Social reorientation in adolescence : neurobiological changes and individual differences in empathic concern

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Chapter 1:

General Introduction

1.1 ADOLESCENCE AS AN IMPORTANT PERIOD FOR GAINING MATURE SOCIAL GOALS

Adolescence, which is the transition stage from childhood to adulthood, is an eventful period in life, as it encompasses major changes in physical appearance and changes in cognition, affect and social orientation. These changes are thought to be related to changes in the social environment, changes in the hormonal systems, and neurodevelopmental changes (Blakemore, 2008; Blakemore, Burnett, & Dahl, 2010). Whereas in childhood parents or caregivers play the most important role, school and playing are central elements, and the contact with friends is still quite 'simple', all of this undergoes major transformations in adolescence (Brown, 2004), and as such, this is one of the most important life period for developing mature social goals and independence.

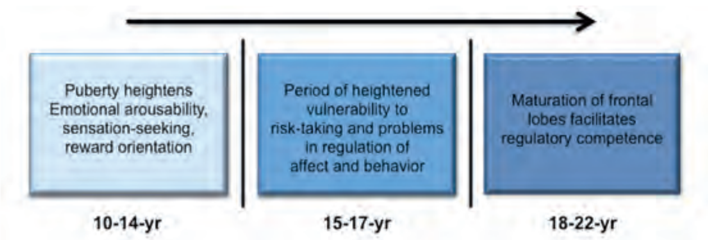

FIGURE 1.1 | Overview of important transitions in adolescence, based on Steinberg (2005).

Adolescence is often divided into three stages: 1) early-adolescence (10-14 years old), 2) mid-adolescence (15-17 years old), and 3) late-adolescence (18-22 years old) (Steinberg, 2005; see Figure 1.1). Although researchers often refer to these stages, the boundaries are quite arbitrary, as they are largely dependent on individual differences in hormonal-, cognitive-, and social-affective levels (Blakemore, 2008; Blakemore, Burnett, & Dahl, 2010). The onset of adolescence is often marked by the onset of puberty, around age 10 for girls and around age 11.5 for boys, although also within the sexes there is large variability in the age of onset (Marshall & Tanner, 1969; Marshall & Tanner, 1970; Shirtcliff, Dahl, & Pollak, 2009). The first signs of puberty are characterized by hormonal changes related to the secretion of estrogen and testosterone leading to maturation in the ovaries and testes, which further result in the development of secondary physical features (e.g., pubic hair growth, breast development) (Shirtcliff, Dahl, & Pollak, 2009). Although puberty is often associated with bodily changes (such as physical appearance, height, and shapes of the body), it goes beyond that, as puberty also plays a pivotal role in neurodevelopmental- and behavioral changes (Blakemore, Burnett, & Dahl, 2010).

Whereas the onset of puberty is often considered as the start of adolescence, defining the end point of adolescence is less clear. Following puberty and moving into adulthood, it is important that adolescents have acquired social and cognitive skills that are important for creating new friendships, obtaining self-confidence, being successful at an educational level, and for becoming an independent individual (Taylor, Barker, Heavey, & McHale, 2013). What is considered as the end of adolescence, and at the same time the start of adulthood, differs across cultures. In western cultures it is often indicated by the ability to manage one's life independently (Blakemore, Burnett, & Dahl, 2010).

One of the most prominent changes in adolescence is social reorientation (Blakemore & Mills, 2014; Steinberg et al., 2008). That is to say, adolescents develop more intimate relationships with peers in which mutual understanding plays an important role (Selman, 1980), they discover what it is like to be involved in a romantic relationship (Zimmer-Gembeck, 2002), and they take (social) risks by for example drinking alcohol for the first time (Brown, 2004) or showing risky driving in the presence of friends (Chein, Albert, O'Brien, Uckert, & Steinberg, 2011). These new experiences go hand in hand with the development of self-consciousness, which makes adolescents more aware of their surrounding peers, their own emotions, and the realization that their behavior will be judged by peers (Somerville & Casey, 2010; Somerville et al., 2013).

Given that adolescence is an important phase for social reorientation, eventually leading to a state of independency and individuality, empathic abilities play a crucial role in successfully reaching these goals. Examples of empathic abilities are sharing and understanding feelings of others and regulating your own emotional responses, which are crucial abilities in social interactions. How individual differences in empathic traits are related to the development of social reorientation is currently not well understood.

It is hypothesized that neural changes are related to the behavioral changes that are classified under the heading social reorientation (Somerville & Casey, 2010; Blakemore & Mills, 2014). In addition, it is hypothesized that the involvement of hormones affects social-affective functions.

Especially testosterone has proven to play an important role in risk-taking behavior during adolescence (Blakemore, Burnett, & Dahl, 2010; Peper, Koolschijn, & Crone, 2013). The current thesis has the purpose to understand the behavioral and neural underpinnings of developmental changes and individual differences in social reorientation and empathic concern across childhood and adolescence.

The questions addressed in this thesis concern: 1) how do brain regions involved in social reorientation develop in adolescence, 2) what is the role of individual differences, and 3) what is the role of pubertal development. These questions are addressed using a multi-method perspective of combining insights from self-report, task behavior, and neural activity on task tapping into components of social reorientation.

1.2 NEURODEVELOPMENTAL CHANGES IN ADOLESCENCE

An influential neural system model that aims to explain social reorientation in adolescence is the Social Information Processing model (SIPN) (Nelson, Leibenluft, McClure, & Pine, 2005; see Figure 1.2). This model describes the overall development of the brain based on three nodes: the detection node, the affective node, and the cognitive-regulation node. Each separate node represents a cluster of brain areas that mediates the processing of social information. The detection node is involved in detecting whether a stimulus is socially relevant, and for recognizing basic social characteristics (e.g. detection of faces). The anterior temporal cortex, the fusiform face area, and the superior temporal sulcus are the brain areas that are involved in this part of social information processing.

The affective node, including the nucleus accumbens (NAcc), ventral striatum (VS), hypothalamus and amygdala, attributes meaning to the perceived social information, for instance by indicating whether information is rewarding or punishing. This cluster of brain areas is thought to be more sensitive during adolescence, resulting in a stronger reaction in these brain areas compared to pre- and post-adolescence. This "hypersensitivity" is linked to changes in gonadal hormones, which affect functional and structural reorganization of the affective node regions (see Herting et al. 2014). This occurs indirectly as gonadal hormones affect neurotransmitters like dopamine, oxytocin, and serotonine that help in the transmission of signals in the brain (e.g. social responsiveness). On a behavioral level, this hypersensitivity is claimed to enhance approaching positive stimuli and to enhance avoiding negative stimuli (Galván, 2010). In daily life, this phenomenon expresses itself in a way that adolescents are taking higher risks when peers encourage them, because being approved and socially accepted by peers is highly rewarding for adolescents (Chein et al., 2011). The downside of this medal is that adolescents who are socially rejected, avoid interactions with peers, possibly due to enhanced activation in the (social) pain related areas like the anterior insula (AI) and the anterior cingulate cortex (ACC), which often brings them in a downhill slide of more social rejection and the accompanied social pain (Masten, Telzer, Fuligni, Lieberman, & Eisenberger, 2012).

Finally, the cognitive-regulation node is involved in controlling and regulating social information (e.g. reasoning about mental states of others) and complex cognitive information (e.g. planning behavioral responses in order to reach a specific goal). The regions that are involved in this node are the dorsal medial prefrontal cortex (dmPFC) and the ventral prefrontal cortex (vPFC) (Nelson, Leibenluft, McClure, & Pine, 2005; Nelson & Guyer, 2011), regions that are still developing during mid to late adolescence, because of synaptic pruning (reduction of neurons and synapses in order to make more efficient neural structures) and myelinization (stimulates fast and guided information transmission) (Shaw et al., 2008). Notably, the detection node, affective node, and cognitive-regulation node are thought to be interrelated within the social information-processing network (Nelson, Leibenluft, McClure, & Pine, 2005).

The SIPN model shares commonalities with a second influential model, which is the dual systems model of adolescent development (Somerville, Jones, & Casey, 2010; Ernst & Fudge, 2009; Steinberg et al., 2008). This model places more emphasis on adolescent specific changes in reward seeking behavior. That is to say, mid-adolescence represents a period in which there is a peak in risk-taking behavior (e.g. having sex without protection, drinking an extensive amount of alcohol, smoking cigarettes). According to the dual systems model, the emotion regions in the brain undergo a sudden change in development, meaning that regions like the ventral striatum (a region important for reward seeking and approach behavior), and the amygdala (a region important for detecting (social) emotions), become “hypersensitive”. These regions are often indicated as subcortical regions being part of the affective node (VS and amygdala) of the SIPN model (Nelson, Leibenluft, McClure, & Pine, 2005).

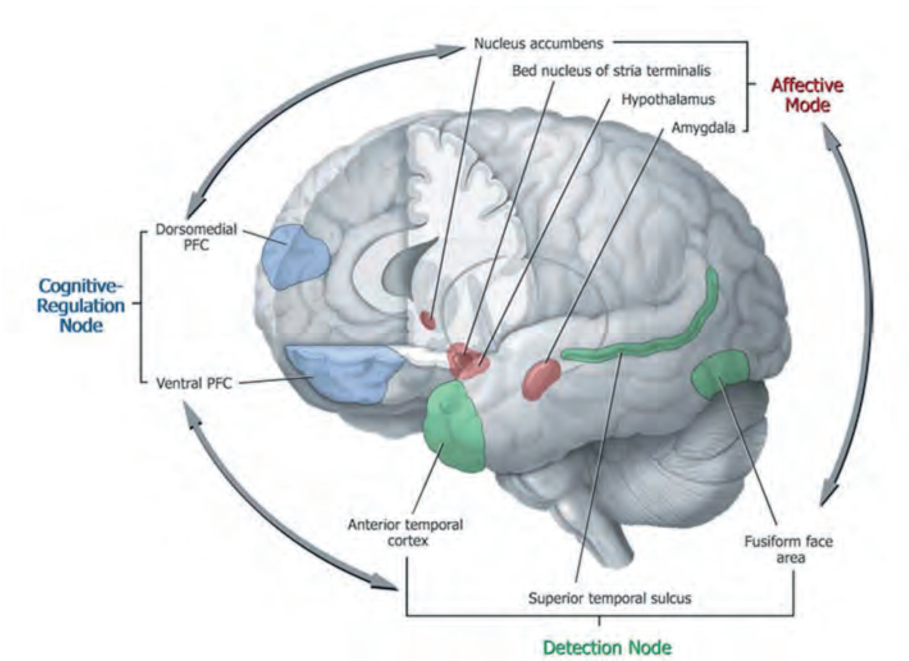

FIGURE 1.2 | Display of the regions involved in the Social Information Processing Network (SIPN) model, based on Nelson et al. (2005)

Similar to the SIPN model, the dual systems model puts emphasis on the development of the prefrontal (cortical) cortex as an important control region in the brain, although whereas the SIPN model places emphasis on both the medial and ventral parts of the prefrontal cortex, the dual systems model puts more emphasis on the lateral prefrontal cortex. The exact differentiation between functions of the medial and lateral PFC are not yet well understood, but a general finding is that the medial regions of the PFC are more involved in social information processing, such as theory of mind and self-referential processing, whereas the lateral regions of PFC are more involved in "cold" cognitive control functions such as working memory and response inhibition (Crone & Dahl, 2012; Blakemore & Mills, 2014; Luna, Padmanabhan, & O'Hearn, 2010). The maturation of the lateral prefrontal cortex continues during adolescence in terms of structure (Shaw et al., 2008) and function (Somerville, Jones, & Casey, 2010). Thus, the dual systems model presents the hypothesis that the affective system (VS, amygdala) matures faster (mid/late adolescence) than the control system (lateral prefrontal cortex). These different developmental trajectories are leading to a discrepancy between the affective system and the control system, and seem to hinder adolescents' abilities to regulate their emotions and to inhibit impulsive reactions (Steinberg et al., 2008).

1.3 EMPATHY DEVELOPMENT FROM CHILDHOOD TO ADULTHOOD

Whereas the SIPN model provides an important working model for understanding changes in social reorientation during adolescence, less attention has been devoted to differences *between* adolescents. That is to say, some adolescents navigate through adolescence relatively well and are less sensitive to, for example, peer pressure, and develop into prosocial helping individuals with strong peer relations. In contrast, other adolescents have difficulty adapting to changing norms in peer relations and are withdrawn, lonely, suffer low self-esteem, and are likely to be at risk for internalizing disorders (Rubin, Bukowski, & Parker, 1998). The absence of social networks is strongly implicated in the development of psychopathology (Deater-Deckard, 2001). In this thesis, the hypothesis is tested that individual differences in empathy are an important predictor for behavioral and neural responses involved in social reorientation.

THE CONCEPTUALIZATION OF EMPATHY

Empathy has many different faces in terms of labels and definitions. Some of the terms that are often used to indicate empathy (or that are closely related to empathy) are: emotional contagion, empathic concern, sympathy, compassion, Theory of Mind, mentalizing, perspective taking, prosocial behavior, and altruism (for a review, see Preston & De Waal, 2002; Zaki & Ochsner, 2012; see Figure 1.3).

A consistent differentiation in the literature is the definition of empathy by two concepts: affective empathy and cognitive empathy. Affective empathy has often been defined as sharing feelings with someone by mirroring the affective state of the person who is experiencing the emotion (De Vignemont & Singer, 2006). Cognitive empathy, on the other hand, has been defined as awareness of the self, the ability to make a self-other distinction and the ability to take another person's perspective (Bernhardt & Singer, 2012).

Prosocial behavior is indicated as an ability rising from cognitive empathy, and is explained by helping someone out of compassion without taking into account self-interest.

Empathic abilities have been found to develop during childhood. An important component of affective empathy is sharing feelings, which already happens in babies, for example when all babies at the nursery start crying because one baby started expressing its sad feeling or ‘cry for help/need’. This does not mean that all the babies are actually sad or in need, just that the emotion of the baby contaminated them (Decety & Meyer, 2008). Making a distinction between one’s own feelings and that of someone else comes along when cognitive empathy develops, mostly around age 4 or 5, when Theory of Mind has been developed (Baron-Cohen, Leslie, & Frith, 1985). However, not all components of cognitive empathy are already in place in 5-year-old children, that is, the more advanced forms of cognitive empathy, such as perspective taking and prosocial development, develops still into adolescence (Güroğlu, van den Bos, & Crone, 2014).

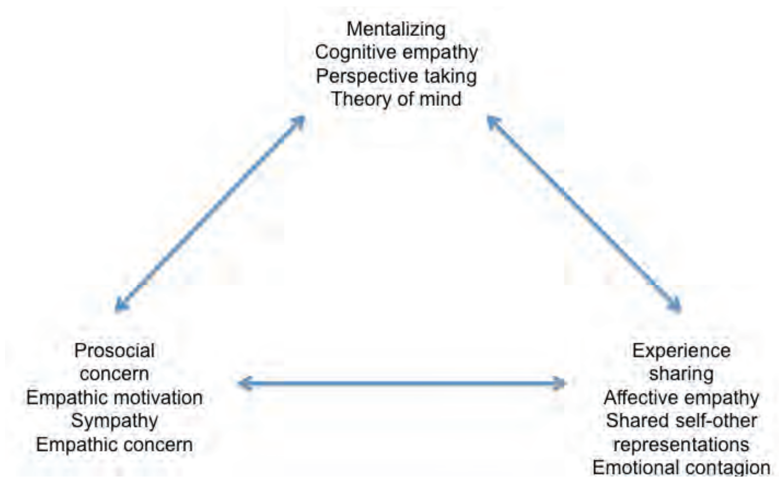

FIGURE 1.3 | Empathy encompasses different processes, which can be categorized as affective empathy, cognitive empathy and prosocial concern, based on Zaki & Ochsner (2012)

1.4 NEURAL CORRELATES OF EMPATHY

EMPATHY MODEL DECETY & MEYER

Developmental and individual differences in empathy have been described in a model by Decety & Meyer (2008), who demonstrated that empathy derives by a ‘bottom-up perception action information process’ in combination with a ‘top-down regulation and control’ information process, whereby past life experiences and specific contexts/situations are of influence. The bottom-up perception action coupling can be explained by underlying biological processes that enable people to learn and share feelings by observing action or mimicry. This biological process has been referred to as the Mirror Neuron System (MNS). When observing someone putting his hands together, the MNS provides activation in the same brain areas in the observer as in the actor, though to a lesser extent. Thus, by ‘mirroring’ the observed action, the mirror neurons are preparing the required brain network for actual performing an action (motor empathy). Besides facilitating action performance, the MNS is also important for perceiving the emotional state of others. Sharing emotions of others by activating the same brain areas helps in empathizing with that other person, i.e. by shared representations. The brain regions that are involved in both the perception and performance of motor empathy (most likely driven by mirror neurons are): the premotor cortex, the inferior frontal gyrus (IFG), the parietal lobule, the supplementary motor area, and the cerebellum.

The ‘top-down regulation and control’ information process is involved in regulating emotions that enable us to make a self-other distinction and to have self-control. Making a self/other distinction requires the ability to know if an action is performed by the self or by the other, and can be determined by: 1) non-overlapping regions in the brain, i.e. regions for self-representation are not involved in other-representations 2) awareness that neural signals of the self are giving immediate feedback, whereas motor empathy representations perceived in others require more processing. The brain regions that have been found to be important for making a distinction between the self and the other are the temporal parietal junction (TPJ) and the paracingulate cortex (PCC). The anterior insula (AI) is an example of a region that has found to become activated when you are responsible for an action, but does not activate when someone else is responsible for an action. In the latter case, the right TPJ has found to be involved (Farrer & Frith, 2002).

In sum, empathy is based on both the 'bottom-up perception action information process' and the 'top-down regulation and control' information process. Difficulties in sharing emotions can lead to shortcomings in understanding what someone else is feeling, whereas difficulties in controlling your own emotions can lead to personal distress and a lack of self-monitoring (Decety & Meyer, 2008). Determining how empathy develops on a behavioral and neural level has been studied extensively by empathy for pain.

EMPATHY FOR PAIN

The literature on the neural correlates of empathy is quite extensive and has focused on various aspects of empathy varying from empathy for physical pain, empathy for social pain (social exclusion), and empathic responses on emotions such as anger, sadness, or happiness (Bernhardt & Singer, 2012). Empathy for pain is by far the most investigated aspect of empathy (Lamm, Decety, & Singer, 2011). When seeing someone in pain, this often gives individuals an unpleasant feeling. For example when observing someone falling of his/her bike, which may lead to the feeling of falling of the bike yourself. Jackson and colleagues have studied participants' reactions on observing pictures in which painful situations were presented (Jackson, Meltzoff, & Decety, 2005; Jackson, Brunet, Meltzoff, & Decety, 2006). The brain areas that became active while watching these disturbing pictures were the anterior insula (AI), the anterior cingulate cortex (ACC), and the anterior mid-cingulate cortex (aMCC). These regions have proven to be mainly involved in the observation of painful situations and are often referred to as the 'pain matrix' (Bernhardt & Singer, 2012).

The regions mentioned above have also been found to be involved in the direct experience of pain (Bird et al., 2010; Hein, Silani, Preuschoff, Batson, & Singer, 2010; Singer et al., 2004; Singer et al., 2006; Singer et al., 2008). Multiple studies have investigated empathy for pain and demonstrated overlap between the regions that became active when observing pain in others compared to experiencing pain. The observation that empathy for pain investigated by pain inflicted pictures, video clips, and by abstract visual cues leading to electric stimulation result in activation in areas that are part of the pain matrix, indicates that empathy for pain is a robust neural mechanism (Lamm, Decety, & Singer, 2011).

Besides activating pain related areas when observing painful situations, another concept is involved as well, namely the contextual or social cues.

For determining the intentions of people involved in a social situation, social cues need to be read. By reading social cues from facial expressions and posture, it is possible to understand a situation and to determine whether the behavior is morally right, wrong or neutral (e.g. harm inflicted accidentally or intentionally) (Pfeifer et al., 2009; Sinke, Sorger, Goebel, & de Gelder, 2010). The areas previously found to be involved in judging social situations and moral behavior are the TPJ, the PCC, and the amygdala (Pfeifer et al., 2009). The TPJ and PCC are regions important for making a self/other distinction and taking other persons' perspective, the oMFC is a reward and punishing related area that monitors positive or negative outcomes, and the amygdala is involved in emotional stimuli and evaluates whether situations are threatening (Decety, Michalska, & Akitsuki, 2008).

Previous studies have examined the developmental changes in activity in these empathy networks (Decety, Michalska, & Kinzler, 2012) and reported developmental changes in several key areas of the network, especially in amygdala-prefrontal cortex coupling, but much less emphasis has been placed on understanding the social-cognitive processing of empathy for pain. In addition, almost nothing is known about individual differences in these trajectories, even though studies in adults reported an important role for individual differences in empathic traits in explaining neural activity during empathy for pain (Decety & Jackson, 2004; Jackson, Brunet, Meltzoff, & Decety, 2006; Van der Heiden, Scherpiet, Konicar, Birbaumer, & Veilt, 2013). Studies that have included groups with psychopathology also show differences in empathy networks in adolescence (Decety, Chen, Harenski, & Kiehl, 2013). This thesis addresses the question how social-cognitive empathy is represented in the adolescent brain and how trait individual differences in empathy explain individual differences in neural responses to social-cognitive empathy.

1.5 OUTLINE CURRENT DISSERTATION

The studies in this thesis are inspired by the combination between the SIPN model for the development of social orientation and the Empathy model to test development and individual differences in cognitive, affective and prosocial empathy. Chapters 2 and 3 use a longitudinal design to examine developmental changes in activity in the detection and affective nodes of the adolescent brain. Most previous research on adolescent brain development has been done cross-sectionally, which gives important information about general neural patterns associated with social and/or cognitive abilities in one or multiple (age) groups. However, the limitation of cross-sectional research is that it does not allow to follow one individual over time and to track how certain abilities change or remain stable within a person. This problem can be resolved by longitudinal research in which it is possible to examine individual trajectories for an individual.

The study presented in **Chapter 2** describes a longitudinal analysis of neural regions involved in mentalizing. Prior studies showed age related changes in the social brain network related to mentalizing, though this was only tested cross-sectionally. The goal of the fMRI study was to test whether the regions involved in mentalizing are consistently active within adolescents across time or whether regions in this network change during development.

Chapter 3 involves a combined cross-sectional and longitudinal study on the relationship between reward processing and puberty in adolescent boys and girls. The hypothesis was that the affective node of the brain, with a specific focus on the ventral striatum, would become increasingly activated in response to rewards with increase age. Second, this node was expected to show individual differences based on self-reported sensation seeking behavior. The first experiment describes a cross-sectional study in which adolescents played a risky decision task. The second experiment describes a longitudinal study of a subset of adolescents who participated in the cross-sectional study (timepoint 1) that were tested again in a follow-up two years later (timepoint 2). As such, this study aimed to examine stability, change, and individual differences in reward processing in adolescence in a cross-sectional and longitudinal comparison.

Next, the cognitive node of the SIPN model was tested in three studies, with a specific focus on cognitive empathy and prosocial behavior. First, in **Chapter 4** a new Empathy Questionnaire was validated that aims to assess different aspects of empathy (affective, cognitive and prosocial) in children and adolescents. Additionally, the study describes how these abilities are linked with positive and negative aspects of social interactions.

Next, in **Chapter 5** a behavioral study examined the role of strategic versus altruistic motivations in bargaining considerations and their developmental trajectories. The reason for using bargaining games was to measure how individuals divide a stake in which two motivational aspects are important: interest in own outcome and concern for the other player (Van Dijk & Vermunt, 2000). Considering that cognitive and prosocial empathy develops over time and that individuals differ in how empathic they behave, a bargaining game in which a stake has to be divided between self and the other can provide relevant information about cognitive empathy and prosocial behavior. More specifically, we tested whether adults show higher levels of concern for others compared to children and have more altruistic motives for offering fair distributions.

In **Chapter 6**, a cross-sectional fMRI study examines the neural responses in response to negative and positive social situations, and whether this is related to self-reported levels of empathy. We were specifically interested in testing whether the regions in the different nodes of the social brain areas were differentially sensitive to the perception of negative social and positive social situations, and whether participants differentiated between the agents in negative social and positive social situations.

Finally, **Chapter 7** integrates the previous chapters and discusses the contribution of the studies to existing literature by drawing attention to possible theoretical and practical implications.