Physiological reactivity to fear in children: effects of temperament, attachment & the serotonin transporter gene

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General introduction

> *Men, during numberless generations, have endeavoured to escape from their enemies or danger by headlong flight (…) and such great exertions will have caused the heart to beat rapidly, the breathing to be hurried, the chest to heave, and the nostrils to be dilated. As these exertions have often been prolonged to the last extremity, the final result will have been utter prostration, pallor, perspiration, trembling of all the muscles, or their complete relaxation. And now, whenever the emotion of fear is strongly felt, though it may not lead to any exertion, the same results tend to reappear, through the force of inheritance and association.* (Darwin, 1872, p. 307).

All children have fears at some point in their life. Fear has been defined as a normal reaction to real or imagined dangers (Gullone, 2000; LeDoux, 1998) and is a common occurrence in daily life. Fears only become abnormal if, for example, they interfere with everyday functioning or persist over a long period of time (Gullone, 2000), becoming clinical fears or phobias. The common "normal" fears, however, typically include fear of social rejection, death, animals, medical treatment, psychic stress, or fear of the unknown (e.g. strangers, ghosts, or violence on television; Burnham & Gullone, 1997; Gullone, 2000). The current thesis addresses the impact of normal fears in young children, induced by media and social fear-inducing tasks, and examines why some children are more fearful than others. Before going into the possible causes of individual differences in fear reactivity, the background of fear reactivity will be discussed, in addition to clarifications of media-induced fear (e.g. frightening film clips) and social-induced fear (e.g. performing a public speech).

Fear

Responding to fear involves activity of the amygdala; almond-shaped groups of neurons located in the medial temporal lobes of the brain (LeDoux, 1998; Debiec & LeDoux, 2004). The amygdala determines the significance of a stimulus and triggers emotional responses (e.g. Lang, Davis, & Öhman, 2000; LeDoux, 1998). Responses to fear typically include increased activity of the autonomic nervous system (increased heart rate, blood pressure, sweating), neuroendocrine responses (excretion of hormones from the pituitary and adrenal glands), and behaviors ("fight or flight", i.e. fighting/attacking or trying to escape). From an evolutionary perspective, responses to fear have evolved through natural selection to cope with dangers. Fast identification of a danger followed by an efficient response increases the chances of survival (Darwin, 1872; Evans & Cruse, 2004).

The knowledge about the amygdala-associated neural network mainly comes from studies of animals. LeDoux (1998, 2003) described the neural pathways underlying fear conditioning in rats. In his studies, a conditioned stimulus (a tone) is paired with an unconditioned stimulus (foot shock). After a few of these pairings, the conditioned stimulus elicits the autonomic, endocrine and behavioral responses that typically occur in the presence of danger. LeDoux reported the importance of the amygdala in the exhibition of responses to a conditioned fear stimulus and described the complex circuits involved in the detection and generation of fear. The central nucleus of the amygdala appears to be interconnected with motor systems involved in the expression of fear responses (LeDoux, 1998). In humans, neural mechanisms have been shown to be very similar. Bechara and colleagues (1995), for example, reported that damage to the human amygdala interferes with the typical autonomic responses. Furthermore, functional magnetic resonance imaging (fMRI) studies in humans have demonstrated that the presentation of fearful facial expressions is associated with increased amygdala activity (e.g. Phan, Wager, Thaylor, & Liberzon, 2002; Whalen et al., 2001), giving more evidence for the key-role of the amygdala in detecting, generating and maintaining fear-related emotions in humans as well.

The amygdala-associated neural network sends signals via the sympathetic and parasympathetic branches of the autonomic nervous system. The sympathetic branch is generally associated with the “fight or flight” response by increasing respiration, blood pressure and heart rate, and decreasing digestion. The actions of the parasympathetic branch are broadly opposed to those of the sympathetic system, by decreasing the blood circulation and stimulating the process of digestion. Berntson et al. (1991) noted that the responses of the two branches are not always reciprocal (sympathetic activation and parasympathetic withdrawal, or vice versa), and proposed a multidimensional system for autonomic regulation (Berntson, Cacioppo, & Quigley, 1991). He showed that the physiological outputs can be both activated or both inhibited, which appears to differ between individuals (Berntson, et al., 1991). Nevertheless, during distress- or fear- inducing stimuli, most people exhibit a reciprocal pattern with increased sympathetic- and decreased parasympathetic activity (Berntson, et al., 1991; Salomon, Matthews, & Allen, 2000).

Heart rate is a common index of physiological activity. However, heart rate is influenced by the sympathetic as well as the parasympathetic nervous systems, which may lead to interpretative difficulties and is therefore a less precise measure of arousal (Ravaja, 2004; Salomon et al., 2000). The separate measurement of sympathetic and parasympathetic activity may be more accurate. A commonly used

index of the parasympathetic influence is heart rate variability (e.g. Fox & Calkins, 2000; Hagemann, Waldstein, & Thayer, 2003). While there are multiple ways to index heart rate variability, a frequently used measure includes RMSSD (the Root Mean of the Squared Successive Differences; Groot, De Geus, & De Vries, 1998; Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology, 1996). RMSSD is a time domain measure of heart period variability and correlates well with other measures assessing the parasympathetic influences on heart rate, like respiratory sinus arrhythmia (RSA; Berntson, Lozano, & Chen, 2005).

Activity of the sympathetic branch can be indexed by measuring electrodermal activity (Dawson, Schell, & Filion, 2000; Hageman, et al., 2003). Electrodermal activity gives direct information about the electrical conductance of the skin that is related to the level of sweat in the eccrine sweat glands. Depending on the sympathetic activity, sweat in the eccrine sweat glands will decrease or increase, producing observable changes in electrodermal activity (Dawson et al., 2000). Physiological responses to fear are often characterized by an increase in electrodermal activity (sympathetic activation), and a decrease in heart rate variability (parasympathetic withdrawal; e.g. Berntson, et al., 1991; Thayer & Lane, 2000).

Media Fear

Only few studies have focused on the fear that children may experience following TV viewing (Van Evra, 2004). Most findings of studies focusing on media fear have emerged from observational studies or research based on questionnaires. In these studies it has been shown, for example, that fright reactions to fear-inducing media stimuli are common (Cantor, 1997; Valkenburg, 2004). Already in 1933, Herbert Blummer studied children's fright reactions to "motion pictures". In response to the question "Were you ever frightened or horrified by any motion picture or scene in any motion picture?", Blummer (1933) reported that 93% of fourth- till seventh- grade children said that they were. More recently, a Dutch study of Valkenburg, Cantor, and Peeters (2000), using telephone interviews, showed that 31% of seven- to twelve-year-old children reported having been frightened by watching television during the preceding year. Of these children, 21% stated that the fear remained for weeks or even months (Valkenburg et al., 2000).

The observational and survey studies have provided a wealth of knowledge about the developmental changes in children's media-induced fears. First, young children (3- to 5-year-olds) appear more likely to be afraid of something that looks scary, while older

children are more affected by how characters behave. Thus, the appearance becomes less important as children mature, while the behavior of television characters becomes more important (Cantor, 2002). Second, fear of fantasy programs appears to decrease with age, while fear of realistic programs (i.e. news) increases. This has been supported by the notion that young children are less capable of making a distinction between reality and fantasy. Young children believe what they see, and they are therefore less likely to dismiss fantasy content as a threat. When children get older, however, realistic contents and abstract concepts of frightening media become more important (Cantor, 2002). Developmental differences have also been reported in how children cope with media-induced fears. Younger children have been reported to benefit less from cognitive coping strategies, while for older children both cognitive (i.e. tell yourself it's not real) and non-cognitive coping strategies (i.e. hugging a teddy bear) can be effective (Cantor, 1997, 2002).

Although these studies have provided greater understanding about media-induced fear, little is known about the physiological impact of fear-inducing films. In a study of Palomba, Sarlo, Angrilli, Mini, and Stegagno (2000), physiological activity was measured in adults during unpleasant (depicting threat and surgery) and neutral film stimuli. The threat film produced larger increases in heart rate and electrodermal activity compared with the neutral film. Not many studies have been conducted on the physiological effects of media-induced fear in young children (e.g., toddlers and preschoolers). Fowles, Kochanska, and Murray (2000) studied electrodermal reactivity in response to neutral, happy and scary film clips in 4-year-olds. They did not find an increase in electrodermal activity during the scary (or happy) film clips and noted that the electrodermal system in young children might not be as responsive to negative film stimuli as it is in adults. However, Osborn and Endsley (1971) reported higher electrodermal responses in 4- and 5-year-olds to fear-inducing, violent film clips compared to neutral, nonviolent clips. The increase to the fear-inducing film clips was especially found when the clips contained human characters in contrast to cartoon characters (Osborn & Endsley, 1971). Furthermore, Kalamas and Gruber (1998) studied electrodermal responses in 10- to 15-year-olds, watching scenes from 'Friday the 13th'. They found increases in electrodermal responses, particularly when the presented violence was implied (e.g. face of a murderer) in comparison with actual violence (e.g. stabbing). The usefulness of measuring physiological reactivity (in particular electrodermal reactivity) during media-fear inducing tasks has thus been demonstrated.

Social Fear

Apart from media-induced fear, this thesis examines individual differences in fear reactivity during a social fear-inducing task. A common social fear is elicited by the need to speak to an audience (Furmark et al., 1999). Public speech tasks performed in the laboratory, where subjects are asked to prepare and present a speech before an audience and/or camera's, have shown to produce enhanced physiological reactivity. For example, Carillo and colleagues (2001) studied public speech in 22-year-olds and reported increased activity in heart rate and electrodermal activity while the subjects prepared and presented the speech in comparison to a baseline period. Jansen and colleagues (2000) studied speaking in public in 9-year-old children with Multiple Complex Developmental Disorder (MCDD) and healthy control children. The public speech task resulted in an increased heart rate and cortisol response in healthy children but not in children with MCDD (Jansen et al., 2000).

The fears of social rejection, or failure, provoked by criticism or making mistakes, are also normally occurring fears (Burnham & Gullone, 1997). A meta-analysis of Dickerson and Kemeny (2004) showed that stressors that include both social-evaluative fear (speaking in the presence of an audience) and lack of control (arithmetic tasks that are impossible to complete within the time constraints) were most effective in triggering physiological reactivity. The Trier Social Stress Test (Kirschbaum, Pirke, & Hellhammer, 1993) is a procedure that includes both public speaking and impossible cognitive tasks and has indeed been shown to be an effective psychosocial stressor (Buske-Kirschbaum et al., 1997).

The Trier Social Stress Test for Children (TSST-C) is an adapted child version of the TSST, developed and evaluated by Buske-Kirschbaum et al. (1997). However, only few studies used this procedure in children. Buske-Kirschbaum and colleagues studied 9- to 14-year-olds (Buske-Kirschbaum et al., 1997) and 7- to 12-year-olds (Buske-Kirschbaum, et al., 2003) and found increased heart rate and cortisol responses during the TSST-C, particularly during the public speaking- and mental arithmetic task. Similar results have been found by Gordis, Granger, Susman and Trickett (2006), who showed that both cortisol and α-amylase increased in response to the TSST-C in 10- to 14-year-old children.

Risk and protective factors

Individual differences in physiological reactivity in response to normal fears, such as the fear that occurs watching fear-inducing film-clips or performing a public speech, may be caused by several factors. Behaviors can be determined by primarily

biological factors (e.g. genes), primarily environmental factors (e.g. parental rearing), or have a mixed causation (e.g., can be determined by an interaction of genetic and environmental factors). One potentially important cause of individual differences in fear reactivity concerns the relationship that a child has developed with his or her attachment figure. Attachment theory suggests that if a child is frightened, the activation of the fear system should be tempered by the (actual or represented) presence of a supportive attachment figure (Cassidy & Shaver, 1999). Children with a secure attachment relationship might show less physiological reactivity in response to fear or distress than children with an insecure attachment relationship, because they are possibly able to cope better with these situations. A secure child has developed a secure internal working model of attachment and therefore may know that their regulatory needs will be met by a sensitive and comforting attachment figure. On the other hand, when parents have been unavailable or inconsistent in previous fearful situations, the child might fear that their regulatory needs will not be fulfilled (Cassidy & Shaver, 1999).

One might also expect that temperament is an important factor in a child's physiological reactions to fear-inducing stimuli. Temperament is defined as the behavioral style that is present from birth, is rather stable across development, and has its influence on adult personality (Fox, 2004). Significant relations between temperamental reactivity and physiological reactivity have indeed been demonstrated in a number of studies (e.g., Kagan, Reznick, & Snidman (1988); Scarpa, Raine, Venables, & Mednick, 1997), indicating that a "difficult" temperament is a risk factor in children, showing larger increases in physiological activity to stressors. A "difficult" temperament typically involves frequent negative emotions, low adaptability, high activity level, and low emotion regulation (Gallagher, 2002). Various characteristics associated with "difficult" temperament (e.g. negative emotionality, high reactivity, high inhibition, high fearfulness) have been used in the literature on temperament. In the current thesis we focus on temperamental fearfulness, as measured by three scales of the Children's Behavior Questionnaire (CBQ; Rothbart, Ahadi, & Hershey, 1994) that are most characteristic for anxiety proneness and fearfulness (Fowles & Kochanska, 2000).

In spite of the rather large role of genetics in temperament (Bokhorst et al., 2003), the continuity of temperament seems to be influenced by the quality of the parent-child relationship as well (Fox, 2004). Certain caregiving influences have been shown to have different effects for children varying in temperaments. Intriguingly, children with a "difficult" temperament seem most susceptible to effects of parenting (Belsky, 1997,

2005; Boyce & Ellis, 2005). The differential susceptibility hypothesis (Belsky, 1997, 2005) indicates that children with a more fearful temperament may profit most from a secure relationship with their parent when confronted with fear-inducing stimuli. On the other hand, fearful children with an insecure attachment relationship may be most vulnerable to fear-inducing stimuli. Belsky's hypothesis (1997, 2005) is based upon an evolutionary perspective. According to evolutionary theory, variation in human characteristics is needed to maximize individual's reproductive success. Beyond genotypical differences, parents would benefit from raising children who differ in their susceptibility to caregiving influences, so that at least some of their offspring would survive even in a drastically changing social or ecological context.

Another potentially important cause of individual differences in fear reactivity concerns the gene that regulates serotonergic function; the serotonin transporter gene-linked polymorphic region (5-HTTLPR). 5-HTTLPR is known to be a promising candidate gene involved in anxiety related personality traits (Lesch & Mössner, 1998; Lesch, 2003). In humans, the alleles of the gene are composed of 14-repeat elements (short allele) or 16-repeat elements (long allele; Lesch, 2003). Carrying two long alleles is associated with increased 5-HTT expression and function compared to carrying one or two short 5-HTT alleles (Lesch & Mössner, 1998). The difference between the long and short 5-HTT alleles in serotonin expression and function has been shown to be associated with depression (Caspi et al., 2003; Kaufman et al., 2004), aggression (Suomi, 2003) and anxiety (Lesch et al, 1996). Both direct and indirect associations between 5-HTTLPR and traits of negative emotionality related to anxiety and depression have been reported. The short allele of the 5-HTTLPR gene proved to be a potential risk factor to psychopathology. However, a risk factor does not determine the outcome on its own, but rather contributes to an outcome (Rutter, 2006). Complex traits, like fear or anxiety, are most likely generated by complex interactions between several factors, like genes, their products, and environmental factors (Lesch, 2003), such as the caregiving environment (Bakermans-Kranenburg & Van IJzendoorn, 2007; Propper & Moore, 2006; Rutter, 2006).

Aims and outline of the thesis

Using a procedure for the simultaneously recording of electrodermal reactivity and heart rate variability, the current thesis investigates young children's fright reactions. The impact of both media fear and social fear were studied. The main question pertains to individual differences in physiological reactivity to fear-inducing stimuli. The possibly relevant factors of attachment security, temperamental fearfulness, and

variations in the serotonin transporter gene are taken into account. Specific aims addressed in the thesis are:

(1) Determining the physiological effects of fear-inducing film clips in 4- and 7-year-old children.
(2) Examining whether individual differences in the impact of fear-inducing film clips are caused by differences in the quality of the parent-child relationship and/or the child's temperamental fearfulness.
(3) Exploring the relation between variations in the serotonin transporter gene (5-HTTLPR; long vs. short allele), attachment security, and the impact of a social fear-inducing task: the Trier Social Stress Test for Children.

Chapter 2 focuses on the impact of fear-inducing film clips in 4-year-olds. Physiological effects of fear-inducing film clips were studied as well as the possible prediction of physiological reactivity from the quality of the parent-child relationship, the child's temperamental fearfulness, and the interaction between those two. This theme is elaborated in Chapter 3, by including 7-year-olds and providing more evidence for Belsky's differential susceptibility hypothesis. Chapter 4 examines individual differences in reactivity during a social-fear inducing task. The effects of attachment security, variations in 5-HTTLPR, and (of special interest) the interplay of these two factors are addressed in this chapter. Finally, in Chapter 5, the main results of the studies are summarized and discussed.