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# Heritability of neural reactions to social exclusion and prosocial compensation in middle childhood



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#### ABSTRACT

Experiencing and observing social exclusion and inclusion, as well as prosocial behavior, are important aspects of social relationships in childhood. However, it is currently unknown to what extent these processes and their neural correlates differ in heritability. We investigated influences of genetics and environment on experiencing social exclusion and compensating for social exclusion of others with the Prosocial Cyberball Game using fMRI in a twin sample (aged 7–9; N=500). Neuroimaging analyses (N=283) revealed that experiencing possible self-exclusion resulted in activity in inferior frontal gyrus and medial prefrontal cortex, which was influenced by genetics and unique environment. Experiencing self-inclusion was associated with activity in anterior cingulate cortex, insula and striatum, but this was not significantly explained by genetics or shared environment. We found that children show prosocial compensating behavior when observing social exclusion. Prosocial compensating behavior was associated with activity in posterior cingulate cortex/precuneus, and showed unique environmental effects or measurement error at both behavioral and neural level. Together, these findings show that in children neural activation for experiencing possible self-exclusion and self-inclusion, and for displaying prosocial compensating behavior, is accounted for by unique environmental factors and measurement error, with a small genetic effect on possible self-exclusion.

#### 1. Introduction

Social exclusion is a common event for school-aged children: in dayto-day interactions they either experience exclusion themselves, or they observe someone else being excluded. Experience of exclusion can lead to personal distress (Saylor et al., 2013), whereas the observation of someone else's exclusion often leads to prosocial compensating behavior (Masten et al., 2011), although in some cases individuals may also join in exclusion to follow group norms, possibly in order to prevent self-exclusion (Over and Carpenter, 2009). However, research to date remained inconclusive with respect to how experiencing exclusion and acting prosocially upon observed exclusion can be distinguished from each other in school-aged children, and whether these processes are differentially influenced by genetic and environmental factors. Earlier studies have indicated that sensitivity to experiencing social exclusion is influenced by personal experiences (Masten et al., 2012), whereas prosocial compensating behavior is both influenced by genetics (Knafo-Noam et al., 2015; Knafo and Plomin, 2006) and by the environment (Menting et al., 2013; Newton et al., 2014). A better understanding of heritability of social exclusion sensitivity and prosocial compensating behavior in middle childhood might help us explain the underlying mechanisms and provides insights for future development of (schoolbased) interventions.

Both social exclusion and subsequent prosocial compensating behavior have previously been studied with the Cyberball Game (Masten et al., 2011; Will et al., 2013; Williams et al., 2000). A four-player adaptation of this paradigm was used to study the experience of social exclusion and prosocial compensating behavior in a situation of observed social exclusion (Tousignant et al., 2017; van der Meulen et al., 2017, 2016). After an initial round of fair play, one player (not the participant) is excluded by the two other players. This manipulation allows the participant to either join in the exclusion or compensate for the exclusion by tossing more balls to the excluded player than to either of the two excluding players (i.e. prosocial compensating). In addition, the participant does not receive the ball for short periods of time from the two excluding players, which might lead to alternating feelings of

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worry about possible self-exclusion and relief about self-inclusion. Neural activation analyses in prior research revealed that experiencing alternating social exclusion was associated with increased activity in left inferior frontal gyrus (IFG) in children (van der Meulen et al., 2017). This finding reflects meta-analyses in adolescents and adults showing that the lateral orbitofrontal cortex (overlapping with the IFG) and subgenual anterior cingulate cortex (sgACC) are more active when experiencing social exclusion (Cacioppo et al., 2013; Rotge et al., 2015; Vijayakumar et al., 2017), as is the amygdala (Eisenberger et al., 2007). Interestingly, studies in which participants experienced exclusion during short intervals showed comparable results to studies examining social exclusion in more prolonged social rejection contexts. For example, it was found that the medial prefrontal cortex (mPFC) was activated during an extended period of exclusion in a classic Cyberball Game (Gunther Moor et al., 2012) as well as during short intervals of rejection in a social judgment task (Gunther Moor et al., 2010a,b). Moreover, studies also report that effects of social exclusion and rejection are sensitive to social experiences, such as a long-term history of social exclusion (Will et al., 2016) or childhood maltreatment (van Harmelen et al., 2014). Social inclusion, in contrast, was previously associated with activity in dorsal ACC (dACC) and the striatum (Davey et al., 2010; van der Meulen et al., 2017), which possibly signals the saliency and reward of this event (Menon and Uddin, 2010; Seeley et al., 2007).

A critical element of the four-player Prosocial Cyberball game is that it also allows for the study of prosocial compensating behavior towards an excluded player. Prior studies using the Prosocial Cyberball Game showed that both adults and children indeed engage in prosocial compensating behavior after observing prolonged social exclusion of a different player (Riem et al., 2013; Tousignant et al., 2017; van der Meulen et al., 2017, 2016; Vrijhof et al., 2016). Interestingly, in adults, but not in children, prosocial compensating behavior was associated with increased activity in the temporo-parietal junction (TPJ; Tousignant et al., 2017; van der Meulen et al., 2016; Will et al., 2015), which is considered to be part of the social brain network (Blakemore, 2008; Frith and Frith, 2007). Moreover, in studies using social dilemma paradigms, it was also found that prosocial behavior was associated with increasing activity in the TPJ over the course of adolescence (Güroğlu et al., 2009, 2014; Güroğlu et al., 2011; Tousignant et al., 2017). Finally, prior studies also showed consistent involvement of the ACC-insula network when participants acted against their own social norms, which was independent of age (Güroğlu et al., 2011). These findings warrant further investigation of the neural regions and motives that children use when acting prosocially towards others.

An important, but understudied question concerns to what extent neural activity in these regions is sensitive to genetic and environmental influences. Earlier studies have focused on heritability of brain volume (Teeuw et al., 2018), brain connectivity (for review see Richmond et al., 2016) and brain activity during cognitive tasks (for review see Jansen et al., 2015), and found significant influences of genetics. A prior study on heritability effects on neural correlates of social rejection showed small influences of genetics in middle childhood (Achterberg et al., 2018b), but to our knowledge there are currently no studies that have directly investigated heritability effects on neural correlates of social inclusion and prosocial behavior. Therefore it remains an important question whether these processes are more sensitive to genetic or environmental influences.

This study therefore had two goals: I) To test the main contrasts and the brain-behavior relations of possible social exclusion, inclusion, and prosocial compensating. II) To examine the heritability of social processes in brain regions that are involved in possible self-exclusion, self-inclusion, and prosocial compensating. Therefore we investigated the genetic versus environmental influences on brain activity in middle childhood using a twin design. First, we expected that experiencing self-exclusion would be associated with activation in IFG and sgACC (Cacioppo et al., 2013; Vijayakumar et al., 2017), as well as mPFC

(Gunther Moor et al., 2012) and amygdala (Eisenberger et al., 2007), whereas experiencing inclusion was expected to lead to activation in bilateral insula/ACC (Menon and Uddin, 2010; Seeley et al., 2007) and the striatum (Van der Meulen et al., 2016). Second, we expected that children would show prosocial behavior in situations of observed exclusion (Masten et al., 2011). Third, we expected that social brain areas (mPFC, precuneus, TPJ and STS) would be activated when acting prosocially (Guroglu et al., 2014; van der Meulen et al., 2016). Finally, we tested the different influences of genetics, shared environment and unique environment on social exclusion sensitivity and prosocial behavior in these brain regions. Given that this is a first study examining heritability of fMRI signals in young children, it is important to validate the approach with measures that are more established in genetic designs. Therefore, we also tested the effects of genetics, shared environment and unique environment on total brain volume, a brain measure that has shown consistent heritability in adults (for reviews see Batouli et al., 2014; Peper et al., 2007) and children (Teeuw et al., 2018). We therefore expected to observe mainly genetic influences on total brain volume in the current sample (see Teeuw et al., 2018, including 9-year-old children).

#### 2. Methods

#### 2.1. Participants

Participants were recruited for the longitudinal twin study of the Leiden Consortium on Individual Development (L-CID). We sent invitations to families with twin children born between 2006 and 2008 in municipalities in the Western region of the Netherlands after obtaining address information from the municipal registries. We included samesex twin pairs that were 7–9 years old at the time of data collection, had normal (or corrected to normal) vision, were fluent in Dutch or English, and did not suffer from psychological or physical conditions that could hinder their performance on the tasks. The study was approved by the Dutch Central Committee on Research Involving Human Subjects (CCMO).

The initial sample for the L-CID study consisted of 512 participants (256 twin pairs). Since our aim was to study a population sample, participants with a psychiatric disorder were included. In the initial sample, 11 participants were diagnosed with an Axis-I disorder (nine with attention deficit hyperactivity disorder (ADHD) and/or attention deficit disorder (ADD); one with generalized anxiety disorder (GAD), and one with pervasive developmental disorder-not otherwise specified (PDD-NOS). An estimate of IQ was obtained via two subscales (Similarities and Block Design of the Wechsler Intelligence Scale for Children, 3rd version (WISC-III); Wechsler, 1991). Estimated IQ was within the normal range (range = 72.5–137.5).

Twelve participants did not have complete data of the Prosocial Cyberball Game and were therefore excluded from further analyses on prosocial behavior, resulting in a behavioral sample of 500 participants (including 244 complete twin pairs in the behavioral twin sample). Of the initial 512 participants, 33 did not perform the Prosocial Cyberball Game in the MRI scanner; 17 due to anxiety, four due to lack of parental consent for the MRI scan, seven due to contra-indications for the MRI scan, and five due to technical errors. Five other participants were excluded from neuroimaging analyses due to anomalous findings, and an additional 191 participants were excluded due to excessive movement (defined as > 3 mm in any volume). This resulted in a MRI sample for the neuroimaging analyses of 283 participants, including 89 complete twin pairs in the MRI twin sample (see Table 1 for demographic characteristics of the different samples). A non-response analysis indicated that the participants included in the MRI sample were older (t(510) = -2.38, p = 0.02), had a higher estimated IQ (t(510) = -2.24, p = -2.240.03), and were more often female ( $X^2$  (1) = 9.34, p = .004) than the participants excluded from the MRI sample. There were no significant differences between the monozygotic (MZ) and dizygotic (DZ) twins in

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