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Genetic and environmental contributions to social anxiety across different ages: A meta-analytic approach to twin data

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ABSTRACT

Social anxiety disorder (SAD) and social anxiety symptoms (SAS) have been largely studied both epidemiologically and genetically, however, estimates of genetic and environmental influences for these phenotypes widely vary across reports.

Based upon available literature, 13 cohorts (42,585 subjects) were included in 3 meta-analytic estimates of the standardized variance components of aetiological influences on SAD/SAS, on the effect of age and of phenotype (symptoms vs. diagnosis). The proportions of variance accounted for by genetic and environmental factors were calculated by averaging estimates among studies, and pondered by the number of individuals in each sample.

Meta-analytic estimations showed that genetic and non-shared environmental factors explain most of individual differences for SAD/SAS. In adults, the genetic contribution was half than that in younger patients, with higher contribution of non-shared environmental influences. In contrast, the shared environmental factors seem to be less relevant.

1. Introduction

Anxiety disorders are the most common psychiatric illnesses, and social anxiety disorder (SAD) (also called Social Phobia) is thought to be one of the most prevalent (Fehm, Pelissolo, Furmark, & Wittchen, 2005; Kashani & Orvaschel, 1990; Kessler et al., 1994; Ruscio et al., 2008; Verhulst, van der Ende, Ferdinand, & Kasius, 1997; Wittchen, Stein, & Kessler, 1999). SAD is characterized by "*a marked and persistent fear of one or more social situations in which the person is exposed to unfamiliar people or to possible scrutiny by other, marked fear or anxiety about one or more social situations in which the individual is exposed to possible scrutiny by others*" (American Psychiatric Association, 2013).

Although the onset of SAD often occurs during adolescence (Wittchen & Fehm, 2001), several studies have shown a childhood onset associated with greater severity (Stein, Chavira, & Jang, 2001; Velting & Albano, 2001). Recently, a bimodal distribution of the age of onset of SP has been described in literature (Stein et al., 2001).

As with adults, children with SAD manifest fear of speaking, reading and eating in public, of going to parties, of speaking to authority figures and of informal social interactions (Beidel, Turner, & Morris, 1999). In these situations SAD patients experience physical symptoms, including choking, flushes or chills, palpitations, fainting, shaking, fear of dying and headache (Beidel et al., 1999). Moreover, during the processing of socially relevant information and functions patients are subject to several cognitive biases and dysfunctional attributional styles implicated in the development and maintenance of SAD (Clark & Wells, 1995; Rapee & Heimberg, 1997). Recent studies indicated the presence of distorted social interpretation in children with social anxiety symptoms also in developmental age (Miers, Blote, & Westenberg, 2011; Vassilopoulos & Banerjee, 2008). Children with SAD report few friends, a very restricted range of social relationships, deficient social skills (Beidel et al., 1999; Scharfstein, Beidel, Sims, & Rendon Finnell, 2011) and sometimes school refusal behaviors (Beidel & Turner, 2007; Bernstein, Bernat, Davis, & Layne, 2008). Moreover, children with primary SAD diagnosis have comorbid diagnoses with other anxiety disorders, such as Separation Anxiety Disorder and Generalized Anxiety Disorder (Lewinsohn, Holm-Denoma, Small, Seeley, & Joiner, 2008; Lipsitz et al., 1994; Otto et al., 2001; Verduin & Kendall, 2003). Implications related to early onset SAD include generalized psychosocial and academic impairment, psychological difficulties, depression (Beesdo et al., 2007; Inderbitzen-Nolan &

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Walters, 2000), and, later, substance abuse (Pine, Cohen, Gurley, Brook, & Ma, 1998; Wittchen et al., 1999). Finally, evidence shows that the strongest predictor of recovery in adulthood is a later age of onset of social fears, suggesting the importance of early diagnosis and intervention (DeWit, Ogborne, Offord, & MacDonald, 1999).

During adulthood, SAD is associated with alcohol abuse problems, higher rates of divorce, suicide risk and different forms of psychopathology (Fehm et al., 2005; Lèpine, Wittchen, & Essau, 1993; Patel, Knapp, Henderson, & Baldwin, 2002; Ameringen, Mancini, Styan, & Donison, 1991).

Unfortunately, only a small number of individuals seek treatment for this condition, both during developmental age and when adult (Masia, Klein, Storch, & Corda, 2001; Oakley Browne, Wells, McGee, & New Zealand Mental Health Survey Research Team, 2006; Wittchen et al., 1999).

While the epidemiology of SAD has been studied in depth, relatively little is known about the aetiological factors. As in many psychiatric disorders, it is not possible to identify a unified theory about the origin of SAD. In fact, multiple pathways are implicated in the development of this condition.

A possible pathway is through genetic transmission. Data from family studies have shown that first-degree relatives of patients with SAD manifest higher rates of SAD than relatives of normal control participants (Fyer, Mannuzza, Chapman, Liebowitz, & Klein, 1993; Reich & Yates, 1988). More recently, a study reported a significant association between SAD in probands and their relatives in contrast with a non-significant association between SAD in probands and panic disorder in relatives (Merikangas, Lieb, Wittchen, & Avenevoli, 2003), suggesting that factors leading to SAD are specific and differ from those linked to panic disorder.

A realistic hypothesis is that vulnerability is acquired through genetic inheritance, but other factors are necessary to develop the disorder (Beidel & Turner, 2007). It is likely that those who are genetically predisposed might be more susceptible to specific environmental situations or to different mechanisms. The disorder could be the result of an interaction between individual vulnerability – such as temperament, stress reactivity and learning experiences – and environmental factors (Merikangas et al., 2003).

Several psychological factors seem to be implicated in the development of SAD (e.g., direct conditioning, observational learning and information transfer (Beidel & Turner, 2007)), with a prominent role of direct conditioning. In fact, different studies (Ost, 1987; Stemberg, Turner, Beidel, & Calhoun, 1995) reported experiences of direct conditioning in patients with SAD, such as specific traumatic experiences that influenced the onset of the disorder. Moreover, additional factors could constitute predisposing and maintenance factors. Family environmental variables, including parental personality and parental style and skills, can contribute to the onset of SAD (Beidel & Turner, 2007). Parental behaviors can influence child psychopathology in at least three ways (Beidel & Turner, 2007). First, parents may transmit genetic predisposition for anxiety. Second, parents may prevent the child's ability to engage in social events. Finally, parents may transmit their anxiety trough observation learning and modeling. In particular, protective parental behaviors seem to maintain avoidance behaviors in anxious children by reinforcing anxious behaviors and discouraging pro-social behaviors (Dadds & Barrett, 1996). Moreover, recent studies have shown an association between parental characteristics of overprotection and rejection of children with social anxiety symptoms (SAS) (Bogels, van Oosten, Muris, & Smulders, 2001; Greco & Morris, 2002; Lieb et al., 2000).

Historically, many of the studies explaining the liability to SAD/SAS used the classic twins design to estimate the relative impact of both genetic and environmental effects. Data from twins are very precious since identical twins share all their genes, while fraternal twins only share half of their segregating genes on average. Thus, any extra similarities of identical twins over fraternal twins can be of genetic origin (R. Plomin, 1991). Quantitative genetic studies have shown that SAD/SAS is highly inheritable and complex, involving multiple risk factors, both genetic and environmental. However, although the relevance of genetic factors has been demonstrated, a lack of consistency is present across the studies (Silove, Manicavasagar, O'Connell, & Morris-Yates, 1995). In particular, the amount of variance explained by genetic factors from twin studies appears to vary widely among twin studies, ranging from 0.13 to 0.60. Also, the estimates of non-shared environmental factors were inconsistent, ranging from 0.31 to 0.78. Moreover, differences related to age seem to be present in the contribution of both genetic and environmental factors. Only few longitudinal studies investigated age differences in SAD/SAS. Kendler and colleagues (Kendler, Gardner, Annas, & Lichtenstein, 2008) found that the common and specific genetic influences declined in importance with increasing age for social fears, whereas the environmental factors grew more important. A similar trend was reported by Lau, Gregory, Goldwin, Pine, and Eley (2007) in an adolescent sample, but not in children. Hallett, Ronald, Rijsdijk, and Eley (2009) evaluated etiology of SAS in middle childhood did not find substantial differences between ages 7 and 9.

Several factors, such as differences in measures, sample size and age, could influence this lack of homogeneity. For example, even though there is considerable support for the use of questionnaires in assessing anxiety symptomatology band in screening for anxiety disorders, it is generally thought that a diagnosis can only be made when the level of impairment is also known (Hodges, 1990). Although it seems unlikely that extreme anxiety and continuous variation in anxiety are underlined by qualitatively different liabilities (Oord, Pickles, & Waldman, 2003), the measures used to assessed these two types of phenotype have different psychometric properties, i.e., they are categorical and semi-continuous, respectively. In structural equation modeling (SEM) applied to twin data these differently distributed variables are approached differently, with ordinal data often implying diminished power (Battaglia et al., 2009; Neale, Eaves, & Kendler, 1994; Spatola et al., 2011).

These inconsistencies call for a systematic re-analysis of the etiology of SAD/SAS and of the possible role played by age. A better knowledge of these issues can help in shaping more effective treatments by understanding the etiological factors that contribute to the development and maintenance of SAD/SAS.

Here, using a meta-analytic approach based upon existing reports, we evaluated the overall magnitude of genetic, shared environmental and non-shared environmental influences on SAD/SAS. Three different meta-analyses were undertaken. The first estimated the proportion of variance accounted for by genetic and environmental factors based on all the different cohorts selected from the available studies. Then, in order to better understand their impact on the estimated causes of SAD/SAS, the meta-analytic standardized variance components were calculated separately by age (childhood vs. adulthood samples), and by phenotype used in the study (diagnosis vs. symptoms).

2. Materials and methods

2.1. Background information: the twin design

The studies examined for this meta-analysis are classic twin studies, which were conducted to determine the sources of individual differences in SAD/SAS by SEM. In SEM applied to twin data the total phenotypic variance can be partitioned into additive genetic factors (identified in the latent variable 'A'), shared environmental factors (including socio-economic level, religion, style of parenting, identified in the latent variable 'C') and non-shared environmental