1972; Nemiah et al., 1976; Taylor, 2000). Some authors have proposed that alexithymic persons might be emotionally aroused just as much as non-alexithymic ones, however, they would report they do not feel anything or do not know how they feel, and consequently can not regulate their emotional states (Lane et al., 1997). Such impairment could lead to a relative inability to use one's own emotions to guide adaptive behaviour (Ogrodniczuk et al., 2011). Alexithymia is also characterised by difficulty in differentiating emotions from physiological states and a tendency to somatization (De Gucht and Heiser, 2003; Taylor and Bagby, 2004). In this context it has been observed association between alexithymia and an impaired capacity for emphaty (Guttman and Laporte, 2002). This relationship might be explained with the model of "shared network" suggesting that the networks responsible for processing of emotions in the self are the same networks used to represent the emotions of others (Singer et al., 2004, 2006; Bird et al, 2010).
2. Alexithymic persons are also characterized by deficits in describing and expressing one's own emotional states with propensity to offering undifferentiated descriptions of emotional experiences. Another typical feature is defined by limited capacity to elaborate upon emotional experience and a limited capacity to symbolize emotions (Nemiah and Sifneos, 1970; Sifneos, 1972; Nemiah et al., 1976, Taylor, 2000). Alexithymic subjects occasionally describe emotional experiences, however that is stereotyped and at time wooden. This observation could be explained by findings, that exteroceptive pathway processing emotional information could be intact, suggesting that in some situations alexithymic individuals describe emotions that they think they should feel based on exteroreceptive cues, but do not consciously experience them (Lane et al., 1997). In this context it has been proposed that alexithymic individuals are like colorblind subjects, who learn to associate certain color words with objects, e.g. , green for grass, even though they do not experience the green per se (Krystal, 1979; Lane et al., 1997).

3. Alexithymic persons have paucity of fantasies, impoverished fantasy life and limited imagination abilities (Sifneos, 1973; Warnes, 1986; Taylor, 2000).
4. It can be also observed an externaly oriented cognitive style that engages in externally oriented rather than psychologically minded thought (Sifneos, 1973; Nemiah et al. 1976).

There are also some other psychological features that are commonly associated with alexithymia. For example, alexithymic subjects sometimes manifest propensity to impulsive behaviour (Warnes, 1986; Taylor, 2000) and flattened emotions accompanied by random and abrupt emotional outbursts which they cannot interpret (Nemiah and Sifneos, 1970). Alexithymia could be also associated with a deficit in maintaining the voluntary control of emotions, overcontrol of their internal needs, exagaggerated defensive system (Gu et al., 2008) and personality dimensions as introversion, neuroticism, and low openness (Bagby et al., 1994b).
In agreement with other authors (Taylor et al., 1985; Hendryx et al., 1991), Bermond et al. (1999, 2006) defines alexithymia as an inability to complete emotional experience, which means, that the person is not able to experience feelings, differentiate between feelings, verbalize emotional experiences, reflect and fantasize about them.

Table 1a. The most and least characteristic features of alexithymia according to the California Q-set (CAQ) (adapted from Haviland and Reise, 1996).

Extremely characteristic	1. Is emotionally bland; has flattened affect. 2. Anxiety and tension find outlet in bodily symptoms. 3. Is concerned with own body and the adequacy of its physiological functioning. 4. Emphasizes communication through action and nonverbal behaviour. 5. Keeps people at a distance; avoids close interpersonal relationships.
Quite Characteristic	1. Has a brittle ego-defense system; has a small reserve of integration; would be disorganized and maladaptive when under stress or trauma. 2. Judges self and others in conventional terms like "popularity," "the correct thing to do," social pressures, etc. 3. Is uncomfortable with uncertainty and complexities. 4. Handles anxiety and conflicts by, in effect, refusing to recognize their presence; repressive or dissociative tendencies. 5. Tends toward overcontrol of needs and impulses; binds tensions excessively; delays gratification unnecessarily.
Extremely Uncharacteristic	1. Engages in personal fantasy and daydreams, fictional speculations. 2. Has insight into own motives and behavior. 3. Has warmth; has the capacity for close relationships; compassionate. 4. Is introspective and concerned with self as an object. 5. Enjoys esthetic impressions; is esthetically reactive.
Quite Uncharacteristic	1. Is skilled in social techniques of imaginative play, pretending, and humor. 2. Is socially perceptive of a wide range of interpersonal cues 3. Responds to humor. 4. Initiates humor. 5. Is concerned with philosophical problems; e.g., religions, values, the meaning of life, etc. 6. Enjoys sensuous experiences (including touch, taste, smell, physical contact). 7. Is facially and/or gesturally expressive.

1.3. STABILITY OF ALEXITHYMIA

A core issue of alexithymic manifestations is a level of their stability during individual life (Sifneos, 1973; Taylor and Bagby, 2004; Luminet et al. 2007). In this context, alexithymia as a stable personality trait has been demonstrated in several longitudinal studies in variuos populations (Schmidt et al., 1993; Salminen et al., 1994; Wise et al., 1995, Porcelli et al., 1996; Luminet et al., 2007; Tolmunen et al., 2011). On the other hand several research data has shown that alexithymia could also present a state-like secondary phenomenon (Freyberger, 1977) and some findings suggest that alexithymia could represent consequence of psychological distress and a response to cope with distress of depressive symptoms like emotional pain, aversive memories and psychological arousal (Freyberger, 1977). These data have led to distinguishing specific forms of alexithymia and definition of primary secondary alexithymia. Primary alexithymia is defined as a disposition factor, and stable long-term trait developed very early in life and possibly genetically and neurologically based. On the other hand secondary alexithymia is defined as state-like phenomenon related to protective and defence mechanisms, frequently developed to psychological trauma or response on serious somatic illness and comorbid conditions (Freyberger, 1977; Wise et al., 1990a, 1990b; Horton et al., 1992; Fukunishi et al., 1997a, 1997b; Honkalampi et al., 2001a, 2001b; Saarijarvi et al., 2000, 2006; Joukamaa et al., 2003; Taylor and Bagby, 2004; Marchesi et al., 2008; Tolmunen et al., 2011). In principle, these data are in agreement with findings reported by cross-sectional and follow-up studies that examined levels of stability in alexithymia (Salminen et al., 2006; Marchesi et al., 2008; Tolmunen et al., 2011) and found absolute, as well as relative stability of alexithymia (Tolmunen et al., 2011). The absolute stability of alexithymia is present when the TAS scores of a subject remain the same during lifetime and is less dependent or independent on actual life events (De Timary et al., 2008a). For example, absolute stability of alexithymia has been observed in the study performed on 755 subjects (from general Finish population) which shown that 63.8% of the subject remained alexithymic after 11-year follow up (Tolmunen et al., 2011). Similarly, Tolmunen et al. (2011) found that correlations of alexithymia and its subscales between baseline and follow-up scores are significantly high ($p = 0.51$-0.63).

Together these findings suggest that relative stability of alexithymia occurs when positive and highly significant correlations between total alexithymia scores and its subscales in several follow-up periods are present (Santor et al., 1997; Mikolajczak and Luminet, 2006; De Timary et al., 2008a).

Based on these findings alexithymia likely is a personality trait as well as a state-dependent phenomenon. A balance between the trait and state components of alexithymia vary among people and situations (Lumley et al., 2007) or it may be understood as a personality trait consisted of both trait and state components (Tolmunen et al, 2011) which may explain its relative stability (Taylor and Bagby, 2004; Marchesi et al., 2008). In this context, the issue of alexithymia stability during the time is likely related to stability of other personality features which may depend on a

level of stressful life events that influence mental instability due to a need to use various forms of adaptive or maladaptive behavior that may significantly change personality profile related to mental and behavioral patterns.

1.4. TYPES OF ALEXITHYMIA

Main historical description of alexithymia types provided Freyberger (1977) in his concept of primary and secondary alexithymia but also other authors such as Bermond (Bermond et al., 2006) and Chen (Chen et al., 2011) described different subtypes of alexithymia based on a distribution of various alexithymic features and its association with occurrence of different behavioural manifestations.

Freyberger´s primary and secondary alexithymia:
Freyberger (1977) has distinguished alexithymia in patients with somatic disorders into two subtypes and defined the terms: primary and secondary alexithymia. Primary alexithymia was defined as a disposition factor, representing a stable long-term trait developed early in life and possibly genetically or neurologically based. On the other hand secondary alexithymia was defined as state-like secondary phenomenon related to protective and defence mechanisms as a response to psychological trauma or serious somatic illness.

Bermond´s three subtypes of alexithymia:
Bermond and coworkers (2006) based upon phenomenological analyses have proposed three subtypes of alexithymia.
Type-1: is characterized by an absence or low level of conscious awareness related to emotional arousal and the emotion accompanying cognitions.
Type-2: is characterized by higher degree of emotional experience but an absence of the normally accompanying cognitions.
Type-3: is characterized by low affective and high cognitive processing of emotions capacities.
Subjects with normal affective and cognitive processing of emotions were asigned as lexithymic.
It has also been suggested that the alexithymia of the Type-1, may be predominantly biologically determined, while alexithymia of the Type-2, may be trauma-related (Bermond et al., 2006). The author has also suggested that each of these alexithymic subtypes might be related to the different neuronal or functional deficit (Bermond et al., 2006).

Chen´s three subtypes of alexithymia:
Chen and collegues (2011) focused their research on assessment of emotional expression and regulation, and studied the alexithymia as a dimensional construct.

They described subtypes of alexithymia in a sample of 1788 healthy students and found that alexithymia scores are differentielly associated with emotional regulation suggesting three subtypes of alexithymia which may be characterised by different behavioural manifestations. They proposed three distinct units related to typology conditions:

1. Extrovert-high alexithymia (EHA) characterized by high score on Externally Oriented Thinking (EOT) subscale of the TAS (Toronto Alexithymia Scale) but normal score on the other alexithymic subscales.
2. General-high alexithymia (GHA) characterized by general high scores on all three factors. This type of alexithymia is similar to the type-I of the Bermond´ classification.
3. Introvert-high alexithymia (IHA) characterized by high scores on Difficulty Identifying Feelings (DIF) subscale and Difficulty Describing Feelings (DDF) subscale, but low score on EOT subscale of the TAS.

The GHA and IHA are defined by suppressive character of emotional regulation and expression with worse emotion status as compared to the EHA and NA. GHA and IHA are marked by poorer emotional regulation and expression with worse emotional status. EHA seems to be modest in emotional status, with better emotion regulating as compared to the GHA (Chen et al., 2011). These findings suggest that several subtypes of alexithymia with different emotional expression and regulation abilities could be present, but further investigation is needed to confirm these results.

1.5 EPIDEMIOLOGY OF ALEXITHYMIA

The prevalence of alexithymia is most frequently described as a percentage of the subjects in population reaching total score of Toronto Alexithymia Scale (TAS) ≥74 (TAS-26) (Taylor and Bagby, 1988) respectively ≥61 (TAS-20) (Bagby et al., 1994a). With respect to this definition the prevalence of alexithymia in the large adult comunity samples was repeatedly amounted to be around 10-20% (Salminen et al., 1999; Honkalampi et al., 2000a; Quinton and Wagner, 2005; Moriguchi et al., 2007). On the other hand the prevalence of alexithymia in clinical samples with some mental health and somatic disorders were significantly higher, amounted to be between 13,8 % (Prochnow et al., 2011) and 77% (Eizaguirre et al., 2004; Parling et al., 2010).

The gender differences in alexithymia epidemiology were not confirmed (Joukamaa et al., 1996; Moriguchi et al., 2007) and the results were variable (Kokkonen et al., 2001; Parker et al., 2003; Franz et al., 2008). Therefore today it is not possible to conclude if any gender associated differences in alexithymia are present or not. Several studies also have shown positive association between alexithymia and age (Salminen et al., 1999; Honkalampi et al., 2000b, Parker et al., 2003; Onor et al., 2010). Some authors tend to explain this observation by age-related poorer neurocognitive abilities (Onor et al., 2010) but there are also several studies that have found conversely negative associations between age and alexithymia (Moriguchi et al., 2007; Säkkinen et al.,

2007). In addition alexithymia has been found associated with some epidemiological data, for example living alone or broken family (Kokkonen et al., 2001; Franz et al., 2008), lack of relationships and close friends (Mattila et al., 2010a), lower educational level, life dissatisfaction (Mattila et al., 2007) and poorer socio-economic situation (Honkalampi et al., 2000b; Kokkonen et al., 2001; Parker et al., 2003; Franz et al., 2008). Worthy of the mentioning is also that several shortcomings of the alexithymic epidemiological studies could be responsible for the equivocal results of some studies. Firstly, use of different alexithymia measures may be partialy responsible for this variability. Moreover the majority of the population studies were performed mostly in countries as Finland, Germany, Japan, USA and Italy. This in fact could also influence previous results, because alexithymia scores may vary across different ethnic groups, populations and language versions (Dion, 1996; Kooiman et al., 2002; Le et al., 2002; Müller et al., 2003; Lumley et al., 2005). It was assumed that these intercultural differences could be results of the differences in the cultural value of attending to and expressing feelings and differences in socioeconomic factors such as education and income (Dion, 1996; Salminen et al., 1999; Lumley et al., 2005).

1.6. MEASUREMENT OF ALEXITHYMIA

Symptoms of alexithymia are generally distributed in the population (Bagby and Taylor, 1997), which enables to establish empirically cut-off scores distinguishing alexithymic and non-alexithymic individuals (Taylor et al., 1988; Bagby et al., 1994a and 1994b; De Gucht and Heiser, 2003). Well-known measure of alexithymia presents self-reported questionnaire Toronto Alexithymia scale (TAS), but also other instruments for assesment of alexithymia have been developed. For example, other useful self-report instruments are the California Q-set (CAQ) (Haviland and Reise, 1996), The Schalling-Sifneos personality Scale (SPSS) (Apfel and Sifneos, 1979), the MMPI alexithymia subscale (Kleiger and Kinsman, 1980), the Amsterdam Alexithymia Scale (AAS) (Bermond et al., 1999), Bermond-Vorst Alexithymia Questionnaire (BVAQ) (Vorst and Bermond, 2001) and also a self-report observer Alexithymia Scale (OAS) (Haviland et al., 2000) that is completed by a subject's close person or relative. Several alexithymia clinical studies also enabled to develop structured interviews such as the Beth Israel Psychosomatic Questionnaire (BIQ) (Taylor et al., 1997), Alexithymia Provoked Response Questionnaire (APRQ) (Krystal et al., 1986), Karolinska Psychodynamic Profile (KAPP) (Weinryb et al., 1991) and other measures. As an important diagnostic complement for assesment of alexithymia may be used projective measures such as the Scored Archetypal Test (SAT9) (Cohen et al., 1985) or the Roschach (Acklin and Alexander, 1988). It is needed to mention that not all those measures have shown satisfactory psychometric characteristics (Linden et al., 1995; Taylor et al., 1997; Kooiman, et al., 2002; De Gucht and Heiser, 2003).

The self-report Toronto Alexithymia scale (TAS) is the first instrument that was made with concern for test development procedures and psychometric quality (De Gucht and Heiser, 2003). In the developing and improving of psychometric characteristics of TAS, subsequenly three versions of the TAS have been evolved: first version was the TAS-26 (with 26 items), second version the TAS-R (Revised Toronto Alexithymia Scale with 23 items) and definite currently used version is the TAS-20 (with 20 items). All the versions of TAS differ from each other with respect to total number of items and factor structure (De Gucht and Heiser, 2003). The basic three dimensions of TAS included in all three versions are: (1.) difficulties to identify feelings and distinguish between feelings and bodily sensations (DIF), (2.) difficulties to describe feelings (DDF) and (3.) externally oriented thinking (EOT) (Bagby et al., 1994a, 1994b). Contrary to the TAS-26, alexithymia measured by the TAS-R and the TAS-20 is not totaly theoretically consistent with the alexithymia construct as originally it was defined because one of the subscales („reduced daydreaming“) was excluded from the subsequent versions of TAS because of theoretical incoherency with the other TAS subscales (De Gucht and Heiser, 2003). Although TAS-20 is reliable, valid and today most used meassure instrument it has several limitations (Taylor and Bagby, 2004). First of these limitations is that DIF and DDF represent very similar constructs (Kooiman, et al., 2002; Hintikka et al., 2001). In addition it has been found that the reliability of the EOT subscale is substantialy lower than other subscales (Bagby et al., 1994a, 1994b; Kojima et al., 2001; Kooiman, et al., 2002) but as a result of various studies has been suggested that total score of TAS-20 presents valid and reliable measure and has been recommended by some authors for clinical assessment (Kooiman, et al., 2002).

Another limitation of the TAS represents the fact, that personal standards might influence TAS score. For example it was observed that respondents with high levels of perfectionism scored higher on the TAS-20 (Lundh et al., 2002, Parling et al., 2010).

In addition, alexithymia might be strongly influenced by depression and other psychopathological states (Wise et al., 1988; Honkalampi et al., 2000b, 2001b, 2010). In this context, later developed clinical instruments such as BVAQ or BIQ (Taylor et al., 1997), have been found as less sensitive to a subjective emotional state and they have been proved as more specific alexithymia measures (Vorst and Bermond, 2001).

Some researchers have also critized the TAS for not taking into account the affective component of alexithymia, and concentrating only on its cognitive component (Bermond et al., 2010). Although alexithymia concept includes cognitive as well as affective dimension (e.g. reduced emotionalizing and fantasizing) (Nemiah and Sifneos, 1970) the TAS scales mainly focus on the cognitive aspects of alexithymia (Bermond et al., 2010). In this context, some authors suggested that several psychological and physiological responses can be differently associated with affective and cognitive component of alexithymia, which could in principle present important limitation of all the TAS versions (Bermond et al., 2010). Therefore some new measures for alexithymia, as for example the BIQ (Taylor et al., 1997) or the BVAQ according to some authors are likely more appropriate (Vorst and Bermond, 2001).

There is also evidence that TAS scores may vary across different populations and language versions (Dion, 1996; Kooiman et al., 2002; Le et al., 2002; Müller et al., 2003; Lumley et al., 2005).

With respect to these limitations, some researchers (Kooiman, et al., 2002) recommended to use the TAS-20 together with the BIQ (Taylor et al., 1997) or the NEO Personality Inventory mainly the subscales focused on „openness feelings" and „openness to fantasy" (Costa and McCrae, 1992). Some authors also recommnend to use Observer Alexithymia Scale (OAS) [completed by a subject's close person or relative] together with TAS to obtain a more complex image of alexithymia (Dorard et al., 2008; Grandi et al., 2011).

Several data suggest that there are also some other measures related to cognitive processing of emotions that may indirectly reflect alexithymia, for example Levels of Emotional Awareness Scale (LEAS) (Lane et al., 1990) or Kellner´s Emotional Inhibition Scale (EIS) (Grandi et al., 2011). The LEAS is a self-reported instrument evaluating written emotional responses to evocative interpersonal situations (Lane et al., 1998; Lumley et al., 2002; Subic-Wrana et al., 2005). Other similar measure related to cognitive processing of emotions represents Kellner´s Emotional Inhibition Scale (EIS) which is self rating scale focused on processes of conscious inhibition of emotional states (Grandi et al., 2011).

1.7. ETHIOLOGY OF ALEXITHYMIA

Although numerous studies have reported associations between alexithymia and various somatic disorders, recently there are only few studies focused on the etiology of alexithymia. Originaly alexithymia construct has been developed in the field of psychoanalysis and applied in psychosomatic medicine, which determined that most of the studies concerned in the ethiology of the alexithymia have examined a role of psychological factors mainly related to childhood family factors etc. (Berenbaum, 1996; Kooiman et al., 2004; Mason et al., 2005). Later research focused on several potential psychosocial, cultural and biological factors that likely play a role in ethiology of alexithymia suggests that ethiology of alexithymia is multifactorial, probably caused by combination of psychosocial and neurobiological factors but without results indicating reliable specificity of psychological and biological factors (Taylor and Bagby, 2004).

1.7.1. Psychosocial and cultural factors

The role of the psychosocial factors in ethiology of alexithymia was mostly developed in the area of psychoanalysis which describe alexithymia as a defense mechanism (Krystal, 1979) as a result of deficit in emotional bonding and communication between mother (caregiver) and child leading to a limited differentiation of affects (Joukamaa et al., 2003). In this context, the importance of enviromental influences on children's psychological development, especially "emotional climate" provided by parents (Nemiah, 1961) and secure attachment to parents (Fonagy and Target, 1997; Taylor et al., 1997) have been studied. The studies demonstrated, that insecure maternal attachment in early childhood (Gündel et al., 2002; Mason et al., 2005), poor family expressivenes during childhood (Berenbaum and James, 1994), overprotection by parents (Kooiman et al., 2004), born as unwanted child (Joukamaa et al., 2003), living in broken family (Joukamaa et al., 2007), general family pathology (Lumley et al., 1996b), domestic violence (Modestin et al., 2005), and history of childhood abuse (Berenbaum 1996; Joukamma et al., 2008; Evren et al., 2009) may present an important role in pathogenesis of alexithymia. Intergenerational continuum of alexithymia in families supporting the role of psychological factors has been also observed (Lumley et al., 1996b; Fukunishi and Paris 2001; Grabe et al., 2008a).

Several studies also proposed that some differences characterizing emotional expression and other differences related to socioeconomic and cultural factors related to education and social-economic status may play a role in alexithymia occurrence (Dion, 1996; Salminen et al., 1999). For example, increased alexithymia was observed in the group of Chinese speaking students compared with native English-speaking students (Dion, 1996) or people from Asian compared with the Caucasian people (Le et al., 2002). In addition, alexithymia is more strongly correlated with physical

symptoms in Asians compared with in Caucasians, which may be interpreted as a result of increased somatization of emotions among Asians (Le et al., 2002). It was also found that elevated alexithymia likely occur in the subjects living in rural areas compared to the urban areas (Joukamaa et al., 2003, 2007).
Together these data suggest that alexithymia construct is valid and its measure is replicable in various socioeconomic, cultural and ethnic environments and in this context may represent universal psychological trait reflecting emotional processing and its conscious reflection (Taylor et al., 2003).

1.7.2. Genetic factors of alexithymia

Recent findings indicate that there are several potential pathways that could be responsible for the association between alexithymia and genetic factors (Plomin and Daniels, 1987, Plomin et al., 2008). In this context, some data suggest that some genes involved in transcription of neural receptors or neurotransmitters influencing and modulating neurodevelopment could play a role in variation of alexithymia expression (Picardi et al., 2011). For example, an association between alexithymia and the stress-related catechol O-methyltransferase Val108/158Met gene polymorphism (Ham et al., 2005) has been found. Also few family studies and four genetic twin studies of alexithymia suggest that intergenerational transmission of alexithymia based on genetic factors may occur (Heiberg and Heiberg, 1978; Valera and Berenbaum, 2001; Grabe et al., 2008a). For example, significant contribution of genetic factors to interindividual differences in alexithymia has been found in two population-based studies with large groups of twin pairs published by Jørgensen et al. (2007) and Picardi et al. (2011). In the Picardi's et al. study genetic factors were accounted to be responsible for almost 42% of individual differences in alexithymia and they found significant "genetic correlation" between alexithymia and depression. They also found probable genetic link between alexithymia and depression (Picardi et al., 2011) which are frequently associated (Parker et al., 1991; Marchesi et al., 2000; Levinson, 2006; Tolmunen et al., 2011).

1.7.3. Neuropsychology of alexithymia

According to some authors alexithymic features can be the caused by different neural dysfunctions, which might result in dysregulation of emotional-physiological responses (Bermond et al., 2006). The fundamental neural structures which relevance for alexithymia is predominantly discussed are right and left hemisphere (Ross and Rush, 1981; Weintraub and Mesulam 1983; Taylor, 1984; Fricchione and Howanitz, 1985; Parker et al., 1992; Berenbaum and Prince, 1994; Spalletta et al., 2001; Aftanas et

al., 2003; Kano et al., 2003), corpus callosum (Galin, 1974; Hoppe and Bogen 1977; Buchanan et al., 1980; Tenhouten et al., 1985, 1986; Krystal, 1988; Zeitlin et al., 1989; Dewaraja and Sasaki, 1990; Ernst et al., 1999; Parker et al., 1999; Lumley and Sielky 2000; Huber et al., 2002; Grabe et al., 2004; Richter et al., 2006; Romei et al., 2008; Lang et al., 2011), anterior commissure (Bermond et al., 2006), anterior cingulate cortex (Lane et al., 1997; Lane et al., 1998; Corbetta et al., 1990, 1991; Frith et al., 1991; Paus et al., 1993; Devinsky et al., 1995; Phan et al., 2002; Gündel et al., 2004b; Bermond et al., 2006), prefrontal cortex (Krystal 1988; Kolb and Whishaw 1990; McDonlad and Prkanin 1990; Aftanas et al., 2003; Kano et al., 2003; Bermond et al., 2006), amygdala (Berthoz et al., 1999; Iversen et al., 2000; Kano et al., 2003; Bermond et al., 2006; Kugel et al., 2008; Sato et al., 2008), and insular cortex (Huber et al., 2002; Kano, et al., 2003; Silani et al., 2008).

1.7.3.1. Alexithymia and right/left hemisphere

Results of numerous studies indicate that in most righ-handed subjects the verbal, conscious and serial information processing takes places in the left hemisphere and the unconscious, non-verbal and parallel holistic information processing takes place in the right hemisphere (Tucker et al., 1986; Miller, 1986-1987; Gazzaniga 1989). In context of emotional processing it is considered that right hemisphere is included predominantly in subjective emotional experience, memorising emotions, communication of emotions to others, and emotional physiological responses while the left hemisphere is supposed to serve to analysis emotions and higher explicit emotional cognitions (Ross and Rush 1981; Fricchhione and Howanitz 1985; Adolphs et al., 2000). In this context it was suggested that inbalance in activation between both hemispheres (hypoactive right hemispehere, or hyperactive left hemisphere) can be implicated in etiopathogenesis of alexithymia (Weintraub and Mesulam 1983; Taylor, 1984; Berenbaum and Prince, 1994). For example it was found that patients with large postraumatic right unilateral cortical lesions are not able to describe their own emotional responses, while are able to describe emotional reactions of others as well as their present emotional reactions from the time before their accident (Ross and Rush, 1981; Fricchione and Howanitz, 1985). Similar observations in the patients with right unilateral hemispheral strokes were found (Spalletta et al., 2001). The role of hemispheric functions in alexithymia was also confirmed in the studies of conjungate lateral eye movements (CLEMs), which are considered to be indicators of relative hemispheric activations. The CLEMs studies have demonstrated relative higher right hemisphere activation in alexithymic subjects (Parker et al., 1992). Also some further studies have shown that brain activity in alexithymic subjects, indicated by PET (Positron Emission Tomography) is decreased in the neocortex of the right hemisphere and conversely increased in the left brain regions (Kano et al., 2003). There are also studies that have observed greater right hemisphere EEG reactivity during evoked

emotions in alexithymia which was interpreted as a sign of "electrocortical effort" reflecting difficulties in symbolization of emotion and resulting from impaired right-hemispheric emotional processing (Aftanas et al., 2003). In this context, there is evidence that alexihymic subjects process emotional words, presented to the right hemisphere, predominantly in their left hemisphere, in contrast to nonalexithymic that process such information in right hemisphere (Bermond et al., 2006). On the other hand few hemispheric specialization studies that did not find a right hemisphere dysfunction in alexithymic subjects were also published (Cole and Bakan, 1985; Grabe et al., 2004). All these data suggest valuable hypothesis for future research, that alexithymia is related to a dysfunction of the right hemisphere although the curent data need further evidence.

1.7.3.2. Alexithymia and interhemispheric transfer

In the previous research the relationship between alexithymia and interhemispheric information transfer via the corpus callosum and the anterior commissure was examined. Data of these studies indicate that the right hemisphere seems to be predominant in perception and motor expression of emotion and uncoscious nonverbal information processing (Ross and Rush 1981; Fricchhione and Howanitz 1985; Adolphs et al., 2000). Together recent data resulted in a hypothesis that neurophysiological corelate of alexithymia could represent a case of “functional commisurotomy” (Galin, 1974; Krystal, 1988; Parker et al., 1999; Lumley and Sielky 2000). For example, several case studies in patients with corpus callosum agenesis reported increased alexithymia scores in this group of patients (Buchanan et al., 1980; Ernst et al., 1999).

Similarly, increased alexithymia scores was observed in patients after commisurotomy (Hoppe and Bogen 1977; Tenhouten et al., 1985, 1986) and some studies have shown that the degree of interhemisferic transmission is significantly correlated with alexithymia and its subscales, but only in men (Zeitlin et al., 1989; Lumley and Sielky 2000). In this context, some PET studies found both decreased activation of corpus callosum after actively remembering on emotional experiences (Huber et al., 2002) and increased activation of corpus callosum by passively watching faces with emotional expressions (Kano et al., 2006). Slowering of transcallosal conduction time in alexithymic subjects was also demonstrated in some studies (Dewaraja and Sasaki, 1990; Romei et al., 2008) and taken together these results emphasize functional differences in transcallosal interactions in high alexithymic subjects and supported the hypothesis of the interhemispheric transfer deficit in alexithymia.

On the contrary few studies indicating that alexithymia is related to the facilitation of transcallosal transfer in the both interhemispheric transfer directions were published (Grabe et al., 2004; Richter et al., 2006; Lang et al., 2011). Grabe et al. (2004) also found a facilitated transcallosal inhibition, but only in alexithymic males. These gender

specific differences could be explained by the hypothesis that cerebral functions are less lateralized in females than in males (Bradshaw, 1989; Zeitling et al., 1989; Canli et al., 1998; Lumley and Sielky, 2000). Based on these findings, results indicating facilitated transcallosal inhibition (Grabe et al., 2004; Richter et al., 2006; Lang et al., 2011) suggest a neurobiological model focused on explanation how facilitated interhemispheric inhibition of right and left hemisphere lead to difficulties in emotional processing, decreased ability to verbalize emotional contents, and presumably also in an externally oriented cognitive thinking style. Authors of facilitated cortical inhibition concept hypothesis suggest that the more expressed left cortical inhibition results in a difficulty in expressing feelings, while a right cortical inhibition results in an externally orienting cognitive style. Base on these results of it has been proposed that facilitated cortical inhibition model may represent a neurobiological correlate of alexithymia (Grabe et al., 2004; Richter et al., 2006; Lang et al., 2011).

In addition, Gazzaniga and LeDoux (1978) imply that also persons with commissure anterior dysfunction are not able to experience emotional feelings however they have access to accompanying cognitions. In this context, these data suggest that in anterior commisurotomy patients the cognitive components of stimuli reach the conscious left hemisphere through the corpus callosum, while the emotional values first projected to the limbic system and from there projects to the left hemisphere by anterior commisure (Bermond et al., 2006). Anterior commisure connects the amygdala and the paleo-cortical parts in both hemispheres, as well as as the anterior temporal lobes, a part of the temporal lobe, to which the corpus callosum does not project (Kolb and Whislaw, 1990). According to Bermond et al. (2006) today is not sufficient information concerning this issue and to date there is no study connecting the anterior commisure directly to alexithymia. Moreover most of the alexithymia studies used TAS, which does not meassure reduction of emotionalising (reduction of affect), which is expected in commisura anterior dysfunction (Bermond et al., 2006). In summary the hypothesis that alexithymia is associated with alterations of interhemispheric transfer of emotional information still needs to be explored further.

1.7.3.3. Alexithymia and anterior cingulate cortex

There is evidence that ventral and dorsal parts of anterior cingulate cortex (ACC) are involved in the affective and cognitive processing of emotions in alexithymia (Lane et al., 1997; Bermond et al., 2006). Several authors suggest that individual variations in the ability to properly recognise emotional signals may be a function of the degree to which the ACC is able to participate in the processing and response to emotional cues (Lane et al., 1997). The role of the ACC in the conscious awarness of emotion has also been suggested (Lane et al., 1997). The results from a PET study by Lane et al. (1998) demonstrated correlations between LEAS and activity in ACC. Presented results are in

aggrement with previous observations showing activity of ACC increasing as a function of attention or conscious awareness with respect to cognitive stimuli (Corbetta et al., 1990, 1991; Frith et al., 1991; Paus et al., 1993). These data are also consistent with the finding that approximately 50% of post-cingulotomy patients have blunted affects postoperatively (Devinsky et al., 1995). In addition, some studies have found that reduced size of right ACC on MRI is positively correlated with TAS score in healthy men (Gündel et al., 2004b). On the other hand there are some studies that are equivocal with the previous findings. For example meta-analysis of PET or fMRI studies has shown that positive emotions activate basal ganglia, but not ACC (Phan et al., 2002). In conclusion, the results of presented studies are not consistent, and the role of ACC in processing of emotions as well as in alexithymia is still not fully understood (Bermond et al., 2006).

1.7.3.4. Alexithymia, prefrontal cortex and amygdala

An important role of the prefrontal cortex (PFC) in emotional experience presents well known observation (Krystal 1988; Kolb and Whishaw 1990; McDonald and Prkachin, 1990). In this context, Trigg (1970) demonstrated that, after frontal lobotomy, the reality is interpreted as before however, these interpretations are accompanied with no emotional feelings. It was observed that patients with prefrontal lesions exhibit a reducted facial expression and a depleted fantasy-life, which is typical alexithymic feature (Krystal 1988; Kolb and Whishaw 1990; McDonald and Prkachin, 1990). It has also been shown that in response to emotional stimuli alexithymic subjects have decreased event related potentials (ERPs) in frontal left hemisphere (Aftanas et al., 2003). Similarly the PET study by Kano et al. (2003), found decreased activations in the right orbitofrontal cortex (O-FC) in alexithymic subjects in reaction to negative emotional stimuli. It was supposed that both orbital and mediotemporal orbitoprefrontal cortices have significant role in affective aspects of alexithymia, while right temporal cortex has functions in cognitive aspects (Bermond et al., 2006).
In addition, the role of amygdala in alexithymia is also discussed and considered to play a key role in processing of emotional stimuli and emotional experience. Various studies indicated that the amygdala is involved in detection of emotional significance of stimuli (Ono et al., 2000; Adams et al., 2003) and in recognition of emotional facial expressions (Lerner et al., 2012). The amygdalae are involved in both cognitive and affective functions (Bermond et al., 2006). There are however only few studies examining amygdala in alexithymia. Berthoz et al. (1999) and Kano et al. (2003) failed to find alexithymia related differences in amygdala function. Another study of Kugel et al. (2008) have found that the difficulties with identifying feelings are negatively correlated with function of the right amygdala in response to the negative emotional stimuli, even when controlling for depressivity and anxiety. For example, decreased ability to recognize fear due to attentional neglect of other people's eyes was observed

in patients with the amygdala lesions (Sato et al., 2008). In this context it was hypothesized that L-DOPA may potentialy activate dopaminergic systems involved in recognition of emotion such as the medial prefrontal cortex (M-PFC) and ACC, and compensate the amygdala dysfunction or activate intact portions of the amygdale (Sato et al., 2008). According to Bermond et al. (2006) on the base of previous research amygdala is primarily involved in implicit processing and identifying emotions as well as explicit identifying emotions. Bermond et al. (2006) suggest that subjects with extremely low capacities to emotionalise would show, in response to emotional stimuly, strong activation in amygdala, and vice versa. Concerning the relationship between amygdala and PFC it is known, that M-PFC and O-FC are related to emotional feeling (Bermond et al., 2006), whereas the amygdala mediates both emotional physiological and inborn, and acquired behavioral responses (Iversen et al., 2000). It is hypothesized that if the M-PFC did not inhibit the amygdala, then this phylogenetically older structure would initiate preprogrammed emotional behaviour (Bermond et al., 2006).

1.7.3.5. Alexithymia, insular cortex and other brain areas

Only few studies examining relationship between insula and alexithymia have been published. For example, hypoactivation of insula in response to angry in alexithymic subjects was observed (Kano, et al., 2003). Also the study by Silani et al. (2008) found that degree of the ability to understand its own emotions is positivelly correlated with activity in the anterior insula. Few previous studies associated insular functions with regulation of negative emotional experiences, such as pain, distress, hunger, thirst, fear, anger, sadness and disgust (Hennenlotter et al., 2004), emotional decision making (Ernst et al., 2003), and production of facial emotional expressions (Carr et al., 2003). It was also reported that alexithymia is related to hypoactivation in the right inferior parietal and occipital cortices, and hyperactivation in left inferior parietal cortex and cerebellum in response to emotional stimuli have been observed (Kano et al., 2003). There is also evidence that higher activation in cuneus and precuneus, thalamus, right inferior temporal and left superior temporal regions, and cerebellum in alexithymia may be influenced by recalling emotional situations (Huber et al., 2002).

1.7.3.6. Alexithymia and emotion processing abnormalities

Recent neurophysiological research focused on evoked potentials provides evidence that alexithymia is related to the impaired processing of emotional stimuli. Franz et al. (2004) found association between alexithymia and deficit in processing of emotional aversive stimuli. The enhanced event-related theta synchronization over right anterior

cortical regions in response to emotional stimuli in alexithymic subjects was also found (Aftanas et al., 2003; Aftanas and Varlamov, 2004, 2007). Some other studies have indicated that also early perceptual-related processes are altered in alexithymia (Schaefer et al., 2007; Pollatos and Gramann, 2011). The authors of theses studies explained this observation by a hypothesis that alexithymia may be associated with a general stimulus augmentation to prevent alexithymic subjects by ignoring stimuli that might be dangerous. This mechanism is also hypothesized as responsible for the high prevalence of alexithymia in patients with chronic or somatoform pain disorders.

1.7.3.7. Summary of the neuropsychological studies in alexithymia

Based on current findings Bermond et al. (2006) suggest that the right hemisphere produces a global, nonverbal overview of emotional information and that the left hemisphere analyses emotions and higher explicit emotional cognition. According to them neural structures mostly important in the affective aspects of alexithymia are the amygdala, both orbitoprefrontal cortices and the two subparts of anterior cingulate. On the other hand neural structures important for the cognitive aspects of alexithymia are only partially different and include right temporal cortex, two subparts of anterior cingulate and also the amygdala (Bermond et al., 2006). But although some specific structures may be involved in alexithymia more than the others, in principle current findings indicate that likely all brain structures are involved in processing related to consciousness (Balduzzi and Tononi, 2008), can modulate one another and create systems of mutual connections and dependences. In this context, alexithymia present specific form of disordered consciousness characterized by a disturbed conscious emotional processing.

1.8. ALEXITHYMIA AND MENTAL HEALTH

1.8.1. Alexithymia and depression

Although alexithymia was first studied in relationship to the psychosomatic illnesses (Taylor et al., 1999) majority of recent research studies is mainly focused on alexithymia symptoms in various psychopathological states, such as depression, anxiety, psychotic episodes etc. Most investigated topic in this area of the research actually is the relationship between alexithymia and depression. Numerous studies have demonstrated that alexithymia and depression are strongly associated in both general and clinical populations (Wise et al., 1990a, 1990b, 1995; Hendryx et al., 1991; Taylor et al., 1999; Honkalampi et al., 1999, 2000a, 2000b, 2001a, 2004; Le et al., 2007; Tolmunen et al., 2011). It has been shown that 39% to 46 % of patients with major depression are alexithymic (Honkalampi et al., 1999, 2000a; Saarijarvi et al., 2001, 2006) and that presence of alexithymia in major depression patients is associated with severity of depression and suicide risk (Bankier et al., 2001; Saarijarvi et al., 2006). According to these studies, average Pearson correlation coeffiecient between depressive symptoms (BDI) and alexithymia (TAS-20) is around 0.25-0.56 (Hintikka et al., 2001; Yalug et al., 2010; Tolmunen et al., 2011). The correlations were even higher in the alexithymic individuals with higher ratings of depressive symptoms (Hintikka et al., 2001; Tolmunen et al., 2011). The results of numerous studies have also shown that the correlations between depression, and alexithymia are high across time and that there are parallel changes of TAS-20 scores and BDI in a follow-up studies (Honkalampi et al., 2001b; De Timary et al., 2008a; Marchesi et al., 2008, Tolmunen et al., 2011).

Because of strong positive correlation between alexithymia and negative affects some authors have concluded that alexithymia could be secondary to depression, or other psychopathological states (Haviland et al., 1988 and 1991). On the other hand some studies have reported relative independence of alexithymia and depressive symptoms (Hintikka et al., 2001; Tolmunen et al., 2011) and factor analysis have shown that alexithymia and depression represent distinct psychological constructs (Parker et al., 1991; Hintikka et al, 2001). It was also found that the TAS-20 and BDI-II items based on separate factors are overlapped only in minority (Hintikka et al, 2001). In this context, there are few studies documenting that alexithymia may present a risk factor of depressive symptoms (Taylor and Bagby, 2004; Tolmunen et al., 2011). In contrast to these findings there is some interesting data that has not found alexithymia as a predictor of depresive episodes in women during pregnancy (Marchesi et al., 2008). In addition, some authors have reported that alexithymic scores can decrease from the acute to the remission phase of depression (Taylor and Bagby, 2004; Saarijarvi et al., 2006; Le et al., 2007).

1.8.2. Alexithymia and other psychopathological states

Several studies have demonstrated a positive association between alexithymia and various other psychopathological symptoms, for example relationship of alexithymia with anxiety symptoms and disorders in clinical as well as non-clinical samples (Yehuda, et al., 1997; Berthoz et al., 1999; Badura, 2003; Tutkun et al., 2004; Marchesi et al., 2005; Mennin et al., 2005; Spitzer et al., 2007; Evren et al., 2008; De Timary et al., 2008a; Frewen et al., 2008a, 2008b; Galderisi et al., 2008, Tselebis et al., 2010; Yalug et al., 2011) and also with obsessive-compulsive disorder (OCD) (De Berardis et al 2005; Grabe et al., 2006; Roh et al., 2011).

In addition, numerous studies of adult and adolescent populations have demonstrated a strong association between dissociative symptoms and alexithymia (Berenbaum and James, 1994; Grabe et al., 2000; Elzinga et al, 2002; Lipsanen et al., 2004; Tutkun et al., 2004; Maaranen et al. 2005; Mason et al., 2005; Sayar et al., 2005; Evren et al., 2007; Evren et al., 2008; Simeon et al., 2009; Tolmunen et al., 2010). In this context it was suggested that some symptoms as well as potential ethiological mechanism of dissociation and alexithymia might be partially shared (Berenbaum, 1996; Simeon et al., 2009). Some researchers explained the relationship between dissociation and alexithymia by mediating factors such as depression (Zlotnick et al., 1996; Wise et al., 2000; Tutkun et al., 2004). Taken together majority of the studies suggest that alexithymia and dissociation present partially overlapping but different phenomena (Berenbaum and James, 1994; Wise et al., 2000; Lipsanen et al., 2004, Evren et al., 2007, Tolmunen et al., 2010).

Several studies have also found that alexithymia is related to symptoms of eating disorders (Corcos et al., 2000; Eizaguirre et al., 2004; Bydlowski et al., 2005; Parling et al., 2010) and reported that prevalence of alexithymia in this population is between 23-77% (Eizaguirre et al., 2004). There are some studies emphasizing that alexithymia might be mediated by negative affects (such as depression and/or anxiety) in this group of patients (Bydlowski et al. 2005; Montebarocci et al., 2006; Parling et al., 2010).

Several studies also support associations of alexithymia with alcohol dependence (Loas et al., 1997; Sakuraba et al., 2005; De Timary et al., 2008a; Evren et al., 2008), substance abuse (Troisi et al., 1998; Farges et al., 2004; Speranza et al., 2004) or internet addiction (De Berardis et al., 2009). For example, the prevalence of alexithymia among alcoholic patients is increased, amounted to be approximately from 40 to 60% (Haviland et al., 1988, 1994; Cecero and Holmstrom, 1997; Taieb et al., 2002). In this context, two longitudinal studies (Ziolkowski et al., 1995; Loas et al., 1997) have demonstrated that higher alexithymic features at onset of withdrawal are predictors of relapse 12 to 15 months afterwards which indicate that alexithymia could represents one of the important risk factors for the relapse of alcoholism. On the other hand some studies have shown alexithymia as a state phenomenon secondary to the depressive and anxiety symptoms in alcohol dependent patients (Haviland et al., 1991, 1994).

There are also studies that have documented relationships between alexithymia and schizophrenia (Maggini and Raballo, 1994; Stanghellini and Ricca, 1995; Nkam et al., 1997a, 1997b). It has been shown that schizophrenia patients with predominant negative symptoms have significantly higher alexithymia (Nkam et al., 1997a, 1997b). For example, alexihymia was related to self-experienced language impairments in nondeficit schizophrenic patients and to the severity of schizophrenia (Stanghellini and Ricca, 1995). Recent data also suggest that alexithymia in schizophrenia is more heterogeneous than was previously recognized, and has several components, some of which are more state-related, and others of which are more like trait features (Maggini and Raballo, 2004).

Current data indicate that prevalence of alexithymia is also significantly higher in borderline-personality disorder (Guttman and Laporte 2002; Modestin et al., 2004, 2005) and autism spectrum disorder (Hill et al., 2004; Tani et al., 2004; Silani et al., 2008). In addition several data suggest that alexithymia is also linked to decreased quality of life (Mattila et al., 2010b), sleep disturbances (Bazydlo et al., 2001; Kronholm et al., 2008) and specific disruptions in dream functions (Lumley and Bazydlo, 2000).

1.9. ALEXITHYMIA AND SOMATIC HEALTH

Recent findings indicate that patients with broad spectrum of somatic disorders are more alexithymic than controls and large amount of the studies have documented significant association between alexithymia and physical illness. For example, it has been reported that prevalence of alexithymia is 13,8-37,1% in multiple sclerosis patients (Bodini et al., 2008; Prochnow et al., 2011), 33-53% in patients with various types of persistent pain (Millard and Kinsler, 1992; Cox et al., 1994; Lumley et al., 2002), 21-24% in Morbus Parkinson patients (Costa et al., 2006, 2010; Poletti et al., 2011), 56% in patients with functional gastrointestinal disorders (Porcelli et al., 2003), 90% in patients with non-epileptic seizures (Bewley et al., 2005) and 31% subjects undergoing upper endoscopy (Mandarelli et al., 2011). Higher prevalence of alexithymia has been also found in patients with psychogenic pain (Sriram et al., 1987), inflammatory bowel disease (Porcelli et al., 1995), essential hypertension (Todarello et al., 1995; Jula et al., 1999), rheumatoid arthritis (Bruni et al., 2006; Vadacca et al., 2008), inflammatory bowel disease (Porcelli et al., 1996), migraine (Muftuoglu et al., 2004; Yalug et al., 2010), bronchial astma (Serrano et al., 2006), chronic obstructive pulmonary disease (Tselebis et al., 2010), female breast cancer (Manna et al., 2007), psoriasis (Conrad et al., 2008), diabetes mellitus (Topsever et al., 2006), cardiac events and fatalities in postmyocardial infarction patients (Berensvaite et al., 2000) and somatisation (de Gucht and Heiser, 2003).

The important shortcoming of these findings presents the fact that psychopathological and socio-demographic variables were not controlled in all of these studies. There are

also few studies that have not found any relationship between alexithymia and somatic illnesses (Ahrens and Defner, 1986).

1.10. ALEXITHYMIA AND PAIN

Several psychopathological symptoms, including alexithymia may be understood as predictors in the onset, chronification, recurrence, and responsiveness to treatment of pain disorders, however, much uncertainty still remains about the weight and functions of these psychological factors (Mehling and Krause, 2007). In this context the association between alexithymia and various pain conditions has been demonstrated in numerous studies. For example, elevated prevalence (33 to 53% patients) of alexithymia among patients with chronic or persistent pain has been observed (Millard and Kinsler, 1992; Zayfert et al., 1992; Cox et al., 1994; Lumley et al., 2002; Sayar et al., 2004; Glaros and Lumley, 2005; Hosoi et al., 2010). In addition, it has been found that alexithymia is positively correlated with acute pain severity and experimental pain tolerance in healthy controls (Nyklicek and Vingerhoets, 2000; Putterman et al., 2001). Alexithymia has also been shown to predict depression (Kosturek et al., 1998; Lumley et al., 2002), anxiety (Kosturek et al., 1998), and physical impairment (Lumley et al., 2002) in patients with various chronic pain conditions and might represents a risk factor for chronic pain, disability, and related health problems in pain patients (Lumley et al., 2002).

Alexithymia is also positively correlated with pain symptoms in patients with chronic myofascial pain (Lumley et al., 2002), temporomandibular disorder (Glaros and Lumley, 2005), rheumatoid arthritis (Fernandez et al., 1989; Lumley et al., 2005), migraine headaches (Lumley et al., 2005; Yalug et al., 2010), systemic lupus erythematosus (Lumley et al., 2005), fibromyalgia (Leichner-Hennig and Vetter, 1986; Sayar et al., 2004; Huber et al., 2009), cancer pain (Porcelli et al., 2007), psychogenic pain (Sriram et al., 1987), inflammatory bowel disease (Porcelli et al., 1995), higher pain intensity and interference in chronic neuromuscular pain patients (Hosoi et al., 2010) and several other types of pain disorders. In this context, several studies have also found association between alexithymia and LBP (Low Back Pain) (Julkunen et al., 1988; Acklin and Bernat, 1987; Kinder and Curtiss, 1990; Viikari-Juntura et al., 1991; Mehling et al., 2005).

Worthy of mentioning are observations that in majority of pain studies there are substantial individual differences in both alexithymia levels and pain severity among people with chronic pain. Only approximately 25-50% of the chronic pain patients were alexithymic, suggesting that there is much variability in alexithymia among people with chronic pain (Lumley et al., 2002). According to previous data, degree of alexithymia should correlate positively with the severity of pain. The evidence for this relationship is however equivocal and there are some studies that have not found any relationship between alexithymia and pain severity (Millard and Kinsler 1992; Zayfert

et al., 1992; Cox et al., 1994; Lumley et al., 2005; Celikel and Saatcioglu, 2006; Friedberg and Quick, 2007; Van Middendorp et al., 2008). In addition, there are recent data documenting that alexithymia is related to the affective but not sensory dimension of pain (Lumley et al., 2002). The possible explanation of these equivocal results is the multidimensional character of pain, which includes a sensory component (intensity and temporospatial characteristics) and also affective or unpleasantness components (Melzack and Katz, 1999). Differentiating these two dimensions seems to be important because they are affected by different psychological and biological processes (Melzack and Katz, 1992). In summary, current data suggest that alexithymia is associated with increased affective pain and hypochondriacal illness behavior which could be mediated, by psychological distress (Hubera et al., 2009). These observations could represent a response to a question, why many studies failed to find an association between alexithymia and unidimensional pain measures.

1.11. ALEXITHYMIA AND PSYCHOTHERAPY

Recent findings indicate that about quarter of an all patients involved in a psychotheraphy are alexithymic and that alexithymia predicts poor therapeutic outcome (Sifneos 1973).

Already the study of Karush et al. (1969) has tested an effect of psychotherapy in subjects with ulcerative colitis and showed that the majority of these patients (80%) exhibit a behavioral pattern strongly suggestive of alexithymia and typically manifested by emotional restriction and unresponsiveness to insight-oriented psychotherapy. Similarly a significant role of alexithymia in psychoterapeutic treatment of posttraumatic stress disorder (PTSD) has been found (O'Brien et al., 2008). In addition, several further studies have also reported poorer psychotherapy outcome in alexithymic individuals (Sifneos 1973; Freyberger 1977; Taylor 1997; Páez et al. 1999; Solano et al. 2003).

On the other hand, numerous data indicating conversely positive effect of psychotherapy in alexithymia have been reported. For example, a study was reported in which on 297 psychodynamic group therapy inpatients has been demonstrated that psychodynamic group therapy may lead to signifiant amelioration of alexithymic features (Grabe et al., 2008b). In addition, Beresnevaite (2000) observed a significant reduction in alexithymia after modified group psychotherapy in post myocardial infarction patients. Similarly Gay et al. (2008) reported interesting data suggesting reduction of alexithymia in hypnotherapy using hypnotic imagery.

In addition, several psychotherapy interventions focused on amelioration of alexithymia have been sucesfully tested and supported creative use of counter-transference (Taylor, 1977), helping the patients to observe the nature of their alexithymic disturbances (Krystal, 1979, 1982-83), empathetic reactions from a physician (Graugaard et al., 2004), cognitive behavioural therapy [especially in high

alexithymic patiens] (Rosenblum et al., 2005), positive reactions from therapist (Ogrodniczuk et al., 2005), short-term supportive or interpretative individual therapy or group psychotherapy focused on patients with lower levels of alexithymia (McCallum et al., 2003), cognitive rather than psychodynamic therapies (Lumley et al., 2007) and some others (Kennedy and Franklin, 2002; Simha-Alpern, 2007; Tulipani et al., 2011). On the other hand, there are also several studies that have not supported negative effect of alexithymia on psychotherapeutic outcome (Lumley, 2004; Spek et al., 2008).

1.12. ASSOCIATION OF ALEXITHYMIA WITH WORSE HEALTH

Previous research have shown a significant association between alexithymia and worse physical and mental health functions, and studied some mechanisms of this association, and processes potentially responsible for this relationship via physiological, behavioral, cognitive or social pathways (Lumley et al., 1996a). In this context, relationship of alexithymia with physiological dysregulation of autonomic, neuroendocrine and immune system dysregulation is mostly discussed. It was suggested that alexithymic subject fail to regulate emotions, particulary negative, which results in chronic alterations of autonomic, endocrine and immune system (Lane et al., 1997; Guilbaud et al., 2009).

Behavioral pathway presents a source of health problems mainly through potentially unhealthy behaviors (Lumley et al., 1996a; Lumley et al., 2007), such as disturbed eating (Bydlowski et al., 2005; Speranza et al., 2007), poor nutrition and sedentary lifestyle (Helmers and Mente, 1999), alcohol consumtion (Loas et al., 1997; Sakuraba et al., 2005; De Timary et al., 2008a; Evren et al., 2008) other substance abuse (Troisi et al., 1998; Farges et al., 2004; Speranza et al., 2004), internet addiction (De Berardis et al., 2009), obesity (Da Ros et al., 2011) or unprotected sex, sleep loss, and nonadherence to medical regimens (Lumley et al., 1996a). In this context, cognitive pathway in alexithymia may potentially influence health by somatic amplification, somatisation, increased seeking of medical care and also various social influences, such as impaired social functioning, deficient social support may play a role (Lumley et al., 1996a).

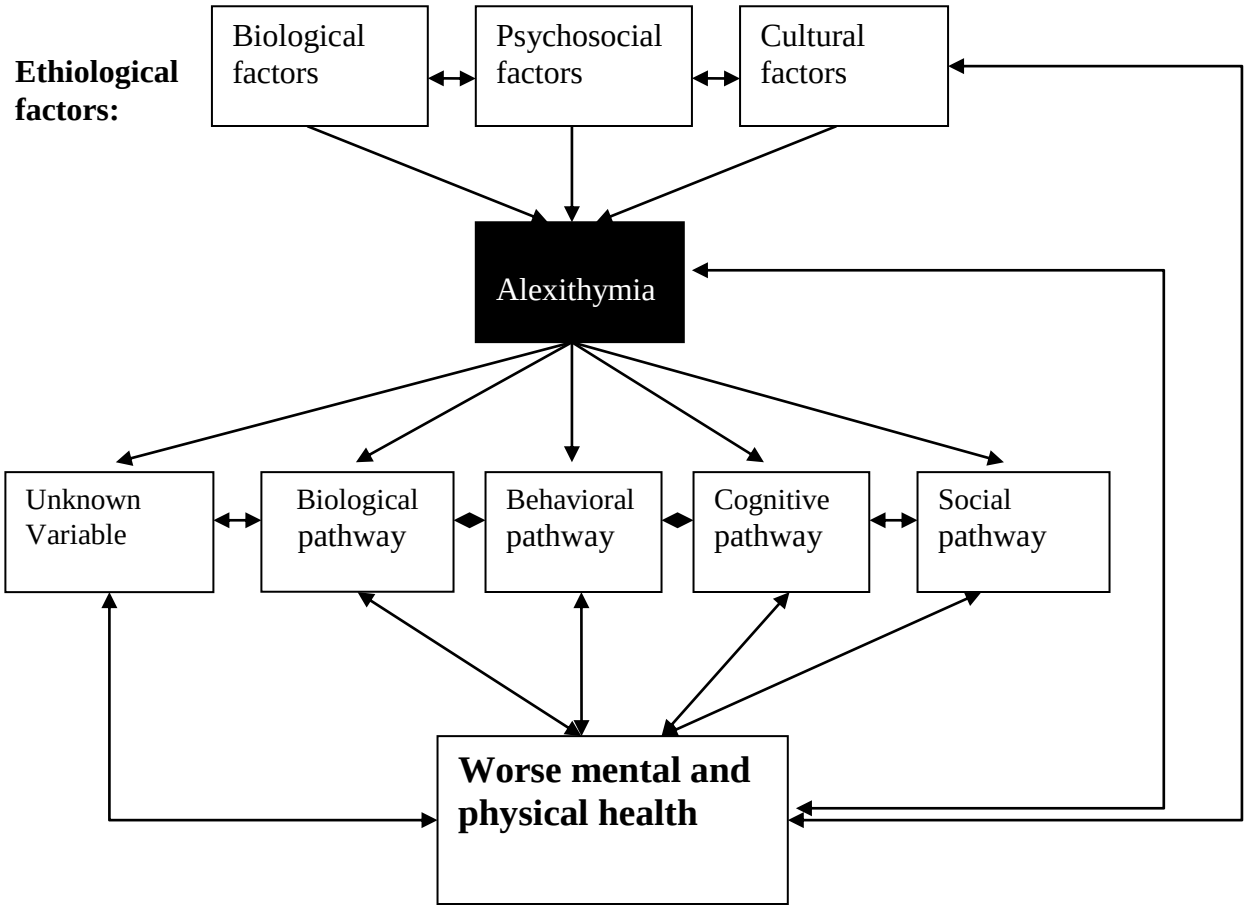


Figure 1a. Overview of potential pathways linking alexithymia and worse health. Adapted and changed from Cohen and Rodriguez (1995).

1.12.1. Alexithymia and autonomic nervous system

According to current findings alexithymia is linked with weakened conscious experience of emotions manifesting in specific responses of the autonomic nervous system (ANS), for example response to emotion-evoked stimuli in alexithymic subjects are exaggerated or excessively persistent (Nemiah, 1975; Martin and Pihl, 1985; Papciak et al., 1985; Gross, 2002; Thayer and Brosschot, 2005).

Current findings show some specific processes related to autonomic changes in alexithymia which enabled to formulate three basic theoretical approaches. First theory presents the so-called "decoupling hypothesis" (Papciak et al., 1985) suggesting that alexithymia is associated with decoupling of peripheral physiological activity and accurate report of feeling state, particulary in response to stress, which result in physiologic dysregulation. Second hypothesis presents the discharge hypothesis that posits inverse relationship between outward expresion of an emotion and the inward autonomic response at any level of emotional stimulation. This conceptualisation suggests that inhibition of expression of emotions cause increased sympathetic activation (Jones, 1935; Cacioppo et al., 1992). Third main explanation presents alexithymia-stress hypothesis (Martin and Pihl, 1985) suggesting that the influence of alexithymia on the expression of stress-related pathological states might involve poor resistance to stress. According to this hypotheses, poor resistance to stress stimuli in alexithymia results in dysregulation of autonomic and neuroendocrine system. Several recent studies also reported basic support for "hypoarousal theory" suggesting that conversely decreased sympathetic responses to emotional provocation in alexithymic individuals may occur (Linden et al., 1996; Bermond et al., 2010).

In agreement with hyperarousal theories, several studies have found relationship between alexithymia and increased baseline levels of sympathetic activation (Martin et al., 1986; Martin and Pihl, 1986; Rabavilas, 1987; Wehmer et al., 1995; Infrasca, 1997; Fukunishi et al., 1999; Gündel et al., 2004a; Bagby et al., 2009). For example, it has been found higher baseline hearth rate (Papciak et al., 1985; Wehmer et al., 1995) and greater tonically basal electrodermal activity (Rabavilas, 1987; Friedlander et al., 1997) in alexithymic individuals. But several studies did not confirm these results (Hyer et al., 1991; Newton and Contrada, 1994; Roedema and Simons, 1999).

Several studies performed in alexithymic individuals have found decreased autonomic responses to stress stimuli (Newton and Contrada, 1994; Wehmer et al., 1995; Friedlander et al., 1997; Fukunishi et al., 1999; Roedema and Simons, 1999). On the other hand some studies have found conversely increased autonomic responses (Papciak et al., 1985; Martin and Pihl, 1986; Infrasca, 1997; Gündel et al., 2004a; Bagby et al., 2009) or unchanged autonomic responses to stress stimuli in alexithymic subjects (Rabavilas 1987; Connelly and Denny, 2007).

Althougt, previous data examining tonic and reactive autonomic functioning in alexithymia are not fully consistent, majority of these studies reported that alexithymia is associated with increased sympathetic baseline levels and decreased sympathetic activation after stress stimuli.

1.12.2. Alexithymia and neuroendocrinne functions

One of the first studies documenting neuroendocrine response in alexithymia was published by Lindholm et al., (1990) in a sample of 266 healthy adults. The authors have demonstrated statistically significant association between alexithymia (BIQ) and abnormal elevated serum cortisol levels following dexamethason administration, which likely indicates an aberrant stress reaction of hypothalamo-pituitary-adrenal (HPA) axis in alexithymic individuals. Worth of the mentioning is the fact that results of the study were unchanged after controlling for depression (PSE-CATEGO), age, social ranking, marital status and other demographic data (Lindholm et al., 1990). Another study by Finset et al. (2006) performed on fibromyalgia patients has shown that an increase in depressed affect (POMS) from pre to post-stress stimulus was associated with significant increase of salivary cortisol, but only in female patients with alexithymia (TAS-20). Suprisingly the increase of salivary cortisol levels was not observed immediately, but up to 24 h after stress stimulus (interview). Authors of this study have suggested that depressed affects could be associated with delayed effects in adrenocortical activity in alexithymic subjects and that alexithymic patients who responded with elevated depressive symptoms failed to elaborate their emotional responses to the consultations (Finset et al., 2006). These findings are in the line with a previous study that has found elevated levels of serum cortisol in alexithymic individuals (Lindholm et al., 1990). In addition, investigation of the De Timary et al. (2008b) performed on 28 healthy male students has shown higher basal stress anticipatory saliva cortisol levels in subjects scoring high on alexithymia score (TAS-20). Multiple regression analyses has shown that the elevated levels of cortisol in high alexithymic subjects was due to only one subfactor of alexithymia, ''the difficulty in describing feelings'' factor (DDF) of TAS-20. DDF scores were positively correlated only with a large increase in cortisol during anticipation but not during exposure of the Trier Social Stress Test (TSST). In this context, De Timary et al. (2008b) reported that association of alexithymia with differences in cortisol levels before social stress exposure raises the possibility that alexithymia modulates cortisol levels, possibly by affecting the anticipatory cognitive appraisal of situations. These findings suggest that affect description, likely through activation of prefrontal cortices, decreases amygdala activation in response to affective stimuli (Lieberman et al., 2007).

Close relationship between alexithymia and neuroendocrine changes documents also study by Lin et al. (2005) performed on 60 male students that has found significant positiv correlation between total score of TAS-26, including also factor I (DIF) and II (DDF), with levels of salivary cortisol.

There are also some studies that have examined relationship between alexithymia and sympathetic adrenal medullary (SAM) system. The first study focused on this topic was performed in 17 nondepressed-recovered alcoholic men. The results indicate significant positive correlations between alexithymia scores (TAS-26) and SAM/HPA ratio (indicated by: urinal 3-methoxy-4-hydroxy-phenyl-ethylene glycol (MHPG)/ plasma adreno-corticotropic hormone (ACTH), respectively urinal MHPG/serum

cortisol level in blood) (Henry et al., 1992). Authors of this study suggested that dissociation of the hemispheres appears to be responsible for the alexithymic avoidance and failure of the cortisol response that so often follow severe psychological trauma (Henry et al., 1992). It was proposed that alexithymia is associated with an increased separation of sympatoadrenal and hypothalamo-hypophyseal system and that this endocrine hemispheral dissociation has an anatomical basis in lateralization of emotions (Henry et al., 1992; Henry 1993, 1997). Similar results documented a study by Spitzer et al., (2005) performed on a sample of 12 major depressive disorder (MDD) patients and 23 healthy controls. Results of this study indicate that alexithymia is associated with an increased noradrenergic activity and a decreased basal activity of the HPA axis among men, indicated by decreased levels of urinary cortisol (Spitzer et al., 2005).

Also McCaslin et al. (2006) examined alexithymia (TAS-20), catecholamine response (salivary 3-methoxy-4-hydroxy-phenylglycol – major metabolite of norepinephrine (MHPG) and HPA axis response (salivary cortisol) in a sample of 160 police academy recruits after exposition to the video stress challenge. Alexithymia scores were negatively associated with catecholamine response after the stress stimulus and no association was observed between alexithymia scores and salivary cortisol reactivity (McCaslin et al 2006). On the other hand, two studies have not confirmed association between alexithymia and HPA response (Pedrosa et al., 2007; Guilbaud et al., 2009).

In addition, there are some findings documenting neuroendocrine changes in alexithymia not directly related to major neuroendocrine stress response axes such as decreased levels of serum prolactin (Söndergaard and Theorell, 2004) and serum oxytocin (Tops et al., 2007) have been found in alexithymic individuals.

In summary, predominant results of previous research indicate that alexithymia is associated with an increased HPA activity (Finset et al., 2006; De Timary et al., 2008; Lindholm et al., 1990; Lin et al., 2005; Finset et al., 2006; De Timary et al., 2008b).

1.12.3. Alexithymia and immune system

1.12.3.1 Introduction

Several studies suggest that alexithymic features are likely related to disturbances of immune functions (Todarello et al., 1997; Guilbaud et al., 2009; Honkalampi et al., 2011). According to several findings this association is likely directly influenced by central nervous system and also mediated by HPA axis, SAM system and autonomic nervous system (Martin and Pihl, 1985; Elenkov and Chrousos, 2002; Gündel et al., 2002).

Close connection between neuroendocrine and immune systems document also recent findings indicating that glucocorticoides and catecholamines present key stress hormones produced by HPA and SAM system, that prompt the production of several anti-inflammantory cytokines such as IL-4, IL-10 and TGF-β, whereas they inhibit production of pro-inflammantory cytokines, such as IL-12, TNF-α (Tumour Necrosis Factor Alpha) and INF-γ (Interferon Gamma) (Elenkov and Chrousos, 2002). According to the recent evidence, cytokine production may be also directly stimulated by stressful experiences and negative emotions (Kiecolt-Glaser et al., 2002) and conversely cytokines may be responsible for influence of the HPA and SAM system (Zarkovic et al., 2008; Marques et al., 2009; Locatelli et al., 2010). Recent findings suggest that interleukine dysregulation presents an important factor responsible for chronic impairment of pro/anti-inflammatory cytokine balance due to psychological and somatic adverse stimuli that play a significant role in alexithymia (Corcos et al., 2004). In this context, Guilbaud et al. (2003) suggests that immune dysregulation observed in alexithymia, in many aspects seems to follow the same pattern as in subjects afflicted with chronic stress with a predominance of depressed cell-mediated immunity and a skewed Th1/Th2 ratio towards Th2 response. Together these findings suggest that alexithymia likely via mechanisms of both acute and chronic stress likely induces dysregulation of immune responses (Elenkov et al., 1996; Marshall et al., 1998; Agarwal and Marshall, 2001; Glaser et al., 2001).

1.12.3.2 Alexithymia and leukocytes

Several studies demonstrated changes of leukocytes counts related to alexithymia. For example, study performed by Todarello et al. (1994) in 62 women (36 healthy and 26 affected by cervical intraepithelial neoplasia - precancerous lesions - CIN I, II, III, who were not aware of their condition) found lower rates of almost all lymphocytic subsets in alexithymic (SPSS) women in comparison to non-alexithymic. These results were successfully replicated by the same author in 1997 performed in bigger sample of 43 women affected by cervical dysplasia and 67 healthy women with use of TAS-20 (Todarello et al., 1997). In the both studies immunological differences were also

observed between alexithymic women affected by CIN and alexithymic healthy women. Women suffering from CIN had higher average TAS-20 ratings than healthy women and the alexithymia scores in the group of women suffering from dysplasia was higher than that of normal women.
Another study performed by Dewaraja et al. (1997) on 97 health male subjects also reported hypoactivation of cellular immunity (Th1 immune functions) in alexithymic subjects (TAS-26). When alexithymia was considered a categorical variable, highly alexithymic men had significantly decreased numbers of the most cytotoxic natural killer (NK) subset, (CD57-CD16+ cells). Similarly, when alexithymia was considered a continuous variable, in addition to the NK subset, killer effector T cell (CD8+CD11a+ cells) count was also significantly decreased.
The both studies by Todarello et al. (1994, 1997) and the study by Dewaraja (1997) are in agreement with results reported by other authors (Temoshok, 1987), who hypothesized that a certain personality trait characterized by emotional inhibition is related to greater cancer vulnerability, and that type of personality might be an important factor responsible for the outbreak of cancer. The results of these studies proposed that immune system has an important role as a possible mediator between personality and cancer and that lowered cytotoxic lymphocytes trigger a mechanism that may be responsible for the association between alexithymia and psychosomatic illnesses (Dewaraja et al., 1997).

1.12.3.3 Alexithymia and cytokines

On the base of previous studies that documented association of alexithymia with hypoactivation of cellular immunity further research has contributed to research of other characteristics of immune dysregulation related to the alexithymia. In this context, study examining cytokines in alexithymia was firstly performed in 17 healthy young women by Corcos et al. (2004). Results of this study demonstrated that total alexithymia score (TAS-26) is significantly positively correlated with serum levels of IL-4 (Corcos et al., 2004). BMI, age, depressed mood and anxiety (HADS) in this study were found as independent variables with respect to IL-4 levels and only alexithymia likely could have predictive value related to increased levels of IL-4. Serum levels of IL-2 and IL-1 were not associated with alexithymia scores in this study. With respect to these findings there is evidence that IL-4 together with IL-10 represent major anti-inflamatory Th2 (type 2) cytokines, which promote humoral immunity and modulate key cytokines regulating the type 1/type2 cytokine balance (Elenkov and Chrousos, 2002). Following these findings Guilbaud et al. (2003) suggested that the neuroendocrine and immune response in alexithymic individuals, are similar to neuroendocrine and immune patterns in subjects afflicted by chronic stress related to up-regulation of Th-2 response and impaired Th-1 response. In this context, increased level of IL-4 likely play a role as an important factor responsible for chronic

impairment of balance of pro/anti-inflammatory cytokines in alexithymia linked to psychological and somatic adverse effects (Corcos et al., 2004). Several researchers also emphasize critical importance of the nervous system on maintenance of the balance between cell-mediated (Th1) and humoral (Th2) immune responses (Tausk et al., 2008). For example, Glaser et al. (2001) observed that chronic stressors are associated with a dysbalance between Th-1 and Th-2 cytokine response.

In this context, further studies assesing Th1/Th2-response and its balance were performed in alexithymia subjects. For example, investigation by Pedrosa et al. (2007) examined 24 subjects with somatoform disorder (SFD) and 9 healthy controls of both genders. They found significant relationship of alexithymia (TAS-26) with decreased Th1-mediated immune functions indicated by decreased serum levels of IL-2 Rα which were negatively correlated with alexithymia [in accordance with previous studies the reduction of IL-2Rα levels presents marker of decreased immune activation and reduction in Th1-mediated immunity]. The serum levels of IL-4 were negatively correlated with the alexithymia, which was incosistent with previous findings of Corcos et al. (2004). It has to be noted, however that IL-4 levels were detectable only in minority of the examined subjects therefore the results must be interpreted whit this important limitation.

Similarly several other studies have demonstrated altered cell-mediated (Th1) immunity in alexithymia. In the study by Guilbaud et al. (2009) performed in 18 alexithymic and 20 non-alexithymic healthy young women have been found significant association between alexithymia (TAS-20) and immune response dysbalance between Th1 and Th2 immune response. In this study alexithymia was related to decreased production of major type 1 cytokines (IL-2, IL-1β) as well as major type 2 cytokine (IL-4), with unchanged levels of the regulatory type 2, represented by cytokine IL-10 in vitro production. Cytokine in vitro production remained significantly diminished in the alexithymic group, even after adjusting for between-group differences in anxiety and depression levels on the HADS. Guilbaud et al. found reduced ratios of Th1/Th2 (IL-2/IL-10) and CD4/CD8, as well as reduced CD4 percentages indicating that alexithymic women have altered immune function, with a predominance of depressed cell-mediated immunity and a skewed Th1/Th2 ratio towards Th2 response. These results confirmed hypothesis of decreased activation of Th1 arms, which is consistent with previous data. In contrast to the data published by Corcos et al. (2004) simultaneous partial downregulation of Th2 response was found. It was also suggested that this contradictory finding could be explained by methodological differences applied in this study because cytokines serum levels but not cytokine production by stimulated peripheral lymphocytes was meassured. In this context Guilbaud et al., proposed that production of IL-4 by other immune cells included in previous studies could influence results of the cytokine levels. Together the results of this study suggest that alexithymia has specific effect on immunity that is probably amplified by anxiety levels and depression. The result of the study also suggests that alexithymia could present a vulnerability factor for infectious and stress-immune related diseases, (Guilbaud et al., 2009).

Recent investigation by Mandarelli et al. (2011) in clinical sample of 68 patients (22 alexithymic, 10 borderline, 36 non-alexithymic), referred for routine upper endoscopy, investigated relationship of alexithymia (TAS-20) with stress (SVS), depression, anxiety (HADS) and several cytokines (IL-4, IL-6, IFN-γ, IL-1β, TNF-α). Alexithymic patients had significantly lower serum levels of IL-4 and IL-6 in comparison to non-alexithymic patients. Statistically significant negative correlations between alexithymia and IL-4, IL-6 were found. The findings of this study were controlled for symptoms of stress, depression, anxiety, BMI, behavioral (smoking, coffee drinking, alcohol intake) and sociodemographical (sex, age, marital status, education) variables. Multiple regression analysis has confirmed these findings and showed that alexithymia is inveresely related to IL-4 as well as IL-6 levels. The correlation between other cytokines (IFN-γ, IL-1β, TNF-α) and other psychopathological symptoms including alexithymia were not statistically significant. The authors suggest that rather than reflecting an isolated shift towards Th2 immune response, the results imply that cytokine profiles differs in alexithymic and non-alexithymic subjects in stresfull conditions, such as endoscopy examination. It is summarized that even though the exact meaning of demonstrated cytokine changes remains unclear, a possible impairment in the mechanisms underlying immune activation might explain the relationship between alexithymia and susceptibility to illness (Taylor et al., 1997).

Another recent study published by Honkalampi et al. (2011) investigated 308 subjects from general population and found that TAS-20 score, and all its factors, correlated positively with hs-CRP and the BDI scores (Honkalampi et al., 2011). Alexithymic subjects had also higher serum levels of IL-6, although this finding did not remain significant after in logistic regression analyses adjusted for several counfounders, such as depression, and several behavioral and sociodemographical variables. The authors suggest that both depression and alexithymia are conditions characterized by a pronounced inflammatory state, and could be considered as state reactions to stressful situations (Martin and Pihl, 1986). However, the underlying mechanisms for these inflammatory changes may differ (Honkalampi et al., 2011). Similar association of serum CRP levels and alexithymia (TAS-20), independently on depression was also observed in the study on 145 patients with major depressive disorder (De Berardis et al., 2008).

Supportive evidence of cytokine dysregulation as related to alexithymia reported also Temoshok et al. (2008), who performed investigation on 184 HIV-infected subjects and found that alexithymic scores (TAS-20) were positively correlated with significantly lower stimulated production of HIV-inhibiting MIP-1 alpha (Macrophage Inflammatory Protein), which blocks HIV entry into CD4(+) lymphocytes and represents key immune parameter implicated in HIV pathogenesis. Increased production of MIP-1 alpha and beta which are β-chemokines is associated with more favourable status, disease-free HIV patients and protection from infection (Garzino-Demo et al., 1999, 2007). An association of strong maladaptive Type C coping with

significantly higher levels of serum IL-6 presenting a second key immune parameter in HIV pathogenesis was also observed.
Similarly Bossù et al. (2009) has found strong positive correlation between pro-inflammantory cytokine IL-18 (member of IL-1 family) serum levels and alexithymia score (TAS-20) in ischemic stroke patients, particularly in patients with right–hemisphere lesions. Multivariate analysis indicated specificity of this association. Serum IL-18 levels, which is implicated in stroke pathophysilogy and outcome, was not significantly corelated with depression severity (HDRS) in this study.
Also the study by Bruni et al. (2006) reported significant association between alexithymia (TAS-20) and serum TNF-α level and between TNF-α level and disease activity in 27 rheumatoid arthritis (RA) patients. However this correlation was not found in the group of 27 systemic lupus erythematosus (SLE) patients and 27 healthy controls. In the similar study by Vadacca et al. (2008) was found increased prevalence of alexithymia (TAS-20) in the small groups of SLE (N=12) and RA (N=13) patients. Moreover alexithymia was positively associated with increased serum levels of IL-6 and TNF-α in the proportion of RA patients with high alexithymia in comparison with non-alexithymic RA patients.
Together results of these studies indicate bidirectional interactions between alexithymia and immune system in patients affected by autoimmune inflammatory diseases. These investigations of autoimmune diseases documented high prevalence of alexithymia and a correlation between immunoendocrine parameters and alexithymic features in SLE and RA proposing that an immunomodulatory pathway could influence this cognitive style in patients with autoimmune disorders. Some authors suggested that future research may help to find common biological pathway linking alexithymia and autoimmunity (Vadacca et al., 2008). These preliminary findings corroborate the integrated bidirectional interactions between neuropsychological mechanisms and the neuroendocrine-immune system in patients affected by autoimmune diseases and might contribute to explanation of common biological pathways linking alexithymia and autoimmune-inflammatory diseases (Bruni et al., 2006).

1.12.3.4 Conclusion

In summary, recent data indicate significant relationships among stress, alexithymia and immune dysregulation although there are certain limitations that mainly include relatively small sample sizes, heterogeneous patient populations and heterogenous methodology of the studies. In the majority of the studies alexithymia was related to the reduction in Th1-mediated immune functions (Todarello et al., 1994, 1997; Dewaraja et al., 1997; Pedrosa et al., 2007; Guilbaud et al., 2009) and the activation of the Th2 immune functions (Pedrosa et al., 2007; Guilbaud et al. 2009). Only few

reported studies have not found any significant association between alexithymia and impaired immune response (Spivak et al., 1997; Koh et al., 2006).
In addition, several studies have observed alexithymia related to dysregulation of some important inflammatory cytokines that are implicated in innate as well as adaptive immunity functions (Corcos et al., 2004; Bruni et al., 2006; Temoshok et al., 2008; Vadacca et al., 2008; Bossù et al., 2009; Honkalampi et al., 2011; Mandarelli et al., 2011).

1.13. CONCLUSIONS BASED ON THE LITERATURE REVIEW

With an attempt to explain basic pathophysiological processes involved in the relationship between psychopatological symptoms and somatic health several theories have been developed. Nemiah and Sifneos in 1970s have observed that many patients with so-called „psychosomatic diseases" have deficits in capacity of symbolization of emotions, verbal behavior, fantasies, and dreams. It was proposed that these psychological features can cause numerous symptoms including physiological dysfunctions that may result to somatic illnesses. This conceptualisation has evolved into the concept of alexithymia that links the influence of emotions and personality on physical illness and health.

In this context, alexithymia could be defined as an inability to complete emotional experience, which means, that the person is not able to experience feelings, differentiate between various emotional feelings, verbalize emotional experiences, reflect and to some extent analyze feelings, or fantasize about them (Bermond, 2006). Alexithymia is today clinically relevant and multidimensional construct (Kooiman et al., 2002; Ogrodniczuk et al., 2011) that reflects general deficit in the cognitive and afective processing of emotions (Taylor et al., 1991; Taylor and Bagby, 2004; Bermond et al., 2010). Alexithymia is characterised by relative and absolute stability (Tolmunen et al., 2011) and is distributed normaly in the general population (Bagby and Taylor, 1997). Alexithymia consists of both, trait and state components (Tolmunen et al, 2011) and the balance between those two components is variable among different subjects and situations (Lumley et al., 2007). The prevalence of alexithymia is amounted to be around 10-20% (Salminen et al., 1999; Honkalampi et al., 2000a; Quinton and Wagner, 2005; Moriguchi et al., 2007) in general population, with significatly higher prevalence in some clinical samples (Eizaguirre et al., 2004; Parling et al., 2010). Despite of the several shortcomings of TAS-20, at present time it remains the most widely used instrument for assesing alexithymia (De Gucht et al., 2003).

Several potential psychosocial, cultural and biological factors are discussed in etiology of alexithymia (Taylor and Bagby, 2004). Among most discussed biological contributors of alexithymia belong genetic and other neurobiological factors. In this context, several recent studies confirmed and strongly supported an important contribution of genetic factors to individual differences in alexithymia (Picardi et al., 2011). According to some authors alexithymic features can be also caused by neural dysfunctions, which might result in different emotional-physiological responses (Bermond et al., 2006). The prominent fundamental neural structures involved in emotional functions, which functional relevance in alexithymia is still discused likely include right and left hemisphere, corpus callosum, anterior commissure, anterior cingulate, prefrontal cortex, amygdala, and insular cortex (Bermond et al., 2006). In spite of the fact that alexithymia was first studied in relationship to the psychosomatic illnesses (Taylor et al., 1999), recent research have largely studied and demonstrated significant association between alexithymia and various psychopathological states, particulary depression, dissociation or anxiety. It is needed to mention that althought

alexithymia has been originally associated with propensity to do poorly in traditional dynamic psychotherapy (Sifneos 1973) several recent studies have described positive effects of psychotherapy (Grabe et al., 2008b).

In this context, also some other recent studies have documented that alexithymia is related to dysregulation of immune and neuroendocrine functions. Up to date it has been published 20 studies examining immune system functions and 10 studies examining neuroendocrine response in alexithymia. Majority of these studies have demonstrated increased levels of some inflammatory cytokines, decreased function of cellular immunity and hyperactivation of HPA axis in alexithymia. In spite of some limitation it could be summarised that stressors related to alexithymia could underlie the process of immune and neuroendocrine dysregulation that likely presents a significant risk factor in pathogenesis of several medical disorders.

The previous research has also shown a significant association between alexithymia and numerous mental health or physical disorders, including also various pain disorders. There are in fact several different pathways potentially acounting for this relationship. In an attempt to explain this association several hypotheses were proposed. Following recent findings this disertation study is focused on some psychoneuroimmunological pathways examining the association between alexithymia and immune dysregulation.

2. Empirical Research

2.1. CEREBROSPINAL FLUID IL-8 LEVELS REFLECT SYMPTOMS OF ALEXITHYMIA IN PATIENTS WITH NON-INFLAMMATORY NEUROLOGICAL DISORDERS

2.1.1. Introduction

Several recent findings indicate that various interactions between nervous and immune system are important in the pathophysiology of alexithymia (Todarello et al., 1994, 1997; Dewaraja et al., 1997; Guilbaud et al., 2003, 2009; Corcos et al., 2004; Pedrosa et al., 2007). These findings strongly suggest that pro-inflammatory cytokines such as IL-1, IL-2, IL- 6, IL-8 and TNF-alpha may play a significant role in developing alexithymia and can mediate its psychological and neurobiological manifestations (Guilbaud et al., 2003, 2009; Corcos et al., 2004). For example, recent study by Vadacca et al. (2008) found increased prevalence of alexithymia (TAS-Toronto Alexithymia Scale) in patients with rheumatoid arthritis (RA) (54%) and also in patients with systemic lupus erythematosus (SLE) (42%). Both groups of patients had increased values of IL-6 and TNF-alpha. Similar study (Bruni et al., 2006) reported association between alexithymia (TAS) and increased TNF-alpha levels in RA patients. According to recent evidence, cytokine production may be also directly stimulated by negative emotions (Kiecolt-Glasser et al., 2002) and conversely cytokines may be responsible for influence of the HPA and SAM system (Zarkovic et al., 2008; Marques et al., 2009; Locatelli et al., 2010). In this context, recent data also indicate that negative emotions related to depressive symptoms and anxiety are related to IL- 8 serum level in patients with major depression (Lehto et al., 2010) and anxiety disorder (Hoge et al., 2009). These findings suggest that IL-8 could present also useful immunological marker related to emotional dysregulation in alexithymia although to this time there is not any study that assessed the relationship between symptoms of alexithymia and IL-8. IL-8, alternatively known as CXCL8, presents a specific pro-inflammatory cytokine, which as a member of the so-called chemokine group with strong chemotaktic properties, mainly for neutrophils, but also for other various immunocompetent cells (Gerszten et al., 1999; Weik et al., 2008). In addition, several data suggest the role of chemokines in cell interaction, neuromodulation, synaptic transmission and neuroendocrine functions which represents factors assumed to be important in pathophysiology of the various neuropsychic disorders (Lehto et al., 2010; Rostene et al., 2010). It has been also documented that IL-8 is related to a variety of inflammatory diseases (Daig et al., 1996; Kraan et al., 2000), and that its excessively production can lead to damage of healthy tissue as seen in such disorders as rheumatoid arthritis, asthma, periodontitis, irritable bowel disease and cancer._They all show a positive association between local as well as systemic levels of IL-8 and severity of diseases symptoms (Daig et al., 1996; Kraan et al., 2000) and are also associated with

psychological stress (Herrmann et al., 2000; Bernstein et al., 2006; Weik et al., 2008). It is also interesting observation that high levels of circulating IL-8 could induce antiinflammatory effect (Kronfol and Remick, 2000; Lehto et al., 2010). Particulary interesting and important is the function of chemokines in neurodevelopment and synaptic transmission. According to its property as a strong proinflammantory agent and its widespread clinical relevance IL-8 seems to be an ideal marker for the assessment of psychological effect on the inflammantory respose (Weik et al., 2008). This observations could explain why IL-8 would be very interesting in relation to alexithymia and anxiety when compare with other proinflammatory cytokines. With the purpose to reexamine relationship of IL-8 with depressive and anxiety symptoms, and assess the relationship between IL-8 level and alexithymia we have performed clinical study of serum and cerebrospinal fluid levels in a group of neurological patients with noninflammatory disorders who undergone cerebrospinal fluid assessment for diagnostic purposes. In order to specify non-inflammatory conditions we have examined serum CRP and also IL-6, immunoglobulines A, G, M and albumin in serum and cerebrospinal fluid.

2.1.2. Methods

2.1.2.1. Participans

In order to examine the above hypothesis, assessment of IL-8 level in CSF during rest conditions and psychometric measures were performed in the selected group of 33 consecutive inpatients with non-inflammatory neurological disorders (NIND). The group patients with NIND were selected from the total group of 210 patients indicated for CSF examination. On the base of exclusion criteria we have selected 110 patients for psychometric evaluation. From this group only 33 patients have fulfiled inclusion criteria and were enroled in this study. The patients were at the time of recruitment treated at the Department of Neurology of the University Hospital in Prague. Psychometric measures were performed within 8h after lumbar punction and blood sample taking. The patients had diagnosis of NIND, which ethiology was related to brain small vessel disease or age related ischemic changes on MRI head scans (n = 8), axonal neuropathy (n = 7), primary headache (n = 10), cervical or lumbar spondylosis (n = 6), and vestibular vertigo (n = 2). The diagnoses were made independently by two neurologists of the neurology department. Complete medical history was taken and physical, neurological and laboratory examinations were performed to establish whether all selected subjects were free of any significant acute or chronic infectious, inflammatory or immune disorders, and endocrine abnormalities. CSF examinations were indicated in order to exclude autoimune demyelinitative disorder, neuroinfection, and other inflammatory states in the context of standard neurological diagnostic procedures. In all patients we have found normal integrity of the brain—

blood barrier, assessed by measurement of CSF/serum albumin quotient with age-dependent reference values. We have also found no evidence of inflammation in serum (no increased number of white blood cells and level of C-reactive protein) and in the CSF analysis we have not found evidence of pleocytosis, CNS autoimmune process with intrathecal immunoglobulin synthesis or oligoclonal bands, monoclonal gammopathy and autoantibodies. We have also excluded patients with psychiatric diagnosis, drug abuse, current pregnancy, lactation and menstruation in women, and also patients with recent history of infectious diseases (influenza or other febril state within past 4 weeks). None of the patients had a psychiatric diagnosis according to detailed examination by a psychiatrist based on criteria MINI version 5.0.0 (Sheehan etal., 1998). All the patients were free of non-steroidal anti-inflammatory medication (NSAIDs), methyldopa, corticosteroids and other hormonal medication, and major psychotropic drugs for at least 2 months prior to testing. None of the patients had received immunomodulatory therapy for 3 months before the lumbar puncture. Actually received medication is summarized in Table 3b. The patients were 9 males and 24 females in average age 38.78 - 12.48 years (age range 21-60) predominantly with high-school education, with adequate nutritional status and body mass index (16-29). The study was approved by the university ethical committee and all patients gave voluntary written informed consent. Patients were informed about the study aims and procedures.

2.1.2.2. Psychometric meassures

While resting after LP in a patient room of the neurologic department, participants completed psychometric questionnaires. Alexithymia was assessed using the validated Czech version of the 20-item Toronto Alexithymia Scale (TAS-20) (Cronbach's alpha 0.81, test - retest reliability after1week 0.77) (Bagby et al., 1994a and 1994b). Each questionis scored on a five - point Likert scale (1 - 5) and the TAS total score has range from 20 to 100. Patients were considered to have alexithymia if their TAS total score was over 61, whereas patients scoring under 50 were classified as non-alexithymic. Patients with TAS-20 total score from 51 to 60 were classified as having borderline alexithymia (Porcelli et al., 2003). For the assessment of depressive symptoms wa sused Czech version of Beck depression inventory BDI-II (Beck et al., 1996) that represents 21-items questionnaire for assessing depression (Cronbach's alpha 0.89, test - retest reliability after week 0.85). Subjects indicate degree of their experience of depressive symptoms on 4-point Likert scale. Levels of anxiety symptoms were assessed using the Czech version of The Zung Self-Rating Anxiety Scale (SAS) (Cronbach's alpha 0.89, test – retest reliability after week 0.85) (Zung, 1971). The SAS is 20-itemself-reporting questionnaire focused on the most common general anxiety symptoms. Each questionis scored on 4-point Likert scale from 1 to 4.

2.1.2.3. Lumbar puncture and immunochemical measures

After a night of fasting with bed rest the subjects received standard carbohydrate breakfast. The subjects were limited to minimal physical activity and kept quietly awake in the neutral environment of the patient room. Usual caffeine intake was allowed. For biochemical assessment CSF was drawn from L4-5 or L3-4 interspace in upright sitting position between 8 and 9 AM using a standard sterile preparation. A total of 8 – 10 ml of CSF was removed and carefully transferred to biochemical department and immediately centrifuged and frozen at - 20 C until assayed. At the same time, the blood samples of 5 ml volumes were collected into sterile tubes according to common procedures and also transferred to the biochemical department and immediately centrifuged and frozen at - 20 C and were kept until assayed. The analyses were performed as soon as possible within 48 hours after serum and CSF sampling. After that serum analyses of CRP and also CSF and serum analyses of IL-8, IL-6, immunoglobulines A, G, M and albumin have been performed according to common analytical procedures. Concentrations of IL-8 in CSF (CSF-IL-8) were measured using double solid-phase chemiluminescent enzyme imunnoassay system based on an Immulite/Immulitwe 1000 (Siemens Medical Solutions Diagnostics). The detection limit for IL-8 was 2pg/ml (picogram/milliliter) and intraassay coefficient of variation amounted to 5.0%.

2.1.2.4. Statistical methods

Statistical evaluation for results of CSF-IL-8 and other immunochemical measures and psychometric measures included means, standard deviations, Mann—Whitney test for independent samples, Spearman correlation coefficients and multiple linear regression analyses. All the methods of statistical evaluation were performed using the software package Statistica version 6.

2.1.3. Results

The results indicate that CSF-IL-8 is significantly correlated to TAS-20 (Spearman $R = 0.46$, $p = 0.007$) and SAS (Spearman $R = 0.44$, $p = 0.009$) but not to BDI-II (Spearman $R = 0.15$, $p = 0.39$) (Table 2b). These correlations show that CSF-IL-8 exhibits relatively strong relationship to alexithymia, anxiety but not to depression. Other statistically significant correlations were also found between psychometric measures of alexithymia, anxiety and depression, and alexithymia and age (Table 2b). Because data did not show presence of significant clusters the

patients (N = 33) were divided into two groups according to values of CSF-IL-8, i.e. higher (N1 = 16, IL-8 - 41.90) and lower (N2 = 17; IL-8 < 41.90) than median. The results show that statistical comparison using Mann-Whitney test between groups of the NIND patients with values of CSF-IL-8 higher and lower than median distinguishes the groups of individuals with higher and lower alexithymia (TAS-20) (Table 1b). Although the Spearman correlation between TAS-20 and CSF-IL-8 is sufficient and it is not necessary to divide the patients in to two groups according to values of CSF-IL-8, we used it as a confirmation method for correlation analysis. This confirmation is particularly useful because Mann - Whitney test usually has higher statistical significance of its results in comparison to Spearman correlation coefficient. In addition, using this statistical test enables to find whether the results of correlation analysis could be influenced by age. In this context, reported data show that the subgroups that are statistically significantly different with respect to CSF-IL-8 and TAS-20 are not statistically different with respect to age (see Table 1b), which indicate that age likely is not responsible for the significant effects observed. Statistical comparison between men and women did not show significant differences in CSF-IL-8 or psychometric measures. To distinguish the effect of TAS and SAS on CSF-IL-8, we have used a multiple linear regression which might be useful, because it is hard to know whether alexithymia and anxiety in their specific interactions are linked to increased levels of CSF-IL-8 and whether alexithymia and anxiety are tightly linked together. The result shows that multiple R = 0.47 is statistically significant ($p = 0.022$; $F = 4.297$). Other correlations of psychometric measures with serum IL-8 and CRP, and with serum and CSF levels of IL-6, immunoglobulines A, G, M and albumin, were not statistically significant. Also we have not found significant correlation between CSF-IL-8 and CSF-IL-6. With exception of the relationship between alexithymia and age we have not found any significant association of psychometric and immunochemical measures with age and BMI. Also we have not found increased CRP in the subgroup with age related ischemic changes as well as the one with axonal neuropathy (Figure 1b, Tables 1b, 2b).

2.1.4. Tables and figure

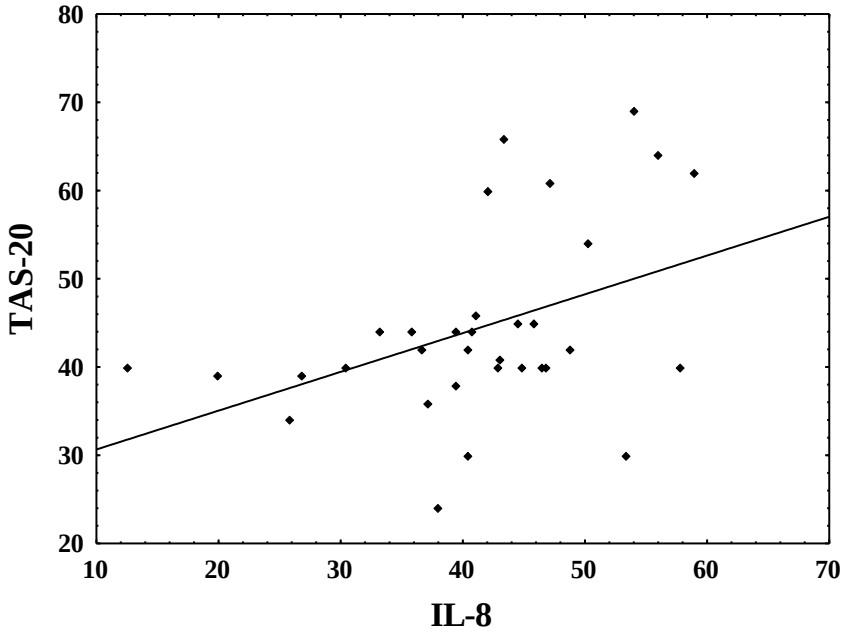


Figure 1b. Dependency graph of CSF-IL-8 and TAS-20 (Spearman R=0.46, p<0.01).

Table 1b. Between group comparison for the NIND patients with higher and lower CSF-IL-8 than median.

	Mean lower IL-8±S.D.	**Mean higher IL-8±S.D.**	**MW-test Z**	**P**
Age	36.87±12.34	40.58±12.71	0.86	0.387
IL-8 (CSF)	33.55±8.41	48.50±5.51	4.89	<0.0001
CRP (ser)	1.79±1.32	1.96±1.83	0.15	0.8843
BDI-II	9.37±10.18	12.70±9.65	1.29	0.1947
SAS	36.75±8.73	41.88±8.06	1.89	0.0586
TAS-20	39.12±5.83	49.35±11.94	2.39	0.0166

Note. TAS-20- Toronto Alexithymia Scale; BDI-II- Beck Depression Inventory; SAS- Self-reported Anxiety Scale; Higher IL-8 (N_1=16, IL-8≥41.90); Lower IL-8 (N_2=17; IL-8<41.90); df=31.

Table 2b. Spearman correlations of CSF-IL-8 with results of psychometric measures.

	Age	**IL-8**	**TAS-20**	**BDI-II**
Age	–	–	–	–
IL-8	0.288	–	–	–
TAS-20	0.346*	0.460**	–	–
BDI-II	-0.166	0.153	0.533**	–
SAS	0.068	0.446**	0.538**	0.581**

Note. *p < 0.05; **p < 0.01.; TAS-20- Toronto Alexithymia Scale; BDI-II- Beck Depression Inventory; SAS- Self-reported Anxiety Scale

Table 3b. Medication used by the patients

Patients	Actual medication
1.-17.	No medication
18.-22.	B complex vitamins only
23.	Telmisartan, Hydrochlorothiazide, Omeprazole, Carbamazepine, Allopurinol, Tamsulosin
24.	Gabapentin, Fenofibrate
25.	Piracetam, Metformin, Ramipril, Atorvastatin, B complex vitamins,
26.	Betahistine, Rilmenidine, B complex vitamins
27.	Atorvastatin, Tramadol, Betahistine, B complex vitamins
28.	Carbamazepine
29.	Mefenoxalone, Sulodexide
30.	Piracetam, Carbamazepine
31.	Cetirizine, Cholecalciferol, B complex vitamins
32.	Quinalapril
33.	Metoprolol

2.1.5. Discussion

Results of the present study are in agreement with recent evidence that various interactions between nervous and immune system are important in the pathophysiology of alexithymia (Todarello et al., 1994; Dewaraja et al., 1997; Todarello et al., 1997; Guilbaud et al., 2003, 2009; Corcos et al., 2004; Pedrosa et al., 2007). In this context, findings of this study show that heightened level of alexithymia within the group of the NIND patients is associated with increased CSF-IL-8. The results also show that CSF-IL-8 level significantly increases with heightened occurrence of anxiety which is in agreement with findings that patients with anxiety disorder exhibit disturbances in IL-8 production (Hoge et al., 2009). In addition we have found that alexithymia and anxiety in their specific interaction is linked to increased levels of CSF-IL-8 and that alexithymia and anxiety are tightly linked together. Worth of mentioning is also result of this study suggesting relationship between alexithymia and age which is in agreement with a few reported studies (Pasini et al., 1992; Mattila et al., 2006; Moriguchi et al., 2007). The results indicate that IL-8 has relationship to alexithymia and anxiety which has not been found in the case of IL-6. The result suggests that IL-8 could have exceptional role in mediation of the relationship of psychopathological symptoms and inflammantory response. This result is particularly interesting although its confirmation needs further research to document whether this relationship is specific for IL-8 or whether it may occur also in other cytokines. A limitation of the present results is that the group of patients assessed in this study appears to be very heterogeneous with regard to their diagnosis and mainly includes patients with primary headache and spondolysis. According to clinical experience both conditions are painful and it is well known that cytokines and chemokines may play a role in inflammatory pain which may implicate that CSF-IL-8 levels in this relatively heterogeneous group of patients may reflect also other not clearly understood processes related to psychopathological symptoms other than alexithymia (Bob, 2008). Other limitation of the present results is that according to the TAS-20 scale only 5 of the patients could be likely diagnosed with alexithymia. Nevertheless the result may present useful finding within the concept of alexithymia continuum where alexithymia is conceptualised preferentially as a dimensional construct, distributed normally in the general population (Bagby and Taylor, 1997; De Gucht and Heiser, 2003). An important explanatory role in this relationship between IL-8 and alexithymia could play corticotropin-releasing hormone (CRH) that is closely related to locus ceruleus-norepinephrine autonomic neurons of the hypothalamus and brainstem and regulate sympathetic nervous activity, and also immune responses (Elenkov et al., 2000; Elenkov and Chrousos, 2002). It corresponds to findings of several recent studies suggesting dysregulation of the HPA (hypothalamic-pituitary-adrenal) axis and SAM (sympatho-adreno-medullary reactivity) in alexithymic subjects (Lindholm et al., 1990; Lin et al., 2005; Finset et al., 2006; De Timary et al., 2008b). In addition, IL-8 was identified in different brain areas (e.g. paraventricular nucleus of the hypothalamus and hippocampus) involved in the HPA axis regulation through

the ACTH [adrenocorticotropic hormone] (Lucinio et al., 1992; Rosténe et al., 2010). Important evidence for the research of interactions between neuroimmune disturbances in alexithymia present data that IL-8 together with other pro-inflammatory cytokines IL-1, IL-6, and TNF-alpha present important regulators of predominantly innate immunity (Medzhitov et al., 1997; Elenkov, 2008). In this context, results of this study present contribution to current findings that also cytokines participating in regulation of predominantly innate immunity play an important role in pathophysiology of immune dysregulation in alexithymia (Bruni et al., 2006; Pedrosa et al., 2007; Vadacca et al., 2008). These findings present a new research direction which is complementary to the recent hypothesis that alexithymia is related to Th1/Th2 cytokines balance dysregulation reflecting disturbances in adaptive immunity (Pedrosa et al., 2007; Guilbaud et al., 2009). Together these findings suggest that immune dysregulations related to alexithymia are more complex than was previously thought and that genetic predispositions may play a significant role in pathogenesis of alexithymia. In this context, future studies focussed on disturbances of innate immunity in alexithymia could provide new research directions and potentially useful clinical findings.

2.2. ALEXITHYMIA AND NEUROPATHIC PAIN IN SCIATICA

2.1.1. Introduction

Low back pain (LBP) is one of the most frequent health problems (Walker, 2000; Strine and Hootman, 2007) and represents one of the most important causes of disability, work absenteeism (Van Tulder et al., 1995) and impact on health resources (Van Tulder et al., 1995; Awad and Moskovich, 2006). Substantial proportion of LBP patients (15%) have sciatica pain, which is considered as a poor prognostic indicator associated with more severe pain, disability, time off work and worse clinical course (Hill et al., 2011). In addition, there is evidence that significant proportion of sciatica patients have neuropathic pain (Baron and Binder 2004; Hassan et al., 2004; Freynhagen et al., 2006a and 2006b; Torrance et al., 2006; Gustorff et al., 2008; Freynhagen and Baron, 2009; Hill et al., 2011) that is associated with higher ratings of pain intensity, co-morbidities such as depression, anxiety, sleep disorders and decreased quality of life (Freynhagen et al., 2006b). Several psychological factors, including alexithymia are implicated as important factors in pathophysiology and management of pain states, however, much uncertainty still remains about the weight and functions of these psychological factors (Mehling and Krause, 2007).

According to current studies there is evidence that psychological factors such as depressed mood, emotional distress and somatization play a significant role in the onset of low back pain (LBP) (Strigo et al, 2010). These factors were also identified as risk conditions for transition of the LBP status to chronicity (Pincus et al., 2002; Frymoyer, 2010; Linton, 2010; Shaw et al., 2010) and may present an antecedent factor predicting development of chronic pain (Fishbain et al., 1997; Shaw et al, 2010).

Alhough the association between depression, anxiety and LBP is relativelly well known (Freynhagen et al., 2006b) the research concerning relationship between alexithymia and LBP is sparse. Indeed, some previous studies have shown that alexithymia symptoms predict depression (Kosturek et al., 1998; Lumley et al., 2002), anxiety (Kosturek et al., 1998), and physical impairment (Lumley et al., 2002) in patients with various types of chronic pain. Alexithymia also represents risk factor for chronic pain, disability, and related health problems (Lumley et al., 2002). In addition it has been shown that association between alexithymia and pain symptoms (persistent pain, acute pain severity and acute pain tolerance) presents clinically significant complication in pain patients (Millard and Kinsler, 1992; Zayfert et al., 1992; Cox et al., 1994; Nyklicek et al., 2000; Lumley et al., 2002; Hosoi et al., 2010). In spite of these findings there are however only few descriptive or cross-sectional studies that have examined relationship between alexithymia and LBP and no study examining alexithymia in sciatica patients. Majority of these studies have found positive relationship between LBP and alexithymia (Acklin and Bernat, 1987; Julkunen et al., 1988; Kinder and Curtiss,

1990; Viikari-Juntura et al., 1991; Mehling et al., 2005) and only one study have found negative association between alexithymia and incidence of LBP (Mehling and Krause, 2007). In addition, to our knowledge and according to PubMed search, there is no study examing relationship between alexithymia and LBP with sciatica as well as study examining relationship between alexithymia and neuropathic pain in sciatica patients. In this context it is also known that alexithymia is related to increased serum levels of C-reactive protein (CRP) (de Berardis et al., 2008; Honkalampi et al., 2011) and that increased levels of CRP are likely associated with neural lesions in the sciatica pain (Stürmer et al., 2005) and may play a role in neuropathic pain generation (Jaggi and Singh, 2011; Noguchi and Okubo, 2011; Pabreja et al., 2011; Takahashi et al., 2011). According to our knowledge the relationship between CRP and alexithymia in sciatica patients have not been reported in recently published studies.

Moreover several authors suggest that majority of the current findings reported in psychological and pain studies of LBP patients are not methodologically integrated and most of these investigations included small and heterogeneous samples of patients (LaCaille et al. 2005; Edwards et al., 2007) with various pain etiology (Carragee, 2001). With respect to the current findings a purpose of this study is to examine a hypothesis wheter there is a relationship between neuropathic pain and alexithymia. Secondly wheter there is a relationship between pain variables (actual pain intensity; maximum pain intensity in last 6 weeks and average pain intensity also within last 6 weeks) and alexithymia in sciatica patients. Further purpose of this study is to examine a hypothesis whether there is a relationship between serum CRP levels and alexithymia.

With the purpose to examine these hypotheses we have investigated a homogenous group of sciatica pain patients with intrervertebral disc herniation or its combination with spondylotic foraminal stenosis divided into three subgroups differentially associated with a level of neuropathic pain component and with different presentations of pain duration, and focal neurological signs on the lower-extremities.

2.1.2. Methods

2.2.2.1. Participans

In order to examine the above mentioned hypotheses we have performed assessment of neuropathic pain, levels of CRP in serum, depressive symptoms, anxiety, alexithymia and BMI data in the patients group consisted of 66 consecutive LBP inpatients suffering from pain related to lower extremity involving radicular pain symptoms (sciatica pain). The patients were 28 males and 38 females in average age 57.93 years (age range 31.00 - 75.00) predominantly with

high-school education and body mass index (18.90 - 43.50). The study was approved by University Ethical Committee and all the patients gave voluntary written informed consent. The patient's had diagnosis of L4, L5 or S1 radiculopathy caused by intervertebral lumbar disc herniation or its combination with spondylotic foraminal stenosis. Complete medical history was taken and physical, neurological and laboratory examinations were performed to establish whether all selected subjects were free of any inflammatory or oncologic disorders that could imitate radiculopathy caused by intervertebral disc herniation. The diagnoses were confirmed independently by two neurologists of the neurology department. The patients were at the time of recruitment treated at the Department of Neurology of the University Hospital in Prague. Exclusion criteria included malignant and systemic inflammatory diseases, rheumatoid arthritis, ankylosing spondylitis, Reiter's syndrome, dementia, psychosis and mental retardation. Other exclusion criteria were steroid medication, recent history of infectious diseases (influenza or other febril state within two past weeks).

2.2.2.2. Psychometric measures

All the participants completed test for neuropathic pain and other psychometric measures. Neuropathic pain component was meassured with Czech version of the Pain DETECT Questionnaire (PD-Q) (Cronbach's alpha 0.87). The PD-Q is a reliable screening tool used for determination of the prevalence of neuropathic pain components in LBP (Freynhagen et al., 2006b). It represents 20-items self-reported questionnaire with high sensitivity, specificity and positive predictive accuracy. A total score of PD-Q above 18 indicates that a predominantly neuropathic pain component is likely, whereas a total score lower than 13 indicates that neuropathic pain is unlikely (Freynhagen et al., 2006b).

Depressive symptoms were assessed using the Czech version of Beck depression inventory BDI-II (Beck et al., 1996) that represents 21-items questionnaire for assessing depression (Cronbach's alpha 0.89, test - retest reliability after week 0.85). Subjects indicate degree of their experience of depressive symptoms on 4-point Likert scale.

Levels of anxiety symptoms were assessed using the Czech version of The Zung Self-Rating Anxiety Scale (SAS) (Cronbach's alpha 0.89, test – retest reliability after week 0.85) (Zung, 1971). The SAS is 20-item self-reporting questionnaire focused on the most common general anxiety symptoms. Each question is scored on 4-point Likert scale from 1 to 4.

Alexithymia was assessed using the Czech version of the 20-item Toronto Alexithymia Scale (TAS-20) (Cronbach's alpha 0.81, test - retest reliability after 1 week 0.77) (Bagby et al., 1994a and 1994b). Each questions scored on a five - point Likert scale (1 - 5) and the TAS total score has range from 20 to 100.

2.2.2.3. Magnetic Resonance Imaging assessment

In order to confirm the clinical diagnosis and for pre-surgical assessment in cases indicated for disc surgery intervention we have performed MRI assessment. The assessment was focused on lumbar spine using 1.5 Tesla scaner (Magnetom Avanto, Siemens) and was performed without Gadolinium contrast.

2.2.2.4. Immunochemical measures of C-reactive protein

Blood samples were taken and immediately transferred for biochemical asessment of serum CRP levels that have been performed according to common analytical procedures. Concentrations of serum CRP were measured using turbidimetric immunoassay method CRP Latex kit (Olympus). The detection limit for CRP was 0.2 mg/mL (milligram/milliliter) and intra-assay coefficient of variation was lower than 4 %.

2.2.2.5. Statistical methods

Statistical evaluation for results of neuropathic pain component, CRP, psychometric measures and BMI included means, standard deviations, Spearman correlation coefficients, Kruskal-Wallis ANOVA and Mann - Whitney test for independent samples. All the methods of statistical evaluation were performed using the software package Statistica version 6.

2.2.3. Results

Because data did not show presence of significant clusters, the patients (N = 66) were divided into three groups according to the presence of neuropathic pain component [i.e. neuropathic pain patients N=29, ambiguous group with possible neuropathic pain component N=18 and non-neuropathic group N=19]. All the differences (Figure 1c) are statistically significant for alexithymia (TAS-20) [at $p<0.01$, $z>4.1$], depression (BDI-II) [at $p<0.01$, $z>3.9$], anxiety (SAS) [at $p<0.01$, $z>4.9$], and pain score (PD-Q) [at $p<0.015$, $z>2.8$]. Also we have found statisticaly significant differences in CRP levels between patients with neuropathic and non-neuropathic pain, and between patients with neuropathic and ambiguous pain [at $p<0.01$, $z>3.8$] (Figure 2c). Other differences were not statistically significant. The results show that pain patients with neuropathic pain have significantly higher alexithymia compared to other pain patients with sciatica symptoms.

The results also indicate that total score of TAS-20 is significantly correlated to depression (BDI) (Spearman R = 0.480, $p<0.01$), anxiety (SAS) (Spearman R = 0.411, $p<0.01$), but not to pain variables (PD-Q – pain detect score; Act P – actual pain intensity; MP – maximal pain intensity last 6 weeks; Aver P – average pain intensity last 6 weeks) (Table1c). These correlations show that alexithymia exhibits relatively strong relationship to depression and anxiety symptoms. Statistical comparison between men and women has not shown significant differences in pain or psychopathology variables measures.

To distinguish the effect of acute pain or its chronicity with respect to the neuropathic pain component, the psychopathological symptoms and CRP levels, we have divided the patients (N= 66) into two subgroups according to sciatica duration. The first group consisted of the acute and subacute sciatica patients [N=40; i.e. non-neuropathic (N=12); ambiguous (N=11); neuropathic (N=17)] with duration of the pain less than 3 months. The second group included the chronic sciatica patients [N=26; i.e. non-neuropathic (N=7); ambiguous (N=7); neuropathic (N=12)] with pain duration more than 3 months. Comparison using Mann-Whitney test have found statistically significant differences between the subgroups for BDI-II and SAS ($p<0.007$, $Z>2.68$) indicating that chronic patients have higher level of depression and anxiety (Mean BDI-II=15.92; Mean SAS=43.73) than patients with acute pain (Mean BDI-II=10.21; Mean SAS=37.16), but we have not found differences for the alexithymia (TAS-20), pain score (PD-Q) and other used measures including CRP.

We have also divided the patients (N=66) into two groups according to the presence of motor [N=29; radicular motor weakness or/and deep tendon hyporeflexia] or sensory [N=37; radicular pain or/and disturbed sensation in the corresponding dermatomes L4-S1] symptoms and found that statistical comparison using Mann-Whitney test did not show significant differences between the subgroups.

2.2.4. Table and figures

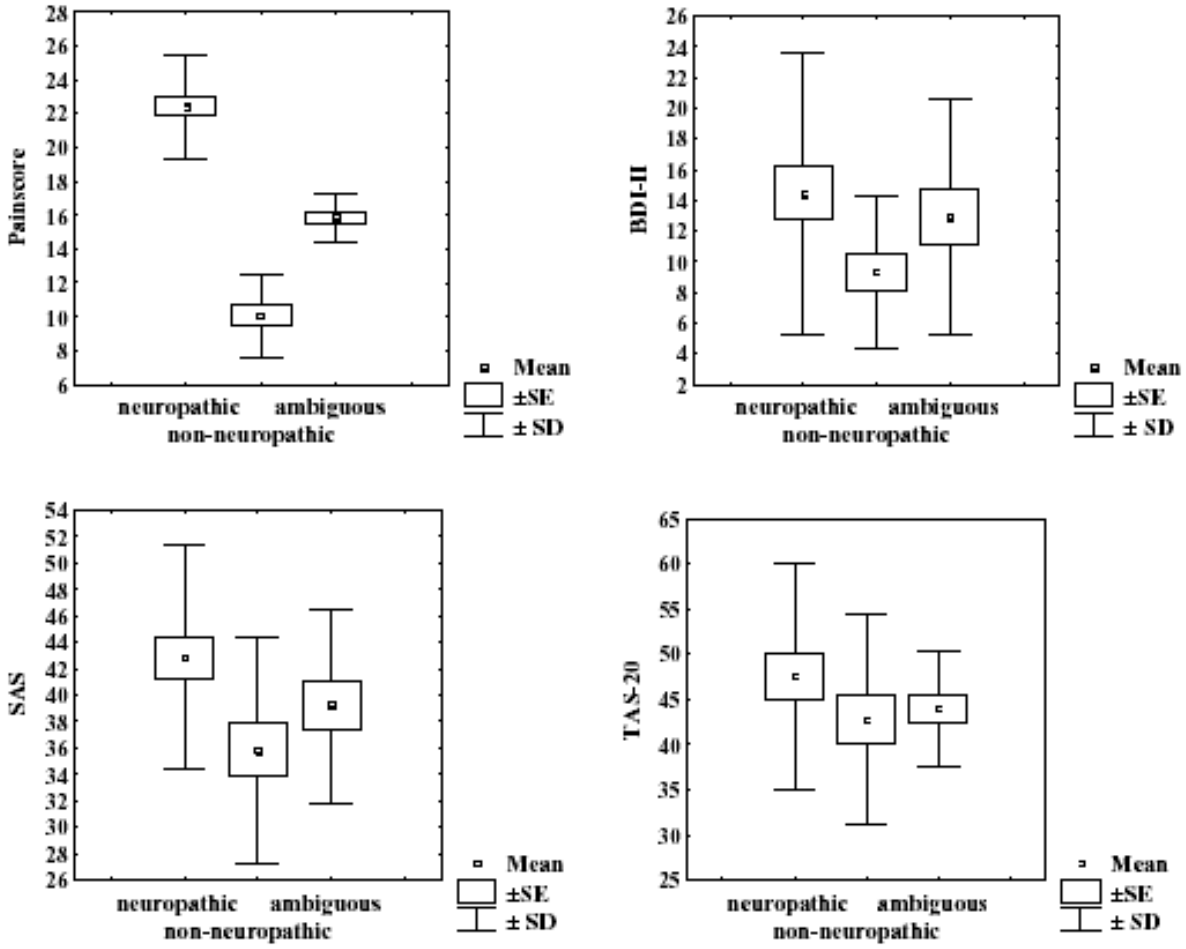


Figure 1c. Scores for the neuropathic, ambiguous and non-neuropathic group. All differences are statistically significant for pain score (PD-Q) at $p<0.015$, $z>2.8$, depression (BDI-II) at $p<0.01$, $z>3.9$, anxiety (SAS) at $p<0.01$, $z>4.9$, alexithymia (TAS-20) at $p<0.01$, $z>4.1$).

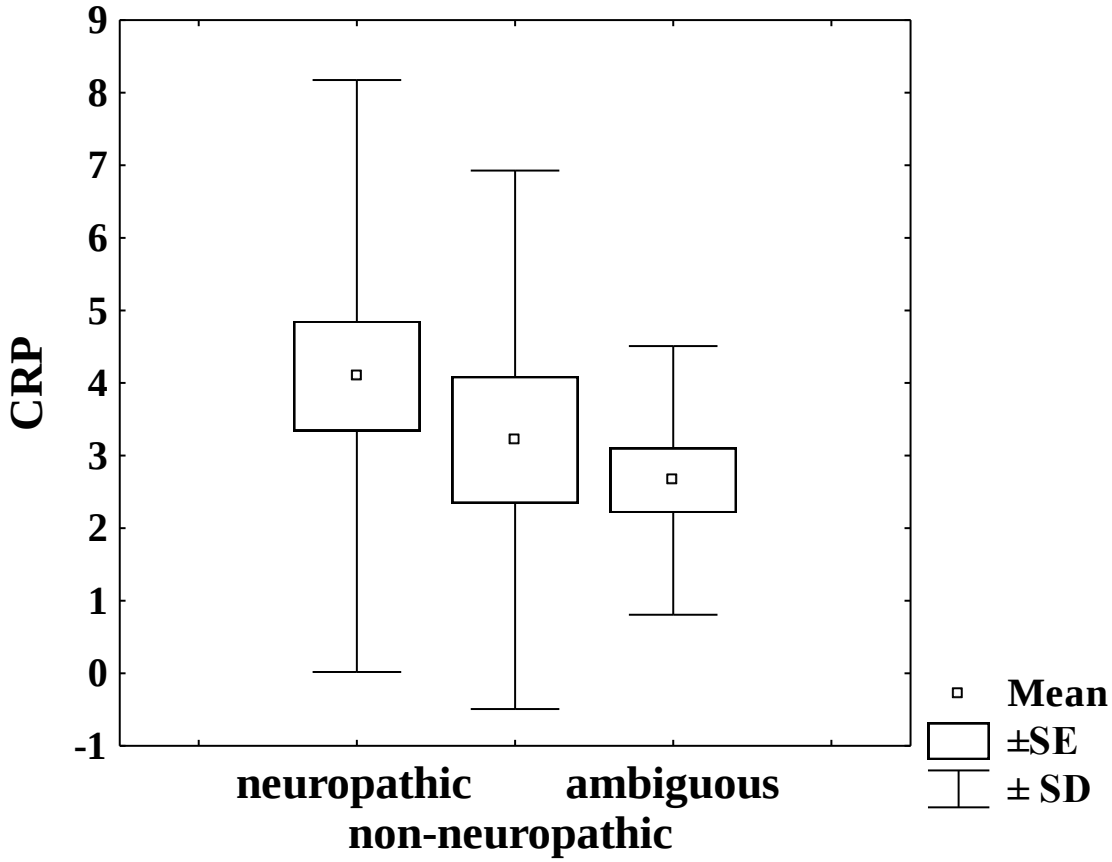


Figure 2c. CRP levels for the neuropathic, non-neuropathic and ambiguous group (differences between neuropathic and non-neuropathic pain, and between neuropathic and ambiguous pain are statistically significant at $p<0.01$, $z>3.8$).

Table 1c. Spearman correlations of pain variables, psychopathological symptoms, BMI, Age and serum CRP in sciatica pain patients (N=66).

	CRP	**TAS-20**	**BDI-II**	**SAS**	**PD-Q**
TAS-20	-0,061	–	–	–	–
BDI-II	0,054	**0,481****	–	–	–
SAS	0,152	**0,411****	**0,704****	–	–
PD-Q	0,051	0,173	0,239	**0,368****	–
Act P	0,187	-0,058	0,268	0,248	0,266
Max P	0,120	-0,047	-0,047	-0,028	0,125
Aver P	0,132	0,077	0,078	0,043	0,346
Age	-0,080	0,077	-0,032	-0,127	-0,118
BMI	**0,399****	0,090	0,211	**0,327***	0,034

Note. *$p < 0.05$; **$p < 0.01$.; TAS-20- Toronto Alexithymia Scale; BDI-II- Beck Depression Inventory; SAS- Self-reported Anxiety Scale; PD-Q – Pain DETECT Questionnaire; Act P – actual pain intensity; Max P – maximal pain intensity last 6 weeks; Aver P – average pain intensity last 6 weeks, BMI – body mass index; CRP – serum level of C-reactive protein

2.2.5. Discussion

Results of this study indicate that increased neuropathic component in sciatica pain is associated with elevated levels of alexithymia, depression, anxiety, and serum CRP. Based on literature review the results of this study likely present the first finding documenting relationship between neuropathic pain and alexithymia in sciatica pain patients. These findings are in agreement with the curent data documented in non-selected LBP patients that has shown significant association between neuropathic pain and the higher ratings of pain intensity, depression and anxiety symptoms (Freynhagen et al., 2006b). Results of this study suggest significant differences in mood factors between nociceptive and neuropathic pain patients.

In this context, there are several data indicating that some patients with other types of "classical" painful neuropathies such as painful polyneuropathies and postherpetic neuralgia do not display differences in pain, cognitive and mood symptoms as well as in a level of physical suffering with respect to the nociceptive pain patients (Haythornthwaite and Benrud-Larson, 2000; Benbow et al., 1998; Galer et al., 2000a, 2000b). With respect to these findings, the result of this study suggest that sciatica neuropathic pain is associated with different sensory symptoms and different mechanisms of neuropathic pain generation in comparson to other painful neuropathies (Baron, 2009; Baron et al., 2010).

Particular importance also has the result indicating significant elevation of serum CRP levels in the neuropathic sciatica patients. This observation is in line with recent studies strongly suggesting that several inflammatory mediators may potentiate neuronal activity and play a role in neuropathic pain generation (Noguchi and Okubo, 2011; Jaggi and Singh, 2011; Pabreja et al., 2011; Takahashi et al., 2011). These results are also in agreement with reported studies indicating that elevated levels of CRP could present systemic inflammatory response related to local nerve root impingement, which is considered as a main mechanism producing sciatica pain (Nygaard et al., 1997; Ahn et al., 2002; Stürmer et al., 2005; Le Gars et al, 2005). In this context, it is known that depression (Miller et al., 2009; Dowlati et al., 2010; Honkalampi et al., 2011) as well as alexithymia (de Berardis et al., 2008; Honkalampi et al., 2011) are related to increased levels of CRP and therefore the inflammatory-cytokine pathway might be responsible for the relationship between neuropathic pain and some psychopathological symptoms in neuropathic pain patients.

3. Appendix – used psychometric meassures

TAS-20

Jméno a příjmení..... Rodinný stav..... Věk .....

Zaměstnání..... Vzdělání.....

Odpověď znázorněte na škále od 1 (neodpovídá to mým zkušenostem a pocitům) do 5 (velmi dobře odpovídá).

1. Bývám často zmatený(-á) pokud jde o to, jaké emoce cítím.	1	2	3	4	5
2. Je pro mne těžké najít správná slova pro mé pocity.	1	2	3	4	5
3. Mám fyzické vjemy, kterým ani lékaři nerozumí.	1	2	3	4	5
4. Jsem snadno schopen(-na) popsat mé pocity.	1	2	3	4	5
5. Dávám přednost analyzování problémů před jejich popisováním.	1	2	3	4	5
6. Když se necítím dobře, nevím jestli jsem smutný(-ná), vyděšený(-ná) nebo rozhněvaný(-ná).	1	2	3	4	5
7. Jsem často zmatený(-ná) z pocitů v mém těle.	1	2	3	4	5
8. Dávám přednost tomu ponechat věcem volný průběh, před tím než abych se snažil(-a) porozumět tomu proč se takto dějí.	1	2	3	4	5
9. Mívám pocity, které nemohu zcela identifikovat.	1	2	3	4	5
10. Být ve styku s emocemi je zásadní.	1	2	3	4	5
11. Zjistil(-a) jsem, že je těžké popsat to, co cítím o lidech.	1	2	3	4	5
12. Lidé mi říkají, abych více popsal(-a) své pocity.	1	2	3	4	5
13. Nevím co se ve mně děje.	1	2	3	4	5
14. Často nevím, proč jsem rozhněvaný(-á).	1	2	3	4	5
15. Raději hovořím s lidmi o jejich denních aktivitách spíše než o jejich pocitech.	1	2	3	4	5
16. Raději se koukám na „lehký“ zábavný pořad než na psychologické drama.	1	2	3	4	5
17. Je pro mne těžké odhalit moje nejvnitřnější city a to i blízkým přátelům.	1	2	3	4	5
18. Cítím se blízko někoho i v okamžicích mlčení.	1	2	3	4	5
19. Zkoumání mých pocitů považuji za užitečné pro řešení osobních problémů.	1	2	3	4	5
20. Hledání skrytých významů ve filmech nebo hrách odvádí od zábavy.	1	2	3	4	5

BDI-II

Jméno a příjmení..... Rodinný stav..... .....Věk.....

Zaměstnání..... Vzdělání.....

Zakroužkujte v každé skupině jeden výrok, který nejlépe vystihuje, jak se cítíte během posledních 14 dnů včetně dneška.

1. Smutek
0 Nejsem smutný[á].
1 Většinou jsem smutný[á].
2 Pořád jsem smutný[á].
3 Jsem tak smutný[á], že se to nedá vydržet.

2. Pesimismus
0 O svou budoucnost nemám obavy.
1 O svou budoucnost se obávám více než dříve.
2 Myslím, že se mi nebude dařit.
3 Moje budoucnost je beznadějná a bude ještě horší.

3. Minulá selhání
0 Nemám dojem, že selhávám.
1 Selhal[a] jsem častěji než bych měl[a].
2 Když se dívám do minulosti vidím spoustu selhání.
3 Jako člověk jsem úplně selhal[a].

4. Ztráta radosti
0 Raduji se stejně jako dříve.
1 Neraduji se stejně jako dříve
2 Téměř nemám potěšení z věcí, které jsem měl[a] rád[a].
3 Vůbec nemám potěšení z věcí, které jsem měl[a] rád[a].

5. Pocit viny
0 Nemívám nijak zvlášť pocity viny.
1 Cítím vinu za řadu věcí, které jsem udělal[a] nebo měl[a] udělat.
2 Mívám často pocity viny.
3 Pořád mám pocity viny.

6. Pocit potrestání
0 Nemyslím, že mě život trestá.
1 Myslím, že by mě život mohl potrestat.
2 Očekávám trest.
3 Myslím, že jsem životem trestán[a].

7. Znechucení ze sebe sama
0 Myslím si o sobě pořád to samé.
1 Ztratil[a] jsem důvěru v sebe sama.
2 Jsem ze sebe zklamaný[á].
3 Sám[a] sebou jsem znechucen[a].

8. Sebekritika
0 Nekritizuji nebo neobviňuji sebe sama více než obvykle.
1 Jsem sám[a] k sobě více kritický[á] než dříve.
2 Kritizuji se za všechny své chyby.
3 Obviňuji se za všechno špatné co se přihodí.

9. Sebevražedné myšlenky nebo přání
0 Nepřemýšlím o tom, že bych se zabil[a].
1 Mám myšlenky o sebevraždě, ale neudělal[a] bych to.
2 Chtěl[a] bych se zabít.
3 Kdybych měl[a] možnost se zabít, tak bych se zabil[a].

10. Plačtivost
0 Neplaču více než dříve.
1 Pláču více než dříve.
2 Pláču kvůli každé maličkosti.
3 Je mi do pláče, ale nejsem toho schopen[na]

11. Agitovanost
0 Nejsem více neklidný[á] nebo napjatý[á] než obvykle.
1 Cítím se více neklidný[á] nebo napjatý[á] než obvykle.
2 Jsem tak neklidný[á] nebo rozrušený[á], že je těžké to vydržet.
3 Jsem tak neklidný[á] nebo rozrušený[á], že nemohu zůstat v nečinnosti.

12. Ztráta zájmu
0 O jiné lidi nebo věci jsem zájem neztratil[a].
1 Méně se zajímám o jiné lidi nebo věci.
2 Mnohem méně se zajímám o jiné lidi nebo věci.
3 Je těžké se zajímat o cokoliv.

13. Nerozhodnost
0 Rozhoduji se stejně dobře jako dříve.
1 Rozhodovat se je obtížnější, než obvykle.
2 Rozhoduji se mnohem obtížněji než dříve.
3 Mám problém udělat jakékoliv rozhodnutí.

14. Pocit bezcennosti

0 Necítím se bezcenný[á]
1 Nemyslím, že mám pro lidi stejnou cenu jako jsem míval[a].
2 Ve srovnání s jinými lidmi se cítím více bezcenný[á].
3 Cítím se úplně bezcenný[á].

15. Ztráta energie

0 Mám stejné energie jako vždy.
1 Mám méně energie než jsem míval[a].
2 Nemám dost energie, abych toho hodně udělal[a].
3 Vůbec na nic nemám energii.

16. Změna spánku

0 Nevšiml[a] jsem si žádných změn u svého spánku.
1a Spím trochu více než obvykle.
1b Spím trochu méně než obvykle.
2a Spím mnohem více než obvykle.
2b Spím mnohem méně než obvykle.
3a Většinu dne prospím.
3b Probouzím se o jednu až dvě hodiny dříve a už nemohu usnout.

17. Podrážděnost

0 Nejsem podrážděný[á] více než obvykle.
1 Jsem více podrážděný[á] než obvykle.
2 Jsem mnohem více podrážděný[á] než obvykle.
3 Bývám pořád podrážděný[á].

18. Změny chutí k jídlu

0 Necítím žádné změny v chuti k jídlu.
1a Mám trochu menší chuť k jídlu než obvykle.
1b Mám trochu větší chuť k jídlu než obvykle.
2a Mám mnohem menší chuť k jídlu než obvykle.
2b Mám mnohem větší chuť k jídlu než obvykle.
3a Vůbec nemám chuť k jídlu.
3b Jíst mohu pořád.

19. Koncentrace

0 Mohu se soustředit jako vždycky.
1 Nejsem schopný[á] se soustředit jako obvykle.
2 Je těžké se na cokoliv delší dobu soustředit.
3 Nejsem schopný[á] se soustředit na nic.

20. Únava

0 Nejsem unavený[á] více než obvykle.
1 Unavím se snadněji než obvykle.
2 Jsem příliš unavený[á], než abych dělal[a] tolik věcí, jako jsem dělával[a].
3 Jsem tak unavený[á], že nedokážu dělat skoro nic.

21. Ztráta zájmu o sex

0 V současnosti jsem nezaznamenal[a] změnu zájmu o sex.
1 Mám menší zájem o sex než obvykle.
2 Mám nyní mnohem menší zájem o sex.
3 Úplně jsem ztratil[a] zájem o sex.

SAS

Jméno a příjmení..... Rodinný stav..... Věk .....

Zaměstnání..... Vzdělání.....

Stupnice hodnocení: 1 – nikdy nebo zřídka, 2 – někdy, 3 – často, 4 – velmi často nebo stále

1. Cítím se více nervózní a úzkostný než je obvyklé.	1	2	3	4
2. Mám strach a vlastně nevím z čeho.	1	2	3	4
3. Snadno se rozruším nebo zpanikařím.	1	2	3	4
4. Mám pocit,že jsem rozvrácený, rozpadlý na kusy.	1	2	3	4
5. Je se mnou všechno v pořádku a neobávám se ničeho nepříjemného	1	2	3	4
6. Cítím chvění a rozklepanost v rukou a nohou.	1	2	3	4
7. Obtěžují mě bolesti hlavy, bolesti v šíji, bolesti v kříži.	1	2	3	4
8. Cítím se slabý a snadno se unavím.	1	2	3	4
9. Jsem klidný a mohu pokojně sedět.	1	2	3	4
10. Cítím,že srdce mi tluče rychleji.	1	2	3	4
11. Obtěžují mě závratě.	1	2	3	4
12. Někdy je mi na omdlení.	1	2	3	4
13. Volně se mi dýchá.	1	2	3	4
14. Mám otupělost nebo brnění v prstech na rukou či nohou.	1	2	3	4
15. Trpím bolestmi žaludku nebo poruchami trávení.	1	2	3	4
16. Mám časté nutkání močit.	1	2	3	4
17. Ruce mám obvykle suché a teplé.	1	2	3	4
18. Mám pocit,že rudnu v obličeji.	1	2	3	4
19. Snadno usínám a dobře se vyspím.	1	2	3	4
20. Mám noční děsy (nepříjemné sny).	1	2	3	4

painDETECT™ Vyhodnocení dotazníku o bolesti

Datum: ..... Pacient: Příjmení: ..... Jméno: .....

Prosím zapište celkové skóre z dotazníku o bolesti:

Celkové skóre ☐☐

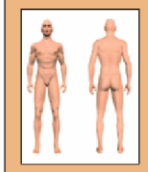
Přičtěte prosím následující čísla podle toho, který příklad průběhu bolesti a vyzařování bolesti byl zakřížkován. Pak vypočítejte konečné skóre:

Trvalá bolest s mírnými výkyvy — 0

Trvalá bolest s občasnými záchvaty silné bolesti — -1 pokud byla zakřížkována tato možnost nebo

Záchvaty silné bolesti, mezi nimi bez bolesti — +1 pokud byla zakřížkována tato možnost nebo

Časté záchvaty silné bolesti, mezi nimi trvalá bolest — +1 pokud byla zakřížkována tato možnost

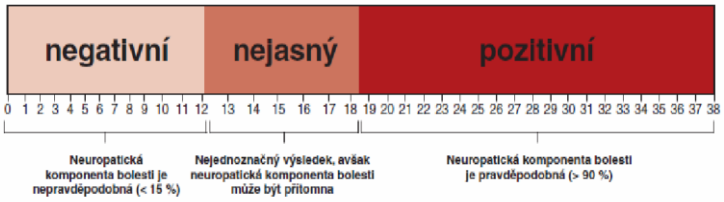


Vyzařující bolest? — +2 pokud bylo uvedeno ano

Konečné skóre ☐☐

Výsledek screeningu

přítomnosti neuropatické komponenty bolesti



Tento dotazník nenahrazuje lékařskou diagnostiku!
Slouží k provádění screeningu přítomnosti neuropatické komponenty bolesti.

DFNS

pain

painDETECT™ DOTAZNÍK O BOLESTI

Datum: ..... Pacient: Příjmení: ..... Jméno: .....

Jak byste ohodnotil/a svou bolest **nyní**, v tomto okamžiku?

0 1 2 3 4 5 6 7 8 9 10

žádná maximální

Jak silná byla Vaše **nejsilnější** bolest během minulých 4 týdnů?

0 1 2 3 4 5 6 7 8 9 10

žádná maximální

Jak silná byla bolest během minulých 4 týdnů **v průměru**?

0 1 2 3 4 5 6 7 8 9 10

žádná maximální

Zakřížkujte políčko vpravo vedle obrázku, který nejlépe vystihuje průběh Vaší bolesti:

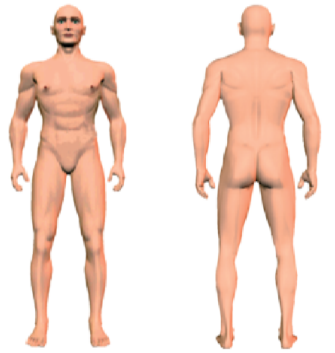
Trvalá bolest s mírnými výkyvy ☐

Trvalá bolest s občasnými záchvaty silné bolesti ☐

Záchvaty silné bolesti, mezi nimi bez bolesti ☐

Časté záchvaty silné bolesti, mezi nimi trvalá bolest ☐

Označte prosím křížkem nebo vystínováním jednu **hlavní oblast své bolesti**



Vyzařuje Vaše bolest i do jiných částí těla? ano ☐ ne ☐

Pokud ano, nakreslete prosím šipkou směr, kterým bolest vyzařuje.

Míváte v této označené oblasti pálivé bolesti (jako např. při popálení kopřivou)?
vůbec ne ☐ takřka ne ☐ málo ☐ středně ☐ silně ☐ velmi silně ☐

Míváte v této označené oblasti pocit brnění nebo šimrání (mravenčení nebo např. jako od elektřiny)?
vůbec ne ☐ takřka ne ☐ málo ☐ středně ☐ silně ☐ velmi silně ☐

Působí Vám lehký dotyk v této označené oblasti (oblečením, přikrývkou) bolest?
vůbec ne ☐ takřka ne ☐ málo ☐ středně ☐ silně ☐ velmi silně ☐

Míváte v této označené oblasti Vaší bolesti vystřelující záchvaty silné bolesti, jakoby od elektrického proudu?
vůbec ne ☐ takřka ne ☐ málo ☐ středně ☐ silně ☐ velmi silně ☐

Je pro Vás chlad nebo teplo (např. voda ve vaně) v této označené oblasti občas bolestivé?
vůbec ne ☐ takřka ne ☐ málo ☐ středně ☐ silně ☐ velmi silně ☐

Trpíte v této označené oblasti pocitem znecitlivění?
vůbec ne ☐ takřka ne ☐ málo ☐ středně ☐ silně ☐ velmi silně ☐

Vyvolává lehký stálý tlak, např. prstem, v této označené oblasti bolest?
vůbec ne ☐ takřka ne ☐ málo ☐ středně ☐ silně ☐ velmi silně ☐

vyplňuje lékař

vůbec ne	takřka ne	málo	středně	silně	velmi silně
☐ × 0 = ☐	☐ × 1 = ☐	☐ × 2 = ☐☐	☐ × 3 = ☐☐	☐ × 4 = ☐☐	☐ × 5 = ☐☐

Celkové skóre ☐☐ z 35

4. References

Acklin MW, Alexander G. Alexithymia and somatization. A Rorschach study of four psychosomatic groups. J Nerv Ment Dis. 1988; 176:343–50.

Acklin MW, Bernat E. Depression, alexithymia, and pain prone disorder: a Rorschach study. J Pers Assess. 1987;51:462–79.

Adams RB Jr, Gordon HL, Baird AA, Ambady N, Kleck RE. Effects of gaze on amygdala sensitivity to anger and fear faces. Science. 2003 Jun 6;300(5625):1536.

Adolphs R, Damasio H, Tranel D, Cooper G, Damasio AR. A role for somatosensory cortices in the visual recognition of emotion as revealed by three-dimensional lesion mapping. J Neurosci. 2000 Apr 1;20(7):2683-90.

Aftanas L, Varlamov A. Associations of alexithymia with anterior and posterior activation asymmetries during evoked emotions: EEG evidence of right hemisphere "electrocortical effort". Int J Neurosci. 2004 Nov;114(11):1443-62.

Aftanas LI, Varlamov AA, Reva NV, Pavlov SV. Disruption of early event-related theta synchronization of human EEG in alexithymics viewing affective pictures. Neurosci Lett. 2003 Apr 3;340(1):57-60.

Aftanas LI, Varlamov AA. Effects of alexithymia on the activity of the anterior and posterior areas of the cortex of the right hemisphere in positive and negative emotional activation. Neurosci Behav Physiol. 2007 Jan;37(1):67-73.

Agarwal SK, Marshall GD Jr. Dexamethasone promotes type 2 cytokine production primarily through inhibition of type 1 cytokines. J Interferon Cytokine Res. 2001 Mar;21(3):147-55.

Ahlberg J, Nikkila H, Kononen M, Partinen M, Lindholm H, Sarna S, Savolainen A. Associations of perceived pain and painless TMD-related symptoms with alexithymia and depressive mood in media personnel with or without irregular shift work. Acta Odontol Scand. 2004;62:119–23.

Ahn SH, Cho YW, Ahn MW, Jang SH, Sohn YK, Kim HS. mRNA expression of cytokines and chemokines in herniated lumbar intervertebral discs. Spine. 2002;27:911–7.

Ahrens S, Deffner G. Empirical study of alexithymia: methodology and results. Am J Psychother. 1986 Jul;40(3):430-47.

Alexander F . Psychosomatic Medicine. New York: Norton, 1950.

Alexander F. Fundamental concepts of psychosomatic research. Psychosom Med. 1943;5:205-10

Apfel RJ, Sifneos PE. Alexithymia: concept and measurement. Psychother Psychosom. 1979;32:180– 90.

Awad JN, Moskovich R. Lumbar disc herniations: surgical versus nonsurgical treatment. Clin Orthop Relat Res. 2006; 443:183-97.

Badura AS. Theoretical and empirical exploration of the similarities between emotional numbing in posttraumatic stress disorder and alexithymia. J Anxiety Disord. 2003;17(3):349-60.

Bagby RM, Taylor GJ, Parker JD. The twenty-item Toronto Alexithymia Scale–II. Convergent, discriminant, and concurrent validity. J Psychosom Res. 1994a;38(1):33-40.

Bagby RM, Parker JD, Taylor GJ. The twenty-item Toronto Alexithymia Scale--I. Item selection and cross-validation of the factor structure. J Psychosom Res. 1994b Jan;38(1):23-32.

Bagby RM, Quiltya LC, Taylor GJ, Grabed HJ, Luminete O, Verissimo R, De Grootte I, Vanheule S. Are there subtypes of alexithymia? Pers Individ Differ. 2009;47: 413–8.

Bagby RM, Taylor GJ, Parker GJ. The twenty-item Toronto Alexithymia cale: II. Convergent, discriminant and concurrent validity. J Psychosom Res. 1994a;38:33 –40.

Bagby RM, Taylor GJ. Affect dysregulation and alexithymia. In: Taylor GJ, Bagby RM, Parker JDA, editors. Disorders of affect regulation: alexithymia in medical and psychiatric illness. Cambridge: University Press, 1997. pp. 26– 45.

Bach M, Bach D. Predictive value of alexithymia: a prospective study in somatizing patients. Psychother Psychosom. 1995;64:43–8.

Balduzzi D, Tononi G. Integrated information in discrete dynamical systems: motivation and theoretical framework. PLoS Comput Biol. 2008;4(6):e1000091.

Bankier B, Aigner M, Bach M. Alexithymia in DSM-IV disorder: comparative evaluation of somatoform disorder, panic disorder, obsessive–compulsive disorder, and depression. Psychosomatics. 2001;42:235–40.

Baron R, Binder A, Wasner G. Neuropathic pain: diagnosis, pathophysiological mechanisms, and treatment. Lancet Neurol. 2010 Aug;9(8):807-19.

Baron R, Binder A. How neuropathic is sciatica? The mixed pain concept. Orthopade. 2004; 33:568-75.

Baron R. Neuropathic pain: a clinical perspective. Handb Exp Pharmacol. 2009;(194):3-30.

Bazydlo R, Lumley MA, Roehrs T. Alexithymia and polysomnographic measures of sleep in healthy adults. Psychosom Med. 2001 Jan-Feb;63(1):56-61.

Beck AT, Steer RA, Brown GK. Manual for Beck Depression Inventory-II. Psychological Corporation, San Antonio, TX, 1996.

Benbow SJ, Wallymahmed ME, Macfairlane IA. Diabetic peripheral neuropathy and quality of life. Quart J Med. 1998;91:733-7.

Berenbaum H, James T. Correlates and retrospectively reported antecedents of alexithymia. Psychosom Med. 1994 Jul-Aug;56(4):353-9.

Berenbaum H, Prince JD. Alexithymia and interpretation of emotion-relevant information. Cogn Emot. 1994;8:231-144.

Berenbaum H. Childhood abuse, alexithymia and personality disorder. J Psychosom Res. 1996;41:585–95.

Beresnevaite M. Exploring the benefits of group psychotherapy in reducing alexithymia in coronary hearth disease patients. Psychother Psychosom. 2000;69:117-22.

Bermond B, Bierman DJ, Cladder MA, Moormann PP, Vorst HC. The cognitive and affective alexithymia dimensions in the regulation of sympathetic responses. Int J Psychophysiol. 2010 Mar;75(3):227-33.

Bermond B, Vorst HC, Moormann PP. Cognitive neuropsychology of alexithymia: implications for personality typology. Cognit Neuropsychiatry. 2006;11: 332–60.

Bermond B, Vorst HCM, Vingerhoets AJ, Gerritsen W. The Amsterdam Alexithymia Scale: its psychometric values and correlations with other personality traits. Psychother Psychosom. 1999;68:241– 51.

Bernstein CN, Walker JR, Fraff LA. On studying the connection between stress and IBD. Am J Gastroentroenterol. 2006;101:782–5.

Berthoz S, Consoli SM, Perez-Diaz F, Jouvent R: Alexithymia and anxiety: compounded relationships? A psychometric study. European Psychiatry. 1999, 14(7):372-378.

Bewley J, Murphy PN, Mallows J, Baker GA. Does alexithymia differentiate between patients with nonepileptic seizures, patients with epilepsy, and nonpatient controls? Epilepsy Behav. 2005 Nov;7(3):430-7.

Bird G, Silani G, Brindley R, White S, Frith U, Singer T. Empathic brain responses in insula are modulated by levels of alexithymia but not autism. Brain. 2010 May;133(Pt 5):1515-25.

Bob P. Pain, dissociation and subliminal self-representations. Conscious. Cogn. 2008; 17:355—69.

Bodini B, Mandarelli G, Tomassini V, Tarsitani L, Pestalozza I, Gasperini C, Lenzi GL, Pancheri P, Pozzilli C. Alexithymia in multiple sclerosis: relationship with fatigue and depression. Acta Neurol Scand. 2008 Jul;118(1):18-23.

Bossù P, Salani F, Cacciari C, Picchetto L, Cao M, Bizzoni F, Rasura M, Caltagirone C, Robinson RG, Orzi F, Spalletta G. Disease outcome, alexithymia and depression are

differently associated with serum IL-18 levels in acute stroke. Curr Neurovasc Res. 2009 Aug;6(3):163-70.

Bradshaw JL: Hemispheric Specialization and Psychological Function. Chichester, Wiley, 1989.

Bruni R, Serino FM, Galluzzo S, Coppolino G, Cacciapaglia F, Vadacca M, Nilo S, Terminio N, Afeltra A. Alexithymia and neuroendocrine-immune response in patients with autoimmune diseases: preliminary results on relationship between alexithymic construct and TNF-alpha levels. Ann N Y Acad Sci. 2006 Jun;1069:208-11.

Buchanan DC, Waterhouse GJ, West SC Jr. A proposed neurophysiological basis of alexithymia. Psychother Psychosom. 1980;34(4):248-55.

Bydlowski S, Corcos M, Jeammet P, Paterniti S, Berthoz S, Laurier C, Chambry J, Consoli SM. Emotion-processing deficits in eating disorders. Int J Eat Disord. 2005 May;37(4):321-9.

Cacioppo JT, Uchino BN, Crites SL, Snydersmith MA, Smith G, Berntson GG, Lang PJ. Relationship between facial expressiveness and sympathetic activation in emotion: a critical review, with emphasis on modeling underlying mechanisms and individual differences. J Pers Soc Psychol. 1992 Jan;62(1):110-28.

Canli T, Desmond JE, Zhao Z, Glover G, Gabrieli JD: Hemispheric asymmetry for emotional stimuli detected with fMRI. Neuroreport. 1998;9:3233–9.

Carr L, Iacoboni M, Dubeau MC, Mazziotta JC, Lenzi GL. Neural mechanisms of empathy in humans: a relay from neural systems for imitation to limbic areas. Proc Natl Acad Sci U S A. 2003 Apr 29;100(9):5497-502.

Carragee EJ. Psychological screening in the surgical treatment of lumbar disc herniation. Clin J Pain. 2001;17:215-9.

Cecero JJ, Holmstrom RW. Alexithymia and affect pathology among adult male alcoholics. J Clin Psychol. 1997 Apr;53(3):201-8.

Celikel F, Saatcioglu O. Alexithymia and anxiety in female chronic pain patients. Ann Gen Psychiatry. 2006;5:13.

Cohen K, Auld F, Demers L, Catchlove R. Alexithymia. The development of a valid and reliable projective measure (the objectively scored Archetypal-9 Test). J Nerv Ment Dis. 1985;173:621– 7.

Cohen SC, Rodriguez MS. Pathways linking affective disturbances and physical disorders. Health Psycho1. 1995;14:374-80.

Cole G, Bakan P. Alexithymia, hemisphericity, and conjugate lateral eye movements. Psychother Psychosom. 1985;44(3):139-43.

Connelly M, Denny DR. Regulation of emotions during experimental stress in alexithymia. J Psychosom Res. 2007;62:649–56.

Conrad R, Geiser F, Haidl G, Hutmacher M, Liedtke R, Wermter F. Relationship between anger and pruritus perception in patients with chronic idiopathic urticaria and psoriasis. Eur Acad Dermatol Venereol. 2008 Sep;22(9):1062-9.

Cooper DE, Holmstrom RW. Relationship between alexithymia and somatic complaints in a normal sample. Psychother Psychosom. 1984;41(1):20-4.

Corbetta M, Miezin FM, Dobmeyer S, Shulman GL, Petersen SE (1990): Attentional modulation of neural processing of shape, color, and velocity in humans. Science. 248:1556 –9.

Corbetta M, Miezin FM, Dobmeyer S, Shulman GL, Petersen SE (1991): Selective and divided attention during visual discriminations of shape, color, and speed: Functional anatomy by positron emission tomography. J Neurosci. 11:2382–402.

Corcos M, Guilbaud O, Paterniti S, Curt F, Hjalmarsson L, Moussa M, Chambry J, Loas G, Chaouat G, Jeammet P. Correlation between serum levels of interleukin-4 and alexithymia scores in healthy female subjects: preliminary findings. Psychoneuroendocrinology. 2004 Jun;29(5):686-91.

Corcos M, Guilbaud O, Speranza M, Paterniti S, Loas G, Stephan P, Jeammet P. Alexithymia and depression in eating disorders. Psychiatry Res. 2000 Apr 10;93(3):263-6.

Costa A, Peppe A, Carlesimo GA, Pasqualetti P, Caltagirone C: Alexithymia in Parkinson's disease is related to depressive symptoms. Eur J Neurol. 2006; 13: 836–41.

Costa A, Peppe A, Carlesimo GA, Salamone G, Caltagirone C: Prevalence and characteristics of alexithymia in Parkinson's disease. Psychosomatics. 2010; 51: 22–8.

Costa PT, McCrae RR. Revised NEO Personality Inventory (NEO PI-R) and NEO Five-Factor Inventory (NEO-FFI) professional manual. Odessa (FL): Psychological Assessment Resources, 1992.

Cox BJ, Kuch K, Parker JD, Shulman ID, Evans RJ. Alexithymia in somatoform disorder patients with chronic pain. J Psychosom Res. 1994;38:523–7.

Cox BJ, Kuch K, Parker JD, Shulman ID, Evans RJ. Alexithymia in somatoform disorder patients with chronic pain. J Psychosom Res 1994;38:523–7.

Da Ros A, Vinai P, Gentile N, Forza G, Cardetti S. Evaluation of alexithymia and depression in severe obese patients not affected by eating disorders. Eat Weight Disord. 2011 Mar;16(1):e24-9.

Daig R, Andus T, Aschenbrenner E, Falk W, Scholmerich J, Gross V. Increased interleukin 8 expression in the colon mucosa of patients with inflammatory bowel disease. Gut. 1996;38:216 –22.

De Berardis D, Campanella D, Gambi F, Sepede G, Salini G, Carano A, La Rovere R, Pelusi L, Penna L, Cicconetti A, Cotellessa C, Salerno RM, Ferro FM. Insight and alexithymia in adult outpatients with obsessive-compulsive disorder. Eur Arch Psychiatry Clin Neurosci. 2005 Oct;255(5):350-8

De Berardis D, D'Albenzio A, Gambi F, Sepede G, Valchera A, Conti CM, Fulcheri M, Cavuto M, Ortolani C, Salerno RM, Serroni N, Ferro FM. Alexithymia and its relationships with dissociative experiences and Internet addiction in a nonclinical sample. Cyberpsychol Behav. 2009 Feb;12(1):67-9.

De Berardis D, Serroni N, Campanella D, Carano A, Gambi F, Valchera A, Conti C, Sepede G, Scali M, Fulcheri M, Salerno RM, Ferro FM. Alexithymia and its relationships with C-reactive protein and serum lipid levels among drug naïve adult outpatients with major depression. Prog Neuropsychopharmacol Biol Psychiatry. 2008 Dec 12;32(8):1982-6.

De Gucht V, Heiser W. Alexithymia and somatisation: quantitative review of the literature. J Psychosom Res. 2003 May;54(5):425-34.

De Timary P, Luts A, Hers D, Luminet O. Absolute and relative stability of alexithymia in alcoholic inpatients undergoing alcohol withdrawal: relationship to depression and anxiety. Psychiatry Res. 2008a Jan 15;157(1-3):105-13.

De Timary P, Roy E, Luminet O, Fillée C, Mikolajczak M. Relationship between alexithymia, alexithymia factors and salivary cortisol in men exposed to a social stress test. Psychoneuroendocrinology. 2008b Sep;33(8):1160-4.

Devinsky O, Morrell MJ, Vogt BA. Contributions of anterior cingulate cortex to behavior. Brain 1995;118:279 –306.

Dewaraja R, Sasaki Y. A left to right hemisphere callosal transfer deficit of nonlinguistic information in alexithymia. Psychother Psychosom 1990;54:201-7.

Dewaraja R, Tanigawa T, Araki S, Nakata A, Kawamura N, Ago Y, Sasaki Y. Decreased cytotoxic lymphocyte counts in alexithymia. Psychother Psychosom. 1997;66(2):83-6.

Dion KL. Ethnolinguistic correlates of alexithymia: Toward a cultural perspective. J Psychosom Res. 1996;41:531–9.

Dorard G, Berthoz S, Haviland MG, Phan O, Coerces M, Bungener C. Multimethod alexithymia assessment in adolescents and young adults with a cannabis use disorder. Compr Psychiatry 2008;49:585-92.

Dowlati Y, Herrmann N, Swardfager W, Liu H, Sham L, Reim EK, Lanctôt KL. A meta-analysis of cytokines in major depression. Biol Psychiatry. 2010 Mar 1;67(5):446-57.

Edwards RR, Klick B, Buenaver L, Max MB, Haythornthwaite JA, Keller RB, Atlas SJ. Symptoms of distress as prospective predictors of pain-related sciatica treatment outcomes. Pain 2007;130(1-2):47-55.

Eizaguirre AE, De Cabezon AO, De Alda IO, Olariaga LJ, Maite J. Alexithymia and its relationships with anxiety and depression in eating disorders. Pers Indiv Differ. 2004;36:321−31.

Elenkov IJ, Chrousos GP. Stress hormones, proinflammatory and antiinflammatory cytokines, and autoimmunity. Ann N Y Acad Sci. 2002 Jun;966:290-303.

Elenkov IJ, Papanicolaou DA, Wilder RL, Chrousos GP. Modulatory effects of glucocorticoids and catecholamines on human interleukin-12 and interleukin-10 production: clinical implications. Proc Assoc Am Physicians. 1996 Sep;108(5):374-81.

Elenkov IJ, Wilder RL, Chrousos GP, Vizi ES. The sympathetic nerve – an integrative interface between two supersystems: the brain and the immune system. Pharmacol Rev. 2000 Dec;52(4):595-638.

Elenkov IJ. Neurohormonal-cytokine interactions: implications for inflammation, common human diseases and well-being. Neurochem Int. 2008 Jan;52(1-2):40-51.

Elzinga BM, Bermond B, van Dyck R. The relationship between dissociative proneness and alexithymia. Psychother Psychosom. 2002 Mar-Apr;71(2):104-11.

Engel G. The need for a new medical model: a challenge for biomedicine. Science. 1977;196:129–36.

Ernst H, Key JD, Koval MS. Alexithymia in an adolescent with agenesis of the corpus callosum and chronic pain. J Am Acad Child Adolesc Psychiatry. 1999 Oct;38(10):1212-3.

Ernst M, Kimes AS, London ED, Matochik JA, Eldreth D, Tata S, Contoreggi C, Leff M, Bolla K. Neural substrates of decision making in adults with attention deficit hyperactivity disorder. Am J Psychiatry. 2003 Jun;160(6):1061-70.

Evren C, Evren B, Dalbudak E, Ozcelik B, Oncu F: Childhood abuse and neglect as a risk factor for alexithymia in adult male substance dependent inpatients. J Psychoactive Drugs. 2009;41:85–92.

Evren C, Sar V, Evren B, Semiz U, Dalbudak E, Cakmak D. Dissociation and alexithymia among men with alcoholism. Psychiatry Clin Neurosci. 2008 Feb;62(1):40-7.

Evren C, Suat C. ClinicalCorrelates of Dissociative Tendencies in Male Soldiers With Conversion Disorder. Isr J Psychiatry Relat Sci. 2007;44(1):33–9

Farges F, Corcos M, Speranza M, Loas G, Perez-Diaz F, Venisse JL, Lang F, Bizouard P, Halfon O, Flament M, Jeammet P. Alexithymia, depression and drug addiction. Encephale. 2004 May-Jun;30(3):201-11.

Fernandez A, Sriram TG, Rajkumar S, Chandrasekar AN. Alexithymic characteristics in rheumatoid arthritis: a controlled study. Psychother Psychosom. 1989;51:45 –50.

Finset A, Graugaard PK, Holgersen K. Salivary cortisol response after a medical interview: the impact of physician communication behaviour, depressed affect and alexithymia. Patient Educ Couns. 2006 Feb;60(2):115-24.

Fishbain DA, Cutler R, Rosomoff HL. Chronic pain-associated depression: Antecedent or consequence of chronic pain? Clin J Pain. 1997;13:116-37.

Fonagy P, Target M: Attachment and reflective function: their role in self-organization. Dev Psychopathol. 1997; 9: 679–700.

Franz M, Popp K, Schaefer R, Sitte W, Schneider C, Hardt J, Decker O, Braehler E. Alexithymia in the German general population. Soc Psychiatry Psychiatr Epidemiol. 2008 Jan;43(1):54-62.

Franz M, Schaefer R, Schneider C, Sitte W, Bachor J. Visual event-related potentials in subjects with alexithymia: modified processing of emotional aversive information? Am J Psychiatry. 2004 Apr;161(4):728-35.

Frewen PA, Dozois DJ, Neufeld RW, Lanius RA. Meta-analysis of alexithymia in posttraumatic stress disorder. Trauma Stress. 2008a Apr;21(2):243-6.

Frewen PA, Lanius RA, Dozois DJ, Neufeld RW, Pain C, Hopper JW, Densmore M, Stevens TK. Clinical and neural correlates of alexithymia in posttraumatic stress disorder. J Abnorm Psychol. 2008b Feb;117(1):171-81.

Freyberger H. Supportive psychotherapeutic techniques in primary and secondary alexithymia. Psychother Psychosom. 1977;28(1-4):337-42.

Freynhagen R, Baron R, Gockel U, Tölle TR. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. Curr Med Res Opin. 2006b; 22:1911-20.

Freynhagen R, Baron R, Tölle TR. Screening of neuropathic pain components in patients with chronic back pain associated with nerve root compression: a prospective observational pilot study (MIPORT). Curr Med Res Opin. 2006a;22:529-37.

Freynhagen R, Baron R. The evaluation of neuropathic components in low back pain. Curr Pain Headache Rep. 2009;13(3):185-90.

Fricchione G, Howanitz E. Aprosodia and alexithymia--a case report. Psychother Psychosom. 1985;43(3):156-60.

Friedberg F, Quick J. Alexithymia in Chronic Fatigue Syndrome: association with momentary, recall, and retrospective measures of somatic complaints and emotions. Psychosom Med. 2007;69: 54–60.

Friedlander L, Lumley MA, Farchione T, Doyal G. Testing the alexithymia hypothesis: physiological and subjective responses during relaxation and stress. J Nerv Ment Dis. 1997 Apr;185(4):233-9.

Frith CD, Friston K, Liddle PF, Frackowiak, RSJ (1991): Willed action and the prefrontal cortex in man: A study with PET. Proc R Soc Lond Biol Sci. 244:241–6.

Frymoyer JW. Epidemiology of spinal disease. In: Mayer TG, Mooney V, Gatchel RJ, eds. Contemporary Conservative Care for Painful Spinal Disorders. Philadelphia: Lea and Febiger; 1991, 10–23.

Fukunishi I, Kikuchi M, Takubo M. Changes in scores on alexithymia over a period of psychiatric treatment. Psychol Rep. 1997a;80:483-9.

Fukunishi I, Kikuchi M, Wogan J, Takubo M. Secondary alexithymia as a state reaction in panic disorder and social phobia. Compr Psychiatry. 1997b;38:166-70.

Fukunishi I, Paris W. Intergenerational association of alexithymic characteristics for college students and their mothers. Psychol Rep. 2001 Aug;89(1):77-84.

Fukunishi I, Sei H, Morita Y, Rahe RH. Sympathetic activity in alexithymics with mother's low care. J Psychosom Res. 1999 Jun;46(6):579-89.

Galderisi S, Mancuso F, Mucci A, Garramone S, Zamboli R, Maj M. Alexithymia and cognitive dysfunctions in patients with panic disorder. Psychosom. 2008;77(3):182-8.

Galer BS, Gianas A, Jensen MP. Painful diabetic polyneuropathy: epidemiology, pain description and quality of life. Diabetes Res Clin Pract 2000a;47:123-8.

Galer BS, Henderson J, Perander J, Jensen MP. Course of symptoms and quality of life measurement in complex regional pain syndrome: a pilot study. J Pain Symptom Manage. 2000b;20:286-92.

Galin D. Implications for psychiatry of left and right cerebral specialization: A neurophysiological context for unconscious processes. Archives of General Psychiatry. 1974;31:572-83.

Garzino-Demo A, Moss RB, Margolick JB, Cleghorn F, Sill A, Blattner WA, Cocchi F, Carlo DJ, DeVico AL, Gallo RC. Spontaneous and antigen-induced production of HIV-inhibitory beta-chemokines are associated with AIDS-free status. Proc Natl Acad Sci U S A. 1999 Oct 12;96(21):11986-91.

Garzino-Demo A. Chemokines and defensins as HIV suppressive factors: an evolving story. Curr Pharm Des. 2007;13(2):163-72.

Gay MC, Hanin D, Luminet O. Effectiveness of an hypnotic imaginery intervention on reducing alexithymia. Contemp Hypn. 2008;25: 1-13.

Gazzaniga M, LeDoux JE. The integrated mind. New York, Plenum, 1978.

Gazzaniga MS. Organization of the human brain. Science. 1989 Sep 1;245(4921):947-52.

Gerszten RE, Garcia-Zepeda EA, Lim YC, Yoshida M, Ding HA, Gimbrone MA Jr, Luster AD, Luscinskas FW, Rosenzweig A. MCP-1 and IL-8 trigger firm adhesion of

monocytes to vascular endothelium under flow conditions. Nature. 1999 Apr 22;398(6729):718-23.

Glaros AG, Lumley MA. Alexithymia and pain in temporomandibular disorder. J Psychosom Res. 2005;59:85–8.

Glaser R, MacCallum RC, Laskowski BF, Malarkey WB, Sheridan JF, Kiecolt-Glaser JK. Evidence for a shift in the Th-1 to Th-2 cytokine response associated with chronic stress and aging. J Gerontol A Biol Sci Med Sci. 2001 Aug;56(8):M477-82.

Grabe HJ, Frommer J, Ankerhold A, Ulrich C, Groger R, Franke GH, Barnow S, Freyberger HJ, Spitzer C. Alexithymia and outcome in psychotherapy. Psychother Psychosom. 2008b;77(3):189-94.

Grabe HJ, Mahler J, Spitzer C, Freyberger HJ. Familial transmission of alexithymia. Eur Psychiatry. 2008a;23:S38.

Grabe HJ, Möller B, Willert C, Spitzer C, Rizos T, Freyberger HJ. Interhemispheric transfer in alexithymia: a transcallosal inhibition study. Psychother Psychosom. 2004 Mar-Apr;73(2):117-23.

Grabe HJ, Rainermann S, Spitzer C, Gänsicke M, Freyberger HJ. The relationship between dimensions of alexithymia and dissociation. Psychother Psychosom. 2000 May-Jun;69(3):128-31.

Grabe HJ, Ruhrmann S, Ettelt S, Muller A, Buhtz F, Hochrein A, Schulze-Rauschenbach S, Meyer K, Kraft S, Reck C, Pukrop R, Klosterkotter J, Falkai P, Maier W, Wagner M, John U, Freyberger HJ. Alexithymia in obsessive-compulsive disorder - results from a family study. Psychother Psychosom. 2006;75(5):312-8.

Grandi S, Sirri L, Wise TN, Tossani E, Fava GA. Kellner's Emotional Inhibition Scale: A Clinimetric Approach to Alexithymia Research. Psychother Psychosom. 2011;80(6):335-44.

Graugaard PK, Holgersen K, Finset A. Communicating with alexithymic and non-alexithymic patients: an experimental study of the effect of psychosocial communication and empathy on patient satisfaction. Psychother Psychosom. 2004 Mar-Apr;73(2):92-100.

Gross JJ. Emotion regulation: affective, cognitive, and social consequences. Psychophysiology. 2002 May;39(3):281-91.

Gu X, Liu X, Guise KG, Fossella J, Wang K, Fan J. Alexithymic trait and voluntary control in healthy adults. PLoS One. 2008;3(11):e3702.

Guilbaud O, Corcos M, Hjalmarsson L, Loas G, Jeammet P. Is there a psychoneuroimmunological pathway between alexithymia and immunity? Immune and physiological correlates of alexithymia. Biomed Pharmacother. 2003 57(7):292-295.

Guilbaud O, Curt F, Perrin C, Chaouat G, Berthoz S, Dugré-Le Bigre C, Wallier J, Strebler M, Touitou C, Jeammet P, Corcos M. Decreased immune response in alexithymic women: a cross-sectional study. Biomed Pharmacother. 2009 May;63(4):297-304.

Gündel H, Ceballos-Baumann AO, Von Rad M. Psychodynamic and neurobiological influences in the etiology of alexithymia. Psychother Psychosom Med Psychol. 2002 Nov;52(11):479-86.

Gündel H, Greiner A, Ceballos-Baumann AO, Ladwig KH, Von Rad M, Förstl H, Jahn T. Alexithymia is no risk factor for exacerbation in spasmodic torticollis patients. J Psychosom Res. 2004a Jun;56(6):699-705.

Gündel H, Greiner A, Ceballos-Baumann AO, Von Rad M, Förstl H, Jahn T. Increased level of tonic sympathetic arousal in high-vs. low-alexithymic cervical dystonia patients. Psychother Psychosom Med Psychol. 2002 Nov;52(11):461-8.

Gündel H, López-Sala A, Ceballos-Baumann AO, Deus J, Cardoner N, Marten-Mittag B, Soriano-Mas C, Pujol J. Alexithymia correlates with the size of the right anterior cingulate. Psychosom Med. 2004b Jan-Feb;66(1):132-40.

Gustorff B, Dorner T, Likar R, Grisold W, Lawrence K, Schwarz F, Rieder A. Prevalence of selfreported neuropathic pain and impact on quality of life: a prospective representative survey. Acta Anaesthesiol Scand. 2008;52:132-6.

Guttman H, Laporte L. Alexithymia, empathy, and psychological symptoms in a family context. Compr Psychiatry. 2002 Nov-Dec;43(6):448-55.

Ham BJ, Lee MS, Lee YM, Kim MK, Choi MJ, Oh KS, et al. Association between the catechol O-methyltransferase Val108/158Met polymorphism and alexithymia. Neuropsychobiology. 2005;52:151–4.

Hassan AE, Saleh HA, Baroudy YM, Abdul-Rahman KI, Najjar MW, Kazi MS, El-Gazar MA, Hafez MA, Abdullah MA, Abdul-Rahman YA, Youseif EA. Prevalence of neuropathic pain among patients suffering from chronic low back pain in Saudi Arabia. Saudi Med J. 2004;25:1986-90.

Haviland MG, Hendryx MS, Cummings MA, Shaw DG, MacMurray JP. Multidimensionality and state dependency of alexithymia in recently sober alcoholics. J Nerv Ment Dis. 1991 May;179(5):284-90.

Haviland MG, Hendryx MS, Shaw DG, Henry JP. Alexithymia in women and men hospitalized for psychoactive substance dependence. Compr Psychiatry. 1994 Mar-Apr;35(2):124-8.

Haviland MG, MacMurray JP, Cummings MA. The relationship between alexithymia and depressive symptoms in a sample of newly abstinent alcoholic inpatients. Psychother Psychosom. 1988;49(1):37-40.

Haviland MG, Reise SP. A California Q-set alexithymia prototype and its relationship to ego-control and ego-resiliency. J Psychosom Res. 1996;41:597– 608.

Haviland MG, Shaw DG, MacMurray JP, Cummings MA. Validation of the Toronto Alexithymia Scale with substance abusers. Psychother Psychosom. 1988;50(2):81-7.

Haviland MG, Warren WL, Riggs ML. An observer scale to measure alexithymia. Psychosomatics. 2000;41:385– 92.

Haythornthwaite JA, Benrud-Larson LM. Psychological aspects of neuropathic pain. Clin J Pain. 2000;16:1-5.

Heiberg AN, Heiberg A. A possible genetic contribution to the alexithymia trait. Psychother Psychosom. 1978;30:205–10.

Helmers KF, Mente A. Alexithymia and health behaviors in healthy male volunteers. J Psychosom Res. 1999 Dec;47(6):635-45.

Hendryx MS, Haviland MG, Shaw DG. Dimensions of alexithymia and their relationships to anxiety and depression. J Pers Assess. 1991 Apr;56(2):227-37.

Hennenlotter A, Schroeder U, Erhard P, Haslinger B, Stahl R, Weindl A, von Einsiedel HG, Lange KW, Ceballos-Baumann AO. Neural correlates associated with impaired disgust processing in pre-symptomatic Huntington's disease. Brain. 2004 Jun;127(Pt 6):1446-53.

Henry JP, Haviland MG, Cummings MA, Anderson DL, Nelson JC, MacMurray JP, McGhee WH, Hubbard RW. Shared neuroendocrine patterns of post-traumatic stress disorder and alexithymia. Psychosom Med. 1992 Jul-Aug;54(4):407-15.

Henry JP. Psychological and physiological responses to stress: the right hemisphere and the hypothalamo-pituitary-adrenal axis, an inquiry into problems of human bonding. Integr Physiol Behav Sci. 1993 Oct-Dec;28(4):369-87.

Henry JP. Psychological and physiological responses to stress: the right hemisphere and the hypothalamo-pituitary-adrenal axis, an inquiry into problems of human bonding. 1. Acta Physiol Scand Suppl. 1997;640:10-25.

Herrmann M, Scholmerich J, Straub RH. Stress and rheumatic diseases. Rheum Dis Clin North Am. 2000;26:737– 63.

Hill E, Berthoz S, Frith U. Brief report: cognitive processing of own emotions in individuals with autistic spectrum disorder and in their relatives. J Autism Dev Disord. 2004 Apr;34(2):229-35.

Hill JC, Konstantinou K, Egbewale BE, Dunn KM, Lewis M, van der Windt D. Clinical outcome among low back pain consulters with referred leg pain in primary care. Spine (Phila Pa 1976) 2011 doi: 10.1097/BRS.0b013e31820712bb

Hintikka J, Honkalampi K, Lehtonen J, Viinamäki H. Are alexithymia and depression distinct or overlapping constructs?: a study in a general population. Compr Psychiatry. 2001 May-Jun;42(3):234-9.

Hoge EA, Brandstetter K, Moshier S, Pollack MH, Wong KK, Simon NM. Broadspectrum of cytokine abnormalities in panic disorder and posttraumatic stress disorder. Depress Anxiety. 2009;26(5):447-55.

Honkalampi K, Hintikka J, Laukkanen E, Lehtonen J, Viinamaki H. Alexithymia and depression: a prospective study of patients with major depressive disorder. Psychosomatics. 2001a;42:229-34.

Honkalampi K, Hintikka J, Saarinen P, Lehtonen J, Viinamäki H: Is alexithymia a permanent feature in depressed patients? Psychother Psychosom. 2000b; 69: 303–8.

Honkalampi K, Hintikka J, Tanskanen A, Lehtonen J, Viinamäki H. Depression is strongly associated with alexithymia in the general population. J Psychosom Res. 2000a Jan;48(1):99-104.

Honkalampi K, Koivumaa-Honkanen H, Hintikka J, Antikainen R, Haatainen K, Tanskanen A, et al. Do stressful life-events or sociodemographic variables associate with depression and alexithymia among a general population? A 3-year follow-up study. Compr Psychiatry. 2004;45:254-60.

Honkalampi K, Koivumaa-Honkanen H, Tanskanen A, Hintikka J, Lehtonen J, Viinamaki H. Why do alexithymic features appear to be stable? A 12-month follow-up study of a general population. Psychother Psychosom. 2001b;70:247-53.

Honkalampi K, Lehto SM, Hintikka J, Koivumaa-Honkanen H, Niskanen L, Viinamäki H: Symptoms of depression and alexithymic burden in middle-aged men. Psychother Psychosom. 2010; 79: 259–61.

Honkalampi K, Lehto SM, Koivumaa-Honkanen H, Hintikka J, Niskanen L, Valkonen-Korhonen M, Viinamäki H. Alexithymia and tissue inflammation. Psychother Psychosom. 2011;80(6):359-64.

Honkalampi K, Saarinen P, Hintikka J, Virtanen V, Viinamaki H: Factors associated with alexithymia in patients suffering from depression. Psychother Psychosom. 1999; 68: 270–275.

Hoppe KD, Bogen JE. Alexithymia in twelve commisurotomized patients. Psychother Psychosom. 1977;28:148-55.

Horton PC, Gewirtz H, Kreutter KJ. Alexithymia—state and trait. Psychother Psychosom. 1992;58:91-6.

Hosoi M, Molton IR, Jensen MP, Ehde DM, Amtmann S, O'Brien S, Arimura T, Kubo C. Relationships among alexithymia and pain intensity, pain interference, and vitality in persons with neuromuscular disease: Considering the effect of negative affectivity. Pain. 2010 May;149(2):273-7.

Huber A, Suman AL, Biasi G, Carli G. Alexithymia in fibromyalgia syndrome: associations with ongoing pain, experimental pain sensitivity and illness behavior. J Psychosom Res. 2009;66:425–33.

Huber M, Herholz K, Habedank B, Thiel A, Müller-Küppers M, Ebel H, Subic-Wrana C, Köhle K, Heiss WD. Different patterns of regional brain activation during emotional stimulation in alexithymics in comparison with normal controls. Psychother Psychosom Med Psychol. 2002 Nov;52(11):469-78

Hyer L, Woods MG, Summers MN, Boudewyns P, Harrison WR. Alexithymia among Vietnam veterans with posttraumatic stress disorder. J Clin Psychiatry. 1990 Jun;51(6):243-7.

Chen J, Xu T, Jing J, Chan RC. Alexithymia and emotional regulation: A cluster analytical approach. BMC Psychiatry. 2011 Feb 23;11:33.

Infrasca R. Alexithymia, neurovegetative arousal and neuroticism. An experimental study. Psychother Psychosom. 1997;66(5):276-280.

Iversen S, Kupfermann I, Kandel ER. Emotional states and feelings. In E. R. Kandel, J. H. Schwartz, & T. M. Jessel (Eds.), Principles of neural science (4th ed.,). McGraw-Hill: New York, 2000, 982-998.

Jaggi AS, Singh N. Exploring the potential of telmisartan in chronic constriction injury-induced neuropathic pain in rats. Eur J Pharmacol. 2011;667:215-21.

Jones HE. The study of patterns of emotional expression. In M.L. Reymert (Ed.), Feeling and emotions. New York; McGraw-Hill, 1935, 161-8.

Jørgensen MM, Zachariae R, Skytthe A, Kyvik K. Genetic and environmental factors in alexithymia: a population-based study of 8785 Danish twin pairs. Psychother Psychosom. 2007;76:369–75.

Joukamaa M, Kokkonen P, Veijola J, et al. Social situation of expectant mothers and alexithymia 31 years later in their offspring: A prospective study. Psychosom Med. 2003;65:307–12.

Joukamaa M, Saarijärvi S, Muuriaisniemi ML, Salokangas RK. Alexithymia in a normal elderly population. Compr Psychiatry. 1996 Mar-Apr;37(2):144-7.

Joukamaa M, Taanila A, Miettunen J, Karvonen JT, Koskinen M, Veijola J. Epidemiology of alexithymia among adolescents. J Psychosom Res. 2007 Oct;63(4):373-6.

Joukamma M, Luutonen S, von Reventlow H, Patterson P, Karlsson H, Salokangas RKR: Alexithymia and childhood abuse among patients attending primary and psychiatric care: results of the RADEP study. Psychosomatics. 2008;49:317–25.

Jula A, Salminen JK, Saarijärvi S. Alexithymia: a facet of essential hypertension. Hypertension. 1999 Apr;33(4):1057-61.

Julkunen J, Hurri H, Kankainen J. Psychological factors in the treatment of chronic low back pain Follow-up study of a back school intervention. Psychother Psychosom. 1988;50:173– 81.

Kano M, Fukudo S, Gyoba J, Kamachi M, Tagawa M, Mochizuki H, Itoh M, Hongo M, Yanai K. Specific brain processing of facial expressions in people with alexithymia: an H2O-PET study. Brain. 2003 Jun;126(Pt 6):1474-84.

Karush A, Daniels GE, O'Connor JF, Stern LO. The response to psychotherapy in chronic ulcerative colitis. II. Factors arising from the therapeutic situation. Psychosom Med. 1969 May-Jun;31(3):201-26.

Kennedy M, Franklin J. Skills-based treatment for alexithymia: An exploratory case series. Behavior Change. 2002;19:158-71.

Kiecolt-Glaser JK, McGuire L, Robles TF, Glaser R. Psychoneuroimmunology and psychosomatic medicine: back to the future. Psychosom Med. 2002 Jan-Feb;64(1):15-28.

Kinder BN, Curtiss G. Alexithymia among empirically derived subgroups of chronic back pain patients. J Pers Assess. 1990;54:351–62.

Kleiger JH, Kinsman RA. The development of a MMPI alexithymia scale. Psychother Psychosom. 1980;34:17 – 24.

Koh KB, Choe E, Song JE, Lee EH. Effect of coping on endocrinoimmune functions in different stress situations. Psychiatry Res. 2006 Aug 30;143(2-3):223-34.

Kojima M, Frasure-Smith N, Lespérance F. Alexithymia following myocardial infarction. Psychometric properties and correlates of the Toronto Alexithymia Scale. J Psychosom Res. 2001;51:487– 95.

Kokkonen P, Karvonen JT, Veijola J, Läksy K, Jokelainen J, Järvelin MR, Joukamaa M. Prevalence and sociodemographic correlates of alexithymia in a population sample of young adults. Compr Psychiatry. 2001 Nov-Dec;42(6):471-6.

Kolb B, Whishaw IQ. Fundamentals of human neuropsychology (3rd ed.). New York: Freeman, 1990.

Kooiman CG, Spinhoven P,Trijsburg RW. The assesment of alexithymia. A critical review of the literature and a psychometric study of the Toronto Alexithymia Scale-20: J Psychosom Res. 2002;53:1083-90.

Kooiman CG, van Rees Vellinga S, Spinhoven P, Draijer N, Trijsburg RW, Rooijmans HG. Childhood adversities as risk factors for alexithymia and other aspects of affect dysregulation in adulthood. Psychother Psychosom. 2004;73:107–16.

Kosturek A, Gregory RJ, Sousou AJ, Trief P. Alexithymia and somatic amplification in chronic pain. Psychosomatics. 1998;39:399–404.

Kraan MC, Patel DD, Haringman JJ, Smith MD, Weedon H, Ahern MJ, Breedveld FC,

Tak PP. The development of clinical signs of rheumatoid synovial inflammation is associated with increased synthesis of the chemokine CXCL8 (interleukin-8). Arthritis Res. 2000;3:65–71.

Kronfol Z, Remick DG. Cytokines and the brain: implications for clinical psychiatry. Am J Psychiatry. 2000 May;157(5):683-94.

Kronholm E, Partonen T, Salminen JK, Mattila AK, Joukamaa M. Alexithymia, depression and sleep disturbance symptoms. Psychother Psychosom. 2008;77(1):63-5.

Krystal H. Alexithymia and psychotherapy. Am J Psychother. 1979 Jan;33(1):17-31.

Krystal H. Alexithymia and the effectiveness of psychoanalytic treatment. Int J Psychoanal Psychother. 1982-1983;9:353-78.

Krystal JH, Giller EL, Cicchetti DV. Assessment of alexithymia in posttraumatic stress disorder and somatic illness: introduction of a reliable measure. Psychosom Med. 1986;48:84–94.

Krystal H. Alexithymia. In H Krystal (Ed.), Integration and self-healing: Affect - trauma - alexithymia. Mahwah, NJ: Analytic Press, 1988, 242-286.

Kugel H, Eichmann M, Dannlowski U, Ohrmann P, Bauer J, Arolt V, Heindel W, Suslow T. Alexithymic features and automatic amygdala reactivity to facial emotion. Neurosci Lett. 2008 Apr 11;435(1):40-4.

LaCaille RA, DeBerard MS, Masters KS, Colledge AL, Bacon W. Presurgical biopsychosocial factors predict multidimensional patient: outcomes of interbody cage lumbar fusion. Spine J. 2005;5:71-8.

Lane RD, Ahern GL, Schwartz GE, Kaszniak AW. Is alexithymia the emotional equivalent of blindsight? Biol Psychiatry. 1997;42:834–44.

Lane RD, Quinlan DM, Schwartz GE, Walker PA, Zeitlin SB. The Levels of Emotional Awareness Scale: a cognitive – developmental measure of emotion. J Pers Assess. 1990;55:124–34.

Lane RD, Reiman EM, Axelrod B, Yun LS, Holmes A, Schwartz GE. Neural correlates of levels of emotional awareness. Evidence of an interaction between emotion and attention in the anterior cingulate cortex. J Cogn Neurosci. 1998 Jul;10(4):525-35.

Lane RD, Sechrest L, Reidel R, Weldon V, Kaszniak A, Schwartz GE. Impaired verbal and nonverbal emotion recognition in alexithymia. Psychosom Med. 1996 May-Jun;58(3):203-10.

Lane RD, Sechrest L, Riedel R: Sociodemographic correlates of alexithymia. Compreh Psychiat. 1998;39:377–85.

Lane RD. Neural substrates of implicit and explicit emotional processes: a unifying framework for psychosomatic medicine. Psychosom Med. 2008 Feb;70(2):214-31.

Lang S, Stopsack M, Kotchoubey B, Frick C, Grabe HJ, Spitzer C, Barnow S. Cortical inhibition in alexithymic patients with borderline personality disorder. Biol Psychol. 2011 Dec;88(2-3):227-32.

Larsen JK, Brand N, Bermond B, Hijman R. Cognitive and emotional characteristics of alexithymia: a review of neurobiological studies. J Psychosom Res. 2003;54: 533–41.

Le Gars L, Borderie D, Kaplan G, Berenbaum F. Systemic inflammatory response with plasma C-reactive protein elevation in disk-related lumbosciatic syndrome. Joint Bone Spine. 2000;67(5):452-5.

Le HN, Berenbaum H, Raghavan C. Culture and alexithymia: Mean levels, correlates and the role of parental socialization of emotions. Emotion. 2002; 2:341–60.

Le HN, Ramos MA, Munoz RF. The relationship between alexithymia and perinatal depressive symptomatology. J Psychosom Res. 2007;62: 215-22.

Lehto SM, Niskanen L, Herzig KH, Tolmunen T, Huotari A, Viinamäki H, Koivumaa-Honkanen H, Honkalampi K, Ruotsalainen H, Hintikka J. Serum chemokine levels in major depressive disorder. Psychoneuroendocrinology. 2010 Feb;35(2):226-32.

Leichner-Hennig R, Vetter GW. Zur Beziehung von Schmerzerleben und psychischen Merkmalen bei Patienten mit Fibrositissyndrom und Patienten mit rheumatoider Arthritis. Z Rheumatol. 1986;45: 139–45.

Lerner Y, Singer N, Gonen T, Weintraub Y, Cohen O, Rubin N, Ungerleider LG, Hendler T. Feeling without Seeing? Engagement of Ventral, but Not Dorsal, Amygdala during Unaware Exposure to Emotional Faces. J Cogn Neurosci. 2012 Mar;24(3):531-42.

Levenson D, James L. Essentials of Psychosomatic Medicine. American Psychiatric Press Inc, 2006.

Levenson D. Mind, Body and Medicine. A History of the American Psychosomatic Society. USA: American Psychosomatic Society, 1994.

Levinson DF. The genetics of depression: a review. Biol Psychiatry. 2006;60:84–92.

Lucinio J, Wong ML, Gold PW. Neutrophil-activating peptide-1/interleukin-8 mRNA is localized in rat hypothalamus and hippocampus. Neuroreport. 1992 Sep;3(9):753-6.

Lieberman MD, Eisenberger NI, Crockett MJ, Tom SM, Pfeifer JH, Way BM. Putting feelings into words: affect labeling disrupts amygdala activity in response to affective stimuli. Psychol Sci. 2007 May;18(5):421-8.

Lin S, Zhao SF, Yan FH. The influence of alexithymia in stress on secretory IgA and cortisol in saliva. Shanghai Kou Qiang Yi Xue. 2005 Dec;14(6):561-4.

Linden W, Lenz JW, Stossel C. Alexithymia, defensiveness and cardiovascular reactivity to stress. J Psychosom Res. 1996 Dec;41(6):575-83.

Linden W, Wen F, Paulhus DL. Measuring alexithymia: reliability, validity, and prevalence. Adv Pers Assess. 1995;10:51–95.

Lindholm T, Lehtinen V, Hyyppä MT, Puukka P. Alexithymic features in relation to the dexamethasone suppression test in a Finnish population sample. Am J Psychiatry. 1990 Sep;147(9):1216-9.

Linton SJ. A review of psychological risk factors in back and neck pain. Spine 2000;25:1148-56.

Lipsanen T, Saarijärvi S, Lauerma H. Exploring the relations between depression, somatization, dissociation and alexithymia--overlapping or independent constructs? Psychopathology. 2004 Jul-Aug;37(4):200-6.

Loas G, Fremaux D, Otmani O, Lecercle C, Delahousse J. Is alexithymia a negative factor for maintaining abstinence? A follow-up study. Compr Psychiatry. 1997 Sep-Oct;38(5):296-9.

Locatelli V, Bresciani E, Tamiazzo L, Torsello A. Central nervous system-acting drugs influencing hypothalamic-pituitary-adrenal axis function. Endocr Dev. 2010;17:108-20.

Luminet O, Rokbani L, Ogez D, Jadoulle V. An evaluation of the absolute and relative stability of alexithymia in women with breast cancer. J Psychosom Res. 2007;62:641-8.

Lumley MA, Bazydlo RA. The relationship of alexithymia characteristics to dreaming. J Psychosom Res. 2000 Jun;48(6):561-7.

Lumley MA, Davis M, Labouvie-Vief G, Gustavson B, Clement R, Barry R, Simon T, Rivard R: Multiple measures of emotional abilities: Their interrelationships and associations with physical symptoms (abstr). Psychosom Med. 2002;64:146.

Lumley MA, Mader C, Gramzow J, Papineau K. Family factors related to alexithymia characteristics. Psychosom Med. 1996b May-Jun;58(3):211-6.

Lumley MA, Neely LC, Burger AJ. The assessment of alexithymia in medical settings: implications for understanding and treating health problems. J Pers Assess. 2007 Dec;89(3):230-46.

Lumley MA, Radcliffe AM, Macklem DJ, Mosley-Williams A, Leisen JC, Huffman JL, D'Souza PJ, Gillis ME, Meyer TM, Kraft CA, Rapport LJ. Alexithymia and pain in three chronic pain samples: comparing Caucasians and African Americans. Pain Med. 2005 May-Jun;6(3):251-61.

Lumley MA, Sielky K. Alexithymia, gender, and hemispheric functioning. Compr Psychiatry. 2000 Sep-Oct;41(5):352-9.

Lumley MA, Smith JA, Longo DJ. The relationship of alexithymia to pain severity and impairment among patients with chronic myofascial pain: comparisons with self-efficacy, catastrophizing, and depression. J Psychosom Res. 2002 Sep;53(3):823-30.

Lumley MA, Stettner L, Wehmer F. How are alexithymia and physical illness linked? A review and critique of pathways. J Psychosom Res. 1996a Dec;41(6):505-18.

Lumley MA. Alexithymia, emotional disclosure, and health: a program of research. J Pers. 2004 Dec;72(6):1271-300.

Lundh LG, Johnsson A, Sundqvist K, Olsson H. Alexithymia, memory of emotion, emotional awareness, and perfectionism. Emotion. 2002 Dec;2(4):361-79.

Maaranen P, Tanskanen A, Honkalampi K, Haatainen K, Hintikka J, Viinamäki H. Factors associated with pathological dissociation in the general population. Aust N Z J Psychiatry. 2005 May;39(5):387-94.

MacLean PD. Psychosomatic disease and the "visceral brain": Recent developments bearing on the Papez theory of emotion. Psychosom Med. 1949; 11(6):338 –53.

Maggini C, Raballo A. Alexithymia and schizophrenic psychopathology. Acta Biomed. 2004 Apr;75(1):40-9.

Mandarelli G, Tarsitani L, Ippoliti F, Covotta F, Zerella MP, Mirigliani A, Biondi M. The relationship between alexithymia and circulating cytokine levels in subjects undergoing upper endoscopy. Neuroimmunomodulation. 2011;18(1):37-44.

Manna G, Foddai E, Di Maggio MG, Pace F, Colucci G, Gebbia N, Russo A. Emotional expression and coping style in female breast cancer. Ann Oncol. 2007 Jun;18 Suppl 6:vi77-80.

Marchesi C, Bertoni S, Cantoni A, Maggini C. Is alexithymia a personality trait increasing the risk of depression? A prospective study evaluating alexithymia before, during and after a depressive episode. Psychol Med. 2008 Dec;38(12):1717-22.

Marchesi C, Brusamonti E, Maggini C. Are alexithymia, depression, and anxiety distinct constructs in affective disorders? J Psychosom Res. 2000;49:43–9.

Marchesi C, Fontò S, Balista C, Cimmino C, Maggini C. Relationship between alexithymia and panic disorder: a longitudinal study to answer an open question. Psychother Psychosom. 2005;74(1):56-60.

Marques AH, Silverman MN, Sternberg EM. Glucocorticoid dysregulations and their clinical correlates. From receptors to therapeutics. Ann N Y Acad Sci. 2009 Oct;1179:1-18.

Marshall GD Jr, Agarwal SK, Lloyd C, Cohen L, Henninger EM, Morris GJ. Cytokine dysregulation associated with exam stress in healthy medical students. Brain Behav Immun. 1998 Dec;12(4):297-307.

Martin JB, Pihl R. The stress-alexithymia hypothesis: Theoretical and empirical considerations. Psychother Psychosom. 1985;43:169-76.

Martin JB, Pihl RO, Young SN, Ervin FR, Tourjman SV. Prediction of alexithymic characteristics from physiological, personality, and subjective measures. Psychother Psychosom. 1986;45(3):133-40.

Martin JB, Pihl RO. Influence of alexithymic characteristics on physiological and subjective stress responses in normal individuals. Psychother Psychosom. 1986;45(2):66-77.

Marty P, de M'Uzan M. 'La pensée opératoire. Rev Fr Psychanal. 1963;27: 345-56.

Mason O, Tyson M, Jones C, Potts S. Alexithymia: its prevalence and correlates in a British undergraduate sample. Psychol Psychother. 2005;78:113–25.

Mattila AK, Luutonen S, Ylinen M, Salokangas RK, Joukamaa M. Alexithymia, human relationships, and mobile phone use. J Nerv Ment Dis. 2010a Oct;198(10):722-7.

Mattila AK, Poutanen O, Koivisto AM, Salokangas RK, Joukamaa M. Alexithymia and life satisfaction in primary healthcare patients. Psychosomatics. 2007 Nov-Dec;48(6):523-9.

Mattila AK, Saarni SI, Alanen E, Salminen JK, Kronholm E, Jula A, Sintonen H, Joukamaa M. Health-related quality-of-life profiles in nonalexithymic and alexithymic subjects from general population. J Psychosom Res. 2010b Mar;68(3):279-83.

Mattila AK, Salminen JK, Nummi T, Joukamaa M. Age is strongly associated with alexithymia in the general population. J Psychosom Res. 2006 Nov;61(5):629-35.

McCallum M, Piper WE, Ogrodniczuk JS, Joyce AS. Relationships among psychological mindedness, alexithymia and outcome in four forms of short-term psychotherapy. Psychol Psychother. 2003 Jun;76(Pt 2):133-44.

McCaslin SE, Inslicht SS, Neylan TC, Metzler TJ, Otte C, Lenoci M, Henn-Haase C, Best S, Yehuda R, Marmar CR. Association between alexithymia and neuroendocrine response to psychological stress in police academy recruits. Ann N Y Acad Sci. 2006 Jul;1071:425-7.

McDonald PW, Prkachin KM. The expression and perception of facial emotion in alexithymia: A pilot study. Psychosom Med. 1990;52:199-210.

Medzhitov R, Preston-Hurlburt P, Janeway CA Jr. A human homologue of the Drosophila Toll protein signals activation of adaptive immunity. Nature. 1997 Jul 24;388(6640):394-7.

Mehling WE, Krause N. Alexithymia and 7.5-year incidence of compensated low back pain in 1207 urban public transit operators. J Psychosom Res. 2007 Jun;62(6):667-74.

Mehling WE, Krause N. Are difficulties perceiving and expressing emotions associated with low-back pain? The relationship between lack of emotional awareness (alexithymia) and 12-month prevalence of low-back pain in 1180 urban public transit operators. J Psychosom Res. 2005;58:73 – 81.

Melzack R, Katz J. Pain measurement in persons in pain. In: Wall PD, Melzack R, editors. Textbook of pain. 4th ed. Edinburgh: Churchill Livingstone, 1999, 409–25.

Melzack R, Katz J. The McGill Pain Questionnaire: appraisal and current status. In: Turk DC, Melzack R, editors. Handbook of pain assessment. New York: Guilford Press, 1992, 152– 68.

Mennin DS, Heimberg RG, Turk CL, Fresco DM. Preliminary evidence for an emotion dysregulation model of generalized anxiety disorder. Behav Res Ther. 2005 Oct;43(10):1281-310.

Mikolajczak M, Luminet O. Is alexithymia affected by situational stress or is it a stable trait related to emotion regulation? Pers Indiv Differ. 2006;40:1399–408.

Millard RW, Kinsler BL. Evaluation of constricted affect in chronic pain: An attempt using the Toronto Alexithymia Scale. Pain. 1992;50:287–92.

Miller AH, Maletic V, Raison CL. Inflammation and its discontents: the role of cytokines in the pathophysiology of major depression. Biol Psychiatry. 2009 May1;65(9):732-41.

Miller L. Is alexithymia a disconnection syndrome? A neuropsychological perspective. Int J Psychiatry Med. 1986-1987;16(3):199-209.

Modestin J, Furrer R, Malti T. Different traumatic experiences are associated with different pathologies. Psychiatr Q. 2005 Spring;76(1):19-32.

Modestin J, Furrer R, Malti T. Study on alexithymia in adult non-patients. J Psychosom Res. 2004 Jun;56(6):707-9.

Montebarocci O, Codispoti M, Surcinelli P, Franzoni E, Baldaro B, Rossi N. Alexithymia in female patients with eating disorders. Eat Weight Disord. 2006 Mar;11(1):14-21.

Moriguchi Y, Maeda M, Igarashi T, Ishikawa T, Shoji M, Kubo C, Komaki G. Age and gender effect on alexithymia in large, Japanese community and clinical samples: a cross-validation study of the Toronto Alexithymia Scale (TAS-20). Biopsychosoc Med. 2007 Mar 6;1:7.

Muftuoglu MN, Herken H, Demirci H, Virit O, Neyal A. Alexithymic features in migraine patients. Eur Arch Psychiatry Clin Neurosci. 2004 Jun;254(3):182-6.

Müller J, Bühner M, Ellgring H. Is there a reliable factorial structure in the 20-item Toronto Alexithymia Scale? A comparison of factor models in clinical and normal adult samples. J Psychosom Res. 2003 Dec;55(6):561-8.

Nemiah JC, Freyberger H, Sifneos PE. Alexithymia: a view of the psychosomatic process. In: Hill O, editor. Modern trends in psychosomatic medicine. Vol 3. London: Butterworth, 1976. 430–9.

Nemiah JC, Sifneos PE. Psychosomatic illness: a problem in communication. Psychother Psychosom. 1970; 18: 154–60.

Nemiah JC. A psychodynamic view of psychosomatic medicine. Psychosom Med. 2000 May-Jun;62(3):299-303.

Nemiah JC. Denial revisited: Reflections on psychosomatic theory. Psychother Psychosom. 1975;24:140-7.

Nemiah JC. Foundations of Psychopathology. Oxford, Oxford University Press, 1961.

Newton TL, Contrada RJ. Alexithymia and repression: contrasting emotion-focused coping styles. Psychosom Med. 1994;56:457-62.

Nkam I, Langlois-Thery S, Dollfus S, Petit M. Alexithymia in negative symptom and non-negative symptom schizophrenia. Encephale. 1997b; 23: 358-63.

Nkam I, Langlois-Thery S, Dollfus S, Petit M. Negative symptoms, depression, anxiety and alexithymia in DSM IIIR schizophrenic patients. Encephale. 1997a; 23: 267-72.

Noguchi K, Okubo M. Leukotrienes in nociceptive pathway and neuropathic/inflammatory pain. Biol Pharm Bull. 2011;34:1163-9.

Nygaard OP, Mellgren SI, Osterud B. The inflammatory properties of contained and non-contained lumbar disc herniation. Spine. 1997;23:2484–8.

Nyklicek I, Vingerhoets AJ. Alexithymia is associated with low tolerance to experimental painful stimulation. Pain. 2000;85:471-5.

O'Brien C, Gaher RM, Pope C, Smiley P. Difficulty identifying feelings predicts the persistence of trauma symptoms in a sample of veterans who experienced military sexual trauma. J Nerv Ment Dis. 2008 Mar;196(3):252-5.

Ogrodniczuk JS, Piper WE, Joyce AS. Effect of alexithymia on the process and outcome of psychotherapy: a programmatic review. Psychiatry Res. 2011 Nov 30;190(1):43-8.

Ogrodniczuk JS, Piper WE, Joyce AS. The negative effect of alexithymia on the outcome of group therapy for complicated grief: what role might the therapist play? Compr Psychiatry. 2005 May-Jun;46(3):206-13.

Ono T, Nishijo H, Nishino H. Functional role of the limbic system and basal ganglia in motivated behaviors. J Neurol. 2000 Sep;247 Suppl 5:V23-32.

Onor M, Trevisiol M, Spano M, Aguglia E, Paradiso S. Alexithymia and aging: a neuropsychological perspective. J Nerv Ment Dis. 2010 Dec;198(12):891-5.

Pabreja K, Dua K, Sharma S, Padi SS, Kulkarni SK. Minocycline attenuates the development of diabetic neuropathic pain: possible anti-inflammatory and anti-oxidant mechanisms. Eur J Pharmacol. 2011;661:15-21.

Páez D, Velasco C, González JL. Expressive writing and the role of alexythimia as a dispositional deficit in self-disclosure and psychological health. J Pers Soc Psychol. 1999 Sep;77(3):630-41.

Papciak AS, Feuerstein M, Spiegel JA. Stress reactivity in alexithymia: decoupling of physiological and cognitive responses. J Human Stress. 1985 Fall;11(3):135-42.

Parker JD, Keightley ML, Smith CT, Taylor GJ. Interhemispheric transfer deficit in alexithymia: an experimental study. Psychosom Med. 1999 Jul-Aug;61(4):464-8.

Parker JD, Taylor GJ, Bagby RM. Relationship between conjugate lateral eye movements and alexithymia. Psychother Psychosom. 1992;57(3):94-101.

Parker JD, Taylor GJ, Bagby RM. The 20-Item Toronto Alexithymia Scale. III. Reliability and factorial validity in a community population. J Psychosom Res. 2003 Sep;55(3):269-75.

Parker JDA, Bagby RM, Taylor GJ. Alexithymia and depression: distinct or overlapping constructs? Compr Psychiatry. 1991;32:387–94.

Parling T, Mortazavi M, Ghaderi A. Alexithymia and emotional awareness in anorexia nervosa: time for a shift in the measurement of the concept? Eat Behav. 2010 Dec;11(4):205-10.

Pasini A, Delle Chiaie R, Seripa S, Ciani N. Alexithymia as related to sex, age, and educational level: results of the Toronto Alexithymia Scale in 417 normal subjects. Compr Psychiatry. 1992 Jan-Feb;33(1):42-6.

Paus T, Petrides M, Evans AC, Meyer E. Role of the human anterior cingulate cortex in the control of oculomotor, manual, and speech responses: A positron emission tomography study. J Neurophysiol. 1993;70:453– 69.

Pedrosa Gil F, Nickel M, Ridout N, Schwarz MJ, Schoechlin C, Schmidmaier R. Alexithymia and interleukin variations in somatoform disorder. Neuroimmunomodulation. 2007;14(5):235-42.

Phan KL, Wager T, Taylor SF, Liberzon I. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. Neuroimage. 2002 Jun;16(2):331-48.

Picardi A, Fagnani C, Gigantesco A, Toccaceli V, Lega I, Stazi MA. Genetic influences on alexithymia and their relationship with depressive symptoms. J Psychosom Res. 2011 Oct;71(4):256-63.

Pincus T, Burton AK, Vogel S, Field AP. A systematic review of psychological factors as predictors of chronicity/disability in prospective cohorts of low back pain. Spine. 2002;27:E109-20.

Plomin R, Daniels D. Why are children in the same family so different from one another? Behav Brain Sci. 1987;10:1–16.

Plomin R, DeFries JC, McClearn GE, McGuffin P. Behavioral genetics. 5th ed. New York: Worth Publishers, 2008.

Poletti M, Frosini D, Pagni C, Lucetti C, Del Dotto P, Ceravolo R, Bonuccelli U. Alexithymia is associated with depression in de novo Parkinson's disease. Psychother Psychosom. 2011;80(4):251-3.

Pollatos O, Gramann K. Electrophysiological evidence of early processing deficits in alexithymia. Biol Psychol. 2011 Apr;87(1):113-21.

Porcelli P, Bagby RM, Taylor GJ, De Carne M, Leandro G, Todarello O. Alexithymia as predictor of treatment out- come in patients with functional gastrointestinal disorders. Psychosom Med. 2003;65(5):911-8.

Porcelli P, Leoci C, Guerra V, Taylor GJ, Bagby RM. A longitudinal study of alexithymia and psychological distress in inflammatory bowel disease. J Psychosom Res. 1996 Dec;41(6):569-73.

Porcelli P, Tulipani C, Maiello E, Cilenti G, Todarello O. Alexithymia, coping, and illness behavior correlates of pain experience in cancer patients. Psychooncology. 2007;16:644–50.

Porcelli P, Zaka S, Leoci C, Centonze S, Taylor GJ. Alexithymia in inflammatory bowel disease: a case– control study. Psychother Psychosom. 1995;64:49 – 53.

Prochnow D, Donell J, Schäfer R, Jörgens S, Hartung HP, Franz M, Seitz RJ. Alexithymia and impaired facial affect recognition in multiple sclerosis. J Neurol. 2011 Sep;258(9):1683-8.

Putterman E, Byrne N, Ditto B. Alexithymia and symptom reporting following blood donation. Psychosom Med. 2001;63:138–9.

Quinton S, Wagner HL. Alexithymia, ambivalence over emotional expression, and eating attitudes. Pers Indiv Differ. 2005;38: 1163−73.

Rabavilas AD. Electrodermal activity in low and high alexithymic neurotic patients. Psychother Psychosom. 1987;47:101-4.

Richter J, Möller B, Spitzer C, Letzel S, Bartols S, Barnow S, Willert C, Freyberger HJ, Grabe HJ. Transcallosal inhibition in patients with and without alexithymia. Neuropsychobiology. 2006;53(2):101-7.

Roedema TM, Simons RF. Emotion-processing deficit in alexithymia. Psychophysiology. 1999;36:379–87.

Roh D, Kim WJ, Kim CH. Alexithymia in obsessive-compulsive disorder: clinical correlates and symptom dimensions. J Nerv Ment Dis. 2011 Sep;199(9):690-5.

Romei V, De Gennaro L, Fratello F, Curcio G, Ferrara M, Pascual-Leone A, Bertini M. Interhemispheric transfer deficit in alexithymia: a transcranial magnetic stimulation study. Psychother Psychosom. 2008;77(3):175-81.

Rosenblum A, Foote J, Cleland C, Magura S, Mahmood D, Kosanke N. Moderators of effects of motivational enhancements to cognitive behavioral therapy. Am J Drug Alcohol Abuse. 2005;31(1):35-58.

Ross ED, Rush AJ. Diagnosis and neuroanatomical correlates of depression in brain-damaged patients. Implications for a neurology of depression. Arch Gen Psychiatry. 1981 Dec;38(12):1344-54.

Rostène W, Guyon A, Kular L, Godefroy D, Barbieri F, Bajetto A, Banisadr G, Callewaere C, Conductier G, Rovère C, Mélik-Parsadaniantz S, Florio T. Chemokines and chemokine receptors: new actors in neuroendocrine regulations. Front Neuroendocrinol. 2011 Jan;32(1):10-24.

Ruesch J. The infantile personality. Psychosom Med. 1948;10:134-44.

Saarijarvi S, Salminen JK, Toikka T. Alexithymia and depression: a 1-year follow-up study in outpatients with major depression. J Psychosom Res. 2001;51:729–33.

Saarijarvi S, Salminen JK, Toikka T. Temporal stability of alexithymia over a five-year period in outpatients with major depression. Psychother Psychosom. 2006;75:107-12.

Säkkinen P, Kaltiala-Heino R, Ranta K, Haataja R, Joukamaa M. Psychometric properties of the 20-item toronto alexithymia scale and prevalence of alexithymia in a finnish adolescent population. Psychosomatics. 2007 Mar-Apr;48(2):154-61.

Sakuraba S, Kubo M, Komoda T, Yamana J. Suicidal ideation and alexithymia in patients with alcoholism: a pilot study. Subst Use Misuse. 2005;40(6):823-30.

Salminen JK, Saarijarvi S, Aairela E, Tamminen T. Alexithymia—state or trait? One-year follow-up study of general hospital psychiatric consultation out-patients. J Psychosom Res. 1994;38:681-5.

Salminen JK, Saarijärvi S, Äärelä E, Toikka T, Kauhanen J. Prevalence of alexithymia and its association with sociodemographic variables in the general population of Finland. J Psychosom Res. 1999 Jan;46(1):75-82.

Salminen JK, Saarijarvi S, Toikka T, Kauhanen J, Aarela E. Alexithymia behaves as a personality trait over a 5-year period in Finnish general population. J Psychosom Res. 2006;61:275-8.

Santor DA, Bagby RM, Joffe RT. Evaluating stability and change in personality and depression. J Pers Soc Psychol. 1997 Dec;73(6):1354-62.

Sato T, Takahashi N, Kawamura M. Impaired recognition of emotion improved by L-DOPA in a patient with amygdala damage, Rinsho Shinkeigaku. 2008 Feb;48(2):139-42.

Sayar K, Gulec H, Topbas M. Alexithymia and anger in patients with fibromyalgia. Clin Rheumatol. 2004;23:441–8.

Sayar K, Kose S, Grabe HJ, Topbas M. Alexithymia and dissociative tendencies in an adolescent sample from Eastern Turkey. Psychiatry Clin Neurosci. 2005 Apr;59(2):127-34.

Serrano J, Plaza V, Sureda B, de Pablo J, Picado C, Bardagí S, Lamela J, Sanchis J; Spanish High Risk Asthma Resrarch Group. Alexithymia: a relevant psychological variable in near-fatal asthma. Eur Respir J. 2006 Aug;28(2):296-302.

Shaw WS, Means-Christensen AJ, Slater MA, Webster JS, Patterson TL, Grant I, Garfin SR, Wahlgren DR, Patel S, Atkinson JH. Psychiatric disorders and risk of transition to chronicity in men with first onset low back pain. Pain Med. 2010;11(9):1391-400.

Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998;59 Suppl 20:22-33;Quit 34-57.

Schäfer R, Schneider C, Tress W, Franz M. Cortical augmenting in alexithymic subjects after unpleasant acoustic stimulation. J Psychosom Res. 2007 Oct;63(4):357-64.

Schmidt U, Jiwany A, Treasure J. A controlled study of alexithymia in eating disorders. Compr Psychiatry. 1993;34:54-8.

Sifneos PE. Affect deficit and alexithymia. New Trends Exp Clin Psychiatry. 1994;10:193–5.

Sifneos PE. Alexithymia: past and present. Am J Psychiatry. 1996;153:137–42.

Sifneos PE. Problems of psychotherapy of patients with alexithymic characteristics and physical disease. Psychother Psychosom. 1975;26:65-70.

Sifneos PE. Short-term psychotherapy and emotional crisis. Cambridge (MA): Harvard University Press, 1972.

Sifneos PE. The prevalence of alexithymic characteristics in psychosomatic patients. Psychother Psychosom. 1973;22:255-62.

Silani G, Bird G, Brindley R, Singer T, Frith C, Frith U. Levels of emotional awareness and autism: an fMRI study. Soc Neurosci. 2008;3(2):97-112.

Simeon D, Giesbrecht T, Knutelska M, Smith RJ, Smith LM. Alexithymia, absorption, and cognitive failures in depersonalization disorder: a comparison to posttraumatic stress disorder and healthy volunteers. J Nerv Ment Dis. 2009 Jul;197(7):492-8.

Simha-Alpern A. „I finally have words!“ Integrating a psychodynamic psychotherapeutic approach with principles of emotional intelligence training in treating trama survivors. J Psychother Integrat. 2007;17:293-313.

Singer T, Seymour B, O'Doherty J, Kaube H, Dolan RJ, Frith CD. Empathy for pain involves the affective but not sensory components of pain. Science 2004; 303: 1157–62.

Singer T, Seymour B, O'Doherty JP, Stephan KE, Dolan RJ, Frith CD. Empathic neural responses are modulated by the perceived fairness of others. Nature. 2006; 439: 466–9.

Solano L, Donati V, Pecci F, Persichetti S, Colaci A. Postoperative course after papilloma resection: effects of written disclosure of the experience in subjects with different alexithymia levels. Psychosom Med. 2003 May-Jun;65(3):477-84.

Söndergaard HP, Theorell T. Alexithymia, emotions and PTSD; findings from a longitudinal study of refugees. Nord J Psychiatry. 2004;58(3):185-91.

Spalletta G, Pasini A, Costa A, De Angelis D, Ramundo N, Paolucci S, Caltagirone C. Alexithymic features in stroke: effects of laterality and gender. Psychosom Med. 2001 Nov-Dec;63(6):944-50.

Spek V, Nyklícek I, Cuijpers P, Pop V. Alexithymia and cognitive behaviour therapy outcome for subthreshold depression. Acta Psychiatr Scand. 2008 Aug;118(2):164-7.

Speranza M, Corcos M, Stéphan P, Loas G, Pérez-Diaz F, Lang F, Venisse JL, Bizouard P, Flament M, Halfon O, Jeammet P. Alexithymia, depressive experiences, and dependency in addictive disorders. Subst Use Misuse. 2004 Mar;39(4):551-79.

Speranza M, Loas G, Wallier J, Corcos M. Predictive value of alexithymia in patients with eating disorders: a 3-year prospective study. J Psychosom Res. 2007 Oct;63(4):365-71.

Spitzer C, Brandl S, Rose HJ, Nauck M, Freyberger HJ. Gender-specific association of alexithymia and norepinephrine/cortisol ratios. A preliminary report. J Psychosom Res. 2005 Aug;59(2):73-6.

Spitzer C, Vogel M, Barnow S, Freyberger HJ, Grabe HJ. Psychopathology and alexithymia in severe mental illness: the impact of trauma and posttraumatic stress symptoms. Eur Arch Psychiatry Clin Neurosci. 2007 Jun;257(4):191-6.

Spivak B, Shohat B, Mester R, Avraham S, Gil-Ad I, Bleich A, Valevski A, Weizman A. Elevated levels of serum interleukin-1 beta in combat-related posttraumatic stress disorder. Biol Psychiatry. 1997 Sep 1;42(5):345-8.

Sriram TG, Chaturvedi SK, Gopinath PS, Shanmugam V. Controlled study of alexithymic characteristics in patients with psychogenic pain disorder. Psychother Psychosom. 1987;47:11-7.

Stanghellini G, Ricca V. Alexithymia and schizophrenias. Psychopathology. 1995; 28: 263-72.

Strigo I, Simmons AN, Matthews SC, Craig AD, Paulus M. Major depressive disorder is associated with altered functional brain response during anticipation and processing of heat pain. Arch Gen Psychiatry. 2008;65:1275-84.

Strine TW, Hootman JM. US national prevalence and correlates of low back and neck pain among adults. Arthritis Rheum. 2007;57:656–65.

Stürmer T, Raum E, Buchner M, Gebhardt K, Schiltenwolf M, Richter W, Brenner H. Pain and high sensitivity C reactive protein in patients with chronic low back pain and acute sciatic pain. Ann Rheum Dis. 2005;64:921–925.

Subic-Wrana C, Bruder S, Thomas W, Lane RD, Köhle K. Emotional awareness deficits in inpatients of a psychosomatic ward: a comparison of two different measures of alexithymia. Psychosom Med. 2005 May-Jun;67(3):483-9.

Taieb O, Corcos M, Loas G, Speranza M, Guilbaud O, Perez-Diaz F, Halfon O, Lang F, Bizouard P, Venisse JL, Flament M, Jeammet P. Alexithymia and alcohol dependence. Ann Med Interne (Paris). 2002 May;153(3 Suppl):1S51-60.

Takahashi Y, Hasegawa-Moriyama M, Sakurai T, Inada E. The macrophage-mediated effects of the peroxisome proliferator-activated receptor-gamma agonist rosiglitazone attenuate tactile allodynia in the early phase of neuropathic pain development. Anesth Analg. 2011;113:398-404.

Tani P, Lindberg N, Joukamaa M, Nieminen-von Wendt T, von Wendt L, Appelberg B, Rimón R, Porkka-Heiskanen T. Asperger syndrome, alexithymia and perception of sleep. Neuropsychobiology. 2004;49(2):64-70.

Tausk F, Elenkov I, Moynihan J. Psychoneuroimmunology. Dermatol Ther. 2008 Jan-Feb;21(1):22-31.

Taylor GJ, Bagby RM, Parker JD. The 20-Item Toronto Alexithymia Scale. IV. Reliability and factorial validity in different languages and cultures. J Psychosom Res. 2003 Sep;55(3):277-83.

Taylor GJ, Bagby RM, Parker JDA. Disorders of affect regulation: alexithymia in medical and psychiatric illness. Cambridge: Cambridge University Press, 1997.

Taylor GJ, Bagby RM, Parker JDA. The alexithymia construct: a potential paradigm for psychosomatic medicine. Psychosomatics. 1991;32:153-64.

Taylor GJ, Bagby RM, Parker JDA: Disorders of Affect Regulation: Alexithymia in Medical and Psychiatric Illness. Cambridge, Cambridge University Press, 1999.

Taylor GJ, Bagby RM, Ryan DP, Parker JDA, Doody KF, Keefe P. Criterion validity of the Toronto Alexithymia Scale. Psychosom Med. 1988;50:500– 9.

Taylor GJ, Bagby RM. Measurement of alexithymia. Recommendations for clinical practice and future research. Psychiatr Clin North Am. 1988 Sep;11(3):351-66.

Taylor GJ, Bagby RM. New trends in alexithymia research. Psychother Psychosom. 2004 Mar-Apr;73(2):68-77.

Taylor GJ, Ryan D,Bagby RM. Toward developement of a new self-report alexithymic scale. Psychother Psychosom. 1985;44:191-9.

Taylor GJ. Alexithymia and the counter-transference. Psychother Psychosom.1977;28(1-4):141-7.

Taylor GJ. Alexithymia: concept, measurement, and implications for treatment. Am J Psychiatry. 1984 Jun;141(6):725-32.

Taylor GJ. Psychosomatic medicine and Contemporary Psychoanalysis. Madison, CT: International Universities Press, 1987.

Taylor GJ. Recent developments in alexithymia theory and research. Can J Psychiatr. 2000;45:134–42.

Temoshok L. Personality, coping style, emotion and cancer: towards an integrative model. Cancer Surv. 1987;6(3):545-67.

Temoshok LR, Waldstein SR, Wald RL, Garzino-Demo A, Synowski SJ, Sun L, Wiley JA. Type C coping, alexithymia, and heart rate reactivity are associated independently and differentially with specific immune mechanisms linked to HIV progression. Brain Behav Immun. 2008 Jul;22(5):781-92.

TenHouten WD, Hoppe KD, Bogen JE, Walter DO. Alexithymia and the split brain. I. Lexical-level content analysis. Psychother Psychosom. 1985;43(4):202-8.

TenHouten WD, Hoppe KD, Bogen JE, Walter DO. Alexithymia: an experimental study of cerebral commissurotomy patients and normal control subjects. Am J Psychiatry. 1986 Mar;143(3):312-6.

Thayer JF, Brosschot JF. Psychosomatics and psychopathology: looking up and down from the brain. Psychoneuroendocrinology. 2005;30:1050–8.

Todarello O, Casamassima A, Daniele S, Marinaccio M, Fanciullo F, Valentino L, Tedesco N, Wiesel S, Simone G, Marinaccio L. Alexithymia, immunity and cervical intraepithelial neoplasia: replication. Psychother Psychosom. 1997;66(4):208-13.

Todarello O, Casamassima A, Marinaccio M, La Pesa MW, Caradonna L, Valentino L, Marinaccio L. Alexithymia, immunity and cervical intraepithelial neoplasia: a pilot study. Psychother Psychosom. 1994;61(3-4):199-204.

Todarello O, Taylor GJ, Parker JD, Fanelli M. Alexithymia in essential hypertensive and psychiatric outpatients: a comparative study. J Psychosom Res. 1995 Nov;39(8):987-94.

Tolmunen T, Heliste M, Lehto SM, Hintikka J, Honkalampi K, Kauhanen J. Stability of alexithymia in the general population: an 11-year follow-up. Compr Psychiatry. 2011 Sep-Oct;52(5):536-41.

Tolmunen T, Honkalampi K, Hintikka J, Rissanen ML, Maaranen P, Kylmä J, Laukkanen E. Adolescent dissociation and alexithymia are distinctive but overlapping phenomena. Psychiatry Res. 2010 Mar 30;176(1):40-4.

Tops M, van Peer JM, Korf J. Individual differences in emotional expressivity predict oxytocin responses to cortisol administration: relevance to breast cancer? Biol Psychol. 2007 May;75(2):119-23.

Topsever P, Filiz TM, Salman S, Sengul A, Sarac E, Topalli R, Gorpelioglu S, Yilmaz T. Alexithymia in diabetes mellitus. Scott Med J. 2006 Aug;51(3):15-20.

Torrance N, Smith BH, Bennett MI, Lee AJ. The epidemiology of chronic pain of predominantly neuropathic origin. Results from a general population survey. J Pain. 2006;7:281-9.

Trigg R. Pain and emotion. Oxford: Clarendon Press, 1970.

Troisi A, Pasini A, Saracco M, Spalletta G. Psychiatric symptoms in male cannabis users not using other illicit drugs. Addiction. 1998 Apr;93(4):487-92.

Tselebis A, Kosmas E, Bratis D, Moussas G, Karkanias A, Ilias I, Siafakas N, Vgontzas A, Tzanakis N. Prevalence of alexithymia and its association with anxiety and depression in a sample of Greek chronic obstructive pulmonary disease (COPD) outpatients. Ann Gen Psychiatry. 2010 Apr 14;9:16.

Tucker DM, Roth DL, Bair TB. Functional connections among cortical regions: topography of EEG coherence. Electroencephalogr Clin Neurophysiol. 1986 Mar;63(3):242-50.

Tulipani C, Morelli F, Spedicato MR, Maiello E, Todarello O, Porcelli P. Alexithymia and cancer pain: the effect of psychological intervention. Psychother Psychosom. 2010;79(3):156-63.

Tutkun H, Savas HA, Zoroglu SS, Esgi K, Herken H, Tiryaki N. Relationship between alexithymia, dissociation and anxiety in psychiatric outpatients from Turkey. Isr J Psychiatry Relat Sci. 2004;41(2):118-24.

Vadacca M, Bruni R, Cacciapaglia F, Serino F, Arcarese L, Buzzulini F, Coppolino G, Rigon A, Terminio N, Afeltra A. Alexithymia and immunoendocrine parameters in patients affected by systemic lupus erythematosus and rheumatoid arthritis. Reumatismo. 2008 Jan-Mar;60(1):50-6.

Valera EM, Berenbaum H. A twin study of alexithymia. Psychother Psychosom. 2001;70:239–46.

Van Middendorp H, Lumley MA, Jacobs JW, van Doornen LJ, Bijlsma JW, Geenen R. Emotions and emotional approach and avoidance strategies in fibromyalgia. J Psychosom Res. 2008;64:159–67.

Van Tulder MW, Koes BW, Bouter LM. A cost-of-illness study of back pain in The Netherlands. Pain. 1995;62: 233-40.

Viikari-Juntura E, Vuori J, Silverstein BA, Kalimo R, Kuosma E, Videman T. A life-long prospective study on the role of psychosocial factors in neck-shoulder and low-back pain. Spine. 1991;16:1056– 61.

Vorst HCM, Bermond B. Validity and reliability of the Bermond-Vorst Alexithymia Questionnaire. Pers Indiv Differ. 2001;30:413-34.

Walker BF. The prevalence of low back pain: a systematic review of the literature from 1966 to 1998. J Spinal Disord. 2000;13:205–17.

Warnes H. Alexithymia, clinical and therapeutic aspects. Psychother Psychosom. 1986;46:96–104.

Wehmer F, Brejnak C, Lumley M, Stettner L. Alexithymia and physiological reactivity to emotionprovoking visual scenes. J Nerv Ment Dis. 1995;183:351-357.

Weik U, Herforth A, Kolb-Bachofen V, Deinzer R. Acute stress induces proinflammatory signaling at chronic inflammation sites. Psychosom Med. 2008 Oct;70(8):906-12.

Weinryb RM, Roessel RJ. Karolinska Psychodynamic Profile; KAPP. Acta Psychiatr Scand. Suppl 1991;83:1–23.

Weintraub S, Mesulam MM. Developmental learning disabilities of the right hemisphere. Emotional, interpersonal, and cognitive components. Arch Neurol. 1983 Aug;40(8):463-8.

Wise TN, Jani NN, Kass E, Sonnenschein K, Mann LS: Alexithymia: relationship to severity of medical illness and depression. Psychother Psychosom. 1988; 50: 68–71.

Wise TN, Mann LS, Hill B: Alexithymia and depressed mood in the psychiatric patient. Psychother Psychosom 1990a;54:26–31.

Wise TN, Mann LS, Mitchell JD, Hryvniak M, Hill B. Secondary alexithymia: an empirical validation. Compr Psychiatry. 1990b;31: 284-8.

Wise TN, Mann LS, Randell P. The stability of alexithymia in depressed patients. Psychopathology 1995;28:173-6.

Wise TN, Mann LS, Sheridan MJ. Relationship between alexithymia, dissociation and personality in psychiatric outpatients. Psychother Psychosom. 2000 May-Jun;69(3):123-7.

Yalug I, Selekler M, Erdogan A, Kutlu A, Dundar G, Ankarali H, Aker T. Correlations between alexithymia and pain severity, depression, and anxiety among patients with chronic and episodic migraine. Psychiatry Clin Neurosci. 2010 Jun;64(3):231-8.

Yehuda R, Steiner A, Kahana B, Binder-Brynes K, Southwick SM, Zemelman S, Giller EL. Alexithymia in Holocaust survivors with and without PTSD. J Trauma Stress. 1997 Jan;10(1):93-100.

Zarković M, Ignjatović S, Dajak M, Cirić J, Beleslin B, Savić S, Stojković M, Bulat P, Trbojević B. Cortisol response to ACTH stimulation correlates with blood interleukin 6 concentration in healthy humans. Eur J Endocrinol. 2008 Nov;159(5):649-52.

Zayfert C, McCracken LM, Gross RT. Alexithymia, disability, and emotional distress in chronic non-malignant pain. Paper presented at the annual meeting of the American Psychosomatic Society, New York, 1992.

Zeitlin SB, Lane RD, O'Leary DS, Schrift MJ. Interhemispheric transfer deficit and alexithymia. Am J Psychiatry. 1989 Nov;146(11):1434-9.

Ziółkowski M, Gruss T, Rybakowski JK. Does alexithymia in male alcoholics constitute a negative factor for maintaining abstinence? Psychother Psychosom. 1995;63(3-4):169-73.

Zlotnick C, Shea MT, Pearlstein T, Simpson E, Costello E, Begin A. The relationship between dissociative symptoms, alexithymia, impulsivity, sexual abuse, and self-mutilation. Compr Psychiatry. 1996 Jan-Feb;37(1):12-6.

Zung WWK. A rating instrument for anxiety disorders. Psychosomatics. 1971;12:371-9.

5. List of original publications

Publications *in extenso* in relationship to the subject of disseration

a) with IF

Tomáš Uher, Petr Bob, Radek Ptáček, Alexithymie a psychosomatická onemocnění, Československá psychologie, ročník LIV, 2010. IF = 0,295

Tomas Uher, Petr Bob , Cerebrospinal fluid IL-8 levels reflect symptoms of alexithymia in patients with non-inflammatory neurological disorders, Psychoneuroendocrinology. 2011 Sep;36(8):1148-53. IF = 5,168

b) without IF

Tomas Uher, Alexithymia and immune dysregulation: A critical review, Activitas Nervosa Superior 2010;52:1,40-44

Total cumulative IF = 5.463

Publications *in extenso* without relationship to the subject of disseration

a) with impact factor --

b) without impact factor --

6. Abbreviations

AAS - Amsterdam Alexithymia Scale
ACC - Anterior Cingulate Cortex
Act P - Actual Pain intensity
ACTH – Adreno-Corticotropic Hormone
ANS - Autonomic Nervous System
APRQ - Alexithymia Provoked Response Questionnaire
Aver P - Average Pain intensity last 6 weeks
BDI - Beck Depression Inventory
BIQ - Beth Israel Psychosomatic Questionnaire
BMI - Body Mass Index
BVAQ - Bermond-Vorst Alexithymia Questionnaire
CAQ - California Q-set
CIN - Cervical Intraepithelial Neoplasia
CLEM - Conjungate Lateral Eye Movements
CNS - Central Nervous System
CRH - Corticotropin-Releasing Hormone
CRP (hs) - C-Reactive Protein (high-sensitive)
CSF - Cerebro-Spinal Fluid
DDF - Difficulty Describing Feelings
DIF - Difficulty Identifying Feelings
EEG – Electroencephalography
EHA - Extrovert-High Alexithymia
EIS - Kellner´s Emotional Inhibition Scale
EOT - Externally Oriented Thinking
ERP - Event Related Potentials
GHA - General-High Alexithymia
HADS - Hospital Anxiety and Depression Scale
HDRS - Hamilton Rating Scale for Depression
HIV - Human Immunodeficiency Virus
HPA axis - Hypothalamic-Pituitary-Adrenal axis
Ig - Imunoglobuline
IHA - Introvert-High Alexithymia
IL - Interleukine
INF - Interferon
KAPP - Karolinska Psychodynamic Profile
LBP - Low Back Pain
L-DOPA – L-Dopamin
LEAS - Levels of Emotional Awareness Scale
MINI - Mini International Neuropsychiatric Interview

MDD - Major Depresive Disorder
MHPG - 3-Methoxy-4-Hydroxy-Phenylglycol
MIP-1 alpha - Macrophage Inflammatory Protein Alpha 1
MMPI - Minnesota Multiphasic Personality Inventory
MP - Maximal Pain
M-PFC - Medial Prefrontal Cortex
MRI - Magnetic Resonance Imaging
N/C ratio - Noepinephrine/Cortisol ratio
NA - Non-Alexithymia
NIND - Non-Inflammatory Neurological Disorders
NK - Natural Killer cell
NSAID - Non-Steroidal Anti-Inflammatory Drugs
OAS - Observer Alexithymia Scale
OCD - Obsessive-Compulsive Disorder
O-FC – Orbito-Frontal Cortex
PD-Q - Pain DETECT Questionnaire
PET – Positron Emision Tomography
PFC - Prefrontal Cortex
POMS - Profile Of Mood States
PSE-CATEGO - computer program for the Present State Examination
PTSD - Postraumatic Stress Disorder
RA - Rheumatoid Arthritis
SAM system - Sympatho-Adrenal-Medullary system
SAS - Zung self-rating Anxiety Scale
SAT9 - Scored Archetypal Test
SCL-90 - Symptom Check List-90
SFD - Somatoform Disorder
SLE - Systemic Lupus Erythematosus
SPSS - Schalling-Sifneos Personality Scale
SVS – Stress Vulnerability Scale
TAS - Toronto Alexithymia Scale
TAS-20 - Toronto Alexithymia Scale with 20 items
TAS-26 - Toronto Alexithymia Scale with 26 items
TAS-R - Revised Toronto Alexithymia Scale with 23 items
TGF - Tumor Growth Factor
Th – T helper Lymphocyte
TNF – Tumor Necrosis Factor
TSST - Trier Social Stress Test

Summary

Alexithymia represents a deficit in identifying and expressing emotions, paucity of fantasies, and an externally oriented cognitive style. Currently, numerous studies document that alexithymia and several mental and somatic disorders are significantly related. Several findings also indicate that this association might be caused by alexithymia related dysregulation of neuroendocrine and immune functions. Together these findings indicate that stressors related to alexithymia could underlie the process of neuroendocrine and immune dysregulation that likely may present a significant risk, sustaining and mediating pathogenesis of several disorders and particulary psychosomatic illnesses. In this context, it is also known that several proinflammatory cytokines may play a role in pain generation and that alexithymia is significantly associated with pain symptoms in several pain disorders.

Following these findings this study includes several new data developing current state of the art and showing some alexithymia specific changes in patients with neurological disorders. Main finding of this study shows that alexithymia and anxiety in their specific interactions are linked to increased levels of interleukine-8 (IL-8) in cerebrospinal fluid (CSF) in the group of patients with non-inflammatory neurological disorders (NIND). This finding suggests that IL-8 could have exceptional role in mediation of the relationship between psychopatological symptoms and inflammatory response.

Other main results of this study indicate that increased neuropathic pain in sciatica patients is associated with elevated levels of alexithymia, depression, anxiety and C-reactive protein (CRP). In this context, several proinflammatory cytokines including IL-8 have been suggested to play an important role in pathogenesis of the neuropathic pain and may link it to psychopatological symptoms.

In this context, future studies focused on disturbances of cytokine production in alexithymia and other psychopatological symptoms could provide new research directions and potentially useful clinical findings in specific groups of neurological patients.

Souhrn

Alexithymie představuje poruchu identifikace a vyjadřování emocí a je navíc spojena s nedostatkem fantazie a externě orientovaným kognitivním stylem. V současnosti je mnoho studií, které popisují významný vztah alexithymie a různých psychických a somatických onemocnění. Některé nálezy poukazují na fakt, že tento vztah může být zprostředkován narušením neuroendokrinních a imunitních funkcí u alexithymických subjektů. Tyto poznatky navíc poukazují na to, že stresové podněty u alexithymických subjektů mohou vést k narušení neuroendokrinních a imunitních funkcí, co může představovat významný rizikový faktor v patogenezi různých psychosomatických onemocnění. V této souvislosti je známo, že pro-zánětlivé cytokiny mohou hrát významnou roli při vzniku neuropatické bolesti, a že alexithymie je dávána do souvislosti se symptomy bolesti u některých poruch.

Vzhledem k těmto nálezům, tato studie přináší některé nové poznatky o alexithymii v případě specifické skupiny neurologických pacientů. Hlavní nález této studie ukazuje, že alexithymie a symptomy úzkosti v jejich specifickém vztahu souvisejí se zvýšenou hladinou interleukinu-8 (IL-8) v mozkomíšním moku (CSF) a to u skupiny pacientů s "nezánětlivými" neurologickými poruchami (NIND). Tyto nálezy také naznačují, že IL-8 může hrát výjimečnou roli zprostředkvávající vztah mezi psychopatologickými příznaky a procesy zánětu.

Další důležitý výsledek této studie představuje sledování, že neuropatická bolest u pacientů s radikulární bolestí je spojená se zvýšenou úrovní alexithymie, symptomů deprese a anxiety a také se zvýšenou hladinou C-reaktívniho proteinu (CRP) v séru. Vzhledem k těmto zjištěním jsou různé pro-zánětlivé cytokiny, včetně IL-8, dávány do souvislosti s patogenezí neuropatické bolesti a uvažuje se o tom, že můžou představovat pojítko mezi neuropatickou bolestí a psychopatologickými symptomy. V tomto kontextu, další studie zaměřené na výzkum cytokinů u alexithymie a u dalších psychopatologických procesů mohou poskytnout nové výzkumné perspektivy a potenciálně užitečné klinické poznatky týkající se některých typů neurologických onemocnění.