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Genetic and environmental influences on relationship between anxiety sensitivity and anxiety subscales in children

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ABSTRACT

Anxiety sensitivity, a belief that symptoms of anxiety are harmful, has been proposed to influence development of panic disorder. Recent research suggests it may be a vulnerability factor for many anxiety subtypes. Moderate genetic influences have been implicated for both anxiety sensitivity and anxiety, however, little is known about the aetiology of the relationship between these traits in children. Self-reports of anxiety sensitivity and anxiety symptoms were collected from approximately 300 twin pairs at two time points. Partial correlations indicated that anxiety sensitivity at age 8 was broadly associated with most anxiety subtypes at age 10 ($r = 0.11–0.17$, $p < 0.05$). The associations were largely unidirectional, underpinned by stable genetic influences. Non-shared environment had unique influences on variables. Phenotypic results showed that anxiety sensitivity is a broad predictor of anxiety symptoms in childhood. Genetic results suggest that childhood is a developmental period characterised by genetic stability and time-specific environmental influences on anxiety-related traits.

1. Introduction

1.1. Anxiety disorders

Anxiety is one of the most prevalent psychiatric conditions amongst young people (Beesdo et al., 2010). About 10% experience anxiety by the age of 16 (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003), with lifetime prevalence estimated at around 29% and mean onset age of 11 years (Kessler et al., 2005). Anxiety disorders have negative impact on child development, disturbing well-being and impairing academic performance and interpersonal interactions (Langley, Bergman, McCracken, & Piacentini, 2004; Van Ameringen, Mancini, & Farvolden, 2003). They are also reliable predictors of long-term mental health difficulties (Gregory et al., 2007; Otto et al., 2001). Anxiety is a broad term bringing together specific disorders, such as generalised anxiety disorder, panic disorder or phobias, that are characterised by excessive, persistent and impairing worry or fear (American Psychiatric Association, 2000). It is important to investigate developmental trajectories of each anxiety disorder in order to learn about the specific as well as shared aetiology.

Although anxiety disorders are characterised by homotypic continuity (prediction of disorder by the same disorder) and heterotypic continuity (prediction of disorder by another disorder), certain anxiety disorders seem to co-vary more than others (Gregory et al., 2007). Panic disorder and separation anxiety are thought to show such close developmental relationship, called the separation anxiety hypothesis (Klein, 1964; Silove, Manicavasagar, Curtis, & Blaszczynski, 1996). The two conditions share common physiological perturbations, such as somatic symptoms (Pine et al., 2005; Slattery et al., 2002). Separation anxiety in childhood has been associated with increased risk of panic disorder in adulthood (Klein, 1995; Silove, Manicavasagar, Vasey, & Dadds, 2001; Kossowsky et al., 2013), a longitudinal relationship which has been shown to be influenced by a shared genetic diathesis (Roberson-Nay, Eaves, Hettema, Kendler, & Silberg, 2012). However, the specificity of this developmental relationship is not clear, as some studies identified separation anxiety as a general risk factor for multiple adult anxiety and nonanxious disorders (Aschenbrand, Kendall, Webb, Safford, & Flannery-Schroeder, 2003; Kossowsky et al., 2013). Despite some evidence of clinical, developmental and biological similarity between separation anxiety and panic disorder, little is known about shared aetiology of these anxiety subtypes in childhood.

1.2. Anxiety sensitivity

Evidence from twin studies suggests moderate genetic and environmental influences on anxiety in childhood and across the lifespan, implicating a complex aetiology (Gregory & Eley, 2009). Another risk factor for anxiety might be biased cognitions. These

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are thought to play a role in both the emergence and maintenance of anxiety disorders (Clark, 1986; Ehlers, 1991). The biases can influence information processing at automatic information encoding stage (attentional biases), as well as at interpretational stage (interpretation and memory biases) (Muris & Field, 2008). Anxiety sensitivity represents one such bias: a tendency to perceive bodily cues related to experiencing anxiety as having threatening or dangerous consequences (Reiss, 1986). It is distinct from trait anxiety, which refers to the extent to which individual is fearful and prone to anxiety, while anxiety sensitivity is a fear of experiencing anxiety symptoms themselves (Taylor, 1996; Zinbarg, Brown, Barlow, & Rapee, 2001). Anxiety sensitivity is thought to be underscored by information processing abnormalities in the brain circuitry (Paulus & Stein, 2006) and variation in the trait is due to both genetic and environmental influences (Zavos, Gregory, & Eley, 2012). Anxiety sensitivity emerges in middle childhood (Reiss, Silverman, & Weems, 2001), a period characterised by a cognitive developmental stage of concrete operations and an overall cognitive maturation (Bibace & Walsh, 1981; Piaget, 1952), corresponding to acquisition of ability to consider physical symptoms in relation to anxiety from the age of 7 (Muris et al., 2008). Childhood anxiety sensitivity shows significant homotypic continuity, as well as predicts future anxiety symptoms when accounting for the current anxious state (Rabian, Embry, & MacIntyre, 1999; Weems, Hammond-Laurence, Silverman, & Ginsburg, 1998). Importantly, anxiety sensitivity and anxiety symptoms both emerge at similar age, making it an ideal time to investigate potential aetiological relationship of the two constructs.

1.3. Anxiety sensitivity – specific or broad risk factor?

Anxiety sensitivity was originally proposed as a specific risk factor for panic disorder. The presence of this cognitive bias in childhood has been found to predict panic attacks concurrently (Calamari et al., 2001; Mattis & Ollendick, 1997), as well as longitudinally in adulthood (Maller & Reiss, 1992; Schmidt et al., 2006). Several studies in adults have found that cognitive-behavioural therapy and pharmaceutical treatment targeted at panic reduce anxiety sensitivity, and this decline in cognitive bias was found to mediate the treatment (Simon et al., 2004; Smits, Powers, Cho, & Telch, 2004). Furthermore, one study found that children with good heart beat perception, which indicates good awareness of and attention to own body state, show the highest level of panic and somatic symptoms, but also heightened separation anxiety symptoms (Eley, Stirling, Ehlers, Gregory, & Clark, 2004). This could be due to a close developmental relationship between panic disorder and separation anxiety. Anxiety sensitivity, therefore, could be investigated as a specific risk factor not only for panic, but also for separation anxiety.

Other studies have shown a much broader relationship between anxiety sensitivity and anxiety subtypes (Schmidt et al., 2010; Taylor, 2003), suggesting that anxiety sensitivity might be a risk factor for a range of internalising symptoms (Plehn & Peterson, 2002). Two recent meta-analyses of adult studies support this view (Naragon-Gainey, 2010; Olatunji & Wolitzky-Taylor, 2009), finding that anxiety sensitivity was significantly related to all anxiety subtypes and depression. The associations were strongest between anxiety sensitivity and panic, general anxiety and post-traumatic stress disorder, suggesting some degree of specificity. A meta-analysis of studies of anxiety sensitivity in childhood (Noël & Francis, 2011) confirmed that anxiety sensitivity was associated with higher anxiety levels. Few studies have looked at the associations between anxiety sensitivity and specific anxiety subtypes in young people, but preliminary results based on 2 studies suggested a degree of specificity to panic symptoms.

The majority of studies that found association between anxiety sensitivity and anxiety are cross-sectional and are therefore not able to establish whether anxiety sensitivity predates anxiety symptoms, or is a consequence of anxiety. Interestingly, some longitudinal studies have directly addressed this question and suggest that the relationship might be bidirectional. For example, one study found a reciprocal longitudinal associations between anxiety sensitivity and both anxiety and depression in adolescence (Zavos, Rijsdijk, & Eley, 2012), while another found that the experience of panic and anxiety symptoms in adulthood lead to an increase in anxiety sensitivity (Schmidt, Lerew, & Joiner, 2000). This suggests that anxiety sensitivity increases subsequent anxiety, but also that symptoms of anxiety themselves increase levels of anxiety sensitivity. However, none of the studies have investigated these reciprocal processes in younger age groups, when both anxiety sensitivity and anxiety disorders emerge and when it might be possible to establish whether anxiety sensitivity predates anxiety symptoms.

1.4. Genetics of anxiety sensitivity and anxiety

Very little is known about the mechanisms underpinning the association between anxiety sensitivity and anxiety symptoms. To date, there are no multivariate twin studies investigating genetic and environmental relationship of these constructs in adults. In adolescence, anxiety sensitivity and anxiety were found to have high and significant genetic correlations (Zavos, Rijsdijk, Gregory, & Eley, 2010). This suggests that genetic factors are important in the concurrent association between anxiety sensitivity and anxiety in young people. In childhood, a very high genetic correlation has been reported between anxiety sensitivity and panic symptoms ($r = 0.98$; Eley, Gregory, Clark, & Ehlers, 2007), suggesting a substantial overlap of genetic influences on the two constructs. This is consistent with the pattern found in the adolescent sample, but longitudinal associations and specificity to other anxiety subtypes have not been addressed. In sum, the genetic and environmental influences underpinning the relationship between anxiety sensitivity and specific anxiety subtypes remain largely unknown.

Recently, twin studies have begun investigating developmental patterns of genetic and environmental effects in longitudinal study designs, in order to see how these influences operate over time (Ronald, 2011). Genetic influences on anxiety sensitivity have been found to be largely stable, with new genetic influences emerging late in adolescence (Zavos, Gregory, et al., 2012). Similarly, genetic stability in anxiety has been observed during childhood, with new genetic influences emerging in early and late adolescence, and in early adulthood (Kendler, Gardner, & Lichtenstein, 2008; Trzaskowski, Zavos, Haworth, Plomin, & Eley, 2011). Unlike genetic effects, environmental influences are more time-specific, possibly because non-shared environmental experiences such as stressful life events are transient (Kendler, Gardner, Annas, et al., 2008; Kendler, Gardner, & Lichtenstein, 2008; Lau & Eley, 2006; Trzaskowski et al., 2011). However, there is also evidence that idiosyncratic experiences may contribute to the continuity of anxiety (Kendler et al., 2011), suggesting some non-shared environment stability over time. Overall, very few studies have addressed these developmental questions and even fewer have explored genetic stability and change on the co-morbidity between two traits or disorders. To our knowledge, the stability of genetic and environmental influences on relationship between anxiety sensitivity and anxiety subtypes during childhood has not been investigated.

1.5. Aims

The current study aimed to investigate the developmental association between anxiety sensitivity and anxiety disorders when these problems first emerge in middle childhood (8–10 years old).