Emergence of higher cognitive functions: Reorganization of large-scale brain networks during childhood and adolescence

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Abstract

In the present chapter, we first review *neurodevelopmental changes in brain structure and function* and the main findings derived from the use of these advanced neuroscientific tools, which can be generalized to the development of higher cognitive functions as well as to other areas of research within developmental cognitive neuroscience. Second, we highlight the main neuroimaging evidence on the *development of working memory and cognitive control processes* and the main neural mechanisms and brain networks supporting them. Third, we review behavioral and neuroimaging research on the *development of memory encoding and retrieval processes,* including *mnemonic control*. Finally, we summarize important *current and future directions* in the study of the neurocognitive mechanisms supporting the development of higher cognitive functions, underscoring the importance of multi-disciplinary approaches, different level of analyses, and longitudinal designs to shed further light on the emergence and trajectories of these functions over development.

Key-words: Developmental cognitive neuroscience, mnemonic control, working memory, cognitive control, episodic memory, prefrontal cortex (PFC), medial temporal lobe (MTL).

Children frequently face situations where they must select among competing choices, such as eating a snack now or save room for dinner, or focus on finishing homework before playing a videogame. In making such decisions, it is necessary to reconcile the conflict between competing options available in the context with a specific set of expectations and rules, as well as to inhibit impulses for immediate gratification in the service of a choice that is less immediate and automatic. Similarly, children often come across challenging cognitive operations that may require, for instance, adding large series of numbers, ordering several pieces of information to build a logical argument, or trying to remember something the teacher said. These operations require retrieving, maintaining, and updating relevant information that is accessible and available for manipulation.

Higher cognitive functions refer to multidimensional executive and control processes characterized by being voluntary and highly effortful. They include the ability to evaluate, organize, and reach goals, as well as the capacity to flexibly adapt behavior when confronted with novel problems and situations. Selective and executive attention, cognitive control, and working memory have been considered as some of the main higher cognitive functions, with developmental improvements in these abilities allowing parallel improvements in other cognitive domains.

Research evidence from developmental cognitive neuroscience has consistently linked improvements on these executive functions with prefrontal cortex (PFC) maturation. Recent views have also underlined the positive consequences of this prolonged prefrontal development trajectory on learning of social and linguistic conventions (Thompson-Schill, Ramscar, & Chrysikou, 2009). The PFC however, does not function alone. Improvements on higher cognitive

functions from childhood to adulthood reflect the integration of complex widely distributed brain systems that are subject to structural and functional changes over development (Fair et al., 2009; Lebel, Walker, Leemans, Phillips, & Beaulieu, 2008). In recent years, developmental scientists have begun to examine how brain *networks*, rather than merely isolated brain regions, develop over time. The ultimate goal of developmental cognitive neuroscientists is to break down high-level human cognition functions into its component processes to examine the emergence and trajectories of these functions over development.

In doing so, developmental cognitive neuroscientists are now drawing on multiple imaging methods and analytic approaches allowing measuring cross-sectional and longitudinal changes over development in brain structure, function, and interactions between structure and function. In the present chapter, we first review *neurodevelopmental changes in brain structure and function* and the main findings derived from the use of these advanced neuroscientific tools, which can be generalized to the development of higher cognitive functions as well as to other areas of research within developmental cognitive neuroscience. Second, we highlight the main neuroimaging evidence on the *development of working memory and cognitive control processes* and the main neural mechanisms and brain networks supporting them. Third, we review behavioral and neuroimaging research on the *development of memory encoding and retrieval processes,* including *mnemonic control*. Finally, we summarize important *current and future directions* in the study of the neurocognitive mechanisms supporting the development of higher cognitive functions, underscoring the importance of multi-disciplinary approaches, different level of analyses, and longitudinal designs to shed further light on the emergence and trajectories of these functions over development.

Neurodevelopmental changes in brain structure and function

Cortical thinning over development

Thanks to the development of powerful analytic tools for measuring longitudinal changes in brain structure, we now have detailed information about within-person changes in cortical thickness over development (Gogtay & Thompson, 2010; Tamnes et al., 2010). These data reveal piecemeal cortical thinning over childhood and adolescence, with association cortices – including but not limited to PFC – maturing later than primary sensory cortices. Within PFC, medial and ventral regions mature most quickly, such that dorsolateral PFC matures later than other prefrontal subregions.

There are several important caveats related to this research. First, these developmental changes are not yet understood at the cellular level. Cortical thinning is likely to reflect multiple changes at the cellular level, including decreased gray matter due to synaptic pruning and increased white matter as a result of myelination and/or increased axon diameter (Giedd, 2008; Tamnes et al., 2010). Indeed, recent structural MRI analyses by Gotgay and Thompson (2010) and Hua et al. (2009) suggest that there is white matter growth underlying areas of thinning gray matter.

Second, the functional significance of these changes in cortical thickness is not yet clear. It is possible to find evidence for positive and/or negative relationships between cortical thickness and cognitive performance. These brain-behavior relationships can be influenced by age, sex (Christakou et al., 2009; Lenroot & Giedd, 2010), and cognitive aptitude (Karama et al., 2009). Further, studies that have compared structural and functional MRI measures of brain development have not provided evidence for a simple relationship between them (Lu et al.,

2009). Thus, each of these measures provides a complementary perspective on brain development. Any one measure considered in isolation, such as cortical thickness (Lenroot and Giedd, 2010) or white matter integrity (Lebel et al., 2008) or functional connectivity (Dosenbach et al., 2010), can provide only an incomplete view of brain maturation.

Strengthening of white matter pathways

Diffusion Tensor Imaging (DTI) provides an indirect measure of white matter tracts *in vivo* in the human brain (Fields, 2008). A recent *post mortem* study has validated DTI probabilistic tractography of a specific neural pathway with tissue samples of the medial temporal lobes (Augustinack et al., 2010). The development of DTI has made it possible to measure within-individual changes in white matter tracts over development, and their relationship to changes in cognition. In a longitudinal study, Giorgio and colleagues (2010) have shown that white matter volume increases over development, likely due to increasing axon diameters within developing tracts. Thus far, however, most developmental DTI research has been cross-sectional, comparing participants of different ages. Lebel and colleagues (2008) have published a large cross-sectional DTI dataset characterizing the developmental trajectories of a number of important white matter tracts (Lebel et al., 2008). Although white matter maturation takes place throughout the brain, it is possible to link cognitive performance to the strength of specific tracts (Johansen-Berg, 2010; Madsen et al., 2010; Niogi, Mukherjee, Ghajar, & McCandliss, 2010; Olson et al., 2009).

We have learned a lot over the last few years about the typical developmental trajectory of cortical thickness and white matter tracts. However, we still know very little about how these changes relate to developmental changes or individual differences in brain function or behavior. Recently, Niogi et al. (2010) have provided evidence of a triple dissociation in the brain-behavior

relationships of the integrity (functional anisotropy, FA) of three white matter tracts to the three attention components identified with the Attention Network Task (ANT): alerting, orienting, and executive attention (specifically, conflict resolution; see Figure 1). Consistent with previous functional imaging evidence indicating that these components of attention are subserved by dissociable networks, this study revealed structure-function positive correlations between alerting and the anterior limb of the internal capsule, orienting and the splenium of the corpus callosum, and conflict resolution and the anterior corona radiata.

- Insert Figure 1 around here -

Developmental changes in functional networks

While techniques like DTI help us to characterize the development of white matter tracts, research on patterns of correlated brain activation provide a complementary picture of developing cortical networks. Functional connectivity analyses identify regions with strongly correlated patterns of BOLD activation over time, either during performance of a cognitive task or at rest. Brain regions that are not directly connected to one another via white matter tracts may nonetheless act in concert as part of a distributed network. Conversely, two brain regions that are anatomically connected may not yet be fully integrated into a shared network (Biswal et al., 2010). Therefore, a promising approach is to integrate these complementary measures of brain connectivity (Rykhlevskaia, Gratton, & Fabiani, 2008). Over the last few years, there have been a number of studies characterizing changes in network connectivity in typically and atypically

developing populations (Cao et al., 2009; Church et al., 2009; Fan et al., 2011; Gao et al., 2009; Superkar et al., 2010; Thomason et al., 2008; see Stevens, 2009, for a review).

One of the central developmental findings in recent functional connectivity work is the progression from short-range connections within cortical areas to longer-range cortico-cortico connections (Church et al., 2009; Fair et al., 2009; Jolles, van Buchem, Crone, & Rombouts, 2011; Stevens, Pearlson, & Calhoun, 2009). As children mature, short-range functional connections become weaker, and long-range connections strengthen (Figure 2). At first, the distributed network is composed of many weak connections, but as children move into adolescence and adulthood, functional connections tend to become stronger but sparser, reflecting the increasing specificity of emerging functional networks (Fair et al., 2009; Superkar et al., 2010). Indeed, Schlaggar, Petersen, and colleagues have shown that it is possible to predict the age of an individual within 2 years with support vector machine-based multivariate pattern analysis based purely on the patterns of functional connectivity measured in a resting-state fMRI scan (Dosenbach et al., 2010).

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Relationships between structural and functional brain changes over development

Broadly, the differences between children and adults in patters of functional connectivity are consistent with the trajectories of gray and white matter development. At the same time that local functional connections within the cortex are weakening, cortical gray matter is thinning – and, as long-range white matter tracts are getting stronger, so is long-range functional connectivity.

Supekar et al. (2010) found that some, but not all, changes in functional connectivity had obvious anatomical correlates. For example, children, who exhibited significantly lower functional connectivity between the posterior cingulate cortex and medial PFC than young adults, also displayed higher gray matter volume and lower white matter density in these regions relative to young adults. On the other hand, while children and adults displayed equally strong functional connectivity between the PCC and the left MTL, children exhibited weak direct anatomical connectivity between these two regions, as measured by DTI. Such findings support the view that these structural and functional measures provide valuable and complementary views of brain development.

Development of higher cognition: working memory and cognitive control

Long-range connections support developmental achievements in higher cognitive functions, such as working memory and cognitive control. Notwithstanding conceptual differences, a general consensus holds regarding working memory and cognitive control as some of the canonical higher cognitive functions in most cognitive developmental theories. *Working memory* refers to the ability to maintain, attend to, and update information that is currently relevant and available on-line for evaluation and manipulation (Baddeley, 1998). *Cognitive control* refers to a set of mental processes that are responsible for the execution, guiding, and monitoring goal-directed behaviors, while inhibiting inappropriate or disadvantageous ones (Braver, Paxton, Locke, & Barch, 2009).

Neuroimaging evidence has shown that frontoparietal circuits implicated in simple *working memory* tasks are already established by middle childhood (e.g., Geier, Garver, Terwilliger, & Luna, 2009; Scherf, Sweeney, & Luna, 2006). Nevertheless, compared to adults, older children and adolescents recruit a more extensive distributed frontoparietal circuitry during working memory maintenance (Geier et al., 2009; Klingberg, 2006) and fail to effectively recruit frontoparietal regions during their performance on more challenging working memory tasks, such as those requiring online manipulation of information (Crone, Wendelken, Donohue, van Leijenhorst, & Bunge, 2006) or maintaining attention on the task by ignoring irrelevant information (Olesen, Macoveanu, Tegner, & Klingberg, 2007). Thus, maturation of the neural circuits supporting working memory processes is characterized by a more consistent recruitment of cortical regions and a refinement in the long-range frontoparietal network connecting these cortical regions.

Response inhibition, attentional regulation, and conflict and error monitoring are cognitive processes that are engaged in the service of *cognitive control*. In adults, cognitive control relies on broad cortical areas, including anterior cingulate cortex, DLPFC, VLPFC/lateral orbitofrontal cortex, as well as temporal and parietal regions, all of which have connections with striatum in the subcortex (e.g., Rubia et al, 2006). Performance on tasks that require suppression of an automatic behavior to perform a less automatic one, such as the Go/No-Go, Stop-signal, Stroop, and Simon tasks does not approach adult levels until late childhood or early adolescence (Davidson, Amso, Anderson, & Diamond, 2006). Evidence from developmental neuroimaging studies suggest that behavioral improvements on cognitive control with age are associated with increasing activation of frontostriatal circuits (Marsh et al, 2006), with a shift from diffuse to focal activation and from posterior to anterior activation (Durston et al., 2006; Rubia et al.,

2006). Moreover, dysregulation or immature frontostriatal control systems has been documented in children, adolescent, and adults with inhibitory control related disorders, such as Tourette's syndrome, Obsessive Compulsive Disorder, and eating disorders (see Marsh, Maia, & Peterson, 2009, for a review); as well as in risk-taking behavior in adolescence paired with increased sensitivity to rewards (Somerville, Hare, & Casey, 2011; van Leijenhorst et al., 2010).

Development of episodic memory and mnemonic control

To evaluate, organize, and adapt behavior and thoughts to reach goals often requires cognitive control mechanisms that allow to codify and to use accessible relevant information, while ignoring irrelevant information. The term *mnemonic control* refers to a set of control processes that, central to higher cognition and key to multiple cognitive operations, determine how relevant information is encoded into, and retrieved from, memory.

Developmental research has revealed strong improvements from early childhood to adolescence in the ability to encode relevant information and to limit interference from irrelevant information (Schneider & Pressley, 1997; Kail, 2002). These developmental achievements are related to control processes at encoding, such as efficient engagement of selective attention to relevant information and elaborative encoding processes leading to a better organization of information in memory (Bauer, 2006). Improvement in memory retrieval processes, including more effective monitoring of the accessed information and better strategic regulation of hippocampal-dependent operations, are usually characterized as showing a slightly more protracted developmental trajectory especially during early and middle childhood years.

In behavioral research, however, is difficult to tease apart the contribution of specific encoding and retrieval processes because dependent measures are obtained principally at retrieval (Bauer, 2006). In contrast, with neuroimaging techniques it is possible to measure brain activation at these specific memory stages separately. Thus, developmental neuroscientific research holds much promise for a comprehensive theory of memory and its development, allowing us to characterize the neural basis of memory related processes and to extant previous evidence from behavioral research in elucidating age-related improvements on mnemonic processes at both encoding and retrieval. Below we describe behavioral research and recent fMRI studies examining age-related changes in activation at encoding and retrieval.

Development of memory encoding processes

Developmental research combining behavioral and electrophysiological measures has underscored that age-related changes in episodic memory during early childhood are especially attributed to more effective and efficient encoding and consolidation processes (Bauer, 2006). For instance, increases in short-term memory span are evident during early childhood, and continue during middle childhood years, indicating that children become increasingly more effective at keeping task-irrelevant information out of short-term memory (Bauer, 2008). Also, with age there are increases in the use of rehearsal to maintain to-be-remembered information over time, reflecting a more organized processing of relevant information (e.g., Bjorklund, Dukes, & Brown, 2008; Schneider & Bjorklund, 1998). During middle childhood children also become increasingly efficient in encoding verbal information, exhibiting gains in remembering verbatim forms and extracting gist information (Brainerd, Holliday, & Reyna, 2004). For

instance, Ghetti and Angelini's (2008) study underscored the role of elaborative processing during encoding, showing that age-related improvements in recollection where only observed when children encoded content semantically. In contrast, recollection of perceptually encoded information did not change over childhood and adolescence.

Increased PFC engagement during encoding over childhood and adolescence

Improvements in memory encoding are associated with age-related changes in the temporo-cortical network that subserves long-term memory. PFC and MTL regions interact during encoding and, as a consequence, structural and functional age-related changes in both regions are likely to contribute to developmental changes in episodic memory. Recent neuroimaging evidence has showed increased activation and selective recruitment of vlPFC and dlPFC regions in encoding processes leading to successful memory formation during middle childhood and adolescence (Ghetti, DeMaster, Yonelinas, & Bunge, 2010; Ofen et al., 2007). Also, increases in the coupling between left dlPFC and left MTL regions during encoding has been observed from middle childhood to adolescence, suggesting that increased functional interactions between PFC and MTL underlie the development of more effective memory encoding strategies (Menon, Boyett-Anderson, & Reiss, 2005).

Nevertheless, although the involvement of MTL regions in encoding processes across development is widely demonstrated, there is still debate in regard to developmental changes in the pattern of activations in this region during encoding processes. Recent evidence from a cortical pattern matching study examining maturational changes in cortical thickness between

ages 4 and 25 revealed cortical thickness reductions in anterior hippocampus over development, with concomitant increases in posterior hippocampus (Gogtay et al., 2006). These findings support the idea that MTL regions do not mature as early as previously thought. Also, developmental fMRI studies have showed increasing functional specialization with age of hippocampus and posterior parahippocampal gyrus for recollective details (Ghetti et al., 2010), and also of posterior parahippocampal gyrus for high complexity scenes (Chai, Ofen, Jacobs, & Gabrieli, 2010; but see Ofen et al., 2007).

Evidence for neurodevelopmental increases in selective encoding

Despite of the importance of the previously reported neurodevelopmental studies in elucidating the role of different MTL and PFC regions, and their interactions during memory encoding, there is sparse neuroimaging research examining developmental changes in mnemonic control processes at encoding. A recent study by Wendelken, Baym, Gazzaley, and Bunge (2011) investigated age-related changes in selective attention processes that allow committing to memory relevant information, while ignoring competing or irrelevant stimuli (Bjorklund & Harnishfeger, 1990).

Results from Wendelken et al's study revealed that top-down recruitment of bilateral parahippocampal place area (PPA) increased from middle childhood to adolescence when participants specifically attended to scene stimuli. Moreover, while younger children appear to be markedly different than young adults, in terms of their capacity to modulate the recruitment of PPA, these differences have practically disappeared by age 14. Children's age-related increases

in PPA enhancement were also matched by age-related increases in the selective activation for attention to scenes versus passive viewing of lateral dlPFC (Figure 3). These findings are consistent with previous evidence showing age-related increases in the selective activation of lPFC on cognitive control tasks (Crone et al., 2006; Konrad et al., 2005) and the role of dlPFC as a primary locus of top-down control (Gazzaley et al., 2007). Additional neuroimaging research on developmental trajectories in mnemonic control processes at encoding is needed to further characterize the neural mechanisms underlying the formation of relevant memories for goal-directed thought and behavior.

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Development of control and monitoring processes over retrieval

Development of retrieval processes can largely contribute to age-related changes in episodic memory performance observed across childhood and adolescence. Overall, there is extensive behavioral evidence showing age-related improvements during middle childhood in the ability to flexible use cues to aid retrieval (Ashcraft, Kellas, &Keller, 1976; Emmerich & Ackerman, 1978). Even assuming that relevant information is successfully encoded and stored across ages, compared to older children and adults, younger children are more heavily dependent of the cues presented in the original context to reinstate encoded information (Ackerman, 1982). Moreover, there is initial evidence showing that detrimental effects of changing cues between encoding and retrieval on memory performance decreases from middle childhood to adulthood, even for

materials that, after encoding, have been repeatedly reinforced in association with their original cues (Paz-Alonso, Ghetti, Matlen, Anderson, & Bunge, 2009).

Similarly, developmental changes in the ability to use strategies and reasoning processes during retrieval may also explain the age-related improvements typically observed in episodic memory during school years. For instance, clustering to-be-remembered information as a function of semantic categories during free recall is a helpful strategy that, relying on knowledge base about the world, improves across childhood years and correlates positively with metamemory skills (Hasselhorn, 1990; Schneider & Pressley, 1997). In fact, together with age-related improvements in the ability to flexibly use different type of cues and strategies to aid memory retrieval, the development of metamemory abilities have an important impact in the final memory output, allowing individuals to monitor the accuracy of the retrieved information (Ghetti, Lyons, Lazzarin, & Cornoldi, 2008) and to evaluate accessible contextual information to locate memories as a function of place and time (Johnson, Hashtroudi, & Lindsay, 1993; Mitchell & Johnson, 2009).

Neurodevelopmental correlates of memory retrieval processes

Developmental achievements in episodic memory retrieval are frequently described as PFC-dependent strategic processes and, as a consequence, they have been linked to PFC maturation (Nelson, 1997; Schwenck, Bjorklund, & Schneider, 2009). Cognitive neuroscience research with adults have underscored the role of lateral PFC in episodic memory retrieval, with vlPFC being implicated in processing item-related cues across different representational domains (e.g., Badre

& Wagner, 2007) and dlPFC aiding monitoring and response selection processes (e.g., Ranganath, Heller, & Wilding, 2007).

We have also shown differentiated patterns of activation with age in vlPFC and dlPFC retrieval reflecting, respectively, development of semantic elaboration processes and decision operations during memory retrieval (Paz-Alonso, Ghetti, Donohue, Goodman, & Bunge, 2008). Together with evidence indicating that developmental changes in PFC cortical thickness occur throughout childhood and adolescence (Gogtay & Thompson, 2010; Tamnes et al., 2010), these findings support the hypothesis that structural and functional development of PFC mediates the development of episodic memory retrieval.

Developmental changes in mnemonic control over retrieval

Sometimes it is possible to suppress the process of memory retrieval, which allows us to focus on goal-relevant memories and to limit the influence of interfering information. Evidence from previous behavioral research using directed-forgetting paradigms suggested increases in memory inhibitory control during middle childhood years (Sahakyan & Kelley, 2002; Wilson & Kipp, 1998). However, directed-forgetting effects can be explained by alternative interpretations to mnemonic control over retrieval, including selective encoding and rehearsal of the to-be-remembered items and contextual shifts (Paz-Alonso et al., 2009; Wilson & Kipp, 1998).

We have recently used the Think/No-Think (TNT) paradigm (Anderson & Green, 2001) to examine developmental changes in mnemonic control over retrieval. The TNT paradigm makes it possible to measure active on-line attempts to prevent and encoded memory to enter

consciousness and their effects in long-term memory. Results from this study revealed age-related improvements in memory suppression (i.e., higher percent recalled for Baseline relative to No-Think items) over middle childhood (Figure 4). Moreover, improvements in memory suppression from age 8 to 12 were observed against a backdrop of overall improvements in declarative memory for to-be-remembered items over this age range.

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Several neuroimaging studies with adults using this paradigm have showed that lateral PFC (lPFC) modulates hippocampal activation during attempts to suppress memory retrieval (e.g., Anderson et al., 2004; Depue, Curran, & Banich, 2007; Depue, Burgess, Willcutt, Ruzic, & Banich, 2010). Thus, it is likely that developmental improvements in the ability to stop memory retrieval are due to age-related refinements in the ability to engage specific lPFC regions or, complementarily, a larger mnemonic control network that modulates activation in MTL areas involved in episodic retrieval. Moreover, the main anatomical fiber tracts that could support lPFC-MTL interactions are the cingulum bundle and the uncinate fasciculus (Figure 5*A*). Compared to other white-matter tracts, these dorsal and ventral fronto-temporal anatomical pathways have the most protracted maturation, reaching the 90% of their development only after 25 years of age (Lebel et al., 2008; see Figure 5*B* & *C*). Current research is testing these hypotheses on the neural mechanisms determining age-related changes in mnemonic control over retrieval in a large fMRI study including children aged 8 to 9 and 11 to 12, and also young adults (Paz-Alonso, Ghetti, Wendelken, Anderson, & Bunge, under review).

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Important current and future directions in developmental cognitive neuroscience

There is still much to be discovered regarding the neural mechanisms that support the emergence of higher cognitive functions over childhood and adolescence. An endeavor of this level of complexity necessitates a multi-disciplinary approach with large research teams, large sample sizes, and data collection at multiple time points per individual. At the same time, it will be important in the coming years for developmental cognitive neuroscience to strike the right balance between high through-put, data-driven research – so-called "discovery science" (Biswal et al., 2010) – and hypothesis-driven research grounded in theories of cognitive development. Below we highlight several important areas for further research.

Cellular basis of macroscopic structural changes observed over development

Before it was possible to measure brain function, anatomical research was the only recourse for a budding neuroscientist. As functional brain imaging techniques have surged, there has been a steady decline in well-trained neuroanatomists. The pendulum must swing back in the other direction if we are to understand the neural basis of developmental changes in brain function and behavior. Structural MRI imaging can provide astonishingly detailed images of the brain; used in combination with sophisticated anatomical techniques in post mortem tissue (Augustinack et al., 2010), it is now possible to begin to explore the cellular underpinnings of macroscopic structural changes over development.

Early brain development

Although most of the behavioral literature on cognitive development has focused on the period of rapid changes observed during early childhood, most of the developmental cognitive neuroscientific studies to date have, for practical reasons, focused on older children and adolescents (Poldrack, 2010). In recent years, researchers have refined pediatric imaging protocols (Nordahl et al., 2008; Raschle et al., 2009) that make it possible to obtain high-quality structural and functional MRI data from infants (Dehaene-Lambertz et al., 2010; Fan et al., 2011; Gao et al., 2009) and young children (Cantlon, Pinel, Dehaene, & Pelphrey, 2011). This advance makes it possible to measure the functional organization of the newborn brain, and to examine the neural changes that support the emergence of new cognitive abilities over early childhood.

Longitudinal research

To examine – and interrelate – developmental trajectories for cognition, brain structure, and brain function, it is necessary to acquire data at multiple time-points per individual. Longitudinal research can provide important insights regarding typical and atypical cognitive development (Reichenberg et al., 2010). Although there are few published longitudinal MRI studies of children (Giedd et al., 2009; Gogtay & Thompson, 2010), and even fewer that include functional as well as structural measures (Fan et al., 2011; Shaw et al., 2009), a number of research groups are conducting this important work now.

External influences on cognitive and brain development

An important next step in developmental cognitive neuroscience is the elucidation of genetic, hormonal, and environmental factors that interact during the development of higher cognitive functions. There has been research on gene x environment influences on behavior during development (Wiebe et al., 2009). Until recently, this work has left the brain out of the equation, but developmental cognitive neuroscience is beginning to examine genetic and/or environmental influences on brain structure and function (Casey, Soliman, Bath, & Glatt, 2010; Chiang et al., 2009; Hackman & Farah, 2009; Lenroot et al., 2009; Thomason et al., 2010), and is also beginning to look at the influence of changing pubertal hormone levels on cognition (Blakemore, Burnett, & Dahl, 2010).

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Figure Legends

Figure 1. Modified with permission from Niogi et al. (2010). In this study, McCandliss and colleagues provide evidence for a triple dissociation in the inter-individual relationships between white matter integrity of three tracts and cognitive performance on the alerting, orienting, and conflict resolution components of the ANT. On this task, participants must decide as quickly as possible whether the central arrow of an array points to the left or to the right. On each trial, one of three cue types is presented, followed closely by a target (sample cues and targets illustrated in gray). Alerting cues indicate that a trial is about to begin, and spatial cues indicate whether the target stimulus is most likely to appear above or below the fixation cross. On incongruent target stimuli, participants must resolve conflict between the responses indicated by the central and flanking arrows. Each of three white matter tracts -posterior limb of the internal capsule, the splenium of the corpus callosum, and the anterior corona radiata, exhibited a positive correlation between FA and cognitive performance on one of the three components of the ANT.

Figure 2. Modified with permission from Church et al. (2009). Red lines indicate functional connections that are stronger in children than in adults; blue lines indicate the connections that are stronger in adults. The inlaid graph shows age-related changes in functional connectivity between the intraparietal sulcus (IPS) and dorsolateral prefrontal cortex (dlPFC) over age.

Figure 3. Modified with permission from Wendelken et al. (2011). *(A)* Mean familiarity rating for adults and children as a function of condition (attended, passive, ignore). Dotted line represents mean familiarity ratings for new scenes presented only during the retrieval phase. *(B)* Coronal view of the Left DLPFC functional ROI, identified from the Scene > Passive contrast

across all participants, showing a positive correlation for dlPFC selective enhancement (Scene-Passive cue) with age.

Figure 4. Modified from Paz-Alonso et al. (2009). Subsequent memory recall on the Same-Probe task for Think, No-Think, and Baseline items as a function of age group from our previous behavioral study including a total of 70 participants (twenty 8-9-year-olds; twenty 11-12-year-olds; and 30 young adults; Paz-Alonso et al., 2009).

Figure 5. Modified with permission from Lebel et al. (2008). The cingulum bundle (*dark blue*) and the uncinate fascilus (*yellow*) are the two white-matter tracts connecting MTL and lPFC regions. *(A)* The cingulum bundle connects posterior hippocampus with posterior parietal cortex and lPFC via the parahippocampal gyrus. The uncinate fasciculus, on the other hand, connects anterior hippocampus with ventral lPFC. *(B)* Age-related FA increases from age 5 to 30 measured by tractography in the cingulum bundle (*dark blue*) and the uncinate fasciculus (*yellow*). *(C)* Magnitude and timing of development in these fronto-temporal white-matter tracts. The length of the colored bar indicates the age at which the region reached 90% of its development plateau from 5 years, as measured by fitting parameters in the exponential equation. The color of each bar represents the percent increase of FA.

Figure 1

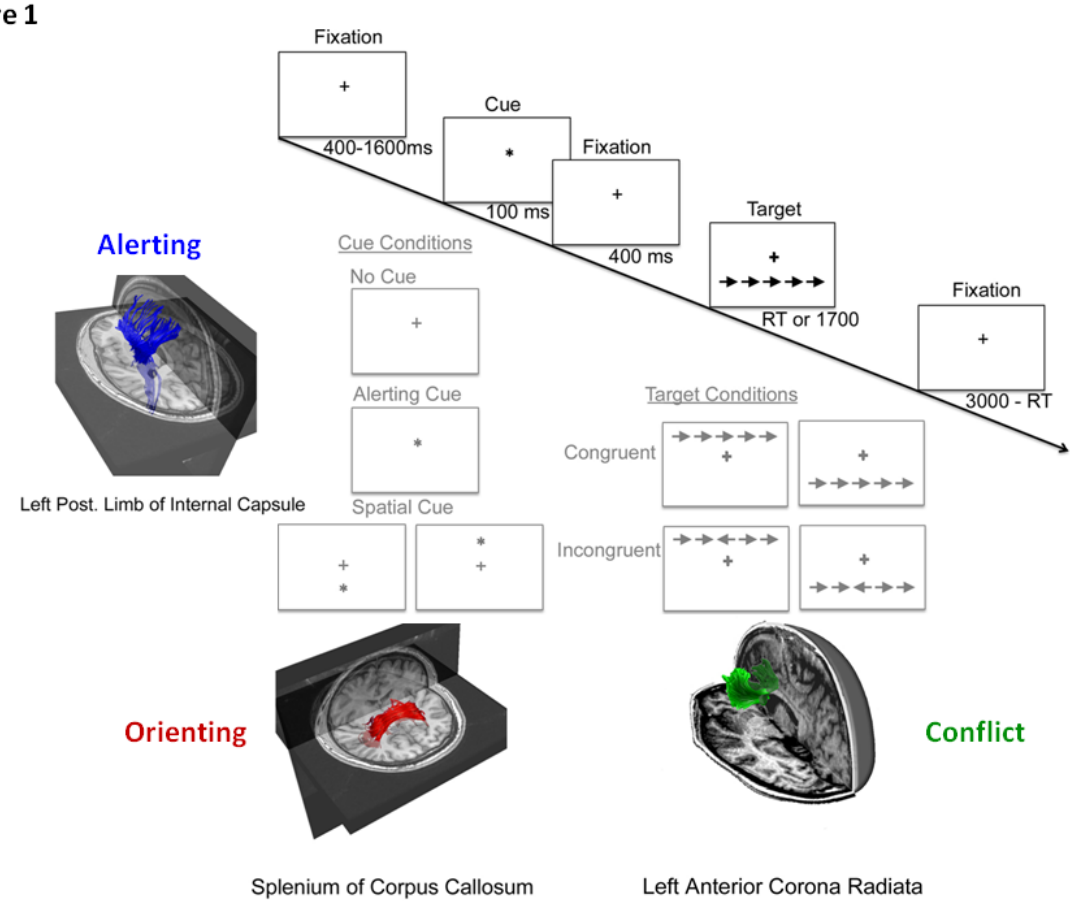

Fixation
400-1600ms
Cue
100 ms
Fixation
400 ms
Target
RT or 1700
Fixation
3000 - RT
Alerting
Cue Conditions
No Cue
Alerting Cue
Spatial Cue
Target Conditions
Congruent
Incongruent
Left Post. Limb of Internal Capsule
Orienting
Splenium of Corpus Callosum
Conflict
Left Anterior Corona Radiata

Figure 2

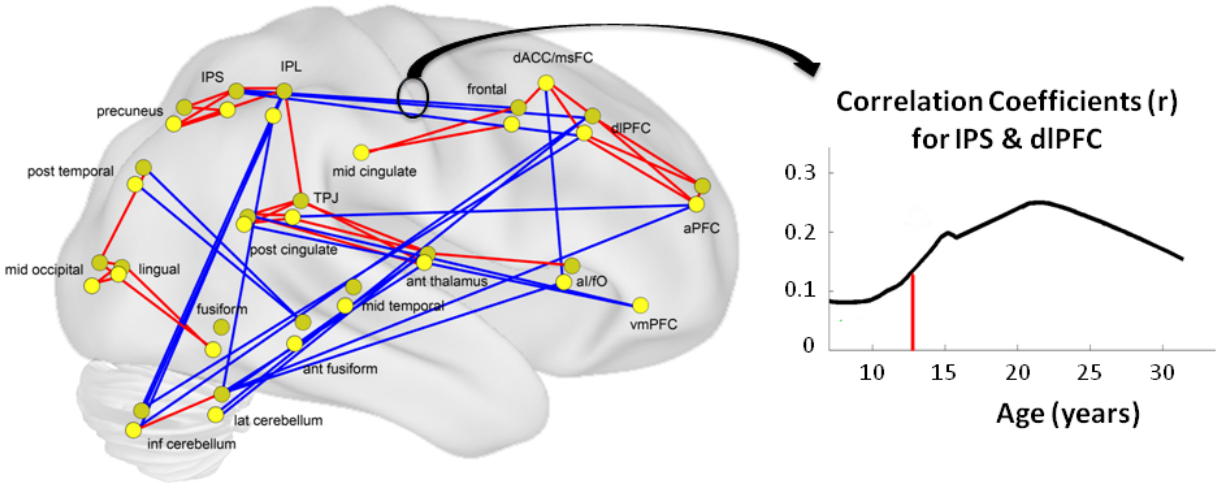

IPS
IPL
dACC/msFC
frontal
precuneus
dlPFC
mid cingulate
post temporal
TPJ
aPFC
post cingulate
mid occipital
lingual
ant thalamus
al/fO
mid temporal
fusiform
vmPFC
ant fusiform
lat cerebellum
inf cerebellum
Correlation Coefficients (r)
for IPS & dlPFC
0.3
0.2
0.1
0
10
15
20
25
30
Age (years)

Figure 3

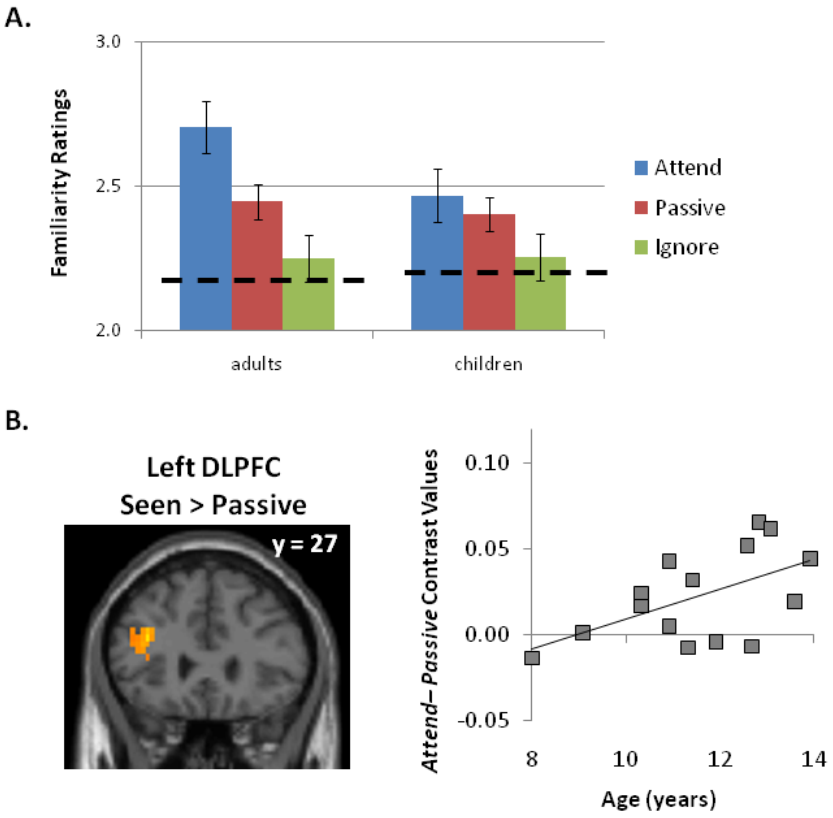
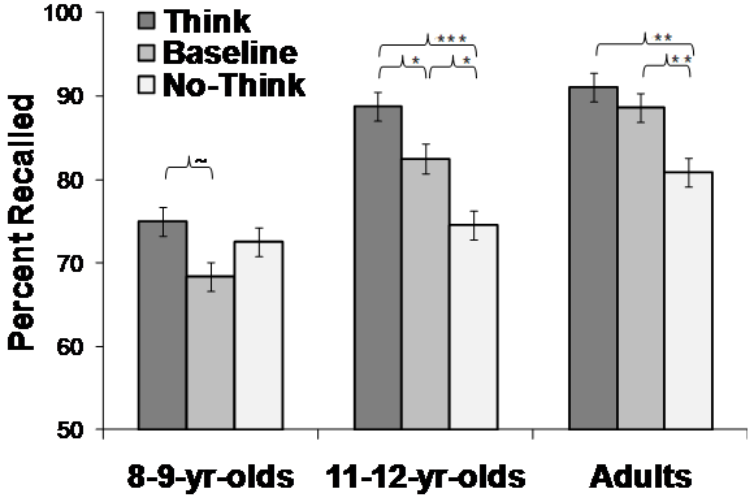

A.
3.0
2.5
2.0
Familiarity Ratings
adults
children
Attend
Passive
Ignore
B.
Left DLPFC
Seen > Passive
y = 27
0.10
0.05
0.00
-0.05
Attend– Passive Contrast Values
8
10
12
14
Age (years)

Figure 4


Think
Baseline
No-Think
Percent Recalled
100
90
80
70
60
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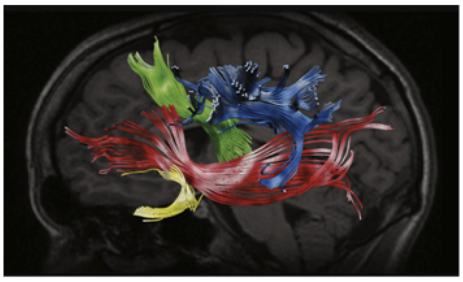
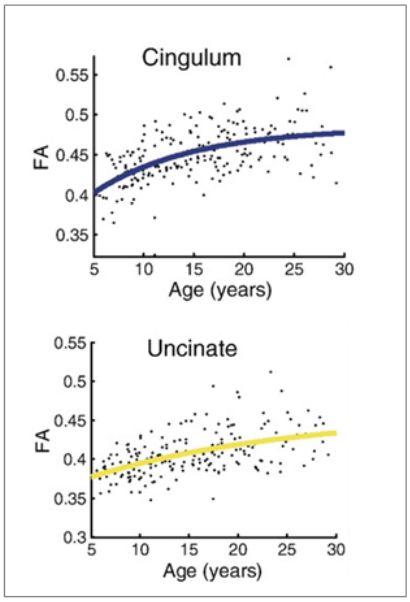
8-9-yr-olds
11-12-yr-olds
Adults

Figure 5

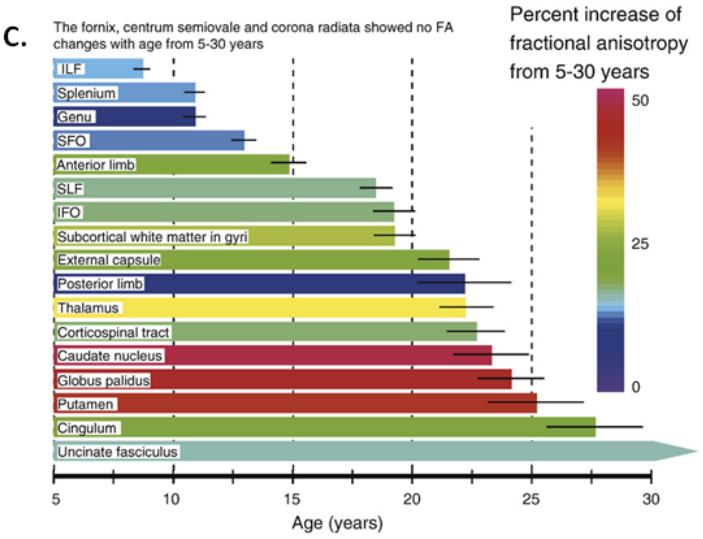
A.



B.


Cingulum
FA
0.55
0.5
0.45
0.4
0.35
5
10
15
20
25
30
Age (years)
Uncinate
FA
0.55
0.5
0.45
0.4
0.35
0.3
5
10
15
20
25
30
Age (years)

C.


The fornix, centrum semiovale and corona radiata showed no FA changes with age from 5-30 years
Percent increase of fractional anisotropy from 5-30 years
50
25
0
ILF
Splenium
Genu
SFO
Anterior limb
SLF
IFO
Subcortical white matter in gyri
External capsule
Posterior limb
Thalamus
Corticospinal tract
Caudate nucleus
Globus palidus
Putamen
Cingulum
Uncinate fasciculus
5
10
15
20
25
30
Age (years)