CHAPTER

21

A Neuroscience Perspective on Empathy and Its Development

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OUTLINE

Abbreviations

aMCC Anterior medial cingulate cortex
CADS Child and adolescent dispositions scale
CD Conduct disorder
dACC Dorsal anterior cingulate cortex
dlPFC Dorsolateral prefrontal cortex
fMRI Functional magnetic resonance imaging
IFG Inferior frontal gyrus
mPFC Medial prefrontal cortex
OFC Orbitofrontal cortex
PAG Periaqueductal gray
SMA Supplementary motor area
SPL Superior parietal lobule
TPJ Temporoparietal junction
vmPFC Ventromedial prefrontal cortex

21.1 INTRODUCTION

Developmental affective neuroscience is an emerging area of research that has the potential to improve one's understanding of human social behavior by integrating theory and research into psychology, neuroscience, clinical psychology, and neuropsychiatry. Among the psychological processes that are the basis for much of social perception and smooth social interaction, empathy and sympathy play key roles. Empathy-related responding, including caring and sympathetic concern, motivates prosocial behavior, inhibits aggression, and paves the way to moral conduct. On the other hand, certain developmental disorders, such as conduct disorder (CD), are marked by psychopathic tendencies and empathy deficits, which likely influence antisocial responses to others' distress, for example, active aggression. Understanding how these behaviors are implemented in the brain, in both typically developing children and children with aggressive tendencies can help elucidate why empathy does or does not automatically lead to prosocial behavior.

This chapter critically examines one's current knowledge about the development of the mechanisms that support the experience of empathy and associated behavioral responses such as prosocial behavior. The affective and cognitive components that give way to empathy are reviewed, starting first with the automatic proclivity to share emotions with others, and then the cognitive processes of perspective taking and executive control, which allow individuals to be aware of the intentions

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and feelings of others and keep separate self and other perspectives. The goal is to address the underlying cognitive and affective neural architecture that instantiates empathy and to examine the dysfunction of these processes in developmental disorders marked by social-cognitive impairments.

Based on the theoretical and empirical evidences from developmental psychology, cognitive neuroscience, and lesion studies, it can be argued that a number of distinct and interacting components contribute to the experience of empathy: (1) affective sharing, a bottom-up process grounded in affective arousal; (2) understanding emotion that relies on a sense of agency, self-awareness, and other awareness and critically involves the medial and ventromedial prefrontal cortex (vmPFC) and temporoparietal junction; and (3) executive functions instantiated in the prefrontal cortex, which operate as a top-down mediator, helping to regulate emotions, appraise social context, and yield mental flexibility (Decety, 2011; Decety and Jackson, 2004; Decety and Meyer, 2008).

Drawing from multiple sources of data can help paint a more complete picture of the phenomenological experience of empathy, as well as an understanding of the development and interaction between the respective mechanisms that drive the phenomenon. Furthermore, studying subcomponents of more complex psychological constructs such as empathy can be particularly useful from a developmental perspective because only some of its components or precursors may be observable. Developmental studies can provide unique opportunities to see how the components of the system interact in ways that are not possible in adults – where all the components are fully mature and operational (De Haan and Gunnar, 2009). Until quite recently, research on the development of empathy-related responding from a neurobiological level of analysis has been relatively sparse. It is believed that integrating this perspective with behavioral work can shed light into the neurobiological mechanisms underpinning the basic building blocks of empathy and sympathy and their age-related functional changes. Such integration can help to understand the neural processes that underpin prosocial behavior including pathological altruism while also benefiting interventions for individuals with atypical development, such as antisocial behavior problems.

21.2 CLEARING UP DEFINITIONAL ISSUES

The construct of empathy is applied to various phenomena that cover a broad spectrum. This spectrum ranges from feeling concern for others (creating a motivation to help them), experiencing emotions that match another individual's emotions, knowing what another is thinking or feeling, to blurring the line between self and other (Hodges and Klein, 2001).

Key concepts

- Empathy is a construct that can be decomposed into a model that includes bottom-up processing of affective sharing and emotion awareness and top-down processing in which the perceiver's motivation, memories, intentions, and self-regulation influence the extent of an empathic experience
- The experience of empathy can lead to sympathy, which refers to feelings of concern for the wellbeing of another. It includes another-oriented motivation or an egoistic motivation to reduce stress by withdrawing from the stressor in the case of personal distress
- Empathy and sympathy play key roles in motivating prosocial behavior and provide the affective and motivational foundation for moral development
- Empathy is implemented by a network of distributed, often recursively connected, interacting neural regions, including the brainstem, hypothalamus, superior temporal sulcus, insula, medial and orbitofrontal cortices, amygdala, and anterior cingulate cortex (ACC), as well as autonomic and neuroendocrine processes implicated in social behaviors and emotional states
- Neurodevelopmental studies provide unique opportunities to explore how the components of empathic responding interact in ways that are not possible in adults
- Investigating dysfunction of the components of empathy provides important clues for understanding deviations that can lead to the lack of empathy and concern for others

In developmental psychology and social psychology (the two academic disciplines that have produced most of the research on this subject), empathy is generally defined as an affective response stemming from the understanding of another's emotional state or a condition similar to what the other person is feeling or would be expected to feel in the given situation (Eisenberg et al., 1991). Other theorists more narrowly characterize empathy as one specific set of congruent emotions – those feelings that are more other-focused than self-focused (Batson, 2009; Batson et al., 1987). Very often, empathy and sympathy are conflated. Here, the authors distinguish between empathy (the ability to appreciate the emotions and feelings of others with a minimal distinction between self and other) and sympathy (feelings of concern about the welfare of others). While empathy and sympathy are often confused, the two can be dissociated. Although sympathy may stem from the apprehension of another's emotional state, it does not have to be congruent with the affective state of the other. The experience of empathy can lead to sympathy (which includes another-oriented motivation) or personal distress (an egoistic motivation to reduce stress by withdrawing from the stressor, thereby decreasing the likelihood of prosocial behavior). Emotion regulation is a critical component of empathy because the modulation of emotional experience allows the person to remain aware of a situation without being overwhelmed or

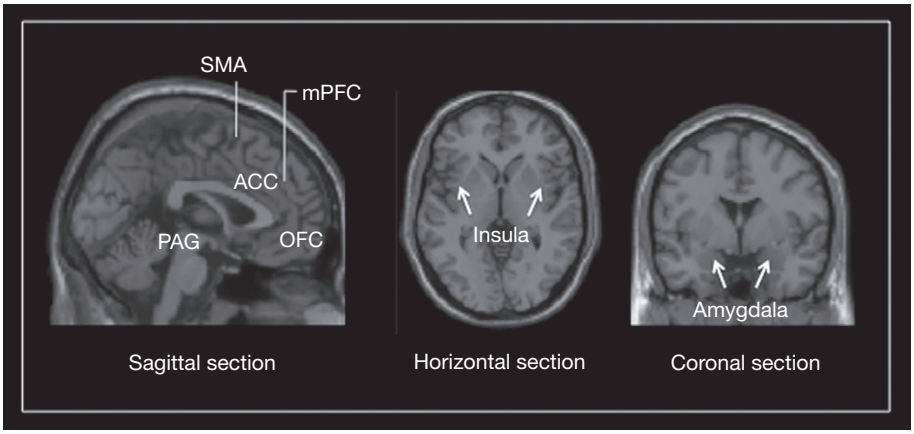

FIGURE 21.1 Brain regions that play crucial roles in the experience of empathy and associated phenomena such as sympathy labeled on sagittal, horizontal, and coronal sections of a structural MRI scan. Functional imaging studies reveal that the anterior insula and the anterior cingulate cortices are conjointly activated during the experience of emotion and during the perception of emotion in others. The insula provides a foundation for the representation of subjective bodily feelings, which substantiates emotional awareness. The ACC can be divided anatomically based on cognitive (dorsal) and emotional (ventral) components: the dorsal part is connected with the prefrontal cortex and parietal cortex as well as the motor system, making it a central station for processing top-down and bottom-up stimuli and assigning appropriate control to other areas in the brain; by contrast, the ventral part of the ACC is connected with amygdala (a structure involved in assigning affective significance to stimuli), ventral striatum, hypothalamus, and anterior insula and is involved in assessing the salience of emotion and motivational information. Many functions are attributed to ACC, such as error detection, anticipation of tasks, motivation, and modulation of emotional responses. The medial prefrontal cortex (mPFC) is critically associated with theory of mind processes and emotion understanding. The orbitofrontal cortex (OFC) is involved in sensory integration, in representing the affective value of reinforcers, and in decision making and expectation. In particular, the OFC is thought to regulate planning behavior associated with sensitivity to reward and punishment and is closely connected to the anterior insula and amygdala.

numbed by it. This is especially important in the case of negative arousal (Decety and Lamm, 2009). Developmental research also indicates that children who can regulate their emotions and emotion-related behavior should be relatively likely to experience sympathy rather than personal distress (Eisenberg and Eggum, 2009).

The complex construct of empathy can be decomposed into a model that includes bottom-up processing of affective sharing and top-down processing in which the perceiver's motivation, intentions, and self-regulation influence the extent of an empathic experience. Shared neural circuits, self-awareness, emotion understanding, and self-regulation constitute the basic macrocomponents of empathy, which are mediated by specific and interacting neural circuits, including aspects of the prefrontal cortex, ACC, medial prefrontal cortex (mPFC), orbitofrontal cortex (OFC), insula, limbic system, and frontoparietal attention networks (Decety, 2011). Consequently, this model assumes and predicts that dysfunction in either of these macrocomponents may lead to an alteration of the experience of empathy and corresponds with selective social cognitive disorders depending on which aspect is disrupted (Blair, 2005; Decety and Moriguchi, 2007; Figure 21.1).

It is also important to keep in mind that both interpersonal as well as contextual factors impact a person's subjective experience of empathy. For instance, mood states, relationship to the person, and the social context in which the interaction occurs influence the way and the extent to which the observer will react.

Recent affective neuroscience research with children and adult participants indicates that the affective, cognitive, and regulatory aspects of empathy involve interacting yet partially nonoverlapping neural circuits. Furthermore, there is now evidence for age-related changes in these neural circuits, which together with behavioral measures reflects how brain maturation influences the reaction to the distress of others (Decety and Michalska, 2010).

21.3 THE DEVELOPMENT OF EMPATHY

Empathy is one of the higher-order emotions that typically emerges as a child comes to a greater awareness of the experience of others, during the second and third years of life, and that arises in the context of someone else's emotional experience (Robinson, 2008). Each of the components of empathy (affective sharing, cognitive understanding, and emotion regulation) will be considered separately from both a developmental and neuroscience perspective. These components are indeed dissociable as documented in neurological patients (Strum et al., 2006), yet mature empathic sensitivity and concern depend on their functional integration in the service of goal-directed social behavior. In addition,

both genetic and environmental factors contribute to the development of empathy and prosociality (Knafo et al., 2008).

21.3.1 Affective Sharing

While there is some controversy concerning the nature of empathic responding in very young children, there is ample behavioral evidence demonstrating that the affective component of empathy develops earlier than the cognitive component. Affective responsiveness is known to be present at an early age, is involuntary, and relies on somato-sensorimotor resonance between other and self (Decety and Meyer, 2008). The general consensus of work in this area is that infants and toddlers are sensitive and responsive to others' emotional cues and that some of the basic building blocks of empathy, such as emotion sharing, are present in the first days of life.

Discrete facial expressions of emotion have been identified in newborns, including joy, interest, disgust, and distress (Izard, 1982), suggesting that subcomponents of full emotional experience and expression are present at birth and supporting the possibility that these processes are hardwired in the brain. Very young infants are able to send emotional signals and to receive and detect the emotional signals sent by others. Human newborns are capable of imitating expressions of fear, sadness, and surprise (Field et al., 1982; Haviland and Lewica, 1987), preparing individuals for later empathic connections through affective interactions with others. Moreover, both infant humans and nonhuman primates are known to respond to others' distress with distress. Infants exposed to newborn cries cry significantly more often than those exposed to silence and those exposed to a synthetic newborn cry of the same intensity (Dondi et al., 1999; Sagi and Hoffman, 1976). A study by Martin and Clark (1987), which examined infants' reactions to audiotapes of neonatal crying, showed not only that 1-day-old babies cry in response to other infant cries but also that newborns do not respond to the sound of their own cries. Together, these findings demonstrate that infants' auditory perception of another's aversive affective state elicits the same distressful emotional state in the self and suggests a neurobiologically based predisposition for humans to be connected to others. The latter results also indicate that there is some self–other distinction already functioning at birth.

Research using measures of facial electromyography (EMG) in adult participants demonstrates that viewing facial expressions triggers distinctive patterns of facial muscle activity similar to that of the observed expression, even in the absence of conscious recognition of the stimulus (Dimberg et al., 2000). In one such study, participants were exposed very briefly (56 ms) to pictures of happy or angry facial expressions and EMG was recorded from their faces (Sonnby-Borgstrom et al., 2003). Results demonstrated facial mimicry despite the fact that the participants were unaware of the stimuli. A study conducted with school-age boys demonstrated that angry and happy facial stimuli spontaneously elicit different EMG response patterns (de Wied et al., 2006). Angry faces evoked a stronger increase in corrugator activity than happy faces, while happy faces evoked a stronger increase in zygomaticus activity than angry faces. Such a mimicry mechanism may be driven by the so-called mirror neuron system (somatosensory motor neurons localized in the premotor, motor, and posterior parietal cortices) that directly links perception and action.

This automatic emotional resonance between other and self provides the basic mechanism on which intersubjective feelings develop. Infant arousal in response to the affects and emotions signaled by others can serve as an instrument for social learning, reinforcing the significance of the social exchange, which then becomes associated with the infant's own emotional experience. As a consequence, infants come to experience emotions as shared states and learn to differentiate their own states partly by witnessing the resonant responses that they elicit in others.

21.3.2 Emotion Understanding

Thus, it is clear that from very early on in development, infants are capable of emotional resonance, which is one important precursor of empathy (Hoffman, 2000). Although the capacity for two people to resonate with each other emotionally before any cognitive understanding is the basis for developing shared emotional meanings, it is not enough for mature empathic understanding. Such an understanding requires forming an explicit representation of the feelings of another person, an intentional agent, which necessitates additional computational mechanisms beyond the emotion-sharing level, as well as self-regulation to modulate negative arousal in the observer (Decety and Moriguchi, 2007; Decety et al., 2008). The cognitive components that give way to empathic understanding have a more protracted course of development than the affective components, even though many precursors are already in place very early in life.

Emotion understanding refers to conscious knowledge about emotion processes or beliefs about how emotions work. Such understanding includes the recognition of emotion expression and knowledge about one's own and others' emotions, the detection of cues for others' feelings, as well as ways of intentionally using emotion

expression to communicate to others (or vice versa; e.g., hiding emotions). Children's development of gradually more sophisticated understanding of emotion fosters many adaptive processes, such as social functioning and coping. Consequently, delayed or limited emotion understanding may place youth at risk for disorders.

As discussed in the previous section, children recognize facial expressions associated with emotions at an early age (Haviland and Lewica, 1987). Some questions remain as to whether these early reactions represent recognition of emotion in another or simple mimicry. Either way, most children are using emotion labels for facial expressions and are talking about emotion topics by the age of 2 years (Gross and Ballif, 1991). Recent work has also documented that even very young children (18–25 months old) can sympathize with a victim even in the absence of overt emotional cues (Vaish et al., 2009), which suggests some early form of affective perspective taking that does not rely on emotion contagion or mimicry. Prior work by Zahn-Waxler et al. (1992) demonstrated that prosocial behaviors (help, sharing, and provision of comfort) emerge between the ages of 1 and 2 and that these behaviors are linked to expressions of concern as well as efforts to understand the other's plight. Regarding the causes and effects of emotion and the cues used in inferring emotion, developmental research has detailed a progression from situation-bound, behavioral explanations of emotion to broader, more mentalistic understandings (Harris et al., 1981). For example, children's early explanations of emotion are largely based on the external world (e.g., 'I am sad because someone took my toy.'), whereas as children develop, their explanations of emotions focus more on internal causes (e.g., 'I am sad because that toy was important to me.'). As children develop, their emotional inferences contain a more complex and differentiated use of several types of information, such as moral variables (Nunner-Winkler and Sodian, 1988), relational and contextual factors, and the target child's goals or beliefs (Harris, 1994). This development appears to be somewhat slower for complex emotions such as pride, shame, or embarrassment (Lewis, 2000). Children also develop an understanding of multiple emotions, comprehending that a person can feel more than one emotion at a time. Development of this understanding proceeds from lack of acknowledgment of multiple emotions in younger children, to acknowledgment, and to an appreciation of different variables, such as emotion valence and emotion intensity (e.g., one very strong and one very weak emotion are easier to understand than two strong ones; Carroll and Steward, 1984).

Understanding that appraisal can modulate a person's emotional experience to a given situation develops from being desire-based to being belief-based. At first, 2- and 3-year-old children understand the role that desires or goals play in determining a person's appraisal and ensuing emotion (Repacholi and Gopnik, 1997). By 18 months, infants can not only infer that another person can hold a desire that may be different from their own but also recognize how desires are related to emotions and understand something about the subjectivity of these desires. By 4 and 5 years of age, this desire-based concept of emotion develops to include beliefs and expectations. Children at this age begin to understand that an emotion is not necessarily triggered by whether or not a desire and an outcome match but rather whether a desire and an expected outcome match. The shift from a desire to a belief–desire conception of mind and emotion is well established. For example, Bartsch and Wellman (1995) have examined children's references to other people's mental states and demonstrated that children talk systematically about desires and goals throughout their third year, but that beginning at about their third birthday, children also begin to make reference to beliefs. At about 5 years of age, talk about beliefs becomes as frequent as talk about desires.

Young children's understanding of emotions has been shown to be related to a number of factors, including children's language ability, family discourse about feelings, and the quality of family relationships. Families vary in the linguistic environment that they offer to children for the interpretation and regulation of emotion. A child with a parent who frequently discusses emotions will have a different kind of conversation partner than a child with a parent who is much more controlled in talking about emotions. Research has established that there is indeed substantial variation among the extent to which emotions are discussed in the home. The frequency with which children engage in discussion about emotions and their causes is correlated with their later ability to identify how someone feels (Brown and Dunn, 1996). While it is possible that such a correlation reflects some disposition of the child that manifests itself in both talking about emotions and sensitivity to emotions, it is more likely that frequent family discussion may prompt children to talk about emotion and increase their understanding and perspective-taking abilities (Harris, 2000). Consistent with this idea, Lewis (2000) demonstrated that 3-year-olds who normally do poorly on a standard test of psychological understanding (the false belief task) perform better if they are prompted to structure the events leading to the false belief into a coherent narrative. Allowing children to express emotion and report on current and past emotions also provides them with an opportunity to share, explain, and regulate emotional experience. Conversation helps to develop empathy, for it is often here that people learn of shared experiences and feelings.

With cognitive empathy, an individual is thought to use perspective-taking processes to imagine or project

into the place of the other in order to understand what she/he is feeling. This aspect of empathy is closely related to processes involved in mental state attribution (also known as theory of mind), which requires executive functions such as cognitive flexibility, inhibitory control, and working memory (Decety and Jackson, 2004; Stone and Gerrans, 2006). While relatively little is known about whether children who have a strong grasp of mental states also are advanced in their understanding of emotions, emotion understanding and mental state understanding seem to engage common, as well as distinct, computational processes. When seeing another child who is upset, a child has to hold two different perspectives in mind in order to correctly identify what that child is feeling and comfort them and their own perspective (and emotions), which may not be congruent with that of the other child, and the point of view of the other child. There is indeed some evidence for a link between understanding of mental state reasoning and emotion. Several studies have shown that by around 4 years of age, children can appreciate that the emotion a person feels about a given event depends on that person's perception of the event and their beliefs and desires about it. Hughes and Dunn (1998) conducted a longitudinal study of 50 children aged 47–60 months, examining developmental changes in understanding of false belief and emotion and mental state in their conversation with friends. They found that individual differences in understanding of both false belief and emotion were stable over this time period and were significantly related to each other.

Emotion recognition continues to develop into later adolescence (Tonks et al., 2007), which might improve social cognition performance. Social performance as a whole continues to improve into adulthood, but it is unclear if this reflects changes in social cognition *per se* or the continued development of cognitive functions that are not specific to social behavior, such as declarative knowledge, metacognition, speed of processing, and working memory.

Neuroimaging studies that have examined the neural systems engaged during mental state understanding in adults consistently identify a neural network involving the mPFC, the posterior temporal cortex at the junction of the parietal cortex (TPJ), and the temporal poles (e.g., Brunet et al., 2000; Frith and Frith, 2003). These regions were activated in children aged 6–11 years, while they listened to sections of a story describing a character's thoughts compared to sections of the same story that described a physical context (Saxe et al., 2009). Furthermore, change in response selectivity with age was observed in the right TPJ, which was recruited equally for mental and physical facts about people in younger children, but only for mental facts in older children. Further support for age-related changes in brain activity associated with metacognition is provided by a neuroimaging investigation of theory of mind in participants whose age ranged between 9 and 16 years (Moriguchi et al., 2007). Both children and adolescents demonstrated significant activation in the neural circuits associated with mentalizing tasks, including the TPJ, the temporal poles, and the mPFC. Furthermore, the authors found a positive correlation between age and the degree of activation in the dorsal part of the mPFC. Direct evidence for the implication of these regions during accurate identification of interpersonal emotional states was documented in a recent functional magnetic resonance imaging (fMRI) study in which participants were requested to rate how they believe target persons felt while talking about autobiographical emotional events (Zaki et al., 2009).

In sum, the neural circuits implicated in emotion understanding largely overlaps with those involved in ToM processing, especially the mPFC and right TPJ. They continue to undergo maturation until late adolescence.

21.4 EMOTION REGULATION

The regulation of internal emotional states and processes is particularly relevant to the modulation of vicarious emotions and the experience of empathy. Given the shared nature of the representations of one's own emotional states and others' emotional states, it would seem difficult not to experience emotional distress while viewing another's distressed state (while personal distress does not contribute to the empathic concern and prosocial behavior). Personal distress can actually deter one's inclination to soothe another person's distress. It is, therefore, adaptive for this automatic sharing mechanism between self and other to be modulated by cognitive control. To this end, executive functions (i.e., the processes that serve to monitor and control thoughts and actions, including effortful control, planning, cognitive flexibility, and response inhibition; Russell, 1996), work in a top-down fashion to regulate one's inclinations to be biased in one's self-perspective while judging another person's emotional state and promoting a sympathetic regard for the other, rather than a desire to escape aversive arousal (Decety, 2005). Difficulty in the ability to regulate emotions can result in deleterious emotional arousal, thereby hindering the ability to socially function adaptively and appropriately.

Although research on emotion regulation has increased rapidly in the past decade, definitions of emotion regulation have typically been implied and not stated. While researchers agree that the construct of emotion regulation involves both emotion as a *behavior regulator* and emotion as a *regulated phenomenon*, the authors

emphasize the latter – that is, how one attempts to regulate emotion – and examine various regulatory processes. As an example, Thomson (1994) defined emotion regulation as the extrinsic and intrinsic processes responsible for monitoring, evaluating, and modifying emotional reactions especially their intensive and temporal features, to accomplish one's goals.

Sympathy is strongly related to effortful control, with children high in effortful control showing greater empathic concern (Rothbart et al., 1994). A number of developmental studies conducted by Eisenberg and her colleagues (1994) found that individual differences in the tendency to experience sympathy versus personal distress vary as a function of dispositional differences in individuals' abilities to regulate their emotions. Well-regulated children who have control over their ability to focus and shift attention have been found to be relatively prone to sympathy regardless of their emotional reactivity. This is because they can modulate their negative vicarious emotions to maintain an optimal level of emotional arousal. In contrast, children who are unable to regulate their emotions, especially if they are dispositionally prone to intense negative emotions, are found to be low in dispositional sympathy and prone to personal distress (Eisenberg et al., 1994).

Interestingly, the development of executive functions is functionally linked to the development of mental state understanding. There is now increasing evidence of a specific link between the development of mentalizing and improved self-control at around the age of 4 years (Carlson and Moses, 2001). Improvement in inhibitory control corresponds with increasing metacognitive abilities (Zelazo et al., 2004), as well as with maturation of brain regions that underlie working memory and inhibitory control (Tamm et al., 2002). A series of studies by Posner and Rothbart (2000) strongly suggest that executive regulation undergoes dramatic change during the third year of life.

Emotion regulation taps into executive function resources implemented in the prefrontal cortex (Zelazo et al., 2008), with different regions subserving distinct functions. Ventral and dorsal regions of the prefrontal cortex have been associated with response inhibition and self-control, which are both key components of emotion regulation (Ochsner et al., 2002). Support for this hypothesis in the domain of empathy comes from a study that compared the neurohemodynamic response in a group of physicians and a group of matched control participants when they were exposed to short video clips depicting hands and feet being pricked by a needle (painful situations) or being touched by a Q-tip (nonpainful situations; Cheng et al., 2007). Unlike control participants, physicians showed a significantly reduced neurohemodynamic empathic response in the anterior insula, anterior medial cingulate cortex (aMCC), and dorsal anterior cingulate cortex (dACC) and no activation of the periaqueductal gray (PAG; a mediator of the flight-or-fight response) when shown video clips of body parts being pricked by a needle. Instead, cortical regions underpinning executive functions and self-regulation (dorsolateral and mPFC) and executive attention (precentral, superior parietal, and temporoparietal junction) were found to be activated. Connectivity analysis further demonstrated that activation in the medial and dorsolateral prefrontal cortices subserving executive control and self-regulation (Ochsner and Gross, 2005) was inversely correlated with activity in the insular cortex in the physicians, indicating executive suppression of the emotional response to the others' pain.

It is well documented that the prefrontal cortex and its functions follow an extremely protracted developmental course and age-related changes continue well into adolescence (Bunge et al., 2002; Casey et al., 2005; Sowell et al., 1999). Frontal lobe maturation is associated with an increase in a child's ability to activate areas involved in emotional control and exercise inhibitory control over their thoughts, attention, and action. The maturation of the prefrontal cortex also allows children to use verbalizations to achieve self-regulation of their feelings (Diamond, 2002). It is, therefore, likely that different parts of the brain may be differentially involved in empathy at different ages. For example, Killgore et al. (2001) and Killgore and Yurgelun-Todd (2007) provided evidence that as a child matures into adolescence there is a shift in response to emotional events from using more limbic-related anatomic structures, such as the amygdala, to using more frontal lobe regions to control emotional responses. Thus, not only may there be less neural activity related to the regulation of cognition and emotion in younger individuals but the neural pattern itself is likely to differ.

21.5 PERCEIVING OTHER PEOPLE IN DISTRESS

Pain evolved as a protective function by not only warning a person suffering that something is awry but also impelling expressive behaviors that attract the attention of others. It has been argued that the long history of mammalian evolution has shaped maternal brains to be sensitive to signs of suffering in one's own offspring (Haidt and Graham, 2007). In many primates and other social animals, this sensitivity extends beyond the mother–child relationship, so that all typically developed individuals dislike seeing others suffering.

A growing number of functional MRI studies have demonstrated that the same neural circuits involved in the experience of physical pain are also involved in the perception or the imagination of another individual in

pain (Jackson et al., 2006). This neural network includes the supplementary motor area (SMA), cerebellum, dACC, aMCC, and anterior insular cortex. In addition, studies using different modalities of neuroimaging including transcranial magnetic stimulation (Avenanti et al., 2005), somatosensory-evoked potentials (Bufalari et al., 2007), functional MRI (Lamm et al., 2007), and magnetoencephalography (Cheng et al., 2008) indicate that areas processing the sensory dimension of pain (the somatosensory cortex and posterior insula) are also activated by the mere visual perception of others' pain. It is worth mentioning, however, that activation of these regions reflects a general aversive response not specific to nociception (i.e., the neural processing of noxious stimuli). This network of regions underpins a physiological mechanism that mobilizes the organism to react – with heightened arousal and attention – to threatening situations. The dACC plays a key role in conflict monitoring; the aMCC is involved in autonomic regulation associated with processing of fear and anxiety; the anterior insula processes visceral bodily sensations; the PAG integrates physiological changes in response to stress, and in the context of danger, the SMA as a result of feedback from the limbic system represents one anatomical substrate for activating motor responses associated with danger and threats (Decety, 2011; Yamada and Decety, 2009).

Distress, of course, often does not occur in a social vacuum. The social context in which pain occurs influences cognitive appraisal and the neural mechanisms underpinning its perception in the observer. To evaluate whether the neural processing in the pain matrix is modulated by social context, a study that compared patterns of brain activation while adult participants observed painful situations occurring by accident and painful situations intentionally caused by another individual (Akitsuki and Decety, 2009). Since pain is the result of a type of social interaction in the latter situation, its recognition is likely to involve not only the perception of pain but also the cognitive evaluation of the social interaction.

Results show that attending to painful situations caused by accident is associated with activation of the pain matrix, including the aMCC, insula, PAG, and somatosensory cortex. Interestingly, when watching another person intentionally inflicting pain onto another, regions that are consistently engaged in mental state understanding and affective evaluation (mPFC, TPJ, OFC, and amygdala) were additionally recruited. Furthermore, stronger connectivity between the left amygdala and the vmPFC was found when participants perceived painful situations caused by another individual relative to situations where pain occurred accidentally. These data demonstrate the impact of social context on the neural response to the perception of others' pain. Similar data were obtained with a group of young children (Decety et al., 2008) and adolescents (Decety et al., 2009). When watching sympathy-eliciting stimuli, increased effective connectivity was found between regions of the mPFC and the frontoparietal supramodal attention network, as well as between the right TPJ and the mPFC.

21.6 NEURODEVELOPMENTAL CHANGES IN EMPATHIC RESPONDING

One limitation of these above-mentioned studies is that they cannot capture any continuous functional changes across age. This is unfortunate because among areas of the brain undergoing considerable remodeling from childhood to adolescence is the prefrontal cortex, both dorsal and ventromedial, which plays a key role in understanding and experiencing social emotions (Kringelbach and Rolls, 2004; Shamay-Tsoory et al., 2006). Furthermore, both the insula and the amygdala may differentially contribute to the experience of interpersonal sensitivity during development. While human neuroimaging studies using pain empathy paradigms all report activations in the insula, no systematic attention has been paid to the anatomical subdivisions of the insula, particularly regarding their respective functional contribution across age.

To examine age-related changes associated with empathy and sympathy, functional MRI and behavioral data were collected from a group of 57 participants ranging from 7 to 40 years of age (Decety and Michalska, 2010). Results at the whole group level showed that attending to accidentally caused painful situations was associated with activation of the pain matrix, including the aMCC, insula, PAG, and somatosensory cortex. Interestingly, when watching one person intentionally inflicting pain onto another, regions that are consistently engaged in mental state understanding and affective evaluation (mPFC, TPJ, and OFC) were also recruited. The younger the participants, the more strongly the amygdala, posterior insula, and SMA were recruited when they watched painful situations that were accidentally caused. While participants' subjective ratings of the painful situations decreased with age and were significantly correlated with hemodynamic response in the mPFC, increases in pain ratings were correlated with bilateral amygdala activation (Figure 21.2).

A significant negative correlation between age and degree of activation was found in the posterior insula. In contrast, a positive correlation was found in the anterior portion of the insula. A posterior-to-anterior progression of increasingly complex rerepresentations in the human insula is thought to provide a foundation for the sequential integration of the individual homeostatic

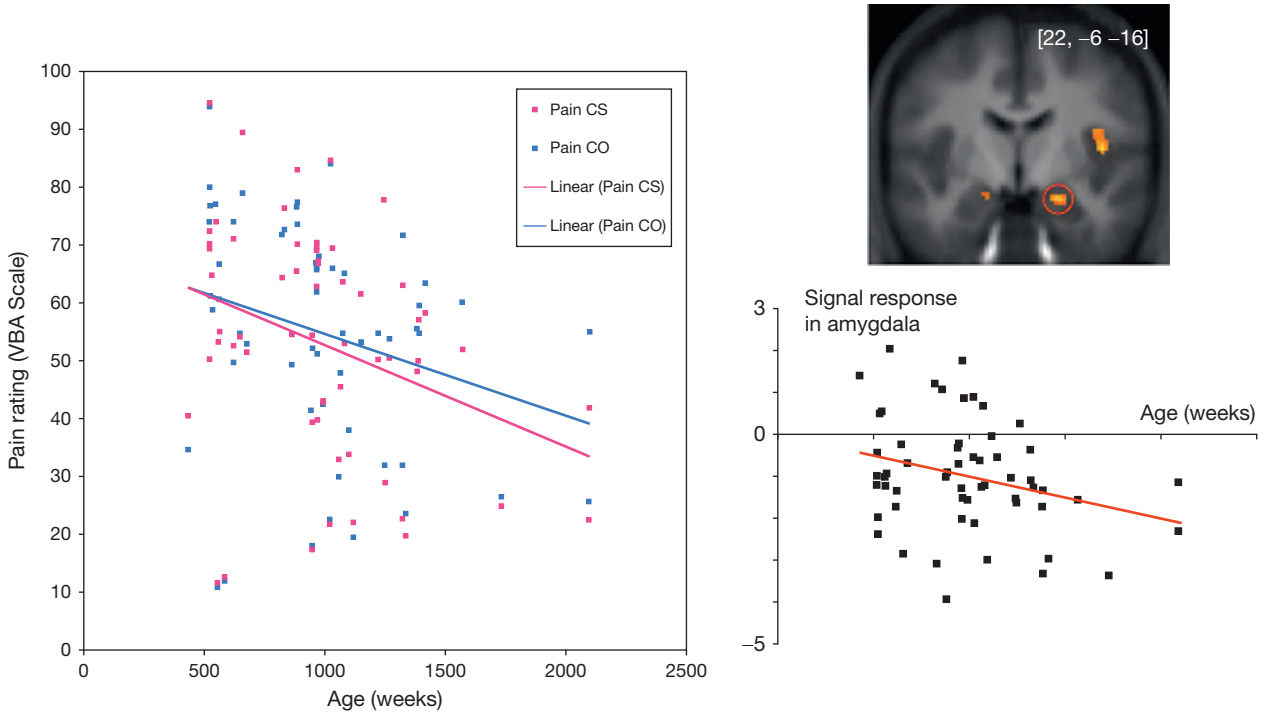

FIGURE 21.2 Left: Subjective ratings to dynamic visual stimuli depicting painful situations accidentally caused by self (Pain CS) and painful situations intentionally caused by another individual (Pain CO) across age (in weeks) in 57 participants (from 7 to 40 years old). A gradual decrease in the subjective evaluation of pain intensity for both painful conditions was found across age, with younger participants rating them significantly more painful than older participants (for Pain CS $r = -0.327$, $p < 0.01$; for Pain CO $r = -0.267$, $p < 0.05$). Further, while on an average participants rated the pain caused intentionally (Pain CO) conditions as significantly more painful than when pain was accidentally caused by self (Pain CS; $t(56) = 2.581$, $p < 0.01$), this effect was not driven by age. Right: Significant negative correlation between age and degree of activation in the amygdala when the participants are exposed to painful situations accidentally caused. *Adapted from Decety J and Michalska KJ (2010) Neurodevelopmental changes in the circuits underlying empathy and sympathy from childhood to adulthood.* Developmental Science *13: 886–899.*

condition with one's sensory environment and motivational condition (Craig, 2004). The posterior insula receives inputs from the ventromedial nucleus of the thalamus that is highly specialized to convey emotional and homeostatic information such as pain, temperature, hunger, thirst, itch, and cardiorespiratory activity. It serves as a primary sensory cortex for each of these distinct interoceptive feelings from the body. The posterior part has been shown to be associated with interoception, due to its intimate connections with amygdala, hypothalamus, and cingulate and orbitofrontal cortices (Jackson et al., 2006). It has been proposed that the right anterior insula serves to compute a higher-order metarepresentation of the primary interoceptive activity, which is related to the feeling of pain and its emotional awareness (Craig, 2003).

Results from this study also showed that activation in the OFC in response to sympathy-eliciting stimuli shifts from the engagement of the medial portion in young participants to the lateral portion in older participants. The medial OFC appears integral in guiding visceral and motor responses, whereas lateral OFC integrates the external sensory features of a stimulus with its impact on the homeostatic state of the body (Hurliman et al., 2005). Greater signal change with increasing age was associated with prefrontal regions that are responsible for cognitive control and response inhibition, such as the dorsolateral prefrontal cortex (dlPFC) and the inferior frontal gyrus (IFG). Indeed, the older the participants the greater the activity in the dlPFC and IFG, which are involved in cognitive control and response inhibition (Kawashima et al., 1996; Swick et al., 2008). This is in line with evidence that regulatory mechanisms continue into late adolescence and early adulthood.

Overall, this pattern in the amygdala and insula can be interpreted in terms of the frontalization of inhibitory capacity, hypothesized to provide a greater top-down modulation of activity within more primitive emotion-processing regions (Yurgelun-Todd, 2007). This finding provides neurophysiological support for developmental studies showing that emotion regulation is an important aspect of empathy and sympathy, especially in relation with prosocial behavior. Indeed, this pattern of developmental change in the OFC appears to reflect a gradual shift between the monitoring of somatovisceral responses in young children, mediated by the medial aspect of the

OFC, and the executive control of emotion processing implemented by its lateral portion in older participants.

In light of these neurophysiological considerations, the authors posited that the anatomical progression (from sensory to emotional awareness) parallels the neurodevelopmental response to seeing people in pain or distress. In other words, a visceral response to painful stimuli associated with danger and negative affect is less likely to occur with increasing age and such a response may be replaced by a more detached appraisal of the stimulus. This was indeed confirmed by having participants rate the pain of the people in the clips outside of the scanner. It was found that on an average, all participants rated the pain caused intentionally conditions as significantly more painful than when pain was caused accidentally by the self. Interestingly, the results also indicated a gradual decrease in the subjective evaluation of pain intensity for both these conditions across age, with younger participants rating them as significantly more painful than older participants. Moreover, while decreases in pain evaluation were significantly correlated with hemodynamic response in the mPFC, increases in pain ratings were correlated with bilateral amygdala and somatosensory cortex activation. These behavioral results are important for interpreting region-specific differences in activation with age as reflecting functional maturation and not simply differences in performance.

In sum, the behavioral evaluations of pain intensity and the pattern of brain activation from childhood to adulthood reflect a gradual change from a visceral emotional response critical for the analysis of the affective significance of stimuli to a more evaluative function.

21.7 ATYPICAL EMPATHIC PROCESSING IN CHILDREN WITH ANTISOCIAL BEHAVIORAL DISORDERS

Children and adolescents diagnosed with antisocial behavioral disorders are marked by lack of regard for others, inability to feel remorse, and even a derivation of pleasure from the distress of others. It has been hypothesized that empathy and sympathetic concern for others are essential factors inhibiting aggression toward others (Eisenberg, 2005; Zahn-Waxler et al., 1995). That is, if a person vicariously experiences the distress that they have caused to others because of their aggression, they will be less likely to continue to hurt others and more likely to help them. Conversely, lack of sympathy is an important risk factor for antisocial behavior problems such as CD (Lahey and Waldman, 2003). The propensity for aggressive behavior has been thought to reflect a blunted empathic response to the suffering of others (Blair and Blair, 2009) and may be a consequence of a failure to be aroused by others' distress (Raine, 1997). It has also been suggested that aggressive behavior can arise from abnormal processing of affective information, resulting in a deficiency in experiencing fear, empathy, and guilt, which in normally developing individuals, inhibits acting out violent impulses (Davidson et al., 2000).

Another hypothesis regarding the relation between affect and aggression can be drawn from the research with animal models and psychiatric populations, which indicates that there may in fact be no blunting of the emotional response toward the other. Rather, heightened emotional reactivity, potentially coupled with diminished regulatory processes may trigger aggressive impulses (Coccaro et al., 2007). This emotional reaction can have either a negative or a positive valence. Previous work has shown that negative affect is generally positively associated with aggression, suggesting that empathic mimicry in conjunction with poor emotion regulation might produce negative affect that increases aggression. For instance, there are numerous empirical studies that document that physical pain often instigates aggressive inclinations (Berkowitz, 1993). The role of heightened negative emotional arousal in antisocial boys, including callous disregard for victims in distress (either caused or observed by aggressive youth) has been examined in young children with normative, subclinical, or clinical levels of behavior problems (Hastings et al., 2000). Results showed that this process can develop early. Boys (but not girls) with clinical levels of aggressive/disruptive problems showed more callous disregard toward victims during simulated distresses than typically developing children (at 4–5 years and again at 7 years). Despite this, 4- to 5-year-old children with clinical problems also showed as much empathic concern as controls at ages of 4–5 years. But by 7 years of age, the clinical group was less empathic than controls according to parent, teacher, and child reports, as well as when observed in the laboratory. Thus, early emotional negativity/callous disregard may have long-term adverse effects.

A recent study by Cheng et al. (2012) found that incarcerated juvenile psychopaths who scored high callous–unemotional traits, compared to participants with low callous–unemotional traits exhibited a reduced frontal N120 (measured with ERPs) in response to visual stimuli depicting people in pain, indicating an absence of early affective arousal. However, there was no deficit in sensorimotor resonance in both groups, as assessed by measures of the *mu* suppression over the sensorimotor cortex, which is considered as a reliable index of the mirror neuron system. This finding indicates that affective arousal is not mediated by the mirror neuron system.

In an fMRI study by Decety et al. (2009), two groups of 16–18-year-olds (matched on age, sex, and race–ethnicity) were scanned using the same animated stimuli and procedures as used with normally developing

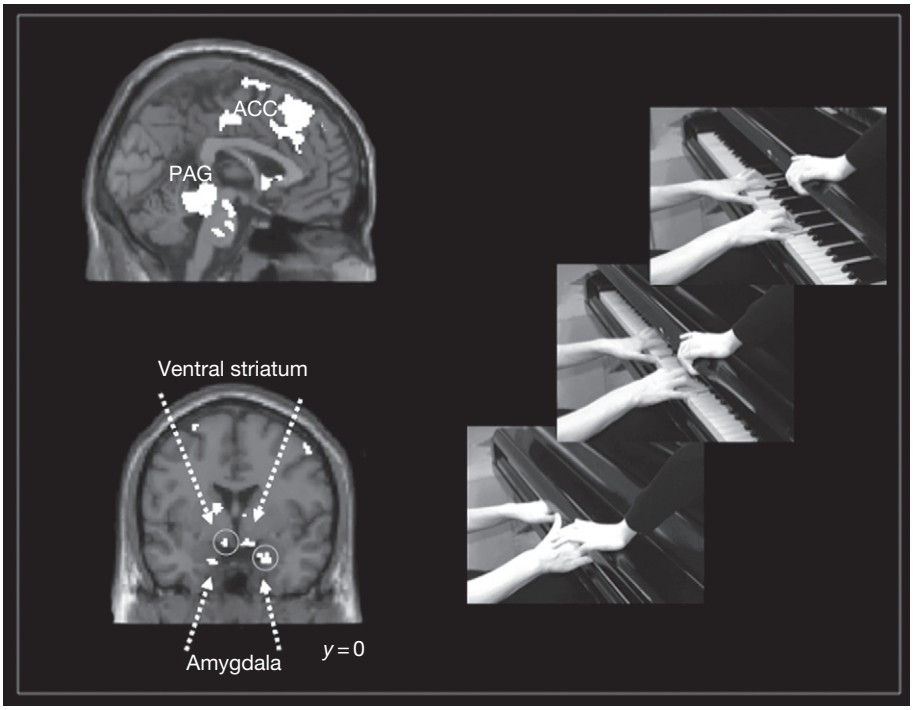

FIGURE 21.3 When youth with aggressive conduct disorder (CD) watch an individual intentionally hurting another (such as closing a piano lid), regions of the brain that process nociceptive information were activated (anterior insula, dorsal and ventral ACC, somatosensory cortex, and PAG), as well as the amygdala and ventral striatum which are part of the neural circuit involved in reward processing. These latter regions were not engaged in healthy control adolescents. Dispositional ratings of daring and sadism in youth with CD correlated with amygdala and striatal response ($p < 0.005$). These adolescents seem to enjoy seeing people in pain, and this may be rewarding and lead to repeated aggression. *Adapted from Decety J, Michalska KJ, Akitsuki Y, and Lahey B (2009) Atypical empathic responses in adolescents with aggressive conduct disorder: A functional MRI investigation.* Biological Psychology *80: 203–211.*

children (Decety et al., 2008, 2010). Results showed that the pain matrix (anterior insula, aMCC, and PAG) was significantly activated in both groups when viewing others in pain, but there was significantly greater activation of the pain matrix and somatosensory cortex in adolescents with CD than in non-CD controls (Figure 21.3).

This suggests that youth with CD do not fail to respond to viewing pain in others. Indeed, this somatic sensorimotor resonance was significantly greater in participants with CD than those without CD. In addition, there was significantly greater activation of the temporal pole in youth with CD than in controls. The temporal pole is part of a system that modulates visceral responses to emotionally evocative stimuli, and electrical stimulation of the TP produces increases in heart rate, respiration, and blood pressure (Gloor et al., 1982). In addition, the temporal poles are tightly connected with the limbic system and project to the hypothalamus, a neuromodulatory region important for autonomic regulation. There is evidence that the temporal pole is involved in the processing of both positive and negative affects (Olson et al., 2007).

Furthermore, adolescents with CD exhibited significantly greater activation of both the amygdala and the ventral striatum when viewing others in pain versus others not in pain. It was also observed that in participants with CD, the extent of amygdala activation to viewing pain in others was positively correlated with their number of aggressive acts and their ratings of daring and sadism scores on the child and adolescent dispositions scale (CADS). This is consistent with greater affective response in youth with CD to viewing others in pain.

What these findings suggest is that individuals with CD actually react to viewing pain in others at least similarly or possibly to a greater extent in some important brain regions than youth without CD, especially in the insula, amygdala, and aMCC. This stands in contrast with one previous fMRI study that reported reduced amygdala response in youth with CD during the viewing of pictures with negative emotional valence (Marsh et al., 2008). The study by Decety and colleagues suggests that youth with CD do not exhibit reduced amygdala response to all negatively valenced stimuli; indeed, they appear to exhibit enhanced response to images of people in pain, including a specific activation of the ventral striatum.

Different patterns of response were detected in the OFC across the two groups. While the lateral OFC was selectively activated in control participants when observing pain inflicted by another, activation of the medial OFC was found in the participants with CD. A direct comparison between the groups confirmed this finding. The OFC/mPFC has been specifically implicated in a variety of areas relevant to CD and aggression, including the regulation of negative affect (Phan et al., 2005). Importantly, functional connectivity analyses demonstrated significantly greater amygdala/PFC coupling when watching pain being intentionally caused by another individual in the control group than those

in the CD group. In particular, in healthy adolescents, left amygdala activity covaried with activity in the prefrontal cortex to a greater extent while watching situations of pain being intentionally caused compared to viewing accidentally caused pain. Adolescents with CD showed no significant functional connectivity between frontal regions and the amygdala.

These findings are consistent with at least two hypotheses that are currently being investigated with younger children who meet diagnosis for CD:

- The first hypothesis is that highly aggressive antisocial youth enjoy seeing their victims in pain and, because of their diminished PFC/amygdala connectivity, may not effectively regulate positively reinforced aggressive behavior. The amygdala is involved in the processing of more than just negative affect. Several studies point to a role for the amygdala in positive affect, and its coupling with the striatum enables a general arousing effect of reward (Murray, 2007). It is possible, therefore, that the robust hemodynamic response in the amygdala to viewing others in pain in youth with aggressive CD reflects a positive affective response (e.g., 'enjoyment' or 'excitement'). The finding that CADS ratings of daring items (which reflect enjoyment of novel and risky situations) and sadism items (which reflect enjoyment of hurting others or viewing people or animals being hurt) correlated positively with amygdala response in youth with CD is in line with this hypothesis. In addition, this interpretation is consistent with the significant activation among youth with aggressive CD of the ventral striatum, which is part of the system implicated in reward and pleasure, among other things.
- The second hypothesis is that youth with CD have a lower threshold for responding to many situations with negative affect, including viewing pain in others, and are less able to regulate these negative emotions through cortical processes. Many studies indicate that individuals with CD tend to respond to aversive stimuli with greater negative affect than most other youth (Lahey and Waldman, 2003). This is potentially important as their negative affect may increase the likelihood of aggression, especially in the absence of effective emotion regulation (Berkowitz, 2003). This interpretation fits well with the hypothesis of a dysfunction in the neural circuitry of emotion regulation (Davidson et al., 2000) and is consistent with the analyses of effective PFC/amygdala connectivity. Aggression may be related to instability of negative affect and poor impulse control (Raine, 2002). Children with aggressive behavior problems have difficulties regulating negative emotions, which may result in harmful patterns of interpersonal behavior. Often triggered by hypersensitivity to specific stimuli, aggressive adults experience escalating agitation followed by an abrupt outburst of aggressive and threatening behavior (Gollan et al., 2005). Failure to discriminate between pain to others and to oneself may further lead to negative emotion when viewing others in pain. Research with nonhumans demonstrates that physical pain often elicits aggression (Berkowitz, 2003). It has been hypothesized that aggressive persons are disposed to experience negative affect (Lahey and Waldman, 2003). This suggests that in certain situations, empathic mimicry might produce high levels of distress in youth predisposed to be aggressive that, ironically, increases their aggression. It is possible that strong activation of neural circuits that underpin actual pain processing is associated with negative affect in youth with CD. This, in conjunction with reduced activation in areas associated with emotion regulation, could result in a dysregulated negative affective state, which may instigate aggression under some circumstances. For example, youth with CD who see an injured friend (or fellow member of a gang) may be more likely to respond aggressively than other youth for this reason. Finally, the strong and specific activation of the amygdala and ventral striatum in the aggressive adolescents with CD during the perception of pain in others is an important and intriguing finding, which necessitates additional research in order to understand the relative roles of negative and positive affect when viewing others in pain in aggression and empathic dysfunction.

Overall, youth with aggressive CD show atypical patterns of hemodynamic response and effective connectivity in regions that regulate emotion when exposed to the distress of others, as well as reward-related activation. More work is needed to disambiguate how such abnormal emotional processing is associated with callous disregard for others, insensitivity to their distress, or even enjoyment that may lead to rewarding offending behavior.

21.8 CONCLUSION

Empathy and sympathy develop as a result of complex biological and psychological processes involving emotion sharing, emotional regulation, mental state understanding, and cognitive abilities that are continuously interactive between the individual and the social environment. Empathy can be viewed as both intrapersonal and interpersonal processes. Breaking down empathy and related phenomena into components and

examining their neurodevelopment can contribute to a more complete model of interpersonal sensitivity. Likewise, drawing from multiple sources of data can improve one's understanding of the nature and causes of empathy deficits in individuals with antisocial behavior disorders. Recent advances in cognitive neuroscience indicate that distinct but interacting brain circuits underpin the different components of empathy, each having their own developmental trajectory.

One important direction for future research is investigating the functional link between empathy, prosocial behavior, and reward. Several studies have documented that the frontomesolimbic reward network is engaged to the same extent when individuals receive monetary rewards and when they freely choose to donate money to charity, and even more so when they are observed by others, suggesting that altruism draws on general mammalian neural systems of reward and social attachment (e.g., Izuma et al., 2010; Moll et al., 2006). Thus, prosocial behaviors may stem from a plurality of motives and intertwined social and motivational contingencies. For instance, witnessing people in pain or distress triggers a neural response associated with aversion. This response, in turn, may initiate helping or soothing behaviors motivated to both reduce one's own discomfort and to feel good about oneself, as well as to lessen another's distress. These behaviors may be reinforced by both endogenous reward (dopamine system) and positive social feedback from others.

Given the importance of empathy for healthy social interaction, it is clear that a developmental approach using functional neuroimaging to elucidate the computational mechanisms underlying affective reactivity, regulation and behavioral outcomes is essential to complement traditional behavioral methods and gain a better understanding of how deficits may arise in the context of development.

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