Like me, or else: Nature, nurture and neural mechanisms of social emotion regulation in childhood

Achterberg, M.

CHAPTER ONE

General introduction

We literally bend over backwards to make a perfect picture, combine it with an inspiring quote, post it on social media and … wait for the likes! Why do we invest so much effort in being recognized and accepted by others? And how come that being rejected can fill us with rage? What are the underlying neural mechanisms of these emotions and behaviors? And how do these mechanisms develop? In this dissertation, I seek out to shed light on the nature, nurture and neural mechanisms of social emotion regulation in childhood.

Social is Salient

The current generation of youth is the first to grow up with smartphones and tablets from birth on. These children are constantly connected to each other through multiplayer video gaming and social media. A 2015 survey amongst over 1200 eight-to-twelve-year-old children revealed that they spend on average six hours on (social) media each day (Common Sense Media Inc., 2015). These statistics show that children deal with social media and social connectedness from an early age on. However, relatively little is known about the influence of this intense form of social connectedness. Some studies have pointed to the potentially addictive aspects of social media (Blackwell *et al.*, 2017), and popular media are warning for a society of social junkies always on the lookout for social confirmation. However, the desire to belong to a social group is not something new: Social acceptance is, and always has been, of key importance in life (Baumeister and Leary, 1995). Receiving positive social feedback increases our self-esteem and gives us a sense of belonging (Leary and Baumeister, 2000; DeWall *et al.*, 2011). Negative social feedback, in contrast, is related to feelings of sadness and depression (Nolan *et al.*, 2003) and can lead to frustration and rage (Twenge *et al.*, 2001). The current dissertation examines how children deal with social evaluation, and what underlying mechanisms come into play. This thesis aims to answer questions such as: How is it that some children are more sensitive to social rejection than others? What are the neural mechanisms of social evaluation and subsequent behavior? And what is a feasible method to examine social evaluation and social emotion regulation in children?

Studying social interactions can be challenging as it is a complex form of behavior that is strongly intertwined with our day-to-day lives. In order to decompose these processes, researchers have often worked with experiments. The advantage of an experiment is that you examine participants in a controlled setting, making it possible to study unique aspects of complex behaviors. Experimental paradigms are also very suitable to use in combination with psychophysiological measures, which enables to additionally study covert

aspects of information processing. Social acceptance and rejection have been studied in a variety of experimental settings, for example by manipulating Instagram likes (Sherman *et al.*, 2018b), by mimicking chat room conversations (Silk *et al.*, 2012) or by simulating peer feedback on the participant's profile (Somerville *et al.*, 2006; Gunther Moor *et al.*, 2010b; Dalgleish *et al.*, 2017; Rodman *et al.*, 2017). These studies showed that social rejection can be quite literally heartbreaking, as negative social feedback can result in cardiac slowing (Gunther Moor *et al.*, 2010a), which was most pronounced in young adolescents compared to adults (Gunther Moor *et al.*, 2014). Other studies found that social rejection resulted in increased pupil dilation (Silk *et al.*, 2012). The pupil becomes more dilated in response to stimuli with a greater emotional intensity (Siegle *et al.*, 2003), and is suggested to reflect increased activity in cognitive and affective processing regions of the brain.

Indeed, a wealth of neuroimaging research has shown that the significance of social evaluation is deeply rooted in our brain. Social acceptance, for example, has been associated with increased activity in striatal regions (Guyer *et al.*, 2009; Davey *et al.*, 2010; Gunther Moor *et al.*, 2010b; Sherman *et al.*, 2018b), specifically in the ventral striatum (VS, **Figure 1**). Numerous studies have shown that the VS is associated with reward processing (Sescousse *et al.*, 2013) and this heightened activation could reflect the rewarding value of positive feedback. Social rejection, in contrast, has been related to increased activation in midline regions of the brain, such as the dorsal and subgenual anterior cingulate cortex (ACC) and medial prefrontal cortex (MPFC) (Cacioppo *et al.*, 2013; Apps *et al.*, 2016), see **Figure 1**. The dorsal ACC, together with the anterior insula (AI, **Figure 1**), have been suggested to signal social pain, as activity in these regions largely overlapped with brain activity after physical pain (Eisenberger and Lieberman, 2004; Kross *et al.*, 2011; Rotge *et al.*, 2015). However, other studies found the dorsal ACC and AI to be sensitive to expectancy violation (Somerville *et al.*, 2006; Cheng *et al.*, 2019) and have suggested that these regions might be important for evaluating social feedback in general, irrespective of its valence (Dalgleish *et al.*, 2017).

Previous experimental studies have thus indicated that different neural processes can be distinguished for social acceptance and rejection in adults and adolescents, but there remain many unanswered questions. Until now the paradigms to study social acceptance and rejections have not been consistently applied to children and young adolescents and there has been little emphasis on behavioral outcomes. To really understand the effects of social acceptance and rejection on children and their development we need a new approach, with a targeted experimental paradigm. Prior studies have provided a solid foundation for studying social evaluation, but an important next step is to disentangle between neural activation that is related to general social saliency and neural activation that is specific for negative social feedback. Understanding the latter

is especially important, as social rejection is often related to negative behavioral outcomes such as anger and frustration.

Regulate or Retaliate?

In some individuals, negative social feedback triggers feelings of anger and frustration, which can lead to reactive aggression (Twenge *et al.*, 2001; Dodge *et al.*, 2003; Leary *et al.*, 2006; Nesdale and Lambert, 2007; Nesdale and Duffy, 2011; Chester *et al.*, 2014). A tragic example of how socially excluded youth can turn violent are school shootings, of which almost all perpetrators have a long history of peer rejection and social exclusion (Leary *et al.*, 2003). But even incidental social rejection can lead to aggression. Reactive aggression after social rejection has been examined experimentally by providing participants with the opportunity to blast a loud noise towards the peer that had just socially excluded them (Bushman and Baumeister, 1998; Twenge *et al.*, 2001; Reijntjes *et al.*, 2010). The participants can set the intensity and duration of the noise blast heard by the other person, providing them with a way to retaliate (Bushman and Baumeister, 1998). These studies consistently showed that rejected participants were considerably more aggressive than accepted participants (Twenge *et al.*, 2001; Leary *et al.*, 2006; Reijntjes *et al.*, 2010; DeWall and Bushman, 2011; Chester *et al.*, 2014; Riva *et al.*, 2015).

The effects of social rejection in terms of behavioral aggression might be associated with a lack of impulse control or inadequate emotion regulation (Chester *et al.*, 2014; Riva *et al.*, 2015). For example, in adults it was found that the extent to which individuals responded aggressively after social rejection was dependent on whether the participant showed high or low executive control (Chester *et al.*, 2014). Participants with high executive control were less aggressive after social rejection, indicating that executive control might down-regulate aggression tendencies. It has been suggested that this form of self-control is dependent on top-down control of the dorsolateral prefrontal cortex (DLPFC, **Figure 1**) over subcortical-limbic regions (such as the VS), to inhibit responses that lead to impulsive actions (Casey, 2015). Evidence for this hypothesis was provided by a study using transcranial direct current stimulation (tDCS), a method to increase neural activation in specific brain regions. Riva and colleagues showed that increased neural activation in the lateral prefrontal cortex during social rejection was related to decreased behavioral aggression, compared to participants that did not receive active tDCS (Riva *et al.*, 2015). Moreover, stronger functional connectivity between the lateral prefrontal cortex and limbic regions was related to less retaliatory aggression (Chester and DeWall, 2016). Similar associations have been found for structural connectivity: stronger connections between subcortical and prefrontal brain regions were related to less

trait aggression (Peper *et al.*, 2015). These studies in adults thus indicate that the lateral prefrontal cortex - and specifically the DLPFC - might serve as a regulating mechanism for aggression after social evaluation. However, relatively few studies have investigated aggression following social rejection in childhood, despite the fact that children deal with social evaluations from an early age. Moreover, as the prefrontal cortex and executive functioning are still developing throughout childhood, children may be more sensitive to aggressive behavior after social rejection, as they might experience more difficulty with social emotion regulation.

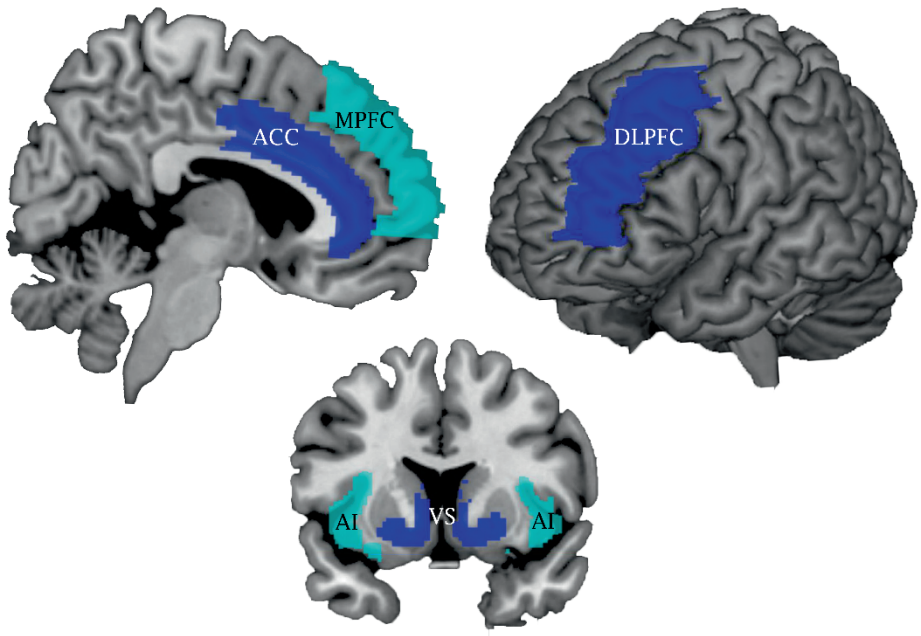

Figure 1. *Brain regions implicated in social evaluation processing and social emotion regulation. ACC- anterior cingulate cortex, MPFF- medial prefrontal cortex, DLPFC- dorsolateral prefrontal cortex, AI- anterior insula, VS- ventral striatum.*

Neurodevelopmental models

When it comes to social evaluation processing, studies in adults have shown that a network of ACC-AI, together with subcortical regions such as the VS, are involved in the direct effects of social rejection and acceptance. With regards to controlling social rejection related aggression, it seems that the DLPFC is involved. Exactly these networks are central to neurodevelopmental models such

as the Social Information Processing Network (Nelson *et al.*, 2005; Nelson *et al.*, 2016) and the Imbalance Model (Casey *et al.*, 2008; Somerville *et al.*, 2010). The Social Information Processing Network (SIPN, Nelson *et al.* (2005); Nelson *et al.* (2016)) states that social information is processed through bi-directional communication between three nodes: the detection node, the affective node, and the cognitive-regulation node (**Figure 2**). The detection node includes regions that have been found to be important to categorize stimuli as being socially relevant, such as the fusiform face area. Once a stimulus has been recognized as a social stimulus, it is further processed by the affective node, which includes - amongst others - the amygdala and the VS (nucleus accumbens). Finally, social stimuli are processed in a network dedicated to complex cognitive operations that is referred to as the cognitive-regulatory node, which includes prefrontal cortical regions. The SIPN model states that goal directed behavior relies on interactions between different (dorsal and ventral) regions within the prefrontal cortex, that process social-emotional information from the affective node (Nelson *et al.*, 2005). Complementary, the Imbalance Model (Casey *et al.*, 2008; Somerville *et al.*, 2010) describes the mismatch in developmental trajectories of subcortical brain regions and the prefrontal cortex. Specifically, the gradual linear increase of prefrontal cortex maturation is slower than the non-linear increase of affective-limbic regions such as the VS. This induces an imbalance between bottom-up limbic regions and top-down control regions, which is most pronounced during adolescence (**Figure 2**). The imbalance model suggests that this imbalance between subcortical and cortical maturation hinders social emotion regulation and can results in risky, reward driven behavior.

Previous studies and theoretical models have shown that social emotion regulation is not solely dependent on isolated brain regions, but relies on a network of integrated connections between subcortical and cortical brain regions (Olson *et al.*, 2009; Chester *et al.*, 2014; de Water *et al.*, 2014; Peper *et al.*, 2015; Silvers *et al.*, 2016b; van Duijvenvoorde *et al.*, 2016a). Most of these studies have focused on adolescence or only included small samples of children. It therefore remains a question whether these integrated subcortical-cortical brain networks are already in place during childhood. The developmental phase towards the teenage years, in which the first friendships are formed, is an underexposed phase in experimental research. Theoretical perspectives have suggested that the increase of executive functions and maturation of DLPFC during childhood are important underlying mechanisms for developing a variety of self-regulation functions in childhood (Bunge and Zelazo, 2006; Diamond, 2013). Few studies have investigated the development of social emotion regulation during childhood, despite empirical findings showing that middle-to-late childhood marks the most rapid changes in executive functions (Luna *et al.*, 2004; Zelazo and Carlson, 2012; Peters *et al.*, 2016). This is a gap in the literature that needs to be investigated. This dissertation takes an important step by focusing precisely on the age of seven to eleven, the pre- to early pubertal years.

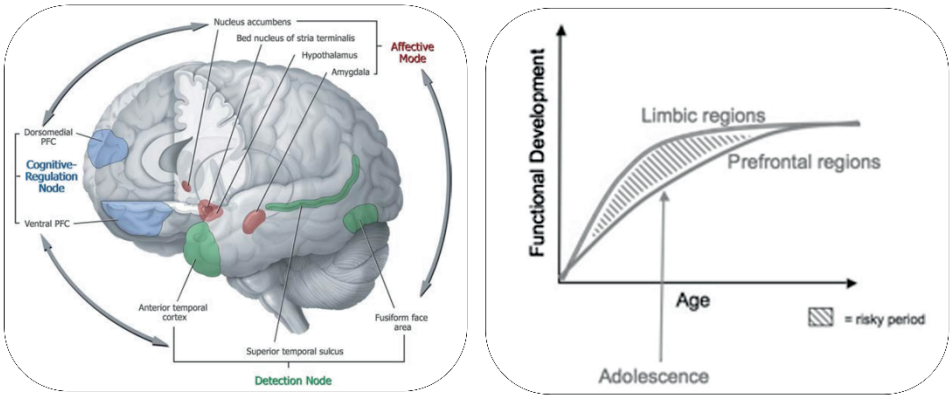

***Figure 2**. Neurodevelopmental models of social emotion regulation. Left: a schematic depiction of the Social Information Processing Network (SIPN), adapted from Nelson, Pine and Tone (2005). Right: the Imbalance model, adapted from Casey, Jones and Hare (2008).*

Hot *vs.* Cool Control

In line with the neurodevelopmental models, previous experimental neuroimaging studies have shown that children become better at regulating their emotions with increasing age (Silvers *et al.*, 2012), which has been suggested to be related to the development of cognitive control (Diamond, 2013; Casey, 2015). The DLPFC has been specifically pointed out as an important region for cognitive control development (Luna *et al.*, 2004; Luna *et al.*, 2010; Crone and Steinbeis, 2017). Most of these studies have focused on *'cool'* cognitive control, that is to say self-control in a non-emotional setting (Welsh and Peterson, 2014). However, whether the same *'cool'* regulatory control functions are also important for regulation of *'hot'* emotions in social contexts is currently unknown (Zelazo and Carlson, 2012; Welsh and Peterson, 2014). Previous studies on '*hot'* emotional control have worked with the now famous delay discounting paradigm (Mischel *et al.*, 1989), which estimates an individual's preference for a smaller immediate reward over larger, delayed rewards (Eigsti *et al.*, 2006; Olson *et al.*, 2007; Scheres *et al.*, 2014). This classic paradigm has been used extensively, as it is suitable for participants in all age ranges, and has shown to be predictive of long-term life outcomes (i.e., Mischel *et al.* (1989); Casey *et al.* (2011); but see Watts *et al.* (2018) for more nuanced findings using a replication design). These studies showed that the ability to delay gratification is very difficult for young children and improves with increasing age (Mischel *et al.*, 1989; Olson *et al.*, 2009; Casey *et al.*, 2011; de Water *et al.*, 2014). Studies in adults and adolescents additionally showed that stronger structural brain connectivity between subcortical (VS)

regions and the prefrontal cortex was related to better delay of gratification abilities (Peper *et al.*, 2013; van den Bos *et al.*, 2015).

Regulating aggression in the case of negative social feedback can been seen as a similar delay of gratification: For some individuals it might feel good to retaliate on the short term (Chester and DeWall, 2016), but on the long term this could result in even more social rejection (Lansford *et al.*, 2010). In fact, examining aggression following social rejection can provide an excellent case to study '*hot'* emotion regulation in an ecological valid social context. This requires a new social evaluation paradigm that exposes the mechanisms through experimental design, ideally combined with neuroimaging measures to inform about brain functions and connections. Such a paradigm can shed light on the underlying neural mechanisms of social acceptance and rejection, and can provide information on why some children are more sensitive to social evaluation than others.

Social Network Aggression Task

In order to gain a better understanding of the mechanisms of social acceptance and rejection, an innovative experimental paradigm is needed that is suitable to combine with neuroimaging. Task-based functional magnetic resonance imaging (fMRI) is based on contrasts between different conditions (for a concise overview of fMRI methodology see Glover (2011)). Most social evaluation studies till date have included only two conditions: participants receive either positive or negative social feedback from unknown, same-aged peers (Somerville *et al.*, 2006; Gunther Moor *et al.*, 2010b; Silk *et al.*, 2014; Rodman *et al.*, 2017). However, such paradigms are unable to investigate brain regions that are active after both positive and negative feedback, as these regions are washed out when both conditions are contrasted against each other. In order to understand the neural mechanisms of social evaluation, it is important to disentangle if regions are specifically sensitive to social rejection, or whether they are sensitive to social evaluation in general, and might signal for social salience (see also Dalgleish *et al.* (2017)). Therefore, we developed a new social evaluation paradigm that included a neutral feedback condition: the Social Network Aggression Task (SNAT), see **Figure 3**. This paradigm enables to study regions that signal for general social salience, by contrasting both positive and negative feedback to a neutral social feedback condition.

Few studies have investigated the neural mechanisms of *'hot'* social emotion regulation during childhood, however, today's youth is constantly connected to each other and they find themselves in an inexhaustible and unceasing pool of social information and subsequent emotions. It is therefore important that we understand how mechanisms of social emotion regulation

develop during childhood. In order to experimentally examine developmental changes in social emotion regulation, we included a retaliation aspect to the Social Network Aggression Task (SNAT, **Figure 3**). After the participants viewed the positive, neutral or negative social feedback, participants got the opportunity to blast a loud noise towards the peer, allowing us to directly examine aggression following social evaluation. By examining differences in aggression regulation after social evaluation within and across individuals, we can examine why some children might be more sensitive for social rejection. By combining this new experimental paradigm with neuroimaging, important insights in the underlying mechanisms of social emotion regulation can be gathered.

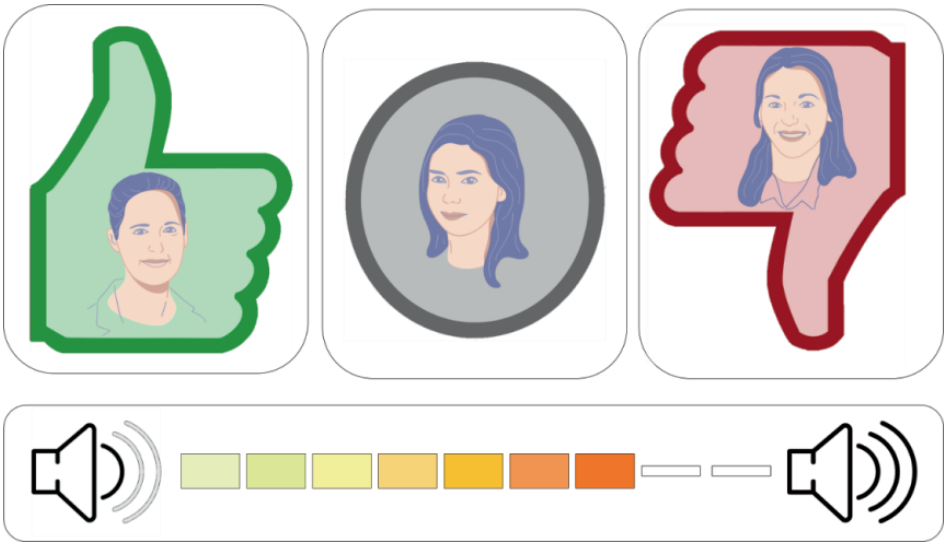

Figure 3. *Social network aggression task (SNAT), a newly developed social evaluation paradigm that includes positive, neutral and negative social feedback from unknown, same-aged peers. In response to the peer feedback, participants are able to blast a loud noise towards the peer, which is used as an index of aggression. The faces used in this figure are cartoon approximations of the photo stimuli used in Achterberg et al. (2016b).*

Nature and Nurture

In a rapid changing digital world with dense social connectedness, it is important to understand why some children are more sensitive to social evaluation than others. Perhaps some children are more sensitive through genetic predisposition. On the other hand, it is possible that specific environments stimulate certain social behavior. An important scientific question is to what extent development

is biologically based or environmentally driven. The caption of this section specifically states nature *and* nurture, as a broad range of literature has shown that these two are strongly intertwined (Polderman *et al.*, 2015). But to what extent nature and nurture contribute to (brain) development has received relatively little attention in developmental neuroscience. One particularly elegant way to study this is using a twin design: Monozygotic (MZ) twins share 100% of their genes, whereas dizygotic (DZ) twins share, on average, 50% of their genes. Therefore, within-twin correlations that are stronger in MZ twins compared to DZ twins indicate heritability (**Figure 4**). Behavioral genetic modeling, a specific structural equation model based on twin similarities, can provide estimates for this heritability (Neale *et al.*, 2016). The 'ACE' model divides similarities among twin pairs into similarities due to additive genetic factors (A) and common environmental factors (C), while dissimilarities are ascribed to unique non-shared environmental influences and measurement error (E), see **Figure 4**. High estimates of A indicate that genetic factors play an important role, whilst C estimates indicate influences of the shared environment. If the E estimate is the highest, the variance is mostly accounted for by unique environmental factors and measurement error (Neale *et al.*, 2016).

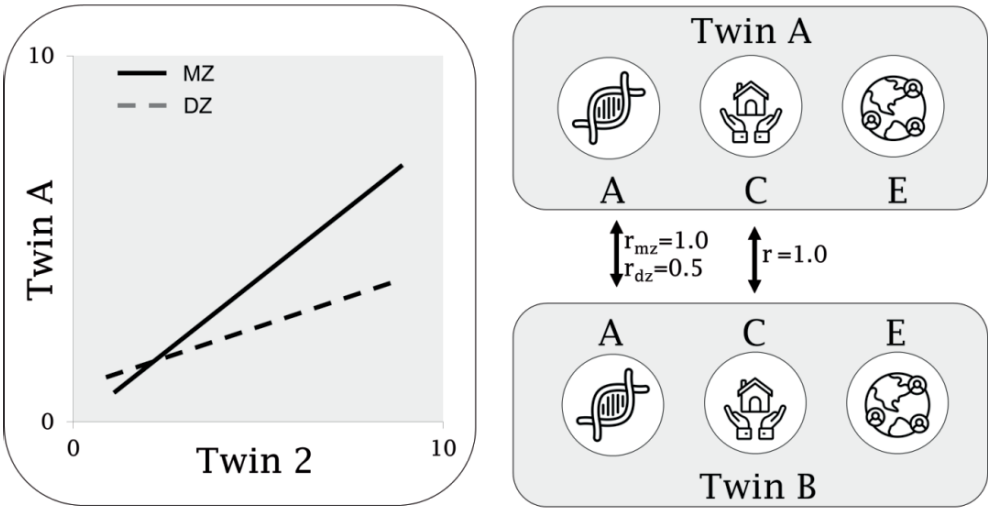

Figure 4. *Twin design: Within-twin correlations that are stronger in monozygotic (MZ) twins compared to dizygotic (DZ) twins indicate heritability (NB: figure is based on hypothetical data). Behavioral genetic modeling can provide heritability estimates by assessing the proportion of variance explained by additive genes (A), common, shared environment (C) and unique environment and measurement error (E). In this ACE model, the correlation between factor A is set to r=1 for MZ twins and to r=0.5 for DZ twins, based on the percentage of overlapping genes. As both MZ and DZ twins share the same environment, the correlation of factor C is set to 1 for all twins. The E factor is freely estimated.*

Previous studies using behavioral data showed high reliability of trait aggression (Miles and Carey, 1997; Rhee and Waldman, 2002; Ferguson, 2010; Tuvblad and Baker, 2011; Porsch *et al.*, 2016). However, the majority of these studies have relied on questionnaire data and very few have used experiments. Also, the number of studies that have investigated heritability of neural mechanisms is scarce. The few studies that investigated genetic and environmental influences on brain function in adults reported significant influences of genetics on functional connectivity, with little shared environmental influences (for an overview, see Richmond *et al.* (2016)). It is important to note that heritability estimates for brain anatomy and connectivity differ across development such that heritability estimates are stronger in adulthood than in childhood (Lenroot *et al.*, 2009; van den Heuvel *et al.*, 2013). Unraveling the extent to which brain development in childhood is influenced by genetics and environment can provide important insights in which neural mechanisms might be more sensitive to environmental influences (Euser *et al.*, 2016). Specifically, using a behavioral genetic approach can provide insights in the etiology of aggression following social evaluation and might offer a starting point for interventions aimed to improve social emotion regulation.

Imaging the Childhood Brain

The majority of previous experimental neuroimaging studies in youth were aimed at adolescence. Some also included children younger than ten years of age, but the sample sizes were often very small. Why has there been so little emphasis on imaging pre-pubertal youth? One possible reason for this could be because scanning children can be very challenging: The MRI scanner is quite imposing and can induce anxiety in children (Tyc *et al.*, 1995; Durston *et al.*, 2009). Such scanner related distress makes it less likely for children to successfully finish an MRI scan, resulting in reduced scan quantity and quality in children compared to older samples (Poldrack *et al.*, 2002; Satterthwaite *et al.*, 2013). However, in order to investigate individual differences (i.e., why are some children more sensitive to social evaluation than others), large sample sizes are required. Not only do we need large sample sizes to investigate inter-individual (between-person) differences in social behavior, multiple waves of that same large sample are needed to capture intra-individual (within-person) differences across development (Telzer *et al.*, 2018). That is to say, to truly capture development we need longitudinal studies. Although more and more studies are using longitudinal methods, these are still not the norm, despite the overall notion that longitudinal research is the golden standard to study changes across development (Pfeifer *et al.*, 2018).

An additional difficulty when it comes to neuroimaging studies in childhood is that different studies seldom used the same experimental paradigm. This makes it difficult to study reproducibility of behavioral and neural findings. Indeed, the (lack of) reproducible results in psychological studies has received a lot of attention (Ioannidis, 2005; Schmidt, 2009; Open Science, 2015). Moreover, findings that show no evidence of significance when analyzed individually (i.e., due to small sample size and/or low statistical power) might provide stronger evidence when collapsed across samples (Scheibehenne *et al.*, 2016). One particularly elegant way to examine a new paradigm is to use a pilot, test and replication design within the same project and combine results meta-analytically. However, to be able to divide a childhood sample into subsamples - again - requires a large sample size.

All of these factors were taken into account when we designed the longitudinal twin study of the Leiden Consortium on Individual Development (L-CID), *Samen Uniek* in Dutch. The L-CID study consists of two cohorts (early childhood and middle childhood) that are being followed for six constructive years, with annual home or lab visits (Euser *et al.*, 2016). The majority of studies in the current thesis (**Chapters 2**, **4**, **5**, **6**, and **7**) are based on data from the middle childhood cohort. Specifically, I made use of the data of the first wave, and a follow up measure two years later. The study included 512 children (256 families) between the ages 7 and 9 at time point 1 (mean age: 7.94±0.67; 49% boys, 55% MZ). This large sample size provides sufficient statistical power to examine childhood brain development, specifically when taken into account that neuroimaging data in developmental samples are more prone to data loss and artifacts due to movement (O'Shaughnessy *et al.*, 2008).

Dissertation Outline

The large sample size of the L-CID study allowed me to test for within-sample replication, thereby contributing to the debate about reproducibility of neuroscientific patterns (Open Science, 2015). In doing so, I first examined the SNAT paradigm using a design with built-in replication and meta-analysis. In **chapter 2**, I tested the SNAT paradigm in separate pilot, test and replication samples and combined the results meta-analytically. The aim of this study was to detect robust behavioral patterns and neural signals related to social feedback, a crucial first step in examining social evaluation processing in childhood. Next, in **chapter 3**, I investigated neural processes of social evaluation in adults, were I additionally investigated brain-behavior associations to shed light on individual differences in the neural mechanisms for social emotion regulation. Unraveling these neural patterns in adults provided an index to compare the results in middle childhood with.

After validating the experimental paradigm in children and adults, the next step was to examine to what extend individual variation in social evaluation were explained by genetics and environmental influences. That is, why are some children more sensitive to social evaluation than others, and how do nature and nurture contribute to this? To examine this, in **chapter 4** I conducted behavioral genetic analyses on neural activation during social evaluation using a large developmental sample. Ultimately, in **chapter 5**, I examined individual differences in longitudinal changes of aggression regulation within childhood. Within-person changes provide a better indication of brain-behavior associations over time and can provide an actual reflection of development. In order to test within-person changes, I examined how neural mechanisms changed within individuals from middle (seven-to-nine-year-old) to late (nine-to-eleven-year-old) childhood, and to what extent these neural changes were related to changes in behavioral aggression.

Taken together, the first four chapters are devoted to an in-depth examination of social emotion regulation using the innovative SNAT paradigm. This paradigm allows to test neural mechanisms of social acceptance and rejection, as well as behavioral aggression in response to social feedback. Previous studies have suggested that social emotion regulation relies on a network of integrated connections between subcortical and cortical prefrontal brain regions (Olson *et al.*, 2009; Chester *et al.*, 2014; de Water *et al.*, 2014; Peper *et al.*, 2015; Silvers *et al.*, 2016b; van Duijvenvoorde *et al.*, 2016a). To date it remains an open question whether these networks are already in place during childhood, as previous studies often used older samples or only included a small sample of children. As L-CID compromises a large and statistically strong sample, I was able to investigate functional brain connectivity specifically in childhood. In **chapter 6**, I investigated the heritability of subcortical-PFC functional connectivity in childhood. The aim of this study was to test whether the subcortical-cortical connections that are central in neurodevelopmental models are already in place in childhood. Here I again made use of the large sample by including an in-sample replication approach to examine the robustness of the findings. Additionally, in **chapter 7**, I provide a comprehensive overview of pitfalls and possibilities in neuroimaging young children, which provides important methodological insights. Specifically, I examined what environmental as well as genetic factors contribute to scan quantity and quality. Here I explicitly compared different MRI modalities, including task-based fMRI, anatomical MRI, and structural and functional brain connectivity measures.

The ultimate goal of developmental neuroscience is to examine brain development from childhood, throughout adolescence, into adulthood and relate neural development to behavioral outcomes. A first step in that direction for social emotion regulation has been taken by relating structural brain connectivity to the ability to delay gratification (Olson *et al.*, 2009; de Water *et al.*, 2014; Peper *et al.*, 2015). In **chapter 8** I investigated the development of structural

subcortical-PFC connectivity and how maturation of this track across development was predictive for delay discounting skills. For this chapter, I used the Braintime data set (van Duijvenvoorde *et al.*, 2016b), a cohort-sequential design including participants aged 8-28, which enabled me to investigate both linear and non-linear brain maturation (see also Braams *et al.* (2015); Peters and Crone (2017). Lastly, in **chapter 9** the findings of the separate chapters are summarized and implications that arise from these findings are discussed in detail.

All empirical chapters are published in, or submitted to international journals. For this, valuable contributions of my co-authors should be acknowledged:

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