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Separation Anxiety in Children and Adolescents

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1. Introduction

Anxiety disorders are among the most common psychological disorders in younger patients, affecting 6% to 20% of developed countries children and adolescents (Walkup et al. 2008). Separation anxiety is the only anxiety disorder restricted to infancy, childhood, or adolescence (APA, 2000). Separation anxiety disorder (SAD) is defined by developmentally inappropriate, excessive, persistent, and unrealistic worry about separation from attachment figures, most commonly parents or other family members. Youths with SAD display distress before separation or during attempts at separation. These children worry excessively about their own or their parents' safety and health when separated, have difficulty sleeping alone, experience nightmares with themes of separation, frequently have somatic complaints, and may exhibit school refusal. Children with separation anxiety disorder exhibit varying degrees of avoidant behaviour that correlate with the severity of their symptoms (Albano et al. 2003). This kind of anxiety in adolescents and schoolchildren significantly interferes with daily activities and developmental tasks. Children with separation anxiety disorder are usually brought to the clinician when SAD results in school refusal or embarrassing somatic symptoms. When analyzing responses to shown images, relative to controls, children with anxiety disorders experience greater negative emotional responses to the presented images, are less successful at applying reappraisals, but show intact ability to reduce their negative emotions following reappraisal. They also may report less frequent use of reappraisal in everyday life (Carthy et al, 2010).

2. The risk factors and background of the separation anxiety

In the aetiology of SAD play a part a complex interplay of biological and genetic vulnerabilities, temperamental qualities, negative environmental influences and negative attachment experiences, parental psychopathology and disadvantageous socio-cultural factors (Pine & Grun, 1999).

Biological risk factors include genetics and child temperament. Studies of environmental risk factors in the development of childhood anxiety disorders have focused on parent-child interactions and parental anxiety.

2.1 Genetic influence

Evidence suggests a genetic link between separation anxiety disorders in children and a history of panic disorder, anxiety, or depression in their parents. Infants with anxious temperaments may have a predisposition toward later development of anxiety disorders. Findings from a number of studies, including Bird et al. (1989), have implicated age of subject and low socioeconomic status as putative risk factors for separation anxiety. Low self-esteem was found to increase risk for the development of anxiety in general. Parental depression played a more important role in the development of anxiety disorders in offspring. Other results of genetic studies of children with separation anxiety (Topolsky et al., 1997) suggested that shared environmental effects are more important than genetic factors in the aetiology of SAD. The liability threshold for SAD is higher for males and increases with age (Tari et al., 1997). Genetic factors seem to play an important role in shaping the co-occurrence of different anxiety dimensions in childhood (Ogliari et al., 2010). Results of a unique 30-year longitudinal study of a group from one town in New Zealand (Gibb et al., 2011) showed that relationship separation is associated with increased rates of depression, suicidal behaviour, and total mental health problems. Parental anxiety disorder has been associated with increased risk of anxiety disorder in offspring. Family aggregation studies suggest that children whose parents have an anxiety disorder are at risk for developing an anxiety disorder themselves. Twin studies also suggest a familial transmission. Separation anxiety disorder in the offspring can be accounted for by the same disorders in the parent (Biederman et al., 2006). Children of anxious parents are likely to have an earlier onset for anxiety disorders than their parents. This phenomenon can be explained as anxious parents can model fear and anxiety, reinforce anxious coping behaviour, and unwittingly maintain avoidance, despite their desire to be of help to their child (Dadds et al., 2001). Lifetime maternal anxiety disorders are related to offspring anxiety disorders. Findings confirm the transmission of anxiety disorders from mother to offspring (Martini et al., 20010).

2.2 Gender

Some studies (Bowen et al. 1990) report a significantly higher prevalence of SAD in girls than boys. In the previously mentioned New Zealand study, an overrepresentation of females was noted among the preadolescent children with separation anxiety disorder (Anderson et al., 1987). Also, higher rates in females than in males were observed among high school students with SAD in Lewinsohn and colleagues (1993) study. It should be noted, however, that there are no reported gender differences in symptomatology (Last et al., 1987). A study including preschool 4-year-old children (Lavigne et al., 2009) showed no gender differences for separation anxiety disorder at any level of impairment, and race or ethnicity differences were not significant. Gender differences have not been observed, although girls do present more often with anxiety disorders in general.

2.3 Temperament

Emotion deregulation is believed to be a key factor in anxiety disorders. Anxious children demonstrate greater intensity and frequency of negative emotional responses relative to controls, deficits in using reappraisal in negative emotional situations and corresponding deficits in reappraisal self-efficacy, and greater reliance on emotion regulation strategies that increase the risk of functional impairment, intense negative emotion, and low emotion regulation self-efficacy (Carthy et al., 2010b). The vigilance-avoidance attention pattern is

found in anxious adults and children, who initially gaze more at threatening pictures than non-anxious adults and children (vigilance), but subsequently gaze less at them than non-anxious adults and children (avoidance) (In-Albon et al., 2010). A Korean study (Soo-churl et al., 2009) evaluated temperament and character of children and adolescents with anxiety disorders, in part subjects with separation anxiety, using the Junior Temperament and Character Inventory (JTCI). Separation anxiety disorder was not associated with any temperament and character on the JTCI, opposite to others anxiety diagnosis. Children and adolescents with anxiety disorders could have different temperaments and character profiles in accordance with diagnostic groups, which imply the specific pathophysiological mechanism of each anxiety disorder (Soo-churl et al., 2009).

2.4 Family parent/child attachment

Parenting stress, parental psychopathology, and family functioning are associated with child anxiety (Victor et al., 2007). Separation anxiety would appear to be a core form of anxiety that is associated with anxious attachment. Overprotective, overcontrolling, and overly critical parenting styles that limit the development of autonomy and mastery may also contribute to the development of anxiety disorders in children with temperamental vulnerability. Rejection and control by parents may be positively related to later anxiety and depression (Rapee, 1997). Insecure attachment relationships with caregivers and, specifically, anxious/resistant attachment can increase the risk of childhood anxiety disorders (Manassis & Hood, 1998; Warren et al., 1997). Different attachment patterns (secure, ambivalent, avoidant, and disorganized) may relate to different types of anxiety symptoms, and that behavioural inhibition may moderate these relations. In a sample of 10 - 12-year olds in Brumariu & Kerns study (2010), security attachment was related to lower levels of all types of anxieties, except separation anxiety. Ambivalence attachment was positively related to separation anxiety, although this relation was stronger for boys. Although avoidance attachment was not related to anxiety and disorganization was positively correlated to somatic symptoms, social phobia, and school phobia. Behavioural inhibition moderated the relations of security with social phobia and of disorganization with school phobia (Brumariu & Kerns, 2010).

2.5 Environmental changes

Anxiety states in children can be associated with exposure to negative life events. Separation anxiety disorder is often precipitated by change or stress in the child's life. Symptoms of separation anxiety disorder may be exacerbated by a change in routine, illness, lack of adequate rest, a family move, or change in family structure (such as death, divorce, parent illness, birth of a sibling), starting a new school, a traumatic event, or even a return to school after summer vacation. The child's symptoms may also be affected by a change in caregivers or changes in parents' response to the child in terms of discipline, availability, or daily routine. Even if changes are positive or exciting, the change may feel uncomfortable and precipitate an anxious response in the child.

2.6 Economical factors

Most children with anxiety disorders are from middle to upper-middle class families; however, 50 to 75% of those with SAD come from low socioeconomic status homes (Last et al., 1987; Last et al., 1992; Velez et al., 1989).

3. The prevalence of the disorder

Anxiety disorders as a whole are the most common psychiatric disorders in children and adolescents, with a reported prevalence ranging from 6 to 18%.

Shaffer et al. found that approximately 20% of American children have an impairing anxiety disorder (Shaffer et al., 1995), but even 25% of Dutch children met criteria for an anxiety disorder (Verhulst et al., 1997). When using a higher impairment threshold, a rate of anxiety disorders was closer to 5% (Costello et al. 1996). In a large sample of adolescents, prevalence rates were found at 3.6% of subjects (Bowen et al., 1990). Different epidemiological studies indicate a prevalence of SAD in 4 to 5% children and adolescents. The 12-month prevalence of SAD is generally estimated at around 5%, but there is a significant variation between studies (2-13%)(Costello & Angold, 1995). Among 11-year-old children from the general New Zealand population was found a 1-year rate of 3.5% for SAD (Anderson et al., 1987). In the same population three years later, the prevalence of SAD decreased to 2% (McGee et al., 1990).

In Bird and colleagues' study, diagnosis of SAD in the sample of 4- to 16-year-old Puerto Rican children was made in 4.7% of the children (Bird et al., 1988). The lifetime prevalence of SAD in a randomly selected sample of adolescents was 4.3% (Lewinsohn et al., 1993). A Canadian epidemiological study (1999) found that the 6-month prevalence of SAD was 4.9% in children aged 6 to 8 years and 1.3% in adolescents aged 12 to 14 years (Breton et al., 1999). A study from an Australian community sample of preadolescent children found a rate of 4.2% for SAD (Prior et al., 1999). Self-report interviews with juvenile subjects yield a higher prevalence of SAD than interviews with adult informants, and agreement between informants ranges between low and moderate (Grills & Ollendick, 2003). Little is known about the development of anxiety symptoms from late childhood to late adolescence. In Van Oort and colleagues' (2009) study, anxiety symptoms were assessed in a large community sample of boys and girls at three time-points across a 5-year interval. In that general population, anxiety symptoms first decrease during early adolescence, and subsequently increase from middle to late adolescence (Van Oort et al., 2009). Prevalence estimates of separation anxiety disorder are between 4 and 5% in the population (Masi et al., 2001). Of those diagnosed with separation anxiety disorder, approximately 75% experience school refusal.

4. Classification criteria of the separation anxiety disorder

Separation anxiety disorder represents a more severe and disabling form of a maturational experience that all children normally have. As specified in DSM-IV-TR criteria, separation anxiety disorders are defined largely by the persistence of such symptoms for long enough duration to be considered pathological (APA, 2000). In DSM-IV, disorders that have been long recognized as manifesting during childhood are placed in a separate category, "Disorders usually first diagnosed in infancy, childhood or adolescence." For the anxiety disorders, this includes only separation anxiety disorder (SAD) in DSM-IV. A DSM-IV-TR-based diagnosis of separation anxiety disorder requires that a child exhibits at least three of the following symptoms for at least four weeks (APA, 2000). The characteristic symptoms include three types of distress or worry, three types of behaviours and two physiological symptoms.

DSM-IV-TR diagnostic criteria for separation anxiety disorder (309.21):

- a. Developmentally inappropriate and excessive anxiety concerning separation from home or from those to whom the individual is attached, as evidenced by three (or more) of the following:
 1. recurrent excessive distress when separation from home or major attachment figures occurs or is anticipated
 2. persistent and excessive worry about losing, or about possible harm befalling, major attachment figures
 3. persistent and excessive worry that an untoward event will lead to separation from a major attachment figure (e.g., getting lost or being kidnapped)
 4. persistent reluctance or refusal to go to school or elsewhere because of fear of separation
 5. persistently and excessively fearful or reluctant to be alone or without major attachment figures at home or without significant adults in other settings
 6. persistent reluctance or refusal to go to sleep without being near a major attachment figure or to sleep away from home
 7. repeated nightmares involving the theme of separation
 8. repeated complaints of physical symptoms (such as headaches, stomach aches, nausea, or vomiting) when separation from major attachment figures occurs or is anticipated
- b. The duration of the disturbance is at least 4 weeks.
- c. The onset is before age of 18.
- d. The disturbance causes clinically significant distress or impairment in social, academic (occupational), or other important areas of functioning.
- e. The disturbance does not occur exclusively during the course of a Pervasive Developmental Disorder, Schizophrenia, or other Psychotic Disorder and, in adolescents and adults, is better not accounted for by Panic Disorder with Agoraphobia.

Specify if:

Early Onset: if onset occurs before age 6 years (APA, 2000).

Diagnostic guidelines of the ICD-10 Classification of Mental and Behavioural Disorders World Health Organization lists similar criteria for separation anxiety disorder (F93.0) (WHO, 1992). The number of studies with clinical samples from zero to 3 year is very limited. The assessments for children zero to 3 years of age are rare and even less common for children aged 0 to 1 year of age. The few prevalence studies in epidemiological samples have concerned preschoolers and reported rates of psychopathology ranging from 7.8 to 50% (Beernink et al., 2007; Skovgaard et al., 2007). In the first study focused on infants younger than 1 year of age, roughly 76% of the infants had an Axis I diagnosis, with anxiety disorders and mixed disorder of emotional expressiveness being the most frequently observed (Viaux-Savelon et al., 2010).

5. Course

The mean age of onset of the disorder is about 7.5 years (Last et al., 1992). Developmental differences have been reported in the presentation of symptoms. Younger children have more symptoms than older children. Children aged 5 to 8 years most commonly report unrealistic worry about harm to attachment figures and school refusal. In children aged 9 to 12 years, the disorder usually manifests as excessive distress at times of separation (Francis

et al., 1987). In adolescents, somatic complaints and school refusal are most common. The most frequently observed ages for occurrence of separation anxiety disorder are in children aged five to seven years and again from aged 11 to 14 years. Many studies report a declining prevalence of SAD as children age into adolescence. Separation anxiety in children with severe school refusal evokes often worry about the future with regard to professional career and social integration. In Von Widdern & Lehmkuhl (2011) study, in the group of inpatient treatment because of a separation anxiety disorder assessed at follow up ranged from 4.3 to 11.1 years (average 7.1 years) was found at least one clinical psychiatric diagnosis in one third of all patients at follow-up. Even more of the formerly inpatients reported subthreshold psychiatric symptoms (55%). Estimated remission rate for the separation anxiety disorder was high (89%). The results revealed an important shift of diagnosis to social phobia in one third of cases. The majority of young people considered academic outcome satisfactory but reported pronounced problems in the social integration (Von Widdern & Lehmkuhl, 2011). In Allen and colleagues' (2010) study, among children aged 4-15 years with a primary DSM-IV diagnosis of SAD, the most frequently reported symptoms were separation-related distress, avoidance of being alone/without an adult and sleeping away from caregivers or from home, with nightmares, the least frequently endorsed criterion. Anxiety disorders in childhood are predictors of a range of psychiatric disorders in adolescence. Results come from the Great Smoky Mountains Study indicated that childhood SAD predicted adolescent SAD (Bittner et al., 2007). Among the participants of the Oregon Adolescent Depression Project SAD was a strong risk factor (78.6%) for the development of mental disorders during young adulthood. The major vulnerabilities were for panic disorder and depression (Lewinsohn et al., 2008). The squeals of childhood anxiety disorders include social, family, and academic impairments. Anxiety separation disorders disrupt the normal psychosocial development of a child. Children with SAD may not have the opportunity to develop independence from adults. Social problems include poor problem-solving skills and low self-esteem. Severe separation anxiety can result intra-familial violence.

6. A normative separation anxiety

The separation anxiety disorder (SAD) is qualitatively different from early worries and the normative anxieties. Fear and worry are common in healthy children. Normal, developmentally, fear does not impair a child's functioning. Infants typically experience fear of loud noises, fear of being startled, and later a fear of strangers. Toddlers experience fears of imaginary creatures, fears of darkness, and normative separation anxiety. School-age children commonly have worries about injury and storms. Older children have worries and fears related to school performance, social competence, and health issues. Fears during childhood become problematic, if they do not subside with time and if they impair the child's functioning. Depending on the age, developmental differences are observed in the expression of childhood anxiety symptoms and fears. Results also point toward specific symptoms predominant at certain ages (i.e., separation anxiety symptoms in youths aged 6-9 years, in partial support of predictions (Weems et al., 2005). Normal separation distress usually intensifies during early childhood, then gradually subsides at 3 to 5 years of age, although a percentage of children continue to present closed relation to parents and separation distress into their first school attendance. Separation anxiety diathesis may manifest itself differently over the life span (Deltito & Hahn, 1993).

7. Neurobiology of separation anxiety disorder

Literature still gives very little information on the nature of separation anxiety and evidence based on longitudinal studies. Contemporary knowledge about anxiety is in a prominent part based on animal studies. Up-to-date research has implicated the amygdala and circuits related to these nuclei as being central to several aspects of fear and fear-related behaviors in animals. It can be concluded that in an emotional response, a limbic system holds a key role. Brain structures building this system determinates processing of information from an emotional angle, and because of many projections from other brain regions it leads the best coping method counteracting a threat stimulus (Cummins & Ninan, 2002; Lucey & Corvin, 2005). The amygdala, and its efferent projections, is mainly concerned with a central fear system involved in expression and acquisition of conditioned fear (Cummins & Ninan, 2002; Davis, 1992). One of important functions of the lateral nucleus is to associate conditioned (particularly aversive) and unconditioned stimuli in the course of the anxiety reaction. Because of this network medial nuclei modulates the autonomous and operational components of a defensive reaction. It also coordinates an anxiety response in which a connection with periaqueductal gray activates a freeze reaction to threatening stimulus. Moreover, the connection with paraventricular nuclei of thalamus modulates the activity of endocrine controlled process involved in regulation of autonomous nervous system reaction. Another role of medial nuclei is due to the connection with the compressed monoaminergic neurons in brainstem and cholinergic in Meynert basal nuclei. These structures modulate nonspecific arousal (excitation) and attention mechanisms, which are important in course of anxiety reaction. Due to numerous neuronal pathways with different brain structures, medial nuclei take part in sensorial information reception from all modalities, access to memory modules, regulation of perception and attention mechanisms, and control of cognitive-motivation processes, which play an important role in decision making and choosing the most adaptive coping reaction. The orbitofrontal cortex dysfunction has been implicated in social anxiety disorder and specific phobia as a direct reaction on a phobic object. Dichotomizing the orbitofrontal cortex into medial versus lateral subdivisions according to positive and negative valence, in reward and punishment expectation is well-founded. The limbic system and specified structures play significant role in anxiety reaction and choice of adaptive coping methods in threatening situation. In separation anxiety, its controlling activity does not seem to work properly. Etiopathogenesis of anxiety disorders is multifactorial with a significant role played by neurotransmitters pathways. Anxiety states are considered to be a result of insufficient inhibitory control. In these disorders, a major role is played by the gamma-amino-butyric acid (GABA) system. There are clinical studies proving a decreased GABAergic inhibition in anxiety disorders (Bremner et al., 2000; Domschke & Zwanzger, 2000; Malizia et al. 1998). Deregulation of serotonergic and noradrenergic functions mediate many symptoms of depression and anxiety disorders. Serotonergic and noradrenergic dysfunction does not cause directly these disorders. Their role in modulating and being modulated by other neurobiological functions underlies abnormality in mood and anxiety states. Abnormal modulation of cortical-hippocampal-amygdala axis contributes to chronic hypersensitive stress, as well as fear responses. Quite possibly, this mechanism mediates features of anxiety (impaired concentration and memory, uncontrollable worry), anhedonia, aggression, affective discontrol (Ressler & Nemeroff, 2000). Schwartz (2003) et al. longitudinal studies showed

that anxiousness correlated with high reactivity of amygdala in response to new stimuli. Among children diagnosed in the age of two as inhibited temperament (timid, anxious, avoidant in new situations) there were more intensive activation of amygdala recorded in contrast to children diagnosed as no inhibited temperament.

7.1 Neuroimaging results in separation anxiety disorder in children

There is very few data about structural and functional neuroimaging in childhood separation anxiety disorder. However, there is an association between separation anxiety disorder and adult panic attacks or panic disorder (Battaglia et al., 1995; Klein, 1995; Pine et al., 1998). Klein and Capps suggested in their investigations that there might be common, heritable biological substrate for both of them (Capps et al., 1996; Klein 1993). The relationship between parental panic disorder or parental depression and childhood separation anxiety disorder is well-defined (Beidel et al., 1997; Capps et al., 1996; Last et al., 1991; Warner et al., 1995; Weissmann et al., 1984). A study by Uchida et al. revealed in adult patients with panic disorder relative increase in gray matter volume in the left insula, in the left superior temporal gyrus, midbrain and pons, as well as relative gray matter deficit in the anterior cingulate cortex of those patients as compared to controls (Uchida et al., 2008). Reduced volume of temporal lobe was detected in other studies (Fontaine et al., 1990; Ontiveros et al., 1989; Vythilingam et al., 2000). However, Massana et al. (2003) didn't find any changes in temporal lobe (probably because of excluding hippocampus and amygdala in his Region of Interest investigations). There is an evidence of a dysfunction in hippocampus, amygdala, cingulate gyrus revealed in functional magnetic resonance imaging (Bystritsky et al., 2001). Grillon et al. (1997) examined enhanced startle reflex in children of patients with anxiety. According to significance of the amygdala in the startle reflex, this data indicates a potential role of amygdala-based circuits (and hypothetic significance of the bed nucleus of the striaterminalis) in familial risk for anxiety. This report is consistent with a study of increased striatal function to reward in adolescents with temperamental anxiety (Guyer et al., 2006). The meta-analysis of functional magnetic resonance and positron emission tomography studies of post-traumatic stress disorder, social anxiety disorder, and specific phobia in adults showed that all three disorders displayed hyperactivity in amygdala and insula (Etkin & Wager, 2007). In adult patients with social anxiety disorder hyperactivity was seen in the amygdala, parahippocampal gyrus, fusiform gyrus, globus pallidus, insula, inferior frontal gyrus and superior temporal gyrus. Adult patients with specific phobia showed hyperactivity in the amygdala, fusiform gyrus, substantia nigra, insula and mid-cingulate (Etkin & Wager, 2007). Separation anxiety disorder exhibits association with depression in adults. Functional brain changes in early stages of depressive disorder in adults were displayed in three frequency bands of electroencephalography (theta 4-7.5Hz, alpha 7.5-14Hz, beta 14-20Hz, both in Eyes closed and Eyes open conditions). A diffuse enhancement of beta power (correlating with anxiety symptoms) and an increase in theta and alpha activity at parietal occipital sites were revealed (Grin-Yatsenko et al., 2010). The presence of structural and functional abnormalities in the superior temporal gyrus and in the amygdala in children and adults with generalized anxiety disorder was found (De Bellis et al., 2000, 2002; Quirk et al., 1997). Adolescents with anxiety disorder displayed more extreme responses in anterior cingulate cortex, dorsolateral prefrontal cortex, medial and lateral orbitofrontal cortex and ventral

striatum than youth with depression (Forbes et al., 2006). A study comparing children with and without anxiety (including separation anxiety disorder) reviewed reduction of the volume of the left amygdala in the morphometric magnetic resonance imaging (Milham et al., 2005). Reduced volume of the brain and of the mediosagittal area of the corpus callosum and increased lateral ventricle (De Bellis et al., 2003), as well as reduced cerebellar volume (De Bellis et al., 2006), but no changes in pituitary gland (Thomas et al., 2004) were found in abused children with post-traumatic stress disorder.

7.2 Cognitive function in separation anxiety disorder

There is a very limited number of data concerning the cognitive functioning of children with a separation anxiety disorder. However, the studies on cognition in anxiety disorders in general, concentrate mainly on biases in attention, information processing, memory and judgment that are considered to underlie them (Bar-Haim et al., 2007). Numerous research studies in adults with anxiety disorders, demonstrating the attentional bias towards threat, are ones of the major findings in this field. They emphasize a role of hyper-vigilance and changes in selective attention in aetiology and maintenance of anxiety (Kindt & van den Hout, 2001). The results of studies performed in anxious children are ambiguous. In the work of Kindt et al. (2003) the processing bias was measured by one of the most often used tools - the emotional Stroop task. It assessed colour-naming latency to threat-relevant and neutral words in children with separation anxiety disorder, social phobia and generalized anxiety disorder and normal controls. It was also controlled whether the bias is domain-specific by monitoring the reactions of children with separation anxiety disorder on words related to separation concerns, social phobia children on words associated with social concerns, and children with generalized anxiety disorder on words linked to physical concerns. They found no evidence for either an anxiety-related bias towards threat or a domain-specificity effect (Kindt et al., 2003). The authors postulate that these discrepancies between adult and children may be connected with age. They suggest that non-anxious children learn with increasing age to inhibit the processing of threat, whereas anxious children do not develop such ability. Thus, only at certain age the differences in processing may be revealed. Moreover, they hypothesize that in adults the content of fear is more stable and represented by domain-specific fear networks, while in children the content of fears changes with the age. It may suggest that representations of fears in children are more flexible and prone to assimilate disconfirming information. In-Albon et al. (2010) performed a study using the eye tracking to identify vigilance-avoidance attention pattern in children with separation anxiety disorder. The model observed in adults with anxiety disorders predicts the initial vigilance for threat stimulus and then its subsequent avoidance. Children were presented with series of pairs of photographs: one with a child separating from an adult woman and the second one with a child reuniting with an adult woman. The results obtained confirmed the vigilance-avoidance model in children with separation anxiety disorder. In the attentional control theory, the influence of anxiety on the main executive functions involving attentional control such as inhibition and shifting is postulated. These changes may affect cognitive performance, e.g. memory. Yet, the effectiveness of performance may not be affected when the compensatory strategies such as e.g. enhanced effort or increased use of processing resources are engaged (Eysenck et al., 2007). The prospective study of Pine et al. (1999) in prepubescent boys aged 7-11 years at risk of delinquency showed verbal and visual memory deficits predicting future anxiety disorders:

social phobia, separation anxiety disorder, overanxious disorder. In addition, the anxiety symptoms were connected more significantly with lower memory ability than with reduced intelligence (Pine et al., 1999). The work of Toren et al. (2000) in a group of children and adolescents aged 6-18 year old presented verbal memory deficits measured by CVLT (California Verbal Learning Test) in separation anxiety and overanxious disorders. Also, the anxiety group performed worse than control group on WCST (Wisconsin Card Sorting Test) measuring working memory, executive function and cognitive flexibility. They found no correlation between anxiety and nonverbal processes (Toren et al., 2000). Vasa et al. (2007) focused on a memory for non-emotional material in offspring with separation anxiety disorder, social phobia and generalized anxiety disorder of parents with panic disorder or major depressive disorder. They presented no relationship between visual memory and verbal memory measured by WRAML (Wide Range Assessment of Memory and Learning) and separation anxiety disorder. The study also indicated that IQ measured using The Kaufman Brief Intelligence Test (K-BIT) is a significant predictor of both visual and verbal memory. What's more, they concluded that anxiety or depressive disorders in parents were unrelated to memory performance in their offspring (Vasa et al., 2007). This finding is in contrary with a study of Merikangas et al. (1999) who found that parental anxiety was connected with visual memory deficits in offspring. They postulated that memory deficits may be considered as a premorbid risk factor for childhood anxiety disorders (Merikangas et al., 1999). A 2009 study of Mikko et al. concentrated on the executive function of 6- 17 year old children of parents with major depression and/or panic disorder and of controls with neither disorder. Children were diagnosed with generalized anxiety disorder, social phobia, separation anxiety disorder and major depression. A large battery of neuropsychological tests was used to assess cognitive performance. The only significant difference in a group of children with separation anxiety related to their better performance on the CPT (Continuous Performance Task) - False Alarms subtest. The main conclusion of this study was that deficits in executive functioning and processing speed do not serve as trait markers for developing depression or anxiety (Micco et al., 2009). In 2007, Mazzone et al. performed a study, in a sample of children and adolescents attending from elementary to high school, assessing a role of anxiety symptoms in school performance. They concluded that frequency of high self-reported levels of anxiety increased with age and was negatively associated with school performance (Mazzone et al., 2007). Such observation may lead to conclusion that poorer performance at school of children with separation anxiety disorder may be a one of the factor maintaining the increased level of anxiety and also leading to school phobia.

8. Assessment

Separation anxiety disorder is usually under-diagnosed and undertreated. The recognition of this kind of anxiety is important, because if not treated, it may affect the child's normal development. Separation anxiety disorder is generally diagnosed by history, including parental reports; however, a few measures of general anxiety exist that can be used to supplement the history. These include Pediatric Anxiety Rating Scale, Children's Global Assessment Scale, Children's Anxiety Scale, Screen for Child Anxiety Related Emotional Disorders (SCARED-R), Multi-Dimensional Anxiety Scale for Children, and Achenbach's Child Behavior Checklist. Separation anxiety disorder can be predicted by the

corresponding subscale of the screening questionnaire - the Anxiety Disorder Interview Schedule (ADIS). Simon and Boegels (2009) rightly concluded that this scale has proved the usefulness of screening for anxiety disorders in primary school children (Simon & Bögels, 2009). A number of simple screening tools have been shown effective in identifying various anxiety disorders in the pediatric population. The Screen for Child Anxiety Related Emotional Disorders (SCARED), a 41-item self-report questionnaire administered to both child and parent, has been shown effective in identifying a pediatric anxiety disorders in both primary care and outpatient settings. The Multidimensional Anxiety Scale for Children (MASC) is a 39-item instrument with both child and parent self-report components available for purchase. The Pediatric Anxiety Rating Scale (PARS) is a clinician-scored instrument that has been used to evaluate the severity of anxiety disorders in children. Researchers conducting a comprehensive review of the most commonly cited and psychometrically valid anxiety scales used in children concluded that the PARS combined with either the SCARED or the MASC, provided an appropriate assessment for pediatric anxiety disorders (Monga et al., 2000). The Separation Anxiety Daily Diary (SADD) assesses the frequency of anxiety-provoking and non-anxiety-provoking separations, along with associated parental anxiety, thoughts, child behaviours, and corresponding parental reactions (Allen et al., 2010). The Revised Child Anxiety and Depression Scale—Parent Version (RCADS-P) is a 47-item parent-report questionnaire of youth anxiety and depression, with scales corresponding to the DSM-IV categories of Separation Anxiety Disorder, Social Phobia, Generalized Anxiety Disorder (GAD), Panic Disorder, Obsessive-Compulsive Disorder, and Major Depressive Disorder (MDD). The RCADS-P demonstrated favourable psychometric properties, including high internal consistency, convergent/divergent validity, as well as strong discriminant validity - evidencing an ability to discriminate between anxiety and depressive disorders, as well as between the targeted anxiety disorders (Ebesutani et al., 2010).

9. Comorbidity

Separation anxiety disorder is closely linked to other anxiety and mood disorders and can also be associated with externalizing psychopathology in children and adolescents. Children and adolescents with anxiety disorders are at risk of developing new anxiety disorders, depression, and substance abuse. Longitudinal studies have suggested that childhood SAD may be a risk factor for other anxiety disorders. It is a question whether this link is specific to, for example, a panic disorder and agoraphobia or whether SAD represents a general factor of vulnerability for a broad range of anxiety disorders (Manicavasagar et al., 1998; Silove et al., 1993). 50 to 75% of children and adolescents with juvenile panic disorder suffer from SAD at the same time (Biederman et al., 1997; Bradley & Hood, 1993; Masi et al., 2000). Some studies confirm the association between separation anxiety in childhood and panic disorder (PD) in adulthood (Capps et al., 1996; Pine et al., 1998). The results from other studies did not confirm a specific link between these two kinds of disorders (Lipsitz et al., 1994; Silove et al., 1996). Some researches consider that a history of SAD identifies a particularly heritable, early-onset form of panic disorder (Battaglia et al., 1995). Fagiolini et al. (1998) hypothesize that childhood SAD cannot transform into panic disorder or other anxiety disorders, but it may simply persist in adulthood, as part of a more comprehensive panic diathesis called panic spectrum. Results from Aschenbrand and colleagues (2003) study argue against the hypothesis that childhood SAD is a specific risk factor for adult panic disorder and agoraphobia. The subjects with a childhood diagnosis of SAD did not

display a greater risk for developing panic disorder and agoraphobia in young adulthood than those with other childhood anxiety diagnoses (Aschenbrand et al., 2003). Results of a 4-year, prospective longitudinal Brückl and colleagues (2007) study of a representative cohort of adolescents and young adults aged 14-24 years at baseline showed an increased risk of developing subsequent not only panic disorder with agoraphobia, but also an increased risk of developing subsequent specific phobia, obsessive-compulsive disorder, bipolar disorder, pain disorder, alcohol dependence and generalized anxiety disorder (Brückl et al., 2007; Masi et al., 1999). Similar patterns of vulnerability to carbon dioxide inhalation have been reported in adults with panic disorder (PD) and children with separation anxiety disorder (SAD), suggesting a link between the adult and child conditions. They might be a subtype of SAD at particularly high risk for adult PD (Roberson-Nay et al., 2010). Anxiety disorders in youth often do not present as a single/focused disorder: such disorders in youth overlap in symptoms and are highly comorbid among themselves (Kendall et al., 2010). Anxiety disorders and depression are frequently comorbid in children and adolescents (Axelson & Birmaher, 2001; O'Neil et al., 2010; Pine et al., 1998). Separation anxiety disorder has an association with higher rates of subsequent depression in a limited number of studies (Horn & Wuyek, 2010). Separation anxiety disorders are among the most common comorbid conditions in youth with bipolar disorder (BP) (Sala et al., 2010). A history of separation anxiety disorder is frequently reported by patients with obsessive-compulsive disorder (Mroczkowski et al., 2011). Anxiety disorders in youth increase a risk for later substance use disorders (O'Neil et al., 2011).

10. School phobia

School refusal could be defined as a difficulty attending school associated with emotional distress, especially anxiety and depression. School refusal is considered a symptom rather than a clinical diagnosis and can manifest itself as a sign of many psychiatric disorders, with anxiety disorders predominant. Identified main predictors of school refusal behaviour were in a connection with distinctive feature of community, school and family (Kearney & Hugelshofer, 2000). The behaviour of those children, who stay home from school because of fear or anxiety, has variously been called an anxious school refusal or a school phobia or a variant of separation anxiety disorder (SAD) (King & Bernstein, 2001).

Separation anxiety disorder, generalized anxiety disorder, social phobia, specific phobia, and adjustment disorder with anxiety symptoms are the most common disorders co-occurring with school refusal (King et al., 1995). Mostly severe separation anxiety can result in school refusal. For separation anxiety disorder, the essential feature is excessive anxiety consuming separation from the home or from those to whom the person is attached, an issue that may first surface when a child begins formal schooling. While separation anxiety disorder is associated with school refusal in younger children, other anxiety disorders, especially phobias, are associated with school refusal in adolescents. School phobia has traditionally referred to the youngsters who refuse school with parental knowledge and because of separation anxiety or specific fears. Terms such as separation anxiety and school phobia are often used interchangeably with school refusal. Johnson et al. (1941) coining the term "school phobia", defined it as an anxious fear of school caused by the child's and mother's separation anxieties (Johnson et al., 1941; Kearney & Silverman, 1996). Such definitions include the youths who are completely absent from school, who initially attend school but then leave during the school day, who go to school after having behavioural

problems such as morning tantrums or psychosomatic complaints, and who display marked distress on school days and plead with their caregivers to allow them to remain home from school. The rates of school absenteeism are much higher in some urban areas. The most common age of onset is 10 to 13 years. Anxious school refuses can be divided into three types: those with separation anxiety, social phobia, and those who are anxious and depressed (King & Bernstein, 2001). The prevalence of school refusal has been reported to be approximately 1% in school-age children and 5% in child psychiatry samples. The prevalence of school refusal is similar among boys and girls. School refusal can occur at any time throughout the child's academic life and at all socio-economic levels. The vulnerabilities associated with pure anxious school refusal include living in a single-parent home, attending a dangerous school, and having a biological or non-biological parent who had been treated for a mental health problem (Egger et al., 2003). Among different kinds of risk factors of school phobia are genetic, biological (obstetric, neonatal), temperament, comorbidity and environmental risk factors such as developmental experience, life events, history of childhood, parent-child relationship (Bernstein et al., 1999; Dabkowska, 1999, 2002; Kearney & Hugelshofer, 2000). The psychiatric disorders are more frequently seen in adult relatives of children with school refusal, which supports a significant role of genetic and environmental factors in the aetiology of school refusal. Approximately 52% of adolescents with school refusal behaviour meet criteria for an anxiety, depressive, conduct-personality, or other psychiatric disorder later in life (Kearney, 2006). Berg et al. (1993) found that a half of the youths with attendance problems had no psychiatric disorder, a third had a disruptive behaviour disorder, and a fifth had an anxiety or mood disorder. School refusal is reported in about 75% of children with SAD, and SAD is reported to occur in up to 80% of children with school refusal (Borchardt et al., 1994; King et al., 1995). Results of studies support the association between anxious school refusal and somatic symptoms (headache, gastrointestinal complaints) occurring mostly in the morning, disturbed sleep, nightmares (Bernstein et al., 1997; Dabkowska, 2006; Egger et al., 2003). The youth with anxiety disorder diagnoses (also separation anxiety disorder) demonstrates significantly lower levels of school functioning than those without anxiety disorders (Mychailyszyn et al., 2010). School refusal behaviour can lead to serious short-term problems, such as distress, academic decline, alienation from peers, family conflict, intrafamilial violence, financial and legal consequences. Long-term consequences may include fewer opportunities to attend facilities of higher education, employment problems, social difficulties, and increased risk for later psychiatric illness (Flakierska-Praquin et al., 1997). Long term follow-up studies of children treated for school refusal due to SAD find that, despite their return to school, many continue to present significant social and affective limitations (Berg & 1985; Flakierska-Praquin et al., 1997). In relation to educational outcomes, about half of school refuses underachieve academically (Flakierska-Praquin et al., 1997; Kearney & Albano, 2000). (Copian et al., 2007; Nelson et al., 2005). Children and adolescents with school refusal are a heterogeneous population and require individualized treatment planning. Variables such as diagnosis and severity at the start of treatment should be taken into consideration when planning treatment. The School Refusal Assessment Scale (revised edition; SRAS-R) is designed to measure the relative strength of the four functional conditions and is given to the child and to both parents. Often children and parents assess basic reasons for school refusal in a different way (Kearney, 2002). Dabkowska study (2007) noticed substantial

disagreement between children and parent in identifying the function of school refusal behaviours. The major aim of the treatment is to help the child return to school in the shortest time possible. The treatment should be carried out in cooperation with the child's parents and the school personnel. A widely accepted approach to the treatment of school refusal is one that is concerned with the application of a multi-faceted treatment. Psychosocial and psychopharmacological approaches constitute the crucial parts of the therapeutic process. Today, cognitive behaviour therapy is the most frequently employed approach in the treatment of school refusal (Bahali & Tahiroğlu 2010). The anxious school refusal can be effectively treated with other behavioural interventions, also pharmacotherapy, where mainly selective serotonin reuptake inhibitors could be useful (King & Bernstein, 2001; Last et al., 1998). Finally, it is important to intervene at school to improve the child's comfort and safety.

11. Adult separation anxiety

Adult separation anxiety disorder (ASAD) has only been recognized as a specific mental disorder in the late 90's, with the pioneering work of professor Vijaya Manicavasagar. Adult separation anxiety disorder is likely to be much more common in adults than previously recognized (Manicavasagar & Silove 1997). This anxiety in adulthood has been associated with severe role impairment at work and in social relationships after controlling for potential confounding effect of anxiety comorbidity. In Pini et al. study (2010), some subjects have exhibited adult separation anxiety disorder without a history of childhood separation anxiety and some have had adult separation anxiety disorder with a history of childhood separation anxiety (Pini et al., 2010). Manicavasagar et al. (1998) indicated that adults might experience wide-ranging separation anxiety symptoms, such as extreme anxiety and fear, when separated from major attachment figures; avoidance of being alone; and fears that harm will befall those close to them. Symptomatology of adult separation anxiety disorder usually has a waxing and waning course, with exacerbation in the presence of threats to intimate bonds, which particularly predisposes to severe anxiety symptoms, including panic attacks (Manicavasagar et al., 1998). Separation anxiety disorder may be a neglected diagnosis in adulthood. Only a single research has examined the relationship of attachment styles to adult separation anxiety disorder. Manicavasagar and colleagues (2009) described how the dimensional associations showed strong correlations with scales measuring anxious attachment and separation anxiety in adults. In a 2006 study, Shear et al. found approximately one-third of adults had a childhood case of separation anxiety disorder that persisted into adulthood. However, a significant part of adults with ASAD recorded its first onset of the disorder in adulthood (Shear et al., 2006). More women than men suffer from ASAD. ASAD often occurs along with other psychiatric conditions, especially other anxiety disorders or mood disorders (Manicavasagar et al., 2009). Abelli et al. (2010) concluded that the platelet 18-kDa translocator protein (TSPO) expression may be a useful biological marker of adult separation anxiety co-occurring with other anxiety and mood disorders, including bipolar disorder. In Silove et al. study (2010) adult separation anxiety disorder was associated with PTSD, but not with complicated grief or depression. Results of Silove and colleagues study found that patients with adult separation anxiety disorder (ASAD) may have elevated early separation anxiety scores but this association is unique in females only. Amongst anxiety patients, those with ASAD recorded more severe symptoms of

depression, anxiety and stress, higher neuroticism scores, and greater levels of disability (Silove et al., 2010).

12. The therapeutic methods of treating separation anxiety disorder

Children are usually brought to the clinician when SAD results in school refusal or somatic symptoms such as recurrent pain of different parts of body occur. Anxiety disorders can be managed by using non-pharmacological and pharmacological options, or a combination of them. Treatment of the separation anxiety disorder includes behavioural, cognitive, and individual psychotherapies, as well as parent counselling and guiding teachers on how to help the child. The most recent evidence for empirically supported treatments shows that the cognitive-behavioural therapy (CBT) and selective serotonin-reuptake inhibitors (SSRI) are the most efficacious for the improvement of the children health with the separation anxiety disorder (Fisher et al., 2006). Different classes of medications have been used in pediatric anxiety disorders, including benzodiazepines, tricyclics and buspirone. Newer antidepressants (SSRIs and beyond) have had fewer side effects, lower toxicity in overdose and a broader range of indications (Masi et al., 2002). Cognitive behavioural therapies have the best evidence-based support for the treatment of the separation anxiety disorder in children and adolescents (Seligman & Ollendick, 2011). Research findings have supported the efficacy of cognitive behavioural therapy in reducing anxiety symptoms and increasing function in anxious children (Schneider et al., 2011). The outcomes of a randomized clinical trial evaluating an individual cognitive-behavioural, family-based cognitive-behavioural, and family-based education, support and attention treatment for anxious youth, also with diagnosis of separation anxiety disorder showed good efficacy of the psychotherapy (Suveg et al., 2009a). Hirshfeld-Becker et al. (2010) found that developmentally modified parent-child CBT may show a promise in 4 to 7 year-old children. The cognitive-behavioural therapy for the anxious youth, also with separation anxiety disorder could change in emotion regulation. The treated youth exhibited a reduction in anxiety and increased anxiety self-efficacy and emotional awareness at post-treatment (Suveg et al., 2009b). Children's coping skills have been considered to be protective factors in childhood anxiety disorders (Dadds et al., 1999). Learning to use active coping strategies, distraction strategies, and problem-focused rather than avoidant-focused coping have been encouraged in the anxious youths (Ayers et al., 1996). Results of the acute outcomes of the Child/Adolescent Anxiety Multimodal Study (CAMS) trial showed that all active treatments of separation anxiety disorder (cognitive-behaviour therapy or sertraline) were superior to pill placebo, that combination treatment (cognitive-behaviour therapy and SSRI) was superior to the monotherapies, and that the monotherapies were equivalent (Compton et al., 2010). The severity of the anxiety in children was found to be reduced with both cognitive behavioural therapy and sertraline (Walkup et al., 2008). Fluoxetine as others selective serotonin-reuptake inhibitors, seemed useful and well tolerated for the acute treatment of the anxious youths, among others in separation anxiety (Birmaher et al., 2003). Non-pharmacological treatments are the first choice approach in separation anxiety disorder or school refusal. This kind of treatment contains psychoeducational intervention (education of child and parents, collaboration with school personnel, training to increase child's autonomy and competence) and psychotherapeutic approach (behavioural, cognitive-behavioural, psychodynamic or family therapy. Pharmacological management of separation anxiety disorder uses mainly selective serotonin reuptake inhibitors; previously used tricyclic antidepressants, possibly

benzodiazepines or buspirone. The use of new drugs (mirtazapine, venlafaxine, nefazodone) needs to be assessed.

13. References

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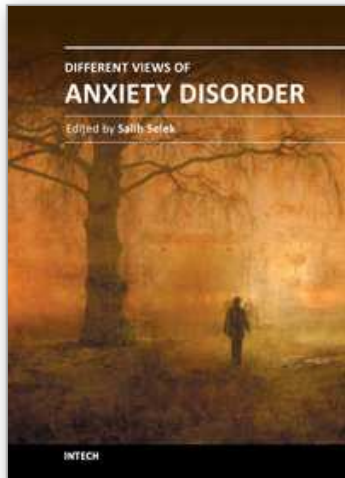
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Anxiety, whether an illness or emotion, is a term with historical roots even in the Bible, but it was not popular until the modern age. Today, we can group, diagnose and treat several anxiety disorders to an extent, but the assessment of symptoms and severity, dealing with resistant conditions, new treatment modalities and specific patient population, such as children, are still the challenging aspects of anxiety disorders. This book intends to present anxiety disorders from a different view and discuss a wide variety of topics in anxiety from a multidimensional approach. This Open Access book addresses not only psychiatrists but also a broad range of specialists, including psychologists, neuroscientists and other mental health professionals.

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