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Empathic responding and hippocampal volume in young children

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ABSTRACT

Empathic responding—the capacity to understand, resonate with, and respond sensitively to others' emotional experiences—is a complex human faculty that calls upon multiple social, emotional, and cognitive capacities and their underlying neural systems. Emerging evidence in adults suggests that the hippocampus and its associated network may play an important role in empathic responding, possibly via its role in processes such as memory of emotional events, but the contribution of this structure in early childhood is unknown. We examined concurrent associations between empathic responding and hippocampal volume in a sample of 78 children (ages 4 to 8 years). Larger bilateral hippocampal volume (adjusted for intracranial volume) predicted greater observed empathic responses toward a stranger in distress, but only for boys. The association was not driven by a specific subregion of the hippocampus (head, body, tail), nor did it vary with age. Empathic responding was not significantly related to amygdala volume, suggesting specificity of relations with the hippocampus. Results support the proposal that hippocampal structure contributes to individual differences in children's empathic responding, consistent with research in adults. Findings shed light on an under-studied structure in the complex neural systems supporting empathic responding and raise new questions regarding sex differences in the neurodevelopment of empathy in early childhood.

Keywords: empathy, hippocampus, structural MRI, early childhood, prosocial behavior

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> "Empathy is really important . . . Only when our clever brain and our human heart work together in harmony can we achieve our full potential."
> – Jane Goodall (2014)

Empathic responding is among the most complex human capacities; it allows us to see the world from others' perspectives, to delight in their joy or feel their pain echo in ourselves, and to respond to others' needs with sensitivity and care. Empathic responding is a multidimensional process that includes resonating with others' affective experience (emotional empathy), feeling concern for others' wellbeing (sympathy), identifying and understanding others' emotional experience, as well as taking others' perspective (cognitive empathy); these internal processes interact to coordinate prosocial behaviors to alleviate others' distress, such as providing comfort to a person in pain or grief (Davis, 1980; Decety, 2010, 2015; Eisenberg, 2017). Supporting empathic responding are concomitant processes such attention and emotion regulation that direct psychological resources to the person in need and reduce self-focused personal distress, which can undermine effective helping (Batson, Fultz, & Shoenrade, 1987; Decety & Lamm, 2009; Eisenberg, 2000; Eisenberg & Eggum, 2009).

Given the complexity and importance of empathic responding to our highly social species, it is no surprise that significant research attention has been devoted to understanding how it is orchestrated by the brain—and how it does so across development. Some of the earliest work in human adults examined which brain regions were related to measures of empathic responding using both structural and functional magnetic resonance imaging (MRI). These studies revealed a complex network of regions—including the ventromedial prefrontal cortex (vmPFC), anterior cingulate cortex (ACC), superior temporal sulcus, insula, and amygdala—with distinct neural networks underlying cognitive empathy, emotional empathy, and personal distress (Decety, 2010, 2015; Shamay-Tsoory, 2011; Zaki & Ochsner, 2012). Neurodevelopmental work suggests that bottom-up affective processes supported by subcortical regions like the amygdala may be functional at birth, then honed over time and with experience to shape emotion understanding, top-down reappraisal, and regulation via connectivity with cortical regions such as the vmPFC (Decety, 2010).

Emerging theoretical perspectives and empirical research have widened the lens, suggesting that additional regions, such as the hippocampus and its associated memory network, also play an important role in empathic responding (see Moscovitch, Cabeza, Winocur, & Nadel, 2016; Laurita & Spreng, 2017). This novel perspective stems from multiple lines of evidence including studies of (1) organization of brain networks in typical adults and (2) adult patients with hippocampal damage. In typical adults, some research has suggested that the hippocampus may be part of a collection of brain regions known as the default mode network. This network has been shown to support social cognitive processes relevant to empathic responding, such as theory of mind (for a review see Spreng, Mar, & Kim, 2009). In adults with hippocampal damage, in addition to widely documented memory impairments, these individuals report lower cognitive and emotional trait empathy, and respond to a person in distress with less empathic emotion and less prosocial behavior compared to healthy controls (Beadle, Tranel, Cohen, & Duff, 2013). Specifically, one study of adults with brain volume loss due to traumatic brain injury found that smaller right hemisphere hippocampal volumes were associated with reduced self-reported empathic emotions in response to others' suffering (Rushby et al., 2016). Indeed, impairment in empathic responding may explain why these individuals often struggle to forge and maintain social bonds (Davidson, Drouin, Kwan, Moscovitch, & Rosenbaum, 2012; Gupta et al., 2009).

Whether the hippocampus is related to empathic responding in childhood—when empathic capacities and the neural structures underlying them are still under construction—is not known. Given that brain structure, function, and connectivity all undergo changes during early childhood—including increasing functional specialization of the hippocampus (Riggins, Geng, Blankenship, & Redcay, 2016) and increasing connectivity between the hippocampus and cortical regions (Blankenship, Redcay, Dougherty, & Riggins, 2017)—it is especially important to examine the neural networks supporting emerging social capacities during this period. Here we bring neurodevelopmental perspectives into conversation with emerging literature on the role of the hippocampus in emotional processes to better understand the neural underpinnings of empathic responding in young children.

Neurodevelopment of Empathic Responding

The developmental roots of empathic responding begin in infancy with early tendencies to orient toward and show concern for others' distress, which become more regulated and differentiated in the second year of life (Roth-Hanania, Davidov, & Zahn-Waxler, 2011; Zahn-Waxler, Radke-Yarrow, Wagner, & Chapman, 1992). By age 2, many children respond to others' distress with concerned attention and comforting behavior (Zahn-Waxler et al., 1992) and engage in affective perspective-taking when others are harmed (Vaish, Carpenter, & Tomasello, 2009). Empathic comforting responses to others' distress tend to increase during the preschool years (Dunfield & Kuhlmeier, 2013) and become increasingly complex as emotion regulation and cognitive skills continue to develop across the school years (Eisenberg, Spinrad, & Knafo-Noam, 2014). Within this picture of normative development, children show striking individual differences, with variation in underlying social-emotional capacities such as emotion regulation predicting lower levels of personal distress and more effective empathic responding across development (see Eisenberg, 2000, 2017).

Alongside these advances, changes in brain structure and function unfold that shape emotional processes and social behavior. Decety's (2010, 2015) model of neurodevelopment suggests that the specific cognitive and affective processes involved in empathic responding are shaped by distinct neural networks with distinct developmental trajectories that interact and feedback on one another in response to social experiences. Specifically, the model proposes that (a) subcortical circuits underlying automatic affective arousal—including the hippocampus, amygdala, hypothalamus, and orbitofrontal cortex—are functional at birth; (b) these affective responses are modulated by prefrontal cortex (PFC) maturation supporting emotion understanding that develops over the second and third years; and (c) the ongoing development of the dorsolateral PFC (dlPFC), vmPFC, and ACC across childhood and adolescence enable greater emotion regulation and increasingly flexible empathic responding in diverse social contexts.

Decety's (2010) model suggests that the hippocampus is among the subcortical structures supporting early-developing processes of emotional resonance (i.e., sharing others' emotional experience; Decety & Meyer, 2008), but further information about its specific role and ongoing development is absent. Given protracted development of the hippocampus (Ghetti & Bunge, 2012) and its central role in cognitive processes across development, might this structure play an additional role in neurodevelopment of empathic responding?

A Possible Role for the Hippocampus

The hippocampus is a critical component of a larger network that supports diverse cognitive processes such as learning and memory, spatial navigation, and HPA regulation, via its reciprocal connections with subcortical regions such as the amygdala and cortical areas such as the prefrontal cortex. The specific role of the hippocampus and associated network in these cognitive processes, and the patterns of hippocampal activity and connectivity, have been shown to vary across development (Ghetti & Bunge, 2012).

A substantial body of research links the hippocampus and networks in which it participates to *episodic memory* ability, or the ability to remember past experiences, along with details and context (for reviews see Ghetti & Bunge, 2012; Spaniol et al., 2009). Although specific relations between subregions of the hippocampus (i.e., head, body, or tail) and memory ability change across development (e.g., DeMaster, Pathman, Lee, & Ghetti, 2014; Ghetti, DeMaster, Yonelinas, & Bunge, 2010; Riggins et al., 2016), individual differences in hippocampal subregion volume (Riggins, Blankenship, Mulligan, Rice, & Redcay, 2015) and functional connectivity (Riggins et al., 2016) have been shown to predict episodic memory ability in early childhood. Specifically, by 6 years of age, episodic memory ability is associated with larger hippocampal head volume (Riggins et al., 2015) and with more adult-like patterns of functional connectivity with cortical regions within the network of regions important for episodic memory (Riggins et al., 2016).

In light of these findings, some researchers have suggested that the hippocampal network may also be important for social cognition and emotion, and that episodic memory may provide a candidate mechanism linking hippocampal structure and function to social processes like empathic responding (see, e.g., Moscovitch et al., 2016; Laurita & Spreng, 2017; Rubin, Watson, Duff, & Cohen, 2014; Spreng, 2013). This proposal is based on theory and research linking empathic abilities with three components of the hippocampal memory system: emotional recall, simulation, and relational binding. First, individuals who can *recall* past emotional information may be better able to understand others’ emotions by relating them to their own past emotional experiences, or by contextualizing them in terms of others’ personal history (Moscovitch et al., 2016). Indeed, research in adults has shown that episodic memory (and the hippocampal memory system) is positively associated with empathy (e.g., Wagner, Handke, & Walter, 2015), as well as related capacities such as thinking about one’s future to plan social interactions (Hassabis, Kumaran, & Maguire, 2007; Hassabis, Kumaran, Vann, & Maguire, 2007; Squire et al., 2010) and social problem-solving (Sheldon, McAndrews, & Moscovitch, 2011).

Second, the ability to vividly imagine or *simulate* the experiences of others may facilitate empathy by allowing individuals to take others’ perspectives in emotionally salient situations (Gaesser, 2013; Laurita & Spreng, 2017; Moscovitch et al., 2016). Simulation ability has been shown to predict greater willingness to help others in distress (Gaesser & Schacter, 2014) and empathy for others in imagined negative situations (Ciaramelli, Bernardi, & Moscovitch, 2013; Gaesser, 2012). Further, neuroimaging research has demonstrated that the hippocampus is similarly activated when recalling one’s own emotional experiences and when imagining the emotional experiences of similar others (Perry, Hendler, & Shamay-Tsoory, 2011).

Third, individuals who are able to integrate (i.e., *bind*) an emotionally salient event with its causes, context, affective associations, and effect on other individuals (who themselves must be represented along multiple integrated social dimensions) may be better able to understand complex emotional situations; greater understanding of others’ emotions, in turn, may facilitate effective empathic responding to others’ distress, especially in complex or ambiguous situations (Decety, 2015; Laurita & Spreng, 2017; see Thompson, 1987). A study by Immordino-Yang and Singh (2013) found that the hippocampus was more strongly activated when individuals processed more cognitively complex situations involving others’ emotions; the authors suggest that the hippocampus helps to integrate social information to facilitate appropriate emotional responses, including empathy. Together, the data suggest that the hippocampal memory system may play an important role in facilitating empathic responding to others' distress.

The Present Study

Despite substantial interest in the neurodevelopmental underpinnings of empathic responding, as well as emerging research on the role of the hippocampus and associated network in supporting social processes in adults, associations between the hippocampus and empathic responding in childhood have not been examined. Thus, the principal goal of the present study was to examine relations between hippocampal volume and observed empathic responding in young children. In general, the volume of a brain structure, such as the hippocampus, is thought to be related to the function of that structure (see Poppenk Evenson, Moscovitch, & Nadel, 2013 for a review). Although the exact nature of this relation is not well delineated, a key advantage of examining structure, as compared to function, is that an individual's structural measurements do not vary based on the performance of a single task as they do with task-based fMRI. Therefore, examining relations between brain structure and behavior is a useful first step in building a research base regarding the neural underpinnings of complex human behaviors.

This investigation focuses on early childhood (age 4 to 8 years) in order to capture both the end of the preschool years and the beginning of the school years, when children begin to display more complex empathic behavior as their cognitive and emotional skills develop through broadening social experiences at school (Eisenberg et al., 2014). Moreover, individual differences in social competencies like empathic responding are especially important for positive adjustment during the transition to kindergarten and grade school (e.g., Blair, 2002; Denham, 2006). From a neurodevelopmental perspective, early childhood is characterized by changes in the hippocampal memory network, with evidence of interactive specialization of this neural system occurring between 4 and 6 years of age (Riggins et al., 2016; Riggins et al., 2018). Thus, understanding how the hippocampus contributes to individual differences in empathic responding in early childhood represents an important area for developmental research.

We assess children's empathic responses to an experimenter's simulated physical pain. We examine both bilateral hippocampal volume as well as volume of hippocampal subregions, given the different functional roles associated with these subregions in adults (e.g., Poppenk, Evensmoen, Moscovitch, & Nadel 2013) and their reported variations across development (e.g., DeMaster et al., 2014; Riggins et al., 2015). Although function and connectivity of the hippocampus were also of interest, given this was an initial investigation, we focused on volume, which is common in the field of developmental cognitive neuroscience. To determine whether the role of the hippocampus is unique, we also examine potential associations between amygdala volume and empathic responding, given its proximity to and connectivity with the hippocampus, as well as their role in emotion-related processes (e.g., Sergerie, Chochol, & Armony, 2008).

In addition, given sex differences in the structural development of the brain (Giedd et al., 1997; Neufang et al., 2008) including the hippocampal network (Koss & Frick, 2017; Riggins et al., 2018) and in the development of empathic responding (Eisenberg et al., 2014), as well as age-related differences in hippocampal structure, connectivity, and function during this period (Riggins et al., 2015; Riggins et al., 2016), a secondary goal was to explore child age and sex as potential moderators of associations between hippocampal volume and empathic responding. Given the exploratory nature of the study, we made no a priori hypotheses. Our approach was to cast a wide net to provide preliminary data on a largely unexplored topic.

This study is the first to examine associations between empathic responding and hippocampal volume in young children. We aim to shed light on an under-studied structure within the neural systems supporting empathic responding in early childhood and to begin to define the roles of specific hippocampal subregions in children's social-emotional processes. The present investigation also serves to provide a point of comparison with the adult literature to demonstrate areas of developmental continuity and change in the hippocampus's role in empathic processes.

Method

Participants

A total of 82 (36 male, 46 female) 4- to 8-year-old children (*M* = 6.47 years, *SD* = 1.26) participated in the present study, which is part of an ongoing longitudinal investigation examining brain and memory development in early childhood. The present paper explicitly focuses on direct associations between the hippocampus and empathetic responding; thus, although additional data were collected (e.g., cortical thickness, IQ, memory ability), they were not utilized in this initial report.

Participants were recruited from the Baltimore–Washington metropolitan area through the use of a University-maintained database of families interested in participating in research and through the distribution of recruitment flyers. Participants were racially diverse (50% White, 22% multiracial, 6% African American, 6% Asian, 16% did not identify). Household income ranged from <$15,000 to >$105,000 (median household income: >$105,000). Children were screened to ensure they had not been premature and had no diagnoses for neurological conditions, developmental delays, or contraindications for MRI.

Once the measure of empathic responding was added to the longitudinal study protocol, all participants provided empathy data; empathy data were not codable for four children (2 children were not recorded due to video equipment malfunction, 1 child was off-camera for the majority of the task, and 1 child interrupted the task to use the restroom), leaving 78 children with empathy data. Of these, 73 children underwent MRI scanning and yielded usable scans for processing (4 children did not undergo scanning because they refused to enter the scanner and 1 of the acquired scans was deemed unusable due to motion artifact). Multiple imputation was used to treat missing hippocampal and amygdala volume data so that all children with empathy data could be included in analyses. Thus, the final analytic sample comprised 78 (34 male, 44 female) 4- to 8-year-old children (*M* = 6.49 years, *SD* = 1.27). The study was approved by the University of Maryland IRB (Approval #569804, "Hippocampal-Memory Network Development and Episodic Memory in Early Childhood").

Procedure

Prior to the experimental session, parents provided written consent and children provided either verbal (< 7 years) or written (> 7 years) assent to participate in the study. Children visited the laboratory and completed both an empathic responding task and a structural MRI scan. Several additional tasks were administered but are not discussed in this paper. Participants received monetary compensation for their participation, along with toy prizes.

Empathic Responding Task. Empathic responding was coded from children's responses to a naturalistic distress task (adapted from Zahn-Waxler et al., 1992, and updated based on Dunfield's work with preschoolers; Dunfield & Kuhlmeier, 2013), in which an experimenter pretends to pinch their finger on a clipboard and then expresses distress for 2 minutes. Versions of this task have been widely used in studies of young children's empathic responding (e.g., Beier et al., 2018; Hastings, Rubin, & DeRose, 2005; Hastings et al., 2000; Kiang, Moreno, & Robinson, 2004; Stern, 2016). In Dunfield's version of the task, an experimenter pretends to hurt themselves and feigns distress for the 2-minute period, at first using subtle cues such as sighs and groans and gradually more overt cues such as statements of distress (e.g., "It hurts really bad") and requests for help (e.g., "Is there anything you can do to help?"). This structure was intended to capture differences in the spontaneity of children's empathic responding, with higher scores awarded to children who responded to the more subtle, indirect distress cues that characterize the beginning of the task (scoring described below); this is important for capturing variation in the present sample of 4- to 8-year-old children, who have more advanced social and regulatory capacities than their younger counterparts (Fox & Calkins, 2003). After 2 minutes, the experimenter "feels better" and re-engages the child in play.

Children's responses were video recorded and later coded for empathy using the Comforting Task Coding Manual (Gross, Brett, Beier, & Cassidy, 2014), which has been used in previous research to code young children's empathy and comforting behavior in response to others' distress (Beier et al., 2018; Stern, 2016). Videos were coded on 10-second time intervals for empathic responses (physical comforting, concerned attention, and verbal soothing) and non-empathic behaviors (negativity/hostility, personal distress, and ignoring the experimenter). Coders assigned a single overall score from 1 (minimal empathic responding; child shows no sign of being concerned about the experimenter's distress, largely ignores the experimenter, is actively negative/hostile, or is too personally distressed to help the experimenter) to 5 (high empathic responding; child comforts experimenter for majority of the task, provides physical comfort such as a hug within the first 30s, or attempts at multiple high-quality strategies to help the experimenter; when not actively comforting, the child shows concerned attention toward the experimenter). Mid-range scores are awarded to children who provide moderate empathic responding or who respond only toward the end of the task when explicitly asked for help.

A team of four coders was trained to reliability (Krippendorff's alpha [K-alpha; Hayes & Krippendorff, 2007)] cutoff = .70), 97% of videos were independently double-coded, and discrepancies were resolved in weekly meetings. K-alpha for overall empathy scores was .90, 95% CI [.86, .93], indicating excellent interrater reliability.

MRI Acquisition. Participants first completed training in a mock scanner in order to become acclimated to the scanning environment and receive feedback regarding motion requirements. Additionally, padding around the participants' head was used to minimize head movement during scan acquisition. Participants were scanned in a Siemens 3.0-T scanner (MAGNETOM Trio Tim System, Siemens Medical Solutions, Erlangen, Germany) using a 32-channel coil. Structural data were collected using a high-resolution T1 magnetization-prepared rapid gradient-echo (MPRAGE) sequence consisting of 176 contiguous sagittal slices (.9 mm isotropic; 1900 ms TR; 2.32 ms TE; 900 ms inversion time; 9° flip angle; pixel matrix = 256 × 256). Children viewed a movie of their choosing while completing the structural MRI scan.

MRI Analysis. Images were analyzed using FreeSurfer Version 5.1.0, a standard automatic segmentation program (surfer.nmr.mgh.harvard.edu; Fischl, 2012; Fischl et al., 2002). Use of FreeSurfer has been validated in children as young as 4 years of age (Ghosh et al., 2010). T1-weighted images of each participant were compared to a probabilistic atlas, generating new surface maps of gray matter, white matter, and pial boundaries. Reconstruction and volumetric calculations were automatized. Resulting hippocampal volumes were aligned into anterior commissure–posterior commissure space, allowing for assessment of hippocampal volumes without distortions introduced by reorientation (Poppenk & Moscovitch, 2011). Hippocampal volumes were further refined using Automatic Segmentation Adapter Tool (ASAT, nitrc.org/projects/segadapter; Wang et al., 2011; see Riggins et al., 2018). The hippocampus was divided into head, body, and tail subregions using manual identification of standard anatomical landmarks. The uncal apex served as the border between the head and body (Weiss, Dewitt, Goff, Ditman, & Heckers, 2005). The boundary between the body and tail was identified as the slice at which the fornix separates from the hippocampus and becomes clearly visible (Watson et al., 1992). Raters were blind to participant age, sex, and empathy score.

In order to ensure that observed effects were not the result of differences in brain size, hippocampal and amygdala volumes were adjusted to control for differences in intracranial volume (ICV) using an analysis of covariance approach (Raz et al., 2005; Van Petten, 2004). Brain extraction was conducted separately in 6 toolboxes including ANTs, AFNI, FSL, BSE, ROBEX, and SPM8. The voxels extracted by at least four toolboxes were included in the brain mask (see Tillman et al., 2017 for similar approach). Exploration of ICV values indicated significant independent influences of age ($\beta = .25$, $p < .05$) and sex ($\beta = -.22$, $p < .05$) on total brain size (adjusted $R^2 = .09$, $F(2, 75) = 4.66$, $p < .05$). Preliminary analyses examining relations between regional volumes and ICV for each age and gender group revealed homogeneity of this relation, therefore the same correction was carried out across age groups, using age and sex to estimate ICV values (adjusted volume = raw volume – b * (ICV – predicted ICV), see Keresztes et al., 2017). Results were first examined for raw volumes and then for adjusted volumes to account for the possibility that observed effects were a product of this adjustment. Given the similarities between the results, only the latter are reported.

Results

Data Preparation

To maximize statistical power, multiple imputation (*N* = 40 imputations, following guidelines by Graham, 2009) was used to handle missing hippocampal and amygdala data; substantial research demonstrates that multiple imputation is a valid and flexible tool for treating missing data in clinical research (e.g., Enders, 2017; Schafer & Graham, 2002). All reported statistics represent pooled results with an analytic sample of *N* = 78. All brain volume data underwent 90% winsorization to treat outliers. For correlational analyses, variables for the individual behaviors coded on the empathic responding task were created by calculating the proportion of 10-second time intervals during which the child displayed a particular behavior. (For example, the number of intervals during which a child showed concerned attention was divided by the total number of intervals in the task (typically 12), in order to account for minor variation in the total time children had to respond during the task.) The dataset is available on Open Science Framework at https://osf.io/d26fy.

Preliminary Analyses

Descriptive statistics and bivariate correlations are presented in Tables 1 and 2, respectively. Empathic responding was significantly greater among girls (*M* = 2.61, *SD* = 1.35) than boys (*M* = 1.99, *SD* = 1.20), *t*(76) = -2.14, *p* = .036, but was unrelated to child age, *r* = .07, *p* = .530. None of the bivariate correlations between empathic responding and ICV-adjusted hippocampal volumes was significant, nor was empathic responding related to ICV, all *p*s > .05.

Does Hippocampal Volume Predict Empathy?

A series of hierarchical linear regressions predicting empathic responding scores was conducted with child age and sex entered in the first step as covariates (selected a priori), each adjusted bilateral hippocampal volume (total, head, body, or tail) in the second step, and two-way interactions between each covariate and hippocampal volume in the third step. Standard statistical assumptions for linear regression were met for all analyses. When interaction terms were non-significant, they were dropped from the final model to preserve power. When significant, interaction terms were probed further using simple slopes analysis in PROCESS (Hayes, 2016). Results are summarized below and in Table 3. (As cross-checks, we also conducted analyses (a) using the original, non-imputed dataset, and (b) using raw (unadjusted) brain volumes, with ICV entered as an additional covariate in Step 1 of the regression. Results were highly similar, with minor variation in statistical significance due to loss of power. Here we report results with the imputed dataset and with adjusted brain volumes to maximize statistical power, following standard practice.)

Controlling for child age and sex, total hippocampal volume positively predicted children’s observed empathic responding to the stranger, $\beta = .23$, $p = .042$, $\Delta R^2 = .05$, a small effect size. This significant main effect was qualified by a significant interaction with sex, such that larger total hippocampal volume predicted greater empathic responding for boys, $\beta = .57$, $p = .003$, but not for girls, $\beta = .05$ $p = .689$ (see Figure 1).

To probe these results further, we examined hippocampal subregions (head, body, tail) as predictors of children’s empathic responding. No main effects of hippocampal subregion volume were significant, and no interactions with child age or sex emerged, all *p*s > .05.

Are Results Specific to the Hippocampus?

Secondary regression analyses were conducted to examine whether the observed effects were specific to hippocampal volume, or whether associations with empathic responding were also observed in a neighboring and functionally connected structure: the amygdala. After controlling for child age and sex, total amygdala volume did not significantly predict empathic responding, and interactions between amygdala volume and age or sex were not significant, *p*s > .05. Moreover, when total hippocampal volume was entered with total amygdala volume in the same step, the unique effect of total hippocampal volume remained significant, and the effect of total amygdala volume remained non-significant (see Table 3).

Discussion

In this study of young children, we observed a positive association between hippocampal volume and observed empathic responding. After controlling for age and sex, larger bilateral hippocampal volumes predicted greater empathic responding, an effect that was not driven by a particular subregion of the hippocampus (i.e., head, body, tail). Results were moderated by sex, with the association between empathic responding and hippocampal volume driven by males. These findings are the first to examine relations between empathic responding and hippocampal structure during childhood. This link is consistent with theory suggesting that the hippocampus and associated network play a role in emotion and social information processing (Immordino-Yang & Singh, 2013; Perry et al., 2011) and with empirical studies showing that adults with hippocampal damage report lower empathic emotions and respond in a less empathic manner to a person in distress (Beadle et al., 2013).

The hippocampal network is vital for a variety of processes related to learning and memory, particularly episodic memory (Eichenbaum & Cohen, 2014; Ghetti & Bunge, 2012). Previous research has shown that episodic memory shows dramatic development in early childhood as the hippocampus becomes structurally and functionally mature (Ghetti & Bunge, 2012; Riggins et al., 2016; Riggins et al., 2018). Thus, associations between empathic responding and hippocampal volume may arise through memory-related abilities such as the ability to *recall* past emotional information, imagine or *simulate* the experiences of others, and/or *bind* emotionally salient events with causes, context, and affective associations. Although our study did not have sufficient power to test this mediation model, our findings suggest that it may be fruitful to test memory capacities as a novel candidate mechanism linking brain structure to children’s empathic development. Further, we note that memory is one of many possible mechanisms explaining the observed links; pathways through capacities such as emotion regulation, inhibitory control, emotion understanding, and HPA-axis response are also possible candidates for future exploration. It is also possible that environmental factors—such as variation in early life stress, quality of parenting, or parents’ own empathy—influence the development of children’s hippocampal structure and empathic responding, but via distinct mechanisms.

Sex emerged as an important factor predicting children’s empathic behavior, with girls demonstrating greater empathic responding, on average, than boys, consistent with previous research (e.g., Lennon & Eisenberg, 1987; Thompson & Voyer, 2014). Sex has also been shown to play a role in hippocampal development, with sex differences observed in hippocampal structure and function from infancy through adulthood in both humans and rodents (see Koss & Frick, 2017; Riggins et al., 2018). In the present study, sex moderated the relation between hippocampal volume and empathic responding, such that hippocampal volume predicted empathic responding for boys, but not for girls. This interactive effect may have been influenced by distributional differences of scores on the empathic responding task, as boys’ data were slightly more positively skewed than that of girls. Alternatively, this interaction may suggest that boys’ empathic capacities are more dependent on the hippocampal system, whereas girls’ empathic responding may rely on other neural systems. Research in adults suggests that males’ empathic responding—and activation of empathy-associated cortical regions—is reduced when they perceive a confederate to be unfair, an effect not observed in females (Singer et al., 2006), suggesting sex-specific influences of contextual cues on empathy-related neural activity. Further, previous research has shown that the same parenting behaviors and parent–child relationship qualities have different influence on boys’ and girls’ prosocial behavior (Hastings, McShane, Parker, & Ladha, 2007); for example, children’s secure attachment to caregivers has been shown to predict greater helping behavior for boys, but not girls (Beier et al., 2018). This suggests that boys and girls may develop empathic and prosocial tendencies via different mechanisms, perhaps with different neural underpinnings. Given cultural norms about gender roles, girls likely receive greater socialization pressures to behave in empathic and caring ways, such that individual differences in girls’ empathic responding may be more likely to reflect these external pressures, rather than factors such as attachment and hippocampal structure. Future research should further investigate the role of sex in shaping the neurodevelopment of empathic responding in children, especially the potentially diverse neural mechanisms underlying individual differences for girls and boys.

Although it is well known that empathic responding continues to develop throughout the school years (e.g., Lennon & Eisenberg, 1987), age was not related to empathic responding in the present study, possibly due to lack of power in this restricted age range. It is also possible that factors related to the empathic responding task (e.g., experimenter was an unfamiliar adult, who older children may not expect to display negative emotion, and who they may be disinclined to approach given increasing awareness of social norms). Age also did not moderate the association between hippocampal volume and empathic responding, suggesting developmental continuity in the role of the hippocampus in empathic responding in this period. It is possible that age becomes a significant moderator when the cognitive demands of the empathic responding task are greater, or that age becomes a significant moderator only later in development, when pubertal development ushers in rapid changes in biological systems underlying social behavior (e.g., Blakemore, Burnett, & Dahl, 2010). Future studies that implement longitudinal designs, follow children through puberty, and integrate multiple measures of empathic responding, including observations in more naturalistic settings with peers (e.g., school), may shed additional light on the role of age.

We did not find associations with specific subregions of the hippocampus (though there was a nonsignificant trend for the hippocampal tail). Hippocampal subregion volumes have been shown to relate differentially with memory tasks in children (DeMaster et al., 2014; Ghetti et al., 2010; Riggins et al., 2015). It is possible that empathic responding simply does not show such specificity; however, it is also possible that measures of subregions were too coarse to detect differences with regard to empathic responding. Examination of hippocampal subfields (i.e. CA1-3, dentate gyrus, subiculum) may provide a more fine-grained way to divide the hippocampus. The dentate gyrus and CA3 are thought to exhibit a protracted development and be especially critical for episodic memory and relational binding (Daugherty, Flinn, & Ofen, 2017; Lee, Ekstrom, & Ghetti, 2014; Riggins et al., 2018). Further, childhood stress has been shown to predict the structure of these subfields, specifically dentate gyrus and CA3 (Teicher, Anderson, & Polcari, 2012), suggesting that they may be especially susceptible to environmental influences that have also been shown to influence empathic responding (e.g., quality of caregiving; Stern & Cassidy, 2018). Given that acquiring subfield volumes requires ultra-high-resolution scans, which last longer and are more susceptible to motion influences, measures of subfield volume were not available for a sufficient number of younger children to examine here. However, these subfields are promising candidate regions to explore in relation to empathic responding and may better account for the observed effects of total hippocampal volume.

Analyses investigating the amygdala revealed that empathic responding was not related to amygdala volume in this sample. Although the amygdala is a core structure implicated in processing of emotional information, it is possible that empathic responding is related to amygdala function, but not structure, or that associations emerge later in development. Research has shown that amygdala function is related to empathy-related emotion processing in children, but that its role changes with age (Rice, Viscomi, Riggins, & Redcay, 2014). Relatedly, it may be that functional connectivity between the amygdala and prefrontal control regions (e.g., medial PFC), which improves rapidly over childhood and supports emotion regulation (Gee et al., 2013), is similarly important for empathic responding. It is also possible that the specific empathic responding task included in the present study was less relevant to the amygdala, as the task presented a mild emotional stressor that was not designed to cause undue stress to the child (indeed, behaviors indicating personal distress were rare in the present sample). Amygdala structure and activity tends to be associated with more stressful and aversive stimuli (e.g., blood) (Phan, Wager, Taylor, & Liberzon, 2002).

Future Directions

As is often the case in cognitive neuroscience, once relations between structure and behavior are identified, this work can be extended by examining whether function (i.e., activation) of the structure mediates this association. To examine activation effectively, age-appropriate, ecologically valid tasks (that can be performed in an MRI scanner) need to be designed that tap the behaviors of interest. For example, empathy tasks could be adapted from recent work in school-aged children using chat-based interactions with peers (Warnell, Sadikova, & Redcay, 2017), passive viewing of videos of a person in distress (e.g., Decety, Michalska, & Akitsuki, 2015), or perceived live face-to-face social interactions (Redcay et al., 2010; Rice, Moraczewski, & Redcay, 2016; see also Redcay & Warnell, 2017). Examining brain activation during these tasks may help clarify how the hippocampal network functions during tasks assessing specific dimensions of empathy, as well as candidate mechanisms such as relational binding, emotion regulation, and memory for social information.

In addition, structural and functional connectivity between regions of interest in the network supporting empathic behavior could also be examined. For example, relations between empathic responding and integrity of the default mode network could be explored, given evidence that this network appears to be important for interpreting social information (Spreng et al., 2009). Previous research has shown that empathic responding in adults is supported by a network of cortical and subcortical brain regions including vmPFC, dlPFC, ACC, superior temporal sulcus, insula, amygdala, and the hippocampus (Laurita & Spreng, 2017; Moscovitch et al., 2016; Shamay-Tsoory, 2011; Zaki & Ochsner, 2012). These regions could be useful starting points for examining patterns of connectivity in early childhood. Further, a recent study employing intracranial electroencephalography recordings (iEEG) demonstrated that communication between the hippocampus and amygdala predicted variation in emotions such as sadness (Kirkby et al., 2018); future research could investigate whether this same hippocampus–amygdala subnetwork predicts variation in children’s empathic responses to others’ sadness. A neural systems perspective is particularly important for understanding how the distributed cognitive and affective systems implicated in empathic responding work together to process social experiences, and how these experiences shape brain structure and function over time.

The age range included in this study allowed us to target an important period of development of both empathic responding and the hippocampus. It would be informative for future studies to extend these findings to middle childhood and adolescence to determine whether the observed continuity in relations between the hippocampus and empathic responding continues throughout the school-aged years and early adolescence, or whether discontinuity becomes apparent as hippocampal subregions and prefrontal regulatory mechanisms become more developed and specialized. Previous research suggests that the hippocampus may support higher-order cognitive processes like working memory during childhood or early adolescence, but not during later adolescence (e.g., Finn et al., 2010); a wider age range would enable researchers to test whether similar effects are observable for social-emotional processes like empathic responding. Inclusion of children in older age groups would also provide a better idea of how individual differences in hippocampal volume may support empathic responding in more cognitively complex and socially demanding contexts that arise in adolescence (e.g., responding to bullying in school).

Although this study is an important step toward understanding the subcortical structures that support empathic responding in early childhood, results should be viewed as preliminary, given the small sample size, especially once separated by sex. Further, the sample was largely high-income, limiting the generalizability of results. Future work would benefit from examining associations in larger, more socioeconomically diverse samples. Such work would also give researchers more power to test mediation models to examine potential mechanisms underlying the relation between hippocampal volume and empathic responding, such as simulation, recall of social information, or memory for personal experience involving emotional distress.

In addition, the present work utilized a behavioral task designed to provide a wholistic assessment of children’s empathic responding in a naturalistic context involving others’ emotional distress; thus, the task drew on multiple components of the empathic process—including identifying the experimenter’s emotion, regulating one’s own attention and emotions, and engaging in sensitive comforting behavior—that are coordinated in effective empathic responding. Although observed comforting behavior and concerned attention are not direct measures of the internal cognitive and emotional processes involved in empathic responding, they reflect children’s attention to and understanding of others’ distress and intention to relieve others’ suffering, and have the benefit of ecological validity. This is in keeping with a long tradition of previous developmental work using behavioral tasks to assess empathy-related processes (e.g., Kestenbaum, Farber, & Sroufe, 1989; Kim & Kochanska, 2017; Spinrad & Stifter, 2006; Stern, 2016; Young, Fox, & Zahn-Waxler, 1999; Zahn-Waxler, Robinson, & Emde, 1992), particularly in studies of young children who may not be able to accurately self-report empathic internal states or trait-like individual differences in empathy-related abilities. However, such behavioral measures are limited in that they do not differentiate the individual subprocesses involved in complex social behavior. Future studies should employ multi-method assessments to target specific subprocesses of empathic responding that may be emerging during this developmental period and may differentially relate to neural systems involving the hippocampus; attention to these subprocesses is crucial for understanding how constellations of cognitive and emotional processes become coordinated through experience and development to shape empathic responding (Pollak, 2005).

Another important consideration for future work is that diverse motivations may underlie children’s empathy-related behavior, including not only altruism and empathic emotion, but also compliance, desire for praise, and other self-focused motives (Eisenberg, VanSchyndel, & Spinrad, 2016). The measure of empathic responding in the present study could not capture children’s underlying motivations. It is possible that the hippocampus plays a role in specific social motivations that could be disentangled in future work that manipulates contextual factors to elicit different motivations; for example, a task involving a same-age peer in distress who makes no direct request for help could reduce the likelihood that behaviors reflect motivations to comply with social norms or an adult experimenter's expectations.

Conclusions

Overall, our findings add to the growing body of research examining the hippocampus and associated network as important for understanding the neural networks that support empathic responding. Specifically, our results indicate that the hippocampus may be important to the development of boys' empathic responding in early childhood. Future research should further explore the nature and timing of hippocampal contributions to empathic development in larger, more diverse samples, test candidate mechanisms linking the hippocampus to empathic responding, and examine how the hippocampus becomes functionally integrated with other regions as children's empathic capacities develop over time and with social experience. Understanding the roots of individual differences in children's empathic responding is particularly important because empathy is critical for a diverse set of processes including prosocial behavior and moral reasoning (Eisenberg & Eggum, 2009; Eisenberg et al., 2010). These findings are an important first step towards unraveling the hippocampus's contribution to the complex neural underpinnings of empathic responding across development.

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Table 1

Descriptive Statistics for Child Empathic Responding and Brain Volumes.

Variable	**Girls**		**Boys**	
	M	(*SD*)	*M*	(*SD*)
Empathic Responding	2.61	(1.35)	1.99	(1.20)
Empathic behaviors				
Concerned attention	.41	(.24)	.31	(.18)
Problem-focused responses	.13	(.13)	.14	(.15)
Emotion-focused responses	.12	(.12)	.08	(.10)
Unempathic behaviors				
Negativity	.00	(.01)	.03	(.14)
Personal Distress	.09	(.22)	.05	(.10)
Ignoring	.41	(.25)	.51	(.26)
Intracranial volume	1316276.64	(97319.27)	1356583.19	(94022.57)
Total hippocampal volume[a]	6471.37	(520.18)	6517.86	(454.87)
Hippocampal head volume[a]	3137.94	(391.51)	3249.55	(396.50)
Hippocampal body volume[a]	2392.13	(267.09)	2355.70	(318.88)
Hippocampal tail volume[a]	938.27	(246.53)	930.01	(260.18)
Total amygdala volume[a]	3064.53	(240.49)	3197.37	(283.67)

Note: Empathic responding (global score) was rated on a 1–5 scale; values for individual empathic behaviors are proportion scores. Brain volumes are in mm^3.

[a] ICV-adjusted volume

Table 2

Bivariate Correlations between Empathic Responding and Brain Volumes.

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Empathic responding	-	.56**	.68**	.68**	-.13	-.08	-.66**	-.12	.17	-.01	.12	.17	-.13
Empathic behaviors													
2. Concerned attention		-	.33**	.37**	.01	0.16	-.79**	-.13	.15	.06	.02	.14	-.06
3. Problem-focused responses			-	.30**	.08	-.06	-.53**	-.11	.21†	.05	.15	.17	-.04
4. Emotion-focused responses				-	-.10	-0.12	-.50**	-.07	.09	.06	.04	<.01	-.06
Unempathic behaviors													
5. Negativity					-	.20†	-.19	.01	-.04	.13	-.07	-.19†	.08
6. Personal Distress						-	-.41**	.07	.06	-.02	.05	.06	.09
7. Ignoring								.06	-.16	-.09	-.06	-.09	.01
8. Intracranial volume								-	.04	.02	-.01	.00	.09
9. Total hippocampus^{a}									-	.52**	.32**	.69**	.41**
10. Hippocampal head^{a}										-	-.49**	<.01	.47**
11. Hippocampal body^{a}											-	.25*	-.01
12. Hippocampal tail^{a}												-	.06
13. Total amygdala^{a}													-

$^{\dagger}p < .10$. $*p < .05$, $**p < .01$.
^{a}ICV-adjusted volume.

Table 3

Regressions Predicting Child Empathic Responding from ICV-Adjusted Hippocampal Volumes.

Model		**β**	***t***	***p***	**Δ*R*²**
1. Total hippocampus					
Step 1	Age	-.12	-1.09	.274	*.07*
	Sex	.26*	2.32	.021	
Step 2	Total hippocampus	.23*	2.04	.042	*.05*
Step 3	Age × Total hippocampus	.09	.81	.419	*.08*
	Sex × Total hippocampus	-.45*	-2.40	.016	
2. Hippocampal head					
Step 1	Age	-.12	-1.09	.274	*.07*
	Sex	.26*	2.32	.021	
Step 2	Hippocampal head	.07	.59	.559	*.01*
3. Hippocampal body					
Step 1	Age	-.12	-1.09	.274	*.07*
	Sex	.26*	2.32	.021	
Step 2	Hippocampal body	.11	.93	.350	*.01*
4. Hippocampal tail					
Step 1	Age	-.12	-1.09	.274	*.07*
	Sex	.26*	2.32	.021	
Step 2	Hippocampal tail	.24	1.62	.104	*.03*

Note. Sex is dummy-coded with 0 indicating boys and 1 indicating girls. Due to constraints on statistical output from imputed datasets, ΔR^2 values were estimated from the original (non-imputed) dataset.

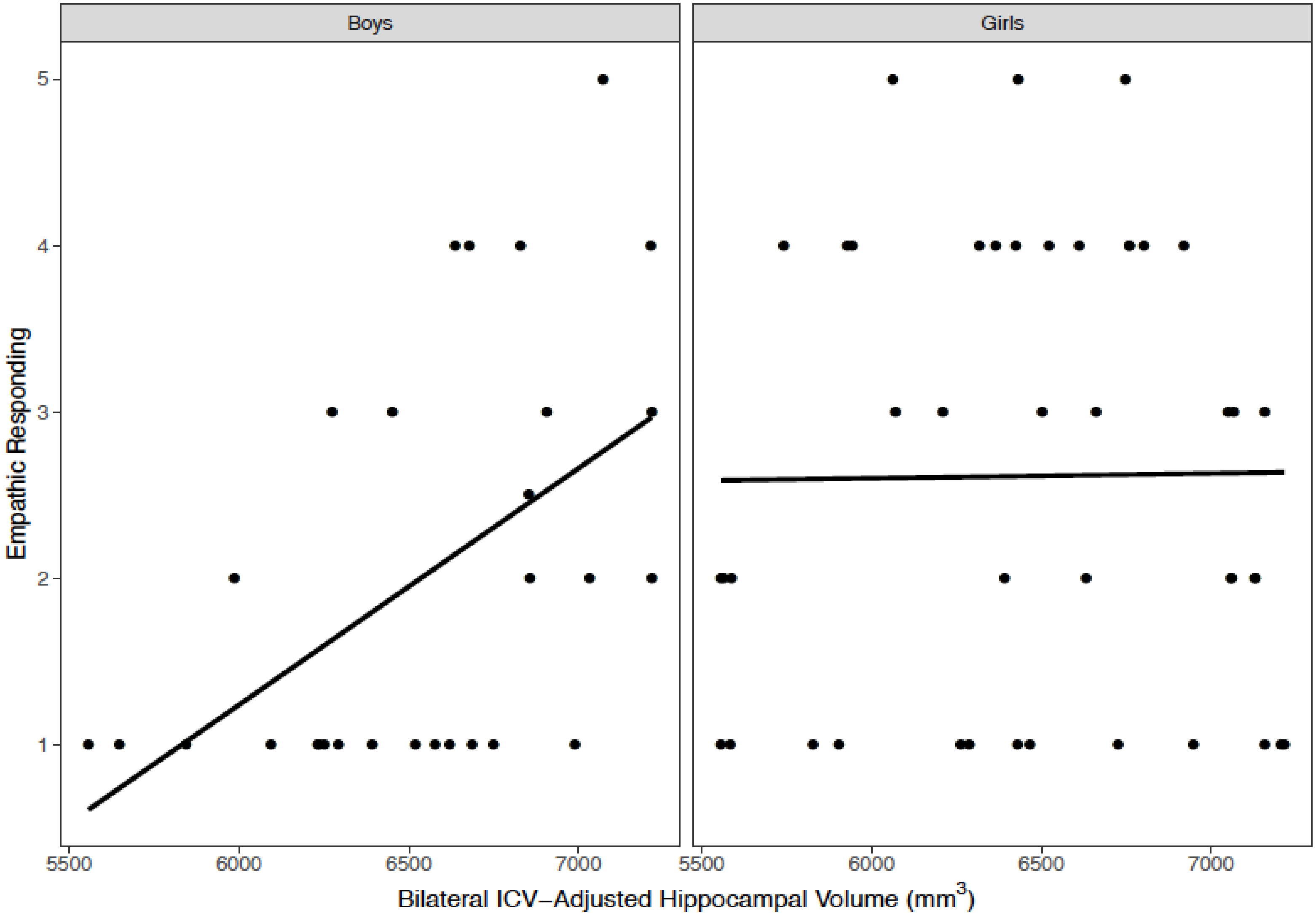

Figure 1. Bilateral ICV-adjusted hippocampal volume predicted observed empathic responding for boys (linear $R^2 = .27$), but not for girls (linear $R^2 < .01$).