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# Behavioral and EEG responses to social evaluation: A two-generation family study on social anxiety

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ABSTRACT

Social anxiety disorder is an invalidating psychiatric disorder characterized by extreme fear and avoidance of one or more social situations in which patients might experience scrutiny by others. The goal of this two-generation family study was to delineate behavioral and electrocortical endophenotypes of social anxiety disorder related to social evaluation. Nine families of patients with social anxiety disorder (their spouse and children, and siblings of these patients with spouse and children) performed a social judgment paradigm in which they believed to be evaluated by peers. For each peer, participants indicated their expectation about the evaluative outcome, after which they received social acceptance or rejection feedback. Task behavior, as well as the feedback-related EEG brain potentials (N1, FRN, P3) and theta power were tested as candidate endophenotypes based on two criteria: co-segregation with social anxiety disorder within families and heritability. Results indicated that reaction time for indicating acceptance-expectations might be a candidate behavioral endophenotype of social anxiety disorder, possibly reflecting increased uncertainty or self-focused attention and vigilance during the social judgment paradigm. N1 in response to expected rejection feedback and P3 in response to acceptance feedback might be candidate electrocortical endophenotypes of social anxiety disorder, although the heritability analyses did not remain significant after correcting for multiple tests. Increased N1 possibly reflects hypervigilance to socially threatening stimuli, and increased P3 might reflect that positive feedback is more important for, and/or less expected by, participants with social anxiety disorder. Finally, increased feedback-related negativity and theta power in response to unexpected rejection feedback compared to the other conditions co-segregated with social anxiety disorder, but these EEG measures were not heritable. The candidate endophenotypes might play a new and promising role in future research on genetic mechanisms, early detection and/or prevention of social anxiety disorder.

## 1. Introduction

Social anxiety disorder (SAD) is a psychiatric disorder characterized by extreme anxiety and avoidance in one or more social situations (APA, 2013). SAD is a common and debilitating internalizing disorder (Furmark, 2002; Rapee and Spence, 2004), and a known precursor to other psychiatric disorders, such as depression and substance abuse disorders (Grant et al., 2005; Rapee and Spence, 2004; Spence and Rapee, 2016). The risk for developing SAD is higher for individuals with a close family member with SAD than for individuals without family members with SAD (Isomura et al., 2015), and heritability of SAD is estimated around 20–56% (Distel et al., 2008; Isomura et al., 2015; Kendler et al., 1992; Middeldorp et al., 2005; Nelson et al., 2000). The genetic basis of psychiatric disorders could be studied by delineating endophenotypes, which are heritable trait markers in between the genotype and phenotype (Glahn et al., 2007; Gottesman and Gould, 2003; Iacono et al., 2016; Miller and Rockstroh, 2013). Electrocortical endophenotypes are specifically useful because they are presumably more closely related to genes than behavioral endophenotypes (Cannon and Keller, 2006). This study aims to delineate candidate endophenotypes of SAD by examining both behavioral and electrocortical responses to social evaluation.

The social judgment paradigm (SJP) (Gunther Moor et al., 2010b; Somerville et al., 2006; Van der Molen et al., 2014) could be useful in delineating candidate endophenotypes of SAD because this task allows for examining behavioral and electrocortical responses to social

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evaluation. In this task, participants receive feedback that communicates social acceptance or rejection, which can either be congruent or incongruent with participants' expectancies (Van der Molen et al., 2014). At the behavioral level, a number of studies have shown an optimism bias in healthy participants, as they more often expect acceptance versus rejection feedback (Dekkers et al., 2015; Gunther Moor et al., 2010a; Van der Molen et al., 2017; Van der Molen et al., 2014; Van der Veen et al., 2016). Patients with SAD expected to be accepted less frequently than healthy controls before the 'Island Getaway task', a task in which participants received social feedback without indicating their expectation in each trial (Cao et al., 2015). This is in line with cognitive-behavioral studies showing that patients with SAD expect negative outcomes of social situations (Clark and McManus, 2002; Hirsch and Clark, 2004). In SAD, the SJP has not been studied yet. Fear of negative evaluation has been studied using the SJP in healthy females, and was not related to feedback expectations during the task (Van der Molen et al., 2014). Notably, fear of negative evaluation was positively correlated with reaction time for indicating feedback expectations in healthy females, suggesting increased self-focused attention and vigilance during the SJP (Van der Molen et al., 2014). So, both feedback expectations and reaction time to indicate these expectations might be candidate endophenotypes of SAD.

At the electrocortical level, two event-related potentials (ERPs) have been examined using the SJP: the feedback-related negativity (FRN) and P3. The FRN (a negative component around 250 ms after feedback) is typically increased for feedback that is unexpected or reflecting poor performance (Ferdinand et al., 2012; Oliveira et al., 2007; Van Noordt and Segalowitz, 2012). However, it is unknown whether the FRN in response to social feedback is modulated by social anxiety in the SJP. There was no relation between fear of negative evaluation and FRN in healthy females (Van der Molen et al., 2014). In the Island Getaway task, the FRN was increased after acceptance feedback in patients with SAD (Cao et al., 2015), whereas FRN was increased after rejection feedback in healthy children with higher levels of parent-reported social anxiety (Kujawa et al., 2014). The effect of social anxiety on feedback valence might be related to feedback expectancies during the task, but this was not assessed on a trial-by-trial basis in the Island Getaway task (Cao et al., 2015; Kujawa et al., 2014). Thus, using the SJP allows for delineating the (differential) effect of feedback valence (acceptance versus rejection) and congruency (expected versus unexpected) on electrocortical responses that might be related to SAD. If there is indeed an effect of valence of social evaluative feedback in social anxiety (Cao et al., 2015; Kujawa et al., 2014), this should be present on both expected and unexpected trials of the SJP.

The P3 (a positive component that peaks around 300–500 ms after stimulus onset) is known to be sensitive to emotionally motivational stimuli (Hajcak et al., 2013). P3 results for healthy participants in the SJP are mixed. Some have found that the P3 was largest in response to expected acceptance feedback, and suggested that this P3 response might be related to the level of reward communicated by expected acceptance feedback (Van der Veen et al., 2016; Van der Veen et al., 2014). However, other studies did not find this P3 effect (Dekkers et al., 2015; Van der Molen et al., 2014). Further, P3 amplitude was not associated with fear of negative evaluation in healthy participants in the SJP (Van der Molen et al., 2014), nor with SAD in the Island Getaway task (Cao et al., 2015). If the social feedback-related P3 indeed reflects reward processing (Van der Veen et al., 2016; Van der Veen et al., 2014), the P3 in response to expected acceptance feedback might be a candidate endophenotype of SAD, based on altered reward-system reactivity in social anxiety (Cremers et al., 2015; Lahat et al., 2016). But, if the social feedback-related P3 rather reflects the processing of emotionally motivational stimuli (Hajcak et al., 2013), the P3 in response to expected and unexpected acceptance feedback might be a candidate endophenotype of SAD, given the importance of positive social evaluation for patients with SAD (Rapee and Heimberg, 1997).

More recently, studies using the SJP have examined neural oscillatory power in response to social evaluation (Van der Molen et al., 2017; Van der Veen et al., 2016). In contrast to ERPs, time-frequency power represents neural activity that is not phase-locked to the onset of a stimulus and this can yield additional insights into the neural dynamics (Cohen, 2014; Makeig et al., 2004; Van der Molen et al., 2017; Van Noordt et al., 2016). Theta oscillatory power seems sensitive to social threat (Cristofori et al., 2013; Van Noordt et al., 2015), and recent SJP studies have reported higher theta power in response to unexpected rejection feedback in healthy participants (Van der Molen et al., 2017; Van der Veen et al., 2016). Although theta power has not yet been studied in social anxiety, increased theta power in response to unexpected rejection feedback might be a candidate endophenotype of SAD, reflecting increased sensitivity to negative feedback in SAD (Clark and McManus, 2002; Heinrichs and Hofmann, 2001; Hirsch and Clark, 2004).

It is argued that endophenotypes could play an important role in understanding the genetic mechanisms underlying SAD (Cannon and Keller, 2006; Glahn et al., 2007; Iacono et al., 2016; Miller and Rockstroh, 2013), because their genetic basis is proposed to be simpler than the genetic basis of complex psychiatric disorders (Cannon and Keller, 2006; Glahn et al., 2007). To meet the criteria of an endophenotype of SAD, behavioral and electrocortical responses to social evaluation should adhere to certain criteria: (1) association with SAD, (2) co-segregation with SAD within families, (3) heritability, (4) state-independence, and (5) increased in non-affected family members compared to the general population (Glahn et al., 2007; Gottesman and Gould, 2003). The first criterion could be studied by comparing patients with SAD and healthy controls (as in Cao et al., 2015). The second and third criterion are based on the observation that psychiatric disorders run in families (Glahn et al., 2007; Gottesman and Gould, 2003). Within these families, the endophenotype should be displayed by persons with the disorder ('co-segregation'). Furthermore, the endophenotype should be heritable. The fourth criterion indicates that persons with the disorder should display the endophenotype whether or not the illness is active (Gottesman and Gould, 2003). The fifth criterion could be studied by comparing family members of patients with SAD with healthy controls.

Although various methods have been used to examine the endophenotype criteria, a family design seems particularly appropriate to assess both the 'co-segregation' and 'heritability' criteria of an endophenotype. Extended families (e.g. including partner and children of patient, and siblings of patient with their partner and children) provide the opportunity to compare family members with and witout SAD ('co-segregation'). Furthermore, we examined extended families instead of twins or sib-pairs, to increase the power to identify genetic variability within the family (because of the many different genetic relations) and thus heritability (Gur et al., 2007; Williams and Blangero, 1999). Moreover, we selected families based on two probands (adult with SAD and child with (sub)clinical SAD) to ensure we focused on a genetic form of SAD and to increase the chance that endophenotypes were related to the genetic factors that influence SAD (Fears et al., 2014; Glahn et al., 2010).

The goal of the current study was to investigate for the first time whether behavioral and electrocortical responses to social evaluation are candidate endophenotypes of SAD. In our two-generation family study, patients with SAD and their family members performed the SJP to assess behavioral and electrocortical responses to social evaluation. For the behavioral data, we expected that the number of trials in which participants expected social acceptance, as well as the corresponding reaction time for indicating feedback expectations are candidate endophenotypes, because previous studies have confirmed the first criterion for endophenotypes ('association') (Cao et al., 2015; Van der Molen et al., 2014). Even though the SJP has not been studied in SAD before, we expected the following electrocortical endophenotypes of SAD: the FRN in response to valence regardless of expectations (Cao et al., 2015; Kujawa et al., 2014), altered P3 in response to expected