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Emotion Understanding in Developmental Disorders
What Can Neuroscience Teach Us?

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Abstract: Empathy is thought to play a key role in motivating helping behavior and providing the affective basis for moral development. Neuroimaging studies clearly document that watching someone in pain elicits a negative arousal response in the observer to a stronger degree in children than in young adults. Findings indicate that although children and adults have similar patterns of brain response to perceiving other people in pain, there are important changes in the functional organization in the neural structures implicated in empathy and sympathy that occur over an extended period from childhood through adulthood.

Keywords: Emotion sharing; moral development; empathy; disorder, developmental; distress; neuroatanomy, fuctional; neuroimaging.

Emotion understanding has many facets. Emotional empathy—the ability to recognize, share, and make inferences about another person's emotional state—is one form of emotion understanding that is fundamental to meaningful social interactions. Responses related to emotional empathy, such as feelings of sympathy and concern, motivate prosocial behavior, inhibit aggression and enable moral reasoning. Conversely, certain developmental disorders, such as conduct disorder (CD), are characterized by deficits in emotional empathy, which likely influence antisocial responses and violent behavior toward others. Over the last two decades, neuroscientists have devoted a large and growing amount of attention to the neural basis of emotional empathy and to deviations from normative emotional responding in the brain. Much can be learned about developmental disorders like CD from the progress that has been made in this domain. Specifically, there are insights into perturbations in emotion understanding that we can glean from work in neuroscience that is not readily available from other measures. The use of neural indices, in addition to the more traditional self-report indices, allows to address questions of clinical and developmental interest.

Based on empirical findings from psychology and cognitive neuroscience, a number of components contribute to the experience of empathy: (i) experience sharing: vicariously sharing the internal states of another, (ii) perspective taking: explicitly considering (and possibly understanding) the others' states and their sources, and (iii) prosocial concern: expressing motivation to improve others' experiences. The vast majority of empirical research on the neuroscience of empathy has focused on characterizing the first two subprocesses: experience sharing and perspective taking. Given that they each represent two routes to the same ultimate goal (that is, understanding and responding to another person's internal states), they are thought to be subserved by surprisingly distinct neural systems.[1] Experience sharing is often associated with a mechanism known as "neural resonance," which is a perceivers' tendency to engage overlapping neural systems when they experience a given internal state and when they observe another person experiencing that same state. Neural resonance is thought to accompany the experience and observation of actions like motor intentions, as well as visceral states such as pain.[2] By contrast, perspective taking, usually observed by asking a person to draw explicit inferences about another's emotional states—engages a system of midline and superior temporal structures that are generally involved in "self-projection": the ability to represent states outside of one's present moment, including the past, the future, and the perspective of another person.

Until relatively recently, the neural activity underpinning these two processes appeared almost entirely non-overlapping. In other words, tasks and social stimuli that engaged one of these systems typically did not concurrently engage the other system.[3] Moreover, lesions to areas in each of these neural systems have been shown to produce dissociable impairments in experience sharing and perspective taking.[4] Together, such findings supported the claim that these two processes are fundamentally dissociable routes to empathy. However, recent cognitive neuroscience research indicates that rather than being engaged in isolation, neural systems that are involved in experience sharing and perspective taking commonly co-activate when an observer encounters complex social cues, such as people engaging others in live joint attention tasks.[5] Researchers also note that although studies of experience sharing and perspective taking clearly draw upon dissociable neural networks, the fact that these studies tend to rely on different stimulus types and task demands (i.e. passively viewing others in pain vs. explicit, active inferences about others) complicates the interpretation of their observed neural distinction. In other words, dissociations between these neural systems could either reflect a separation between the two empathic subprocesses, or they could reflect less interesting variation in the types of stimuli exposed to perceivers (*NEP*).

To provide some background and with these caveats in mind, each of the components of empathy (experience sharing, perspective taking) is described here separately from both a developmental and a neuroscience perspective, followed by a review of recent research with atypical populations.

Experience Sharing

While there is some disagreement about the nature of empathic responding in very young children, there is considerable evidence demonstrating that the affective component of empathy develops earlier than the cognitive component. Many aspects of experience sharing are present at an early age and thought to rely on involuntary processes like mimicry and neural resonance.[6] A general consensus is that infants are sensitive and responsive to the emotional cues of others and that some of the basic building blocks of emotional empathy, like emotion sharing, are already present in the first days of life. For example, discrete facial expressions of emotion have been observed in newborns, including joy, interest, disgust and distress,[7] which suggests that subcomponents of

1 Jamil Zaki and Kevin N. Ochsner, "The Neuroscience of Empathy: Progress, Pitfalls and Promise," *Nature Neuroscience* 15/5 (2012), 675-680. [Henceforth refered to as *NEP*]

2 Claus Lamm and Tania Singer, "The Role of Anterior Insular Cortex in Social Emotions," *Brain Structure & Function* 214/5-6 (June 2010), 579-591.

3 Frank Van Overwalle and Kris Baetens, "Understanding Others' Actions and Goals by Mirror and Mentalizing Systems: A Meta-Analysis," *NeuroImage* 48/3 (November 2009), 564-584.

4 Simone G. Shamay-Tsoory, Yasmin Tibi-Elhanany, Judith Aharon-Peretz, "The Ventromedial Prefrontal Cortex Is Involved In Understanding Affective But Not Cognitive Theory Of Mind Stories," *Social Neuroscience* 1/3-4 (2006), 149-166.

5 See Elizabeth Redcay, David Dodell-Feder, Mark J. Pearrow, Penelope L. Mavros, Mario Kleiner, John D. E. Gabrieli, Rebecca Saxe, "Live Face-to-Face Interaction during fMRI: A New Tool for Social Cognitive Neuroscience," *NeuroImage* 50/4 (May 2010), 1639-1647.

6 Jean Decety and Meghan Meyer, "From Emotion Resonance To Empathic Understanding: A Social Developmental Neuroscience Account," *Development and Psychopathology* 20/4 (Fall 2008), 1053-1080.

7 Carroll E. Izard and Peter B. Read, eds, *Measuring Emotions in Infants and Children*, Cambridge: Cambridge University Press, 1982-1986.

mature emotional experience and expression might already be present very early on. Infants are able to both send emotional signals and detect emotional signals communicated by others around them. Human newborns are capable of imitating expressions of fear, sadness, and surprise,[8] thus preparing them for later emotional empathic responses through interaction with others. Moreover, both human infants and nonhuman infant primates are known to respond to the distress of others with distress. Infants who hear newborn cries cry significantly more often than those who listen to silence and those who hear simulations of a newborn's cry.[9] It appears that from early on in development, infants are capable of emotional resonance.[10] However, while the capacity for two people to resonate with each other emotionally might form the basis for developing shared emotional experiences, it is not enough for mature empathic understanding. Such an understanding requires forming an explicit representation of the feelings of another person, which requires additional computational mechanisms above and beyond the emotion sharing level.[11] The cognitive components that give way to such empathic understanding have a more protracted course of development than the affective components, even though some precursors are already in place early in life.

Perspective Taking

Perspective taking refers to explicitly considering and potentially understanding the others' emotional states and their sources. Such consideration includes the knowledge of one's own and others' emotions and the acknowledgement that these may not be aligned. Children's development of such understanding of emotion fosters many adaptive processes, like peer relationships and prosocial behavior. Consequently, delayed or compromised emotion understanding may place youth at risk for developmental disorders, such as autism spectrum disorder (ASD) or conduct disorder (CD). The individual uses perspective-taking processes to project themselves into the shoes of the other in order to understand what they are feeling. This aspect of empathy appears to require what is called "executive functions," including cognitive flexibility, inhibitory control and working memory.[12] For example, when seeing another child in distress, a child has to hold two different perspectives in mind in order to correctly identify what the other child is feeling and potentially comfort it—their own perspective, which may not be congruent with that of the other child (such as, being in a state of happiness), and the point of view of the other child (who might be in distress). Several studies have shown that, by approximately 4 years of age, children can appreciate that the emotion a person feels about a given event depends upon that person's perception of the event, as well as that person's beliefs about it.[13]

Functional magnetic resonance imaging (fMRI) studies investigating the neural processes that are engaged during perspective-taking in adults have consistently identified a neural network involving the medial prefrontal cortex (MPFC), the posterior superior temporal cortex at the junction of the parietal cortex (pSTS/TPJ), and the temporal poles.[14] Support for age-related changes in neural activity associated with perspective taking comes from a neuroimaging investigation of "theory of mind," or false belief

[8] Jeannette M. Haviland and Mary Lelwica, "The Induced Affect Response: 10-Week-Old Infants' Responses to Three Emotion Expressions," *Developmental Psychology* 23/1 (1987), 97-104.

[9] Abraham Sagi and Martin L. Hoffman, "Empathic Distress in the Newborn," *Developmental Psychology* 12/2 (1976), 175-176; and Marci Dondi, Francesca Simion, Giovanna Caltran, "Can Newborns Discriminate Between Their Own Cry And The Cry Of Another Newborn Infant?" *Developmental Psychology* 35/2 (1999), 418-426.

[10] Martin L. Hoffman, *Empathy And Moral Development: Implications For Caring And Justice*, New York: Cambridge University Press, 2000.

[11] Jean Decety, Kalina J. Michalska, Yuko Akitsuki, "Who Caused The Pain? An fMRI Investigation Of Empathy And Intentionality In Children," *Neuropsychologia* 46/11 (2008), 2607-2614.

[12] Valerie E. Stone and Philip Gerrans, "What's Domain-Specific About Theory Of Mind?" *Social Neuroscience* 1/3-4 (2006), 309-319.

[13] Claire Hughes and Judy Dunn, "Understanding Mind And Emotion: Longitudinal Associations With Mental-State Talk Between Young Friends," *Developmental Psychology* 34/5 (1998), 1026-1037.

[14] Utah Frith and Christopher D. Frith, "Development And Neurophysiology Of Mentalizing," *Philosophical Transactions of the Royal Society B* 358/1431 (March 2003), 459-473.

reasoning, in 9 to 16 year old youth.[15] Children as well as adolescents exhibited activation in the neural circuits associated with perspective taking tasks, including the TPJ, the temporal poles, and the MPFC. Furthermore, a positive correlation was observed between age and the degree of activation in the dorsal part of the MPFC.

Regulating one's visceral states and emotions is especially important for the expression of vicarious emotion and the experience of emotional empathy. As discussed above, emotion sharing involves an affective response that is congruent with what the observed other is feeling, which may motivate helping behavior. But emotion sharing may also give rise to negative reaction in the form of personal distress.[16] For instance, when I witness a person who is cringing in pain, I might be incited to empathize with and help that person, but I might also be very upset at seeing him hurt and just want to avoid the situation altogether. Not only does personal distress not always contribute to helping behavior, but it can also inhibit one's inclination to soothe the person's distress.[17] It is therefore adaptive if the neural resonance between self and other is curbed by cognitive control. Executive functions—the processes that control thoughts and actions, such as effortful control, flexibility and response inhibition[18]—work to regulate our predisposition to be self-focused while appraising another persons' emotional states, and promoting a sympathy for the other, rather than a desire to escape one's aversive feelings.[19]

Sympathy is strongly related to emotion regulation, or effortful control, with children high in effortful control showing greater sympathy.[20] A number of developmental studies conducted by Nancy Eisenberg and her colleagues 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 override their negative vicarious emotions and sustain a more optimal level of arousal. Conversely, children who are unable to regulate their emotions, particularly if they are dispositionally irritabile, have been observed to be low in dispositional sympathy and prone to personal distress.[21]

Improvement in emotional regulation corresponds with increasing cognitive abilities,[22] as well as with maturation of brain regions which underlie working memory and inhibitory control.[23] Emotion regulation abilities are largely instantiated in the prefrontal cortex (PFC),[24] with various subcomponents subserving

[15] Yoshiya Moriguchi, Takashi Ohnishi, Takeyuki Mori, Hiroshi Matsuda, Gen Komaki, "Changes Of Brain Activity In The Neural Substrates For Theory Of Mind In Childhood And Adolescence," *Psychiatry and Clinical Neuroscience* 61/4 (2007), 355-363.

[16] Mark H. Davis, "The Effects of Dispositional Empathy on Emotional Reactions and Helping: A Multidimensional Approach," *Journal of Personality* 51/2 (June 1983), 167-184.

[17] Nancy Eisenberg and Natalie D. Eggum, "Empathic Responding: Sympathy and Personal Distress," in *The Social Neuroscience of Empathy*, eds. Jean Decety and William J. Ickes, Cambridge: MIT Press 2009, pp. 71-83.

[18] James Russell, *Agency and its Role in Mental Development*, Hove, East Sussex: Erlbaum (UK) Taylor & Francis, 1996.

[19] Jean Decety, "Perspective Taking as the Royal Avenue to Empathy," in *Other Minds: How Humans Bridge the Divide between Self and Others*, eds. Bertram F. Malle and Sara D. Hodges, New York: Guilford Press 2005, pp. 135-49.

[20] Mary K. Rothbart, Stephan A. Ahadi, Karen L. Hershey, "Temperament and Social Behavior in Childhood," *Merrill-Palmer Quarterly* 40/1 (1994), 21-39.

[21] Nancy Eisenberg et al., "The Relations of Emotionality and Regulation to Dispositional and Situational Empathy-Related Responding," *Journal of Personality and Social Psychology*, 66/4 (April 1994), 776-797.

[22] Philip D. Zelazo, Fergus I. M. Craik, Laura Booth, "Executive Function Across the Life Span," *Acta Psychologica* 115/2-3 (Feb-Mar 2004), 167-183.

[23] Leanne Tamm, Vinod Menon, Allan L. Reiss, "Maturation of Brain Function Associated with Response Inhibition," *Journal of American Children and Adolescent Psychiatry* 41/10 (October 2002), 1231-1238.

[24] Philip D. Zelazo, Stephanie M. Carlson, Amanda Kesek, "The Development of Executive Function in Childhood," in *Handbook of Developmental Cognitive Neuroscience*, eds. Charles A. Nelson III and Monica L. Collins, Cambridge: MIT Press 2008, pp. 553-74.

distinct functions. Ventral and dorsal regions of the PFC have been associated with response inhibition and self-control, which are both key components of emotion regulation.[25] It is well documented that the PFC follows an extended developmental trajectory, and age related changes continue well into adolescence and early adulthood.[26] Frontal lobe maturation is associated with an increase in a child's ability to exercise inhibitory control over their thoughts, attention, and behaviors. The maturation of the prefrontal cortex also allows children to use explicit language to achieve self-regulation of their feelings.[27] It is therefore likely that different parts of the brain may be differentially involved in empathy at different ages.

Perceiving Other People In Distress

Physical pain warns of potential threat and danger on the one hand, and indexes an opportunity to help the person in pain on the other. The perception of pain in others has been used as a way to investigate the neurophysiological mechanisms that underlie the experience of emotional empathy. One particularly widely used paradigm employs visual stimuli depicting individuals being harmed, and some studies further distinguish intentional and accidental harm.[28] Research with this paradigm in healthy adults and adolescents reveals consistent patterns of activation in a network encompassing sensory regions such as the somatosensory cortex, affective-motivational regions such as the periaqueductan gray (PAG), anterior insula (aINS), medial/anterior cingulate cortex (aMCC), caudate/striatum and amygdala, and regulatory/attention/evaluation regions such as the inferior frontal gyrus (IFG), and ventromedial prefrontal cortex (vmPFC).[29]

Neurodevelopmental Changes In Empathic Responding

One limitation of many of these studies is that they often do not capture any continuous changes across age. As children enter adolescence, levels of empathic concern, personal distress, and helping behavior all change,[30] and neurobiological systems implicated in affective resonance undergo substantial transformation,[31] making this a critical period of development in which to examine these phenomena. Besides the prefrontal cortex, which plays a key role in understanding and regulating social emotions,[32] also the insular cortex, which is critical for the elaboration of visceral states and their contextual regulation, belongs to the areas of the brain undergoing considerable remodeling from childhood to adolescence. The insula receives inputs from incoming fibers that carry information concerning the internal state of the body. Research suggests that the posterior insula codes lower-level basic interoceptive and somatosensory information, and that as one

[25] Kevin N. Ochsner, Silvia A. Bunge, James J. Gross, John D. E. Gabrieli, "Rethinking Feelings: An fMRI Study of Cognitive Regulation of Emotion," *Journal of Cognitive Neuroscience* 14/8 (15 Nov 2002), 1215-1229.

[26] For example, B. J. Casey, Nim Tottenham, Conor Liston, Sarah Durston, "Imaging the Developing Brain: What Have We Learned About Cognitive Development?" *Trends in Cognitive Sciences* 9/3 (2005), 104-110.

[27] Adele Diamond, "Normal Development of Prefrontal Cortex from Birth to Young Adulthood: Cognitive Functions, Anatomy, and Biochemistry," in *Principles of Frontal Lobe Function*, eds. Donald T. Stuss and Robert T. Knight, New York: Oxford University Press 2002, pp. 466-503.

[28] For example, Jean Decety, Laurie Skelly, Kent A. Kiehl, "Brain Response to Empathy-Eliciting Scenarios Involving Pain in Incarcerated Individuals with Psychopathy," *JAMA Psychiatry* 70/6 (June 2013), 638-645.

[29] For example, the meta-analysis in Claus Lamm, Jean Decety, Tania Singer, "Meta-Analytic Evidence for Common and Distinct Neural Networks Associated with Directly Experienced Pain and Empathy for Pain," *NeuroImage* 54/3 (February 2011), 2492-2502.

[30] For example, Nancy Eisenberg, Amanda Cumberland, Ivanna K. Guthrie, Bridget C. Murphy, Stephanie A. Shepard, "Age Changes in Prosocial Responding and Moral Reasoning in Adolescence and Early Adulthood," *Journal of Research on Adolescence* 15/3 (September 2005), 235-260.

[31] Jennifer H. Pfeifer and Sarah-Jayne Blakemore, "Adolescent Social Cognitive and Affective Neuroscience: Past, Present, and Future," *Social Cognitive and Affective Neuroscience* 7/1 (January 2012), 1-10.

[32] Morten L. Kringelbach and Edmund T. Rolls, "The Functional Neuroanatomy of the Human Orbitofrontal Cortex: Evidence from Neuroimaging and Neuropsychology," *Progress in Neurobiology* 72/5 (2004), 341-372.

progresses toward the front, this low-level sensory information is linked with higher level cognitive and affective networks that impart salience and meaning to these basic interoceptive signals.[33] Thus, the posterior insula appears to be a key region for perception of interoceptive feelings, whereas the anterior insula appears to be critical for contextual integration of interoceptive input, association of interoception and emotion, and cognitive regulation of the integrated interoceptive representations. To examine age-related changes associated with empathy and sympathy, we collected MRI and behavioral data from a group of 57 participants ranging from 7 to 40 years of age.[34] 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. Results from this study also showed that activation in the OFC in response to empathy-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. Thus, 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.

Atypical Empathic Processing In Children With Antisocial Behavioral Disorders

Childhood-onset conduct disorder (CD) may lead to serious public health consequences, which impact the child, family, and community.[35] Preliminary studies, for example with functional magnetic resonance (fMRI), are underway to examine the neurological mechanisms underlying CD in this age group.[36] More work is needed, particularly at younger ages and related to sex differences in CD pathophysiology, given already established evidence of sex differences in prevalence and outcomes.[37] Very limited fMRI work has used an emotional empathy task to examine pre-adolescents with CD, and the few available studies of CD in older children focus on male children only.

The propensity for aggressive behavior has been thought to reflect a blunted empathic response to the suffering of others,[38] and may be a consequence of a failure to be aroused by others' distress.[39] It has also been suggested that aggressive behavior can arise from abnormal processing of emotional information, resulting in a deficiency in experiencing fear and empathy, which in typically developing individuals deters the acting out of violent impulses.[40]

Another hypothesis regarding the relation between emotion and aggression states that there may in fact be

[33] See W. Kyle Simmons, Kristina M. Rapuano, John E. Ingeholm, Jason Avery, Seth Kallman, Kevin D. Hall, Alex Martin, "The Ventral Pallidum and Orbitofrontal Cortex Support Food Pleasantness Inferences," *Brain Structure and Function* 219/2 (March 2014), 473-483.

[34] Jean Decety and Kalina J. Michalska, "Neurodevelopmental Changes in the Circuits Underlying Empathy and Sympathy from Childhood to Adulthood," *Developmental Science* 13/6 (November 2010), 886-899. [Henceforth refered to as *NCC*]

[35] Walter Matthys and John E. Lochman, *Oppositional Defiant Disorder and Conduct Disorder in Childhood*, Oxford: Wiley-Blackwell, 2009.

[36] For example, Catherine L. Sebastian, Nathalie M. G. Fontaine, Geoffrey Bird, Sarah-Jayne Blakemore, Stephane A. De Brito, Eamon J. P. McCrory, Essi Viding, "Neural Processing Associated with Cognitive and Affective Theory of Mind in Adolescents and Adults," *Social Cognitive and Affective Neuroscience* 7/1 (2012), 53-63.

[37] For example, Benjamin B. Lahey and Irwin D. Waldman, "A Developmental Propensity Model of the Origins of Conduct Problems during Childhood and Adolescence," in *Causes of Conduct Disorder and Juvenile Delinquency*, eds. Benjamin B. Lahey, Terrie E. Moffitt, Avshalom Caspi, New York: Guilford Press 2003, pp. 76-117. [Henceforth refered to as *CCD*]

[38] R. James R. Blair, "Responding to the Emotions of Others: Dissociating Forms of Empathy through the Study of Typical and Psychiatric Populations," *Consciousness and Cognition* 14/4 (December 2005), 698-718.

[39] Adrian Raine, "Antisocial Behavior and Psychophysiology: A Biosocial Perspective and a Prefrontal Dysfunction Hypothesis," in *Handbook of Antisocial Behavior*, eds. David M. Stoff, James Breiling, and Jack D. Maser, New York: Wiley 1997, pp. 289-304.

[40] Richard J. Davidson, K. M. Putnam, C. L. Larson, "Dysfunction in the Neural Circuitry of Emotion Regulation—A Possible Prelude to Violence," *Science* 289/5479 (July 2000), 591-594.

no blunting of an emotional response towards the other. Rather, heightened emotional reactivity, potentially coupled with diminished regulatory processes may trigger aggressive impulses.[41] This emotional reaction can have either a negative or positive valence. Previous work has shown that negative emotions are sometimes positively associated with aggression, suggesting that emotional empathy together with poor emotion regulation might produce negative emotions that increase, not decrease, aggression. For instance, there are several empirical studies that document that physical pain often prompts aggressive inclinations.[42] Other studies indicate that individuals with CD tend to respond to aversive stimuli with greater negative affect than most other youth (*CCD*). This is potentially important as their negative affect may increase the likelihood of aggression, especially in the absence of effective emotion regulation.[43] This suggests that, in certain situations, empathic resonance might produce high levels of distress in youth predisposed to be aggressive that, ironically, increases their aggression.

If the blunted empathic emotional response hypothesis is correct, children and adolescents with aggressive CD should react less to stimuli depicting others in pain than healthy controls. If the pain-aggression hypothesis is correct, however, youth with aggressive CD should exhibit greater activation than healthy controls in the amygdala, PAG, and related areas in response to stimuli depicting others in pain. Notably, the amygdala is involved in the processing of both negative and positive emotions and its coupling with reward circuitry (i.e. in the striatum) enables a general arousing effect of reward.[44] It is possible, therefore, that the response in the amygdala to viewing others in pain in youth with aggressive CD reflects a positive affective response (for example, enjoyment).

Past neuroimaging research, conducted almost exclusively in male subjects, presents a mixed picture concerning the relationship between CD and emotional empathy, particularly in response to viewing others in pain, being harmed, or in emotional distress. One set of studies reports reduced emotional responsiveness in youth with CD compared to youth without CD, particularly in individuals with elevated callous-unemotional (CU) traits.[45] CU traits are sometimes viewed as early signs of later psychopathy and reflect an important dimension of heterogeneity among children with CP.[46] Another set of studies finds an opposite profile of responses. These studies reported a positive relationship between levels of aggression and affective responses,[47] including a hyper-reactive neural response profile to stimuli depicting of people being harmed[48] and atypically elevated threat-circuitry

[41] Emil F. Coccaro, Michael S. McCloskey, Daniel A. Fitzgerald, K. Luan Phan, "Amygdala and Orbitofrontal Reactivity to Social Threat in Individuals with Impulsive Aggression," *Biological Psychiatry* 62/2 (2007), 168-178.

[42] Leonard Berkowitz, "Pain and Aggression: Some Findings and Implications," *Motivation and Emotion* 17/3 (1993), 277-293.

[43] Leonard Berkowitz, "Affect, Aggression, and Antisocial Behavior," in *Handbook of Affective Sciences*, eds. Richard J. Davidson, Klaus R. Scherer, and H. Hill Goldsmith, New York: Oxford University Press 2003, pp. 804-823.

[44] Elisabeth A. Murray, "The Amygdala, Reward and Emotion," *Trends in Cognitive Sciences* 11/11 (November 2007), 489-497.

[45] For example, Abigail A. Marsh, Elizabeth C. Finger, Katherine A. Fowler, Christopher J. Adalio, Ilana T. N. Jurkowitz, Julia C. Schechter, Daniel S. Pine, Jean Decety, R. J. R. Blair, "Empathic Responsiveness in Amygdala and Anterior Cingulate Cortex in Youths with Psychopathic Traits," *Journal of Child Psychology and Psychiatry* 54/8 (August 2013), 900-910.

[46] Paul J. Frick, James V. Ray, Laura C. Thornton, Rachel E. Kahn, "Can Callous-Unemotional Traits Enhance the Understanding, Diagnosis, and Treatment of Serious Conduct Problems in Children and Adolescents? A Comprehensive Review," *Psychological Bulletin* 140/1 (January 2014), 1-57.

[47] Soo Hyun Rhee, Naomi P. Friedman, Debra L. Boeldt, Robin P. Corley, John K. Hewitt, Ariel Knafo, Benjamin B. Lahey, JoAnn Robinson, Carol A. Van Hulle, Irwin D. Waldman, Susan E. Young, Carolyn Zahn-Waxler, "Early Concern and Disregard for Others as Predictors of Antisocial Behavior," *Journal of Child Psychology and Psychiatry* 54/2 (February 2013), 157-166.

[48] Jean Decety, Kalina J. Michalska, Yuko Akitsuki, Benjamin B. Lahey, "Atypical Empathic Responses in Adolescents with Aggressive Conduct Disorder: A Functional MRI Investigation," *Biological Psychology* 80/2 (February 2009), 203-211. [Henceforth refered to as *AER*]

responsiveness.[49]

Two findings emerge from studies using the empathy for pain paradigm when examining CD in youth. First, an inverse association arises between levels of callousness (CU) and neural response in affective-motivational regions.[50] Second, enhanced responses occur in affective-motivational regions in individuals with reactive aggression (RA), relative to low levels of aggression.[51] Consistent with such work, a preliminary study found that adolescents with early-onset CD, relative to adolescents without CD, exhibited greater activation in such regions (AER). However, this study did not include pre-adolescents, nor did it assess CU or RA traits. Moreover, none of these previous studies on emotional empathy examined sex differences, which are known to contribute to heterogeneity in CD.[52]

In a large recent study of 107 nine to eleven years old children (52 female subjects), recruited from pediatric and mental health clinics, representing a wide range of CD symptoms, it was found that children with greater CD and callousness exhibit dampened hemodynamic response to viewing others being harmed in the insula, while children with increased RA scores had enhanced responses. Sex differences in the neural correlates of CD were also observed.

The findings extend our understanding of atypical emotional empathy in preadolescent children with CP. First, both when viewing harm-*vs*-no-harm scenarios, hemodynamic response in the right insula and aMCC was inversely associated both with the number of conduct problems and with callousness ratings. Second, the opposite pattern was observed with levels of reactive aggression scores, whereby increased RA scores were associated with stronger signal responses in these regions in the harm-vs-no-harm condition. Third, sex-by-CP interactions in STS and MFG were observed. Sex differences in these regions were supported by post hoc tests revealing robust inverse associations in the STS and MFG in female subjects only. There is considerable evidence that CD symptoms lie on a continuum.[53] Our study represents the first attempt to investigate neural processing of sensitivity to others harm in a large sample that includes both pre-adolescent girls and boys with a wide range of CD symptoms. Importantly, while not all children exhibited symptom threshold for CD, the level of symptoms in the current study still represents substantial risk for serious adverse outcomes. These data contribute to elucidating the functional neuroanatomy of CP in several important ways. Using a well-validated emotional empathy-eliciting paradigm, the study shows reduced neural response to others' harm in children at high levels of CP and document sex differences in the association between CP and functional neuroanatomy, suggesting early emergence of sexual dimorphism in correlates of aggressive behavior.

Conclusions

Empathy is thought to play a key role in motivating helping behavior and providing the affective basis for moral development. Emotional empathy develops as a result of complex biological and psychological processes involving emotion sharing, emotional regulation, and cognitive perspective taking that are continuously evolving and interacting with an individuals social environment. Breaking down empathy and related phenomena into components and examining their neurodevelopment can contribute to a more complete model of interpersonal sensitivity. Likewise, drawing

[49] S. L. Crowe and R. James R. Blair, "The Development of Antisocial Behavior: What Can We Learn from Functional Neuroimaging Studies?" *Development and Psychopathology* 20/4 (Fall 2008), 1145-1159.

[50] For example, Jean Decety, Chenyi Chen, Carla Harenski, Kent A. Kiehl, "An fMRI Study of Affective Perspective Taking in Individuals with Psychopathy: Imagining Another in Pain does not Evoke Empathy," *Frontiers in Human Neuroscience* 7/489 (September 2013) online.

[51] Sabine C. Herpetz, "Emotional Processing in Conduct Disorder: Data from Psychophysiology and Neuroimaging," *European Psychiatry* 23/2 (April 2008), S9.

[52] For example, Graeme Fairchild, Cindy C. Hagan, Luca Passamonti, Nicholas D. Walsh, Ian M. Goodyer, Andrew J. Calder, "Atypical Neural Responses During Face Processing in Female Adolescents With Conduct Disorder," *Journal of the American Academy of Child & Adolescent Psychiatry* 53/6 (June 2014), 677-687.

[53] Benjamin B. Lahey, Brooks Applegate, Keith McBurnett, Joseph Biederman, Laurence Greenhill, George W. Hynd, Russell A. Barkley, Jeffrey Newcorn, Peter Jensen, John E. Richters, et al., "DSM-IV Field Trials for Attention Deficit Hyperactivity Disorder in Children and Adolescents," *American Journal of Psychiatry* 151/11 (November 1994), 1673-1685.

from multiple sources of data can improve our understanding of the nature and causes of empathy deficits in individuals with antisocial behavior disorders. Neuroimaging studies clearly document that watching someone in pain elicits a negative arousal response in the observer (underpinned but the anterior cingulate cortex, insula, and PAG), to a stronger degree in children than in young adults (*NCC*). Findings indicate that although children and adults have similar patterns of brain response to perceiving other people in pain, there are important changes in the functional organization in the neural structures implicated in empathy and sympathy that occur over an extended period from childhood through adulthood. Moreover, given the importance of empathy for healthy psychological and 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.