Title

From bottom-up to top-down : an fMRI study of language development

Authors

Parks, Erin Nicole

Parks, Erin Nicole

Publication Date

2012

UNIVERSITY OF CALIFORNIA, SAN DIEGO

SAN DIEGO STATE UNIVERSITY

From Bottom-up to Top-down: An fMRI Study of Language Development

A dissertation submitted in partial satisfaction of the
requirements for the degree Doctor of Philosophy

in

Clinical Psychology

by

Erin Nicole Parks

Committee in charge:

University of California, San Diego

Professor Frank Haist
Professor Doris A. Trauner

San Diego State University

Professor Ralph-Axel Müller, Chair
Professor Vanessa L. Malcarne
Professor Judy S. Reilly

2012

The Dissertation of Erin Nicole Parks is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

Chair

University of California, San Diego

San Diego State University

2012

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACKNOWLEDGMENTS

I want to acknowledge and thank my mentor and committee chair, Dr. Ralph-Axel Müller for inviting me to join the Brain Development Imaging Laboratory and accepting me into the Clinical Psychology Joint Doctoral Program. Thank you Axel for encouraging my critical thinking and for modeling eloquent, beautiful, *and* concise writing that will always inspire me. You are an outstanding mentor who has always treated me, and all of your students, with incredible respect.

I also want to acknowledge and thank my peers in the JDP, particularly my neuropsych cohort. You were my teammates and I loved that we had a collaborative class that cheered each other on through practicums and stats and comps and grants, oh my! And a special thank you to my dear friend Dr. Vaurio; while Andrea was right, "grad school is *not* a walk in the park," we managed to occasionally make it a poolside mimosa flight, (metaphorically of course!).

Lastly, thank you to my labmates at the BDIL who provided invaluable assistance, support, and friendship, with extra kudos to Brandon, Erin, Becky, and Sarah. Thank you to all of the children and families who participated in this study, my dissertation committee, and the NIH for funding this project. Finally, thank you to my family for their unwavering support and encouragement.

Chapter 3, in part, is a reprint of a section of the article "An fMRI study of sentence-embedded lexical-semantic decision in children and adults" published in Brain and Language in 2010. Moore-Parks, E. N., Burns, E. L., Bazzill, R., Levy, S., Posada, V., & Muller, R. A. The dissertation author was the primary investigator and author of this paper.

VITA

2002	Bachelor of Science, Northwestern University, Chicago, IL
2009	Master of Science, San Diego State University
2010-2011	Predoctoral Internship, San Francisco VA Medical Center
2012	Doctor of Philosophy, University of California, San Diego

FIELDS OF STUDY

Major Field: Clinical Psychology
Minor Field: Neuropsychology

ABSTRACT OF THE DISSERTATION

From Bottom-up to Top-down: An fMRI Study of Language Development

by

Erin Nicole Parks

Doctor of Philosophy in Clinical Psychology

University of California, San Diego, 2012
San Diego State University, 2012

Professor Ralph-Axel Müller, Chair

A growing number of functional MRI studies have examined age-related changes in language organization. However, existing studies have predominantly examined differences between children and adults using cross-sectional designs and have been limited to a single language component studied at a single point in time. Thus the mechanisms by which cognitive changes occur over time are still uncertain. A better understanding of developmental changes in the brain organization for

language might broaden our understanding of cognitive development, elucidate the causes of atypical development, and could potentially inform our diagnosis, treatment, and prevention of developmental disorders. The current project is founded on a comprehensive theory of language development, which predicts organization from predominantly sensorimotor-based (bottom-up) processing in early stages to more strongly top-down controlled processing in later childhood and adulthood. Applied to two language tasks that tap into the two primary components of language development (lexicosemantic and morphosyntactic), this theoretical perspective generates specific hypotheses about developmental change, which were tested both in cross-sectional and longitudinal analyses.

Subjects completed two language tasks: lexical semantic decision (assessing the semantic congruency of sentences describing objects) and morphosyntactic judgment (assessing the grammaticality of sentences) during functional MRI. Forty-one children in two age groups (7 and 9 years) were scanned and brought back for a second scan (n=30) after twelve months, providing a longitudinal component to the study. An adult group (n=15) was scanned at one time point as a comparison. Longitudinal and cross-sectional analyses of the data were performed to examine the interactions and main effects of group (7-year olds, 9-year olds, adults), task (lexicosemantic or morphosyntactic) and time.

We found that both the lexical-semantic and morphosyntactic judgment tasks were associated with left lateralized fronto-temporal networks that were overall similar to those seen in adults. Our findings of age- and time-dependent activation increases in left frontal and parietal networks are consistent with a model of age-

dependent strengthening of ‘top-down’ control mechanisms during language processing. However, we did not find evidence of language development emerging from sensorimotor abilities. In fact, we found inverse results with age- and time-dependent *increases* in bilateral middle and superior occipital gyri for both tasks.

This dissertation is only the second longitudinal study of neurolinguistic development in children and the first to utilize sentence-embedded tasks for two language domains. While our results provide additional evidence for increased top-down control in the process of language learning, more time points are needed in future longitudinal studies to examine possible non-linear development in sensorimotor regions. The present study, which was largely exploratory due to its novel methodology, provides regions of interest for correlation analysis with behavioral developmental markers for future longitudinal studies.

Background

Language is the basis of communication. Reading, writing, gesturing, listening, and speaking are all forms of language. When language is impaired, it can affect an individual's ability to form interpersonal relationships, learn new tasks, seek and maintain employment, and live independently. Language impairment is coincident, concomitant or resultant with a wide range of neurodevelopment disorders including autism, fetal alcohol syndrome, epilepsy, Williams Syndrome, and Down's syndrome and can be consequent to incidents of childhood such as traumatic brain injury, perinatal stroke, and pediatric cancer.

A better understanding of developmental changes in the brain organization for language may broaden our understanding of cognitive development, elucidate the causes of atypical development, and could potentially inform our diagnosis, treatment, and prevention of neurodevelopmental disorders. As an example, when treating children with seizure disorders, one method of intervention is to identify and surgically remove the seizure focus. During surgical planning, functional magnetic resonance imagine (fMRI) is sometimes used to map the child's cortical language networks to determine if the seizure focus is near the language cortex, and thus potentially too risky to remove. It is unclear the role that seizures play in the reorganization of language networks and thus it is unknown how to best time surgery: as soon as the seizure focus can be identified, or after a period of seizures which may reorganize language away from the seizure focus to allow safe surgical removal. To begin to answer these questions, a better understanding of the cortical network for typical language development is needed. It is not known if the cortical regions for language acquisition develop differentially and whether they are consistent across different linguistic elements. This proposal aims to add to the current literature on language development by using fMRI to investigate the neural correlates of lexical semantics and morphosyntax longitudinally in a group of school-aged children.

This proposal will first review typical language acquisition, brain development, and neurodevelopment theories supporting the current proposal. Next, a review of the behavioral and fMRI literature for lexical semantics and morphosyntax, the two language aspects we wish to study, will be presented. Finally, previous fMRI studies of language development is reviewed, along with the methodological considerations they raise, followed by the complete methodology for the proposal.

Language Acquisition

The literature would suggest that language acquisition begins *in utero* due to prenatal experience with maternal speech. Studies with newborns have indicated that not only can they distinguish their mother's voice from that of another female (DeCasper & Fifer, 1980), they are also able to distinguish their mother's language from a foreign language (Mehler et al., 1988), and can discriminate between a familiar passage (read to them *in utero*) and an unfamiliar passage (DeCasper & Spence, 1986). Functional imaging data support these findings of early language acquisition with 3-month-old infants showing increased left-lateralization and activation in left superior temporal and angular gyri, similar to the cortical networks seen in adult language listening, when processing normal speech compared to reversed speech (Dehaene-Lambertz, Dehaene, & Hertz-Pannier, 2002).

At 6 months of age, babies often begin babbling and produce intonation contours resembling that of adults (Petitto & Marentette, 1991). Between 8 to 10 months of age, babies begin to show word comprehension and utilize gestures to communicate. While the average age of first-word production is around 12 months, initially children demonstrate a larger productive repertoire of action-gestures than vocalizations (Caselli & Casadio, 1995) and have a larger comprehension vocabulary than production vocabulary (Fenson et al., 1994). Between 16 and 18 months, when children reach the 50-word milestone, most children experience a word spurt and the rate at which they acquire new words increases from 8 to 11 words per month to an average of 22 to 37 words per month (Benedict, 1979). By 20 to 24 months, children are producing two word utterances and by 36 months they are able to form complex sentences. On average, children are able to produce scripts and simple stories by their fourth birthday.

Children’s utterances are not simply words that are randomly strung together, but from a very early stage, children reveal their grasp of the principles of sentence formation or syntax. Around 2 years of age, children start to acquire grammatical morphemes (e.g., plural, possessive, past regular). Though children acquire these grammatical morphemes at different ages, most interesting is the fact that the order of acquisition across more than a dozen grammatical morphemes is approximately the same for all children (R. Brown, 1973).

By the age of 5, children are very competent speakers. Their phonology skills are similar to adults as they’ve typically mastered all vowels and may only struggle to articulate a few consonants (Ingram, 1989). Semantically, children know the meaning of at least 10,000 different words (Clark, 2003), understand common idioms and concrete metaphors, and can produce humor intentionally (McGhee, 1979; Nippold, 1985). By the age of 5, children's syntax and morphology are also well developed. They have a mean length of utterance of six or more morphemes, have mastered Brown's 14 grammatical morphemes, and can produce sentences with relative, adverbial, and nominal clauses. Five-year-olds are also able to use multiple embedding, infinitives, gerunds, and negation, can produce compound and complex sentences, ask wh- questions, and use past, present, and future tense verbs (Paul, 1981). Although still developing, children's discourse and pragmatics by the age of 5 are well formed as children can take turns within a conversation, can maintain the topic of a conversation, ask and answer questions, and can tell simple narratives (Preece, 1987).

At the age of 5, children can sight-read a few common words, sing the "Alphabet Song," identify words that rhyme, comprehend simple stories, and possibly write the names of some family members. Though literacy is the most obvious way in which children linguistically differ from adults, other aspects of language are still developing throughout childhood and adolescence. For instance, though many aspects of lexical-semantics are developed by the age of 5, children continue to add new words to their lexicon and old words take on new and subtle meaning throughout development. The ability to articulate one's knowledge of words also improves, as does the speed and accuracy in calling up words well into adulthood. Children also experience continued development in their spoken and written morphosyntactic skills with the eventual use of low-frequency syntactic structures and increasingly complex and cohesive discourse.

Lexical semantics and morphosyntax provide a good context for investigating the neural correlates of language development because these language aspects are both well developed *and* still developing in childhood. On a number of lexical-semantic and morphosyntactic tasks, children are able to perform at the same level as adults, thus allowing for the removal of performance-related effects and the isolation of age-related effects. Yet the gradual, subtle, and protracted nature of lexical semantic and morphosyntactic acquisition (Nippold, 2007) provide a unique opportunity for studying development. These two language domains are discussed in greater detail in the following sections.

Brain Development

Brain development can be understood as a complex sequence of constructive and regressive events (Kandel, Jessell, & Sanes, 2000; Quartz & Sejnowski, 1997; Rakic, Ang, & Breunig, 2004). In the early postnatal brain, there is an excess of synaptic connections, and through regressive events, in particular synaptic pruning, many early connections are subsequently lost. However, pruning and the concurrent constructive process of synaptic stabilization are not random, but driven by activity and experience to support the emergence of functional networks (Kandel et al., 2000). From childhood into adulthood, a second major type of constructive process is also observed in the steady increase in white matter (Giedd et al., 1999) due to myelination. This combination of regressive and constructive events aids the formation of highly specialized neural networks. The typically developing brain is characterized by plasticity, meaning that experience, learning, and environmental interaction impact functional brain organization via these constructive and regressive events.

Cognitive development is a protracted process (Paus, 2005) during which changes in ability are seen in diverse domains such as language, memory, and executive functioning throughout childhood, adolescence, and – for some domains – even young adulthood. Such age-dependent improvement in cognitive ability is theorized to arise from the emergence of specialized functional networks that perform a particular type of processing with greater efficiency (Johnson, 2003; Quartz & Sejnowski, 1997).

Behavioral studies have shown that language development benefits heavily from developmental plasticity. Plasticity is at work in the typically developing brain, although its effects are much more pronounced in brain-damaged children. Unlike adults who sustain a stroke, most children with early brain damage go on to develop relatively normal language functioning, regardless of lesion location (Reilly, Bates, & Marchman, 1998). However, some studies have shown that these children may not fully "catch up" to their healthy peers in all linguistic abilities. Rather, deficits may surface as children face new linguistic challenges, as for example in processing complex morphosyntactic or narrative stimuli (Dennis, 1980; Reilly et al., 1998). Thus when studying language development, it is important to examine multiple aspects of language functioning.

Neurolinguistic Theory

This proposal is theoretically guided by models of language acquisition according to which language emerges from sensorimotor abilities in the first years of life. Rather than developing autonomously from prespecified genetic information, as claimed by proponents of Chomskian generative grammar (Chomsky, 1965), behavioral and neuroscientific evidence of the past decade has favored approaches viewing language acquisition as founded upon and embedded in development in a variety of sensorimotor and cognitive domains (Bates, Thal, Finlay, & Clancy, 2003; Müller, 1996). The conceptual background of this proposal is more specifically informed by the theory of 'progressive neural scaffolding' (T. T. Brown et al., 2005; Petersen, van Mier, Fiez, & Raichle, 1998), which posits that in the process of learning, when performance is still immature, large sets of lower-level sensory brain regions are recruited for novel tasks. As novel tasks become learned, top-down support is provided through higher-level control mechanisms. The progressive neural scaffolding model does not imply that the former neural networks are specific to language, but rather that they are recruited to aid in the learning of language.

In addition to the scaffolding model, Johnson's interactive specialization (IS) model (Johnson, 2001, 2003) provides a theoretical basis for the dissociation between performance and the neural networks underlying the performance. The IS model hypothesizes that during development, cortical regions may initially be involved in processing a range of tasks or stimuli and with maturation these cortical regions become specialized, or tuned, to specific tasks or stimuli. This theory posits that localization, as frequently discussed in language development, is a result of specialization of cortical networks and pathways, possibly through selective pruning or inhibition of alternative pathways. Johnson (Johnson, 2003) also points out that similar levels of performance between children and adults for a given task do not imply identical underlying neurofunctional organization. This is relevant to the present study because children are expected to perform at high levels on lexical-semantic and morphosyntactic tasks, but at the same time are hypothesized to recruit different neural networks than adults during task performance.

Among the studies supporting these models, two reports by Schlaggar and colleagues (T. T. Brown et al., 2005; Schlaggar et al., 2002) suggested that posterior regions, in particular extrastriate cortex presumably involved in visual functions, participated heavily in lexical retrieval and word generation in children up to age 10 years, but not in older children and adults. These results prompt the intriguing general hypothesis that children may process at least some aspects of language with greater reliance on lower-level perceptuo-motor components. Frontal top-down control, in this view, would increase with age.

Several functional activation and effective connectivity studies also support theories of developmental increases in top-down control processes in the development of language. In a series of studies by Booth, Bitan and colleagues, age was related to increased activation in the dorsal portion of the left inferior frontal gyrus and decreased activation in the dorsal left superior temporal gyrus (Bitan et al., 2007) for a phonological task of rhyming judgment on visually presented words. For that same task, they also found age-related increases in the influence (i.e., effective connectivity) of the inferior frontal gyrus and fusiform gyrus on the lateral temporal cortex (Bitan, Cheon, Lu, Burman, & Booth, 2009). Developmental increases in dorsal connections with the inferior frontal gryus were also shown in a visual and auditory spelling task

(Booth, Mehdiratta, Burman, & Bitan, 2008). When comparing children and adults on the spelling tasks, children had significantly weaker top-down modulatory influences emanating from the inferior frontal area (Bitan et al., 2006). These results have also been replicated in children passively listening to a narrative where the effective connectivity from Broca's area to the superior temporal gyrus in the left hemisphere was shown to increase with age (Schmithorst, Holland, & Plante, 2007).

Language Components to be Studied

While linguistic theories vary greatly with regard to specific organizational principles of language, there is relative agreement on the existence of at least two distinct components within the language system, i.e., the lexical-semantic and the morphosyntactic components. Ullman’s declarative/procedural model (Ullman, 2001) is an example of a dual-mechanism model relating to these distinct components. In this model, the declarative memory system and the medial temporal lobes subserve the learning of words (including phonology and semantics), which are eventually represented in temporal and temporal-parietal regions. Acquisition of grammar (syntax and morphology), on the other hand, is supported by the procedural memory system, including the basal ganglia and their projections to frontal cortex as well as inferior parietal regions. There are competing psycholinguistic models for the processing of semantic and syntactic information during language comprehension (Friederici, 2002). Serial or syntax-first models posit that syntactic information is processed before semantic information during sentence comprehension. Interactive or constraint-satisfaction models claim that semantic and syntactic information interact throughout language comprehension. This proposal will examine the developmental properties of both the lexical-semantic and morphosytactic language components.

Lexical Semantics. Semantic comprehension refers to the meaningful interpretation of language elements (morphemes, words, sentences). Lexical semantics more specifically relates to single-word meanings. In this section, the development of lexical semantics is reviewed followed by a summary of the fMRI literature on lexical semantic development.

Development. Studies have shown that children as young as 5 months are comprehending and selectively responding to words (Mandel, Jusczyk, & Pisoni, 1995), typically their name, and by 8 months, children often understand a few phrases (Fenson et al., 1994). Around this time, children begin to use gestures to communicate. Even after children speak their first words, initially children demonstrate a larger productive repertoire of action-gestures than vocalizations (Caselli & Casadio, 1995) and have a larger comprehension vocabulary than production vocabulary (Fenson et al., 1994). Between 10 and 15 months, children produce their first words (Fenson et al., 1994). First words tend to be context bound (Barrett, 1995), as in the only *dog* is the family's dog and the child does not use this word when looking at dogs in a book or seeing other dogs. Eventually some words also become overextended and *dog* was used to describe all animals with four legs. Between 16 and 18 months, when children reach the 50-word milestone, most children experience a word spurt and the rate at which they acquire new words increases from 8 to 11 words per month to an average of 22 to 37 words per month (Benedict, 1979). By the time a child is 5-years-old, they will know approximately 10,000 words (Clark, 2003), understand some common idioms and concrete metaphors, and can produce humor intentionally by misnaming objects during play (e.g., You're a doorknob!) or by repetitive rhyming to create nonsense words (e.g., Daddy, saddy, waddy, caddy) (McGhee, 1979; Nippold, 1985).

Though much attention has been paid to this initial word spurt during toddlerhood, vocabulary growth continues at an even more rapid pace after early childhood (Anglin, 1993) with a typical school-age child acquiring 5 to 8 new words per day (Nagy & Scott, 2000) for a total of approximately 40,000 unique words by high school graduation (Nagy & Herman, 1987). This vocabulary growth is supported by several new developments in childhood, the first of which is reading. Studies have shown that around the age of 9 years, children who are active readers develop larger vocabularies than their peers who read less (Nagy, Herman, & Anderson, 1985) and that the amount of time spent reading continues to be a strong predictor of lexical development throughout adolescence and into adulthood (Echols, West, Stanovich, & Zehr, 1996; Stanovich & Cunningham, 1992). As children leave the preschool years, and develop increased literacy, they also begin learning more of their words from context (as opposed to direct instruction) and the new words they acquire are increasing obscure and complex (Nagy, Diakidoy, & Anderson, 1993). Lexical development is also a result of conceptual development, as children must acquire new words for their newly developed concepts.

Lexical-semantic development involves more than just the acquisition of new words. Nippold (1992) found that between the ages of 5 and 9 years, children develop an increasingly organized semantic network. Children were presented with a word (e.g., dog) and were asked to say the first word that came to their mind. Younger children responded syntagmatically (e.g., barks) but older children responded with semantically related words (e.g., cat, collie, or animal). An increasingly organized semantic network is also likely associated with the increase in lexical retrieval ability and increasingly complex semantic categories and category networks. Consistent with several similar studies, children between the ages of 4 and 8 years were instructed to name pictures of animals, food, and musical instruments (Fried-Oken, 1984 as cited in Nippold, 2007 #3900). The researchers found that naming speed and accuracy increased with age and high-frequency words were always produced more quickly than low frequency words. Finally, development of the semantic network is also seen as children begin to appreciate both the physical and psychological meanings of words like *cold, sweet,* and *crooked* (Nippold, 1992).

Lexical-semantic development is also the result of a child's development of morphological knowledge, typically between grades three and five, that enable them to decipher what new words mean (Anglin, 1993). In a classic study by Berko (1958), children ages 4 to 7 years were shown a picture of a bird-like creature and told, "This is a wug." Though they had never heard the word "wug" before, they were able to produce inflectional morphologies (e.g., There are two – wugs) but were unable to use derivational morphology to answer questions like "What would you call a very tiny wug?" (e.g., wuggie, wuglet, wugling) or "What would you call a house a wug lives in?" (e.g., wughouse, wuggery, wughut). Derving (1976), Tyler and Nagy (1989) showed that children first learned how to use compound words and then had a protracted course of development for derivational morphology into adulthood.

Carlisle and Nomanbhoy (1993) used a derivational morphology task to compare production and judgment in 101 six-year-olds. Subjects either responded "yes" or "no" to a sentence (e.g., A person who makes dolls is a dollar) or produced the final word in a sentence (e.g., Help. Father tells me I am a good ____). They found that the children performed significantly better on the receptive tasks (mean accuracy = 88%) than on the production task (41%). Carlisle and Nomanbhoy suggested that using production tasks alone may underestimate a child's knowledge of the linguistic skill being studied.

In summary, school-aged children already have a wide repertoire of lexical-semantic skills and can perform at adult-like levels on a number of tasks. However, lexical-semantic skills continue to develop throughout the school years and even into adulthood. Lexical-semantic development is seen in children's growing lexicon, increased literacy, conceptual development, increasingly organized semantic network, faster word retrieval, and use of derivational morphology. Thus, the present study is proposing to investigate lexical-semantic development in school-aged children, age 7-10 years, because lexical semantics are both well developed *and* still developing during this age range. Based on the previous review of lexical-semantic development, a lexical-semantic judgment task (as opposed to production task) is proposed to investigate the underlying cortical networks. A judgment task should help to ensure that children's lexical-semantic abilities aren't underestimated and that all children are able to perform at high levels of accuracy on the task. A high level of accuracy is needed in order to isolate age-related effects from performance-related effects. This will allow for the identification of cortical regions that are specific to lexical-semantic development.

fMRI Studies. From lesion literature, left posterior superior temporal gyrus (corresponding to part of classical Wernicke's area) has been implicated in the processing of lexical semantics. It has been considered that the temporal lobes may "store" semantic representations (Bookheimer, 2002; Fiez, 1997). However, the more recent neuroimaging literature has tended to suggest a distributed network for lexical-semantic processing, also including inferior parietal regions, the cerebellum, and some regions related to category specific (potentially sensorimotor-based) components of lexical representations (Hwang, Palmer, Basho, Zadra, & Müller, 2009; Martin, 2007). Prominent among those additional regions is left inferior frontal cortex (Broca's area), which may provide top-down control and on-line manipulation of elements of semantic representations.

FMRI studies of lexical-semantic processing in adults have implicated activation in the inferior frontal gyrus (IFG) (J. R. Binder, 1997; J.R. Binder et al., 1997) and more specifically pars orbitalis of the left inferior frontal lobe (BA 47) in semantic processing and retrieval of semantic information (Bookheimer, 2002). Ruff and colleagues (Ruff, Blumstein, Myers, & Hutchison, 2008) demonstrated that prefrontal cortex is recruited in both lexical decision and semantic judgment tasks and additionally found increased activation in the superior temporal gyrus (STG) associated with both the storage and retrieval of lexical-semantic information.

While there is a large literature describing the distributed organization of the lexical-semantic system in adults, developmental changes of lexical-semantic organization in childhood are less understood. Lexical-semantic skills undergo prolonged development throughout childhood and adolescence, thus making these tasks highly amenable to developmental studies (Holland et al., 2001; Vannest, Karunanayaka, Schmithorst, Szaflarski, & Holland, 2009). Few studies have examined lexical-semantic processing in children using complete sentences. Brauer and Friederici (2007) had young children (ages 5 and 6 years) passively listen to correct, syntactically incorrect, and semantically incongruous sentences. They found that cortical activation in children was less left-lateralized than in the adults. However, in both children and adults they observed bilateral activation in the anterior STG for all three conditions, and left lateral IFG and frontal operculum in the semantically incongruous condition.

Virtually all other lexical-semantic fMRI tasks have been limited to single-word or word-pair tasks, outside a sentence context. Frequently used paradigms include lexical association, generation, or naming. Word-pair tasks, for example, typically require participants to make decisions about word pairs (e.g., do the words rhyme?) or complete a word-pair through antonym generation, rhyme generation, or verb generation in response to a noun (T. T. Brown et al., 2005). These single-word and word-pair tasks have been associated with mostly similar activation patterns in young adults and children in left inferior frontal, superior and middle temporal, and anterior cingulate gyri (Blumenfeld, Booth, & Burman, 2006; Bookheimer, 2002; Chou et al., 2006; Gaillard et al., 2000; Gaillard et al., 2003; Holland et al., 2001; Kotz, Cappa, von Cramon, & Friederici, 2002; Schlaggar et al., 2002).

Despite overall strong similarities, differences between children and adults have been found in several respects. Some studies have reported generally greater left lateralization in adults than in children (Holland et al., 2001; Holland et al., 2007; Szaflarski, Holland, Schmithorst, & Byars, 2006). Other studies have yielded more region-specific findings of greater activation in adults in left dorsal frontal cortex (Schlaggar et al., 2002), left inferior and middle frontal gyri (Gaillard et al., 2003), left middle temporal gyrus (MTG) (Chou et al., 2006) and left parietal cortex (T. T. Brown et al., 2005). Conversely, children have shown greater activation than adults in left extrastriate regions (Schlaggar et al., 2002). In a more recent study by this latter group that combined large sample size with thorough isolation of performance and age-related effects, greater activation in children (inverse correlation between activity and age) was detected in medial frontal and anterior cingulate cortex, right inferior frontal gyrus, medial parietal and posterior cingulate cortex, and bilateral occipitoparietal cortex (T. T. Brown et al., 2005).

Intriguingly, although the study by Brown and colleagues (2005) also reported age-dependent increases in lateral frontal cortex of the left hemisphere, the effect did not occur in inferior frontal gyrus, as to be expected from several previous studies (Brauer & Friederici, 2007; Gaillard et al., 2003; Schlaggar et al., 2002; Szaflarski, Holland, et al., 2006), but rather in BA 6, which is considered premotor cortex. The question remains to what extent this finding may relate to overt speech responses. Many previous lexical-semantic studies have resorted to covert responses (Gaillard et al., 2000; Gaillard et al., 2003; Holland et al., 2001; Szaflarski, Holland, et al., 2006) given that overt speech can cause artifacts related to increased head motion and changes in magnetic susceptibility, which is particularly problematic in a pediatric population where minimizing movement is already challenging. However, there is a serious trade-off since covert word generation prevents response monitoring, which is clearly needed in children who may not always be as task-compliant as the investigator hopes.

Morphosyntax. Morphemes are the smallest units of meaning. In the word *books* there are two morphemes – the word (i.e., free morpheme) *book*, and the bound morpheme *s* indicating plurality. Morphology refers to how morphemes are combined. Morphosyntax refers to the internal structure of words (i.e., morphology) and the way in which words are combined or ordered to form phrases and sentences (i.e., syntax). In this section, the development of morphosyntax was reviewed followed by a summary of the fMRI literature on morphosyntactic development.

Development. When children are approximately 20 to 24-months old, they begin producing two word utterances. Children's utterances are not simply words that are randomly strung together, but from a very early stage, children reveal their grasp of the principles of sentence formation. In his seminal work, Brown (1973) researched the acquisition of 14 grammatical morphemes. Grammatical morphemes include the present progressive (+ *ing*), possessive (+ *'s*), and past regular (+ *d*), as examples. Around two years of age, children start to acquire these grammatical morphemes. Brown's initial data on three children suggested, and de Villiers and de Villiers (1973) confirmed, that though children acquire these grammatical morphemes at different ages, the order of acquisition across the 14 grammatical morphemes is approximately the same for all children.

While early utterances are often telegraphic or simple declarative sentences, as children begin to acquire grammatical morphemes, they start producing different sentence forms. Negation is expressed early on, though the utterances are not adult-like until children have learned to use auxiliairies (e.g., am, is). Likewise, children begin asking questions and using wh- words, but their utterances are still not adult like until they acquire auxiliaries towards the end of the pre-school years. The next development is the use of complex sentences, or sentences that contain more than one clause. Though the first complex sentences occur when children are producing four-word utterances (e.g., I want go outside) (Bowerman, 1976), this skill is not well developed until around age 4 (Bowerman, 1979). Well these different developments in the use of morphosyntax occur at a wider range of ages, what is consistent is the relative order that children proceed through these developmental milestones.

Even from the beginning, it is clear that children's use of grammar is more than a parroting of words or phrases they've heard, they are actually learning the rules of their language. Comprehension studies have shown that children as young as 16 months, who were only producing one-word utterances, understood the relational meanings in word combinations (e.g., kiss keys) (Sachs & Truswell, 1978). The previously described study by Berko (1958) also illustrates that children are not simply repeating words they'd heard as they were able to produce correct inflectional morphologies to words they'd never heard before (e.g., There are two – wugs). Finally, overregularization errors, where children incorrectly apply the rules of the language such as pluralizing *foot* as *footses*, further suggest that children are acquiring the rules and not simply repeating words or phrases they've learned.

By the age of 5, children are able to use a large number of grammatical rules in their utterances, and their syntax and morphology is well developed. They have a mean length of utterance of 6 or more morphemes, have mastered Brown's grammatical morphemes, and can produce sentences with relative, adverbial, and nominal clauses. Five-year-olds are also able to use multiple embedding, infinitives, gerunds, and negation, can produce compound and complex sentences, ask wh-questions, and use past, present, and future tense verbs (Paul, 1981).

Beyond the preschool years, considerable growth in syntax occurs both at the level of the individual sentence and in joining adjacent sentences (Karmiloff-Smith, 1986). Regular increases in sentence length and complexity for spoken and written language has been seen throughout development from age 6 to 18 years (Loban, 1976). This increased length and complexity is often due to greater use of subordinate clauses, though increased syntactic sophistication is also seen through the increased use of participial, infinitive, and gerund phrases (Scott, 1988). Researchers have examined development of comprehension for conjunctions (e.g., *although*, *but*) by having participants listen to sentences, and judge if they are grammatically correct. Katz and Brent (1968) found an increase in performance from ages 6 to 12 years, and Flores d'Arcais (1978) found the same gradual growth in children ages 7, 8, 10, and 12 years. Other studies of conjunction development had very high metalinguistic demands (i.e., being asked to reflect on the grammaticality of language). Wing and Scholnick (1981) asked children as young as 6 to determine if an "astronaut studying animals on a new planet was expressing belief, disbelief, or uncertainty" for a series of 5 questions on the same topic (e.g. *This is a monkey because it has two hands, This is a monkey if it has two hands*). The youngest children performed near chance, highlighting the necessity of making sure that the metalinguistic demands are suitable for the age group being studied. However, the majority of studies examining morphosyntactic development in school-age children have participants produce oral or written narratives. In order to use fMRI to study the neural correlates of morphosyntactic development, such metalinguistic tasks of grammaticality judgment are needed as producing narratives in the MRI environment is not possible.

Another approach to studying morphosyntax that does not involve narrative production is the implementation of tag questions. Tag questions consist of a question added, or “tagged”, to the end of a declarative sentence (e.g., You are going to the show, *aren’t you?*). Multiple morphosyntactic operations are required to produce and judge tag questions, given the complex combination of parameters such as subject and number agreement, along with syntactic rules of inversion. Both tag production and tag judgment have been used to investigate syntactic development in children.

McGrath and Kunze (1973) studied tag production in three groups of typically developing children (i.e., 5, 8, and 11 years). The children were given the first part of a sentence (e.g., You didn’t buy ice cream) and the children had to produce the tag (i.e., did you?). Errors were categorized into four categories: 1.) polarity (i.e., didn’t you?), 2.) auxiliary verb selection, 3.) pronoun selection, and 4.) inversion of the pronoun and auxiliary verb (i.e., you did?). Throughout the age range, children produced errors in the previously listed hierarchy, with most errors due to polarity and fewest errors due to inversion. In each error category, each older group had significantly fewer errors than the younger groups.

In another cross-sectional study of tag production (Dennis, 1982), five groups of typically developing children (ages 6, 8, 10, 12, and 14 years) added tags to 48 declarative statements. The authors observed that tag production improved from 6 to 8 years, but did not see significant improvement thereafter. Further, they found that the various tag rules were acquired at different ages, with inversion already well established in half of the youngest group and polarity only mastered in half the oldest group.

Weckerly et al (1998) used the Dennis (1982) tag production paradigm in children with language impairments and typically developing controls aged 5 to 16 years. Consistent with previous results, they found that both of their groups scored lowest on polarity and produced errors in the same rank order. They also reported a significant main effect for age, with fewer violations with increased age. However, even their oldest group (12 to 16 years) only responded correctly on 79% of the items. In another study by the same group (2004) of children ages 4-16 years, they again found the greatest number of errors due to polarity and found that the older children (12 -16 years) performed significantly better than the younger two groups.

In designing a functional magnetic resonance imaging (fMRI) study for children, tag production may be challenging as overt speech can cause movement artifact. Instead, tag judgment tasks are proposed for the current study. The tag judgment paradigm consists of a declarative statement followed by a grammatical or ungrammatical tag question (e.g., “Tom combs his hair, doesn’t he?” and “Sue is writing a letter, aren’t she?”). Participants are asked to decide if the sentence is grammatically correct. We have recently presented behavioral data (Moore et al., 2007) on typically developing children aged 7 to 11 years, and adults completing a tag judgment task. Adults performed significantly better than the children for the judgment task. An ANOVA indicated that there were no significant performance differences for the three types of violations (i.e., inversion, subject agreement, and number agreement). Finally, a linear regression analysis showed that age was a marginally significant predictor of hit rate. Similar to previous studies, a significant amount of errors were due to the polarity violations and the polarity errors accounted for the significant performance differences between the adults and the children. As this proposal wishes to neutralize performance to isolate cortical regions that show age-related effects, polarity violations are not being proposed for the current study.

fMRI Studies. Syntactic structures, unlike lexical semantics, are said to be hierarchical in that the processing of complex sentences (e.g., The girl that the man saw drinks the milk) includes syntactic relations between non-neighboring constituents (e.g., “girl” and “drinks”). In a study where healthy adults learned simple artificial grammar rules, Friederici and colleagues (Friederici, Bahlmann, Heim, Schubotz, & Anwander, 2006) suggested that the left inferior frontal cortex (Brodmann Area [BA] 44/45) was crucial for processing hierarchically structured sentences. This was consistent with several other studies investigating increasing morphosyntactic complexity using hierarchical sentences (Ben-Shachar, Hendler, Kahn, Ben-Bashat, & Grodzinsky, 2003; Grodzinsky, 2000; Tettamanti et al., 2002). It has been suggested, however, that activation in BA 44, may be related to working memory rather than syntactic complexity (Fiebach, Schlesewsky, & Friederici, 2001; Heim, 2005, for a review).

Syntactic violations (compared to syntactically correct or semantically incorrect sentences) have been associated with activation in left temporal regions (Friederici, 2004; Friederici, Ruschemeyer, Hahne, & Fiebach, 2003), and left posterior inferior frontal gyrus (Démonet, Thierry, & Cardebat, 2005), pars opercularis, and pars triangularis (S. D. Newman, Just, Keller, Roth, & Carpenter, 2003). A number of other studies involving processing of syntactic violations found bilateral activation, particularly in BA 44 (Kaan & Swaab, 2002) and right anterior superior temporal sulcus (A. J. Newman, Pancheva, Ozawa, Neville, & Ullman, 2001).

Tag paradigms have, to our knowledge, not been implemented in published fMRI studies. In one study of tag judgment in healthy adults (M. A. Rubio et al., 2004; M. A. Rubio et al., 2004), which served as a pilot for the present project, activation was seen in left inferior frontal gyrus (BA 44), similar to studies of syntactic complexity. Task related activations were also found in anterior cingulate gyrus (BA 32) and left middle temporal gyrus (BA 21). While tag paradigms have been applied in several pediatric and adult behavioral studies (described above), no fMRI studies using such paradigms are available.

Metalinguistic Competence

In addition to using comprehension and production tasks to study language, researchers also use judgment tasks. In judgment tasks, participants are asked to listen to or read a sentence and make a judgment, such as judging if the sentence is grammatically correct. Several of the previously described behavioral and fMRI studies utilize judgment tasks to study language. These judgment tasks require metalinguistic competence, or the “ability to reflect upon or analyze language as an entity itself" (Nippold, 2007). Around the age of 7 years, children begin to show increased metalinguistic competence and employ this skill in a variety of language domains including the use and understanding of lexical semantics and morphosyntax (Gombert, 1992). Grunwell (1986) and van Kleeck (1994) concluded that language development in children and adolescents is heavily dependent upon metalinguistic competence. This dependence is reflected in several ways including children's ability to use context to identify the meaning of an unfamiliar word or an unfamiliar metaphor (Nippold, 2007). As metalinguistic competence is so integral to later language development, the proposed study will employ judgment tasks to examine the neural correlates of lexical semantics and morphosyntax.

fMRI Studies Comparing Lexical Semantics and Morphosyntax

Some studies have utilized fMRI to compare the activation networks for semantic and syntactic processes. Dapretto and Bookheimer (Dapretto & Bookheimer, 1999) concluded that a section of Broca's area, the inferior frontal pars opercularis (BA 44), was critical for syntactic processing while BA 47 in lower inferior frontal gyrus (pars orbitalis) was implicated in semantic processing. In a similar study by Friederici et al. (Friederici et al., 2003), participants listened to sentences that were correct, semantically incorrect, or syntactically incorrect to differentiate between the two language components. They found that a temporo-frontal language network supported both semantics and syntax, although there were cortical regions with differential activation. Semantically incorrect sentences were associated with greater bilateral activation in the medial superior temporal regions and insula. Syntactic violations were associated with more left-hemisphere activation in the anterior superior temporal gyrus, frontal operculum, and basal ganglia. Lastly, they found increased superior temporal activation for syntactic violoations when compared to the semantically and syntactically correct sentences.

To our knowledge, only one group has utilized fMRI in children to examine differential cortical involvement for semantic and syntactic processing. As mentioned previously, Brauer and Friederici (Brauer & Friederici, 2007) had 12 children (4 boys), ages 5 and 6 years, listen to sentences and respond via a button press using two response boxes in their left and right hands, to indicate whether the sentence was correct or incorrect. They found that unlike adults, children had strong overlapping activation in the superior temporal gyrus for both semantically and syntactically incorrect sentences and recruited additional areas in bilateral inferior frontal gyrus. They concluded that by the age of 6, the semantic and syntactic language networks are not yet specialized as had been seen in adults. In a reanalysis of the same data (Brauer, Neumann, & Friederici, 2008), they observed that while the two groups had similar activation patterns, the children's BOLD activation time course had an overall later peak than the adults, with inferior frontal cortex responding later than superior temporal cortex. They concluded that the overall latency differences were "in line with the assumption of ongoing maturation in perisylvian brain regions and the connections between them". In the proposed study, tent functions was used to model each individual participant's hemodynamic response to account for latency differences between children and adults.

Paradigm Design

Almost all imaging studies of lexical-semantic development have been cross-sectional, showing mixed patterns of regional increases and decreases in activation associated with age (T. T. Brown et al., 2005). Cross-sectional designs and are limited as they only capture development at a single point in time and only look at a single language component. Thus the mechanisms by which these cognitive changes occur over time are still uncertain. Further, although children have been shown to acquire several linguistic skills in the same rank order, the ages at which children acquire these different skills varies significantly. Thus comparing a group of 7-year-olds to a group of 8-year-olds may be difficult as some of the 7-year-olds may be performing at the same level as the 8-year-olds and vice versa. Longitudinal studies are able to control for these within group variability as each child acts as their own control or comparison point at each time point. In longitudinal analyses, by identifying those observations that are measured on the same individuals, it is possible to focus on changes occurring within subjects and to make population inferences that are not as sensitive to between-subject variation.

In the only longitudinal study of pediatric language development that we know of, thirty typically developing children showed age-dependent activation increases in the left inferior/middle frontal, middle temporal, and angular gyri and the right inferior temporal gyri for a block-design verb generation task. Among the regions with age-dependent decreases were left extrastriate cortex, anterior cingulate gyrus, and thalamus (Szaflarski, Schmithorst, et al., 2006).

There are several methodological weaknesses in this longitudinal study

(Szaflarski, Schmithorst, et al., 2006) that the proposed study wishes to improve upon. First, the longitudinal study utilized a block design fMRI task. Block designs have several limitations including stimulus predictability, low temporal resolution, and inability to separate trial types and to estimate HRF shapes. In the proposed longitudinal-sequential study, we will therefore use an event-related design, which will also allow us to control for performance-related differences and confounds through trial-wise modeling in performance regressors and post-hoc sorting into correct and incorrect responses.

Szaflarski et al. (2006) also utilized a silent verb generation task and were thus not able to control for performance or ensure that the children were engaged in the task. The proposed study will use a button-press for participants to indicate whether the sentence they heard was correct or incorrect, thus avoiding speech-related artifacts while still monitoring performance. Contrary to the previous pediatric morphosyntax study by Brauer and Friederici described above (Brauer & Friederici, 2007), participants in our study will respond only with their left hand, which will provide differentiation between language-related effects in the left hemisphere and those related to motor response in the right hemisphere. All of our participants are right-handed as ambidexterity and left-handedness has been shown to be associated with more frequent atypical language lateralization (Knecht et al., 2000). In the Szaflarski's longitudinal study, four of the 30 participants were not right-handed.

Szaflarsky et al. (2006) further asked participants to silently generate verbs to nouns (presented binaurally). Single-word and word-pair paradigms are generally 'non-ecological', creating highly artificial task demands that differ dramatically from actual language use in linguistic environments encountered by children. The proposed study, on the contrary, will use a sentence-embedded lexical-semantic and morphosyntactic tasks. Finally, unlike previous adult (Friederici et al., 2003) and pediatric studies (Brauer & Friederici, 2007), the proposed study has separate, but parallel, tasks for examining lexical semantics and morphosyntax. Thus participants will be asked to explicitly judge if a sentence is semantically correct or incorrect for the entire lexical-semantic task, and will explicitly judge if a sentence is syntactically correct or incorrect for the morphosyntactic task. This is in contrast to the previously mentioned studies where participants are told to decide if a sentence is incorrect regardless of the error type.

Finally, unlike the study by Szaflarsky et al. (2006), the present study will apply two tasks to tap into the two main aspects of language: lexical semantics, and morphosyntax. These linguistic components have different rates and ages of acquisition and are therefore suitable for the investigation of development with a longitudinal-sequential design. The tasks also target different cortical areas, which allows for the examination of neural language networks.

The proposed project aims to strengthen the previous findings by examining developmental change longitudinally, as well as cross-sectionally and by broadening the scope of language tasks beyond single word processing. A better understanding of developmental changes in the brain organization for language might broaden our understanding of cognitive development, elucidate the causes of atypical development, and could potentially inform our diagnosis, treatment, and prevention of developmental disorders.

Aim 1. To examine neural correlates of morphosyntactic development

To our knowledge, there has been no published fMRI study of morphosyntactic judgment in children. Since the task is entirely novel, our hypotheses cannot be directly derived from existing child studies, but are instead derived from adult work. The theoretical background, as described above, encompasses models of progressive neural scaffolding (Petersen et al., 1998), interactive specialization (Johnson, 2001, 2003), and the procedural bases of grammar (Ullman, 2001). Changes in BOLD (blood oxygen level dependent) response during an event-related fMRI task of lexical-semantic decision will be analyzed to detect brain regions showing age-related effects. Brain regions showing age-related effects will be tested for direction of change. It is expected that age-related effects will be seen in sensorimotor regions, such as the basal ganglia and posterior cortices, which are hypothesized to show decreases in activation with age. It is hypothesized that there will be age-related activation effects in top-down processing regions in frontal and parietal lobes, which are expected to show increases of activation with age.

Aim 2. To examine neural correlates of lexical-semantic development

Changes in BOLD response during an event-related fMRI task of lexical-semantic decision will be analyzed using the same theorietical models and methods as in Aim 1. Based on previous cross-sectional studies (T. T. Brown et al., 2005) it is expected that age-related activation effects will be seen in sensorimotor regions, such as bilateral extrastriate and occipitoparietal cortices, which are hypothesized to show decreases in activation with age. It is also hypothesized that there will be age-related activation effects in top-down processing regions in frontal and parietal cortices, which are expected to show increases of activation with age.

Aim 3. To test for brain regions differentially activated for the two language components

This is an exploratory analysis to examine the relationship between the two language components (i.e., lexical-semantic and morphosyntactic decision) and their inferred neural correlates. This exploratory analysis aims to identify the brain regions that are associated with both language components and those brain regions that are differentially activated. Further, the aim is to look at the interaction between language components and development to examine whether there are activated brain regions that have age-related effects for one language component, but not the other.

Research Design and Methods

Participants

The experimental group consisted of two groups of typically developing children; children aged 7 years (i.e., Young Children group) and children aged 9 years (i.e., Old Children group). Typically developing children were studied at two time points, 12 months apart. Adults, aged 21-25 years, were included as a reference group.

Table 1: Anticipated enrollment without attrition

Group	Age at 1st Scan	Age at 2nd Scan	*n*
Young children	7 years	8 years	20
Older children	9 years	10 years	20
Adults	21-25 years	n/a	15

Recruitment

Participants were recruited from San Diego State University and University of California San Diego campuses and the surrounding community through institutional review board (IRB) approved advertisements and word of mouth. The Brain Development Imaging Lab has access to San Diego State students who participate in experiments for course credit. In addition, the laboratory has established contacts with local schools for recruitment of children in kindergarten through high school, and has a database of participants in the appropriate age range. Finally, IRB approved fliers were posted on online community message boards, community centers, and around both campuses and were responsible for recruiting the majority of participants.

Retention

It was expected that attrition would be no greater than 25%, i.e., complete datasets for both time points would be available for at least 15 participants per child group. In order to minimize attrition, the following steps were taken.

Both at first contact by phone and again during the parental consent and child assent in the first session, participants and their parents were told that the study consists of three sessions (neuropsychological assessment, scan one, and scan two) and the study was explained to them so that they understood the importance of each session. Children and their parents were asked to commit to participating in all three sessions “so that we can see how the child’s brain is growing and changing due to age and learning”. Note, however, that we could not and did not do anything to coerce parents and their children to return for subsequent sessions, in accordance with strict IRB guidelines. As such, payment was separate for each session.

In addition to explaining the purpose of the second scan to increase commitment to the study, it was important to create and maintain a relationship with the participants and their parents to reduce attrition between the first and second imaging time points, one year apart. This was accomplished in two ways. First, we sought to make the study pleasurable for the children and their parents. This included having a comfortable waiting room for the parents and other children that they may have brought along, and having drinks and snacks for participants and their families.

We also offered convenient testing and scanning sessions after school, during holidays, and weekends. In addition to compensating the participants for their time and the parents for travel expenses, we gave the children and their siblings toy brains and pencils to remind them of their time with us.

Finally, we initiated multiple points of contact with the participants throughout the year in between scanning sessions. This included sending them a thank you letter a week after their participation, sending them pictures of their brain one month after participation, and sending them congratulatory cards at the end of the academic school year. We also sent families a reminder letter and email two months before the second scan, and we called and emailed one month before the second scan to schedule a convenient time for them to come in. Finally, all appointments were confirmed via email and a phone call the week of the appointment.

Final Participation

Forty-two children participated in the first time point, 21 per group. Thirty-three of those children participated in the second time point, 16 older children and 17 younger children. Of those 33 participants, three were removed from the final analysis as more than 25% of their fMRI data points were unusable due to motion greater than 2.0 mm or performance at chance levels. Nine children who participated in the first time point did not participate in the second time point for the following reasons: two moved out of the area, two had orthodontic work that excluded them from participating in an MRI due to the possibility of ferromagnetic materials, four children could not be reached, and one child did not receive consent to participate from his non-custodial parent who had previously consented to participation for the first time point.

Table 2: Final enrollment and data used for analysis

Group	**Age 1st Scan**	***n***	**Age 2nd Scan**	***n***	**Used in final analysis (*n*)**
Young Children	7 years	21	8 years	17	15 (7 females)
Older Children	9 years	21	10 years	16	15 (7 females)
Adults	21-25 years	15	n/a	n/a	15 (8 females)

Group Characteristics and Exclusionary Criteria

Participation was based on multiple criteria. All participants were monolingual native speakers of English (without significant exposure to another language before age 5). For MRI safety reasons, subjects had no metal in their body, no history of claustrophobia, nor any other condition for which MRI is contraindicated. Subjects were administered the Wechsler Abbreviated Scale of Intelligence (WASI-III) and had a Full Scale IQ at or above 70. All subjects were able to complete the two language tasks. The subjects practiced the tasks outside of the scanning environment and were able to complete these practice tasks at a set criterion (≥70% of responses correct). All subjects were right-handed, free from any neurological, psychological, or psychiatric diagnosis and/or finding, with no chronic use of any psychotropic pharmaceutical agent.

Procedure

Participants were scheduled for the first two sessions on different days, scheduled over a period of 1 week. For the child participants, a third session was scheduled for 12 months after the second session.

Cognitive testing and mock scanning session. The first session lasted approximately 2 hours and took place at the Brain Development Imaging Lab (BDIL) at San Diego State University. It began with an introduction to the study, consenting, and screening for MRI compatibility. For the participants meeting eligibility criteria and wishing to continue with the study, the cognitive battery was administered (described below). The final 20 minutes of the session was dedicated to standardized practice of the fMRI tasks in the "mock scanner." This protocol involved having the child enter a tube that resembles the bore of the magnet, hear recorded MRI gradient noise at appropriate volumes, and practice pressing buttons on a response pad while lying as motionless as possible. The children also learned the importance of not moving while in the scanner and had the opportunity to ask questions or discuss concerns regarding the MRI component of the study. Adult subjects practiced the fMRI tasks, but did not participate in the mock scanner protocol.

fMRI session time point 1. The second session was the fMRI scan and took place at the Center for fMRI at the University of California, San Diego. This session lasted approximately 2 hours and included safety screening, task review, careful positioning of participants to avoid discomfort in the magnet, acquisition of high resolution structural images, and acquisition of functional images during performance of the language tasks. Participants spent approximately 45-60 minutes in the magnet.

fMRI session time point 2. For all children, the imaging session was repeated on a subsequent visit after 12 months. The EVT-II and PPVT-III (see Cognitive Battery), which has a strong correlation with verbal IQ (Bell, Lassiter, Matthews, & Hutchinson, 2001), was administered again at the final visit, to provide a longitudinal measure of verbal development. This session was approximately 2 hours and included consenting, screening for MRI compatibility, and reviewing the tasks before completing the fMRI protocol from the first time point.

Practice Effects

As subjects practiced the language tasks in session one and again in session two and three prior to performing the tasks in the scanner, the possibility of practice effects were considered. However, such practice effects are not expected to be an issue because (a) stimuli used during practice was different from those used during fMRI scanning, and (b) these are cognitive tasks in which gains in accuracy from practice are minimal as long as novel stimuli are used throughout. Practicing the tasks was beneficial as participants were more comfortable and confident during the actual fMRI scan.

Practice effects are also of concern between the first and second imaging sessions, as the same stimuli were used at both time points. Practice effects are expected to be minimized as (a) the two sessions are 12-months apart, and (b) the stimuli are administered in random order. Cross-sectional analysis was used to check for practice effects. The young children at the first time point (age 7) were compared to the old children at the first time point (age 9). Any difference between the groups cannot be attributable to practice effects. Additionally, the young children at the second time point (age 8) were compared to the old children at the second time point (age 10) and again differences between these groups cannot be attributable to practice effects.

Lexical-Semantic paradigm

The lexical-semantic decision task was adapted, with permission, from a series of paradigms from Gaillard and colleagues (Gaillard et al., 2007). Similar to the majority of lexical-semantic tasks, the original version was a covert generation task. The participants heard a question (e.g., What is a king's hat called?) and were supposed to silently generate the response (e.g., *crown*). This silent generation made it impossible to ensure task participation and assess performance. Conversely, in overt lexical-semantic fMRI tasks, speech is associated with head movement and susceptibility artifact. Thus the lexical-semantic paradigm in this study implemented a button press response, ensuring performance monitoring while avoiding overt speech.

In the lexical-semantic decision task, a descriptive statement is followed by a noun (e.g., Something you sit on is a *chair*" or "Something you sit on is *spaghetti*") and participants were asked to respond via button press and push one button if the sentence was congruous and a different button if the sentence was incongruous (with button assignments counterbalanced across participants). Participants responded using their non-dominant left index and middle fingers. All stimuli were presented binaurally for 2.75 seconds through noise-reduction headphones (Resonance Technology; www.mrivideo.com) specially designed for use with fMRI, followed by 1.25 seconds to provide time to respond.

Experimental trials were presented at two levels of difficulty (e.g., Easy and Hard), as determined by Hyperspace Analogue to Language (HAL) frequency norms (Lund & Burgess, 1996), with less frequent (i.e., low log of frequency) words being considered more difficult than more frequent (i.e., high log of frequency) words. All words in the Easy stimuli have a log of frequency greater than 8.50. All of the Hard stimuli contain target words with a log of frequency less than 7.50. By varying the difficulty of the stimuli, it was possible to isolate main effects of task from those of task difficulty.

The original version of the lexical-semantic task used a block design format. For the proposed study, the task was converted into an event-related fMRI design, which allows for post hoc sorting of trials with correct versus incorrect responses and allows timecourses of brain activity to be measured. To control for auditory and motor processing, Control stimuli consist of 2.75 seconds of reversed speech and participants were instructed to push the button for “incorrect” when they hear the reversed speech.

All participants completed two 6-minute runs of the lexical-semantic decision task. Each run consists of 40 lexical-semantic stimuli (20 semantically congruous, 20 incongruous) and 20 Control stimuli. Temporal jittering with 60 two-second null baseline trials (presenting only a visual crosshair) was optimally randomized through both runs using Optseq (surfer.nmr.mgh.harvard.edu/optseq/). Runs of the lexical-semantic task were administered back-to-back with a one-minute break between runs.

Morphosyntactic Judgment paradigm

The morphosyntactic judgment task was adapted from Weckerly, Wulfeck, & Reilly (Weckerly et al., 2004) and was designed to be parallel to the lexical-semantic decision task. Stimuli in this paradigm consist of a declarative statement followed by a grammatical or ungrammatical tag question (e.g., “Tom combs his hair, doesn’t he?” and “Sue is writing a letter, are she?”). Experimental stimuli were presented binaurally for 2.75 seconds as described above. Participants had 1.25 seconds to respond via button press using their non-dominant left index and middle fingers to push one button if the sentence was grammatically correct, and the other button if the sentence was grammatically incorrect. Button presses were counterbalanced across participants and were consistent across the two tasks.

There were two types of experimental stimuli: no grammatical violation and morphosyntactic violations (i.e. number, inversion, or subject violation). Behavioral data (Moore et al., 2007) on tag judgment has shown that there is no significant difference in performance for the three types of violations in the age group to be studied. There were equal numbers of trials for each violation type.

The morphosyntactic paradigm also used an event-related fMRI design, with the experimental and control conditions optimally randomized with temporal jittering using 2-second null trials of visually presented crosshairs. The same control condition as in the lexical-semantic paradigm was used (i.e., reverse speech and a button press).

The event-related design allowed for analysis of different types of grammatical violations and performance. Participants completed two 6-minute runs of this task.

fMRI Data Acquisition

FMRI sessions took place at the UCSD Center for Functional Magnetic Resonance Imaging (CFMRI). Brain images were acquired on a General Electric (GE) 3 Tesla magnet, using an 8-channel gradient head coil. Blood Oxygenation Level Dependent (BOLD) imaging data were acquired with single shot echoplanar imaging (EPI), using an Array Spatial Sensitivity Encoding Technique (ASSET), a parallel imaging method developed by GE, which is a version of Sensitivity Encoding (SENSE) (Pruessmann, Weiger, Scheidegger, & Boesiger, 1999). 180 full image volumes were collected for each run. Image volumes contain 39 axial slices, with a 2000ms repetition time (TR), 30ms echo time (TE), 90°flip angle, 3mm slice thickness, and $4mm^2$ in-plane voxel size for complete coverage of the brain. A high-resolution T1-weighted anatomical scan (TR = 7400 ms, TE = 3.0 ms, flip angle = 12 degrees, 256x192 matrix, 1-mm slice thickness, field of view = 24 cm, 3 minute and 36 second acquisition time) was collected in the sagittal plane for co-registration with the functional protocol.

All participants completed two runs each for two language tasks; lexical-semantic decision, and morphosyntactic judgment. All stimuli were presented on a Macintosh G4 Powerbook computer (Apple Computer, Inc., Cupertino, CA) using PsyScope X software (Robosoft and the SISSA Language, Cognition and Development Lab). Auditory stimuli were presented binaurally through noise-reduction headphones designed for use with MRI. All stimuli were recorded in the same female voice using Sound Studio software and were cleaned and edited with Audacity software. For the lexical-semantic decision and morphosyntactic judgment paradigms, responses were made using the top two keys on an MR-compatible, vertically oriented four-key response pad (Current Designs, Inc., Philadelphia, PA), with key press (top or bottom) and response times logged by PsyScope X. Utilizing button press responses, overt speech responses, which are known to be associated with motion and susceptibility artifact, can be avoided. Visual stimuli were projected on a screen, which is easily viewed from the bore of the scanner through a mirror positioned on the headcoil.

Each run and task paradigm was 6 minutes in length. Between runs, the author spoke with the participant through the scanner intercom to ensure comfort and provide a brief break.

Cognitive Battery

These measures were administered during the first session. They provided general psychometric data for all participants in the study along with a means of tracking language development in the longitudinal component of the study. The measures were selected because they have literature supporting their reliability and are extensively used in studying language.

Children’s Cognitive Battery

- Wechsler Abbreviated Scale of Intelligence (WASI)
- Letter-Word ID, Word Attack; Woodcock Johnson-3rd Edition

- Sentence Repetition; Clinical Evaluation of Language Fundamentals (CELF-4)
- Peabody Picture Vocabulary Test (PPVT–4)*
- Expressive Vocabulary Test (EVT-2)*

Adult Cognitive Battery

- Wechsler Abbreviated Scale of Intelligence (WASI-III)
- Peabody Picture Vocabulary Test (PPVT–4)
- Expressive Vocabulary Test (EVT-2)

Analysis of Behavioral Data

Neuropsychological test data were converted to standard scores using age-corrected norms to compare the two groups of children (i.e., 7-year olds, 9 year-olds, adults) to ensure there were no group differences.

Performance data (response time, accuracy) were also collected on the language tasks acquired during fMRI. These data were included as regressors in fMRI analyses to account for performance. Data were also analyzed for group differences between the two groups of children and the two imaging time points.

fMRI Data Processing

Imaging data were processed using local software and the Analysis of Functional NeruoImages (AFNI) library (Cox, 1996), and the fMRIB Software Library (FSL) (S. M. Smith et al., 2004; Woolrich et al., 2009).

Preprocessing. The first five volumes of each run were discarded to remove signal equilibration effects. All data were examined for excessive movement, outliers, and significant distortions before and during preprocessing. Each run was corrected for inter- and intra-run motion using AFNI to register each volume to the middle (89^{th}) volume of the first run. Field inhomogenieties were corrected using FSL and each volume was slice-time corrected using AFNI. The two runs (of each task) were concatenated to create a single time-series with 360 volumes and smoothed with a 6-mm^3 full-width at half-maximum Gaussian kernel.

Signal Processing. To analyze time series data on the individual level, the MR signal was deconvolved and fit to a general linear model (GLM). Tent functions were used to estimate the amplitude and shape of the hemodynamic response (HR) for each stimulus type in the behavioral paradigm. The six motion parameters corresponding to translation and rotation were included as orthogonal regressors. A multiple regression analysis was performed on the estimated impulse response functions and the stimulus time series and mean peak activation were examined for each of the stimulus conditions.

Group Analyses. To account for inter-subject variability in gyral anatomy, the anatomical images were transformed into standard Talairach atlas space (Talairach & Tournoux, 1988). Functional image data sets were similarly normalized using the same parameters as the anatomical image acquired in the same session using AFNI auto-Talairach procedures and interpolated to 3 mm^3 isotropic voxels. The literature has shown that children has young as 7 years can be normalized to the adult Talairach template without excessive distortions (Muzik, Chugani, Juhasz, Shen, & Chugani, 2000).

A pair-wise t-test was used to examine the main effect of time (i.e., time point 1 vs 2), across groups (i.e., Young and Older children) and across language tasks (i.e., lexical-semantic and morphosyntactic judgment). An independent two-sample t-test examined an interaction between group and time point by comparing the change seen between time points for the two groups, across language tasks. Lastly, a pair-wise t-test was used to examine an interaction between language task and time by comparing the change seen between time points for each language task, across groups.

A longitudinal analysis of each language task, for each group, was performed with pair-wise t-tests to examine the directionality of change. A cross-sectional analysis was performed with independent t-tests with the youngest group at their first time point (7 years) and the older group at their last time point (10 years).

Testing the Specific Aims

Aim 1 & 2. To examine the hypotheses of age-related activation effects in sensorimotor regions and top-down processing regions, whole-brain analysis with independent and pair-wise t-tests were performed to determine magnitude and directionality of longitudinal and cross-sectional changes across time, across and between groups, and across and between tasks.

Aim 3. For an exploratory analysis of differential activation in brain regions between tasks, 2-way interactions between task and time were explored with paired t-tests. Further, regions showing task-related activation in within group analyses were examined between tasks to see if some regions showed age-related effects for one language component but not the other.

Results

Behavioral Results

All participants scored within or above the normal range for their age on a neuropsychological test battery (i.e., inclusionary criteria for study) and their age-corrected scores are presented in Table 3. As expected, there were no significant differences in age-corrected scores between the three groups (i.e., Young Children, Older Children, Adults). While all of the children demonstrated age-appropriate reading levels for word reading (Letter-Word ID) and phoneme reading (Word Attack) on the Woodcock Johnson-3rd Edition, their raw scores were compared with two-sample independent t-tests and as expected, the Older children were reading at a significantly higher level than the Young children.

Table 3: Behavioral results for the three study groups: 7-year-olds (YOUNG), 9-year-olds (OLD), and Adults.

	YOUNG (n = 15)	OLD (n = 15)	ADULTS (n =15)	*p*	Group Comparisons
Full Scale IQ[a] (WASI)	113.1 (11.0)	113.7 (11.4)	113.2 (6.4)	0.983	-----
Verbal IQ[a] (WASI)	113.1 (8.4)	112.0 (10.7)	110.1 (6.9)	0.632	-----
Non-verbal IQ[a] (WASI)	110.5 (13.7)	112.4 (13.5)	113.2 (8.9)	0.821	-----
Sentence repetition[b] (CELF-4)	58.3 (15.4)	49.7 (32.7)	---	0.364	
Word reading[c] (WJ-3)	45 (8.94)	53.6 (5.11)	---	0.003	
Phoneme reading[c] (Word Attack, WJ-3)	19.6 (5.32)	22.5 (4.91)	---	0.136	
Timepoint 1					
Age (years)	7.56 (0.25)	9.60 (0.32)	23.1 (1.33)	---	-----
Receptive vocabulary[a] (PPVT-4, A)	103.7 (30.5)	111.7 (11.5)	108.2 (5.9)	0.529	-----
Expressive vocabulary[a] (EVT-2, A)	110.1 (10.5)	111.3 (9.9)	108.0 (9.0)	0.659	-----
Lexical-semantic decision[d] (LSD)	88.2 (6.9) / 87.2 (7.6)	93.8 (7.4) / 93.8 (8.2)	99.0 (2.6) / 98.8 (2.3)	< 0.001	Young < Old < Adult
Morphosyntactic judgment[d] (TAG)	65.4 (23.7) / 77.9 (16.3)	74.6 (11.1) / 85.4 (9.2)	92.9 (7.0) / 92.1 (6.2)	< 0.001 / 0.006	Young = Old < Adult
Timepoint 2					
Age (years)	8.59 (0.25)	10.67 (0.34)	---	---	
Receptive vocabulary[a] (PPVT-4, B)	76.1 (20.2)	76.3 (18.7)	---	0.978	
Expressive vocabulary[a] (EVT-2, B)	66.0 (20.5)	65.8 (26.0)	---	0.981	
Lexical-semantic decision[d] (LSD)	90.5 (6.6) / 86.7 (10.5)	93.0 (9.3) / 92.8 (6.7)	---	0.079 / 0.013	
Morphosyntactic judgment[d] (TAG)	71.9 (17.5) / 81.7 (15.5)	76.5 (17.8) / 88.3 (7.5)	---	0.483 / 0.146	

Values represent the sample mean (standard deviation)

[a] Age-corrected Standard Scores with a mean of 100 and standard deviation of 15

[b] Age-corrected percentile scores

[c] Raw scores

[d] Percent accuracy hits / correct rejection

Lexical-semantic decision (LSD) task. All participants were able to complete both runs of the LSD task and their performance is presented in Table 3. Mean hit rate was 99.0% (SD = 2.6%) in the adults, 88.2% (SD = 6.9%) in the Young Children, and 93.8% (SD = 7.4%) in the Older Children. A one-way ANOVA with follow-up two-sample independent t-tests revealed that the Adults performed significantly better than Older Children, and the Older Children's performance was significantly better than the Young Children. Finally, paired t-tests demonstrated that neither the Young Children nor the Older Children's performance significantly improved from their first- to second administration (i.e., 1 year apart), (t(14) = 1.07; p = 0.301) and (t(14) = 0.24; p = 0.817) for hit rate respectively.

Morphosyntactic tag judgment (TAG) task. All participants were able to complete both runs of the TAG task and their performance is presented in Table 3. Mean overall hit rate was 92.9% (SD = 7.0%) in the adults, 65.4% (SD = 23.7%) in the Young Children, and 74.6% (SD = 11.1%) in the Older Children. A one-way ANOVA with follow-up two-sample independent t-tests revealed that while the Adults performed significantly better than the Older Children, the Older Children's performance was not significantly different than the Young Children. Finally, paired t-tests demonstrated that neither the Young Children nor the Old Children's performance significantly improved from their first- to second administration (i.e., 1 year apart), (t(14) = 1.03; p = 0.32) and (t(14) = 0.55; p = 0.59) respectively.

fMRI Results

Within-group language networks. Within-group results are presented here, and illustrated in Figures 1 and 2, with full cluster listings in Tables 4-7 to provide additional context for the cross-sectional and longitudinal analyses of development presented in the following sections. Within-group data analyses for LSD have been published (Moore-Parks et al., 2010) and are presented here with permission from the authors.

Lexical-semantic decision (LSD) task v. control condition (reversed speech). Adults showed a large activation cluster that extended from the left inferior frontal gyrus (IFG) to the left middle (MTG) and superior temporal gyrus (STG) (Table 4; Figure 1A). Significant activation was also detected in the right hemisphere including a large cluster peaking in the right superior temporal gyrus and extending to the right temporal pole. The adult group also showed activation in bilateral medial frontal cortex (mostly in SMA), right insula, bilateral pre- and postcentral gyri, as well as in left inferior temporal and inferior parietal regions. Activation outside cerebral cortex was observed in left thalamus and in the cerebellum (predominantly the right hemisphere). Deactivations (greater activity for the reverse speech control condition than for LSD trials) were detected in right inferior parietal lobe, precuneus and posterior cingulate gyrus (mostly in the right hemisphere), as well as in anterior cingulate, middle frontal, and postcentral gyri of the left hemisphere.

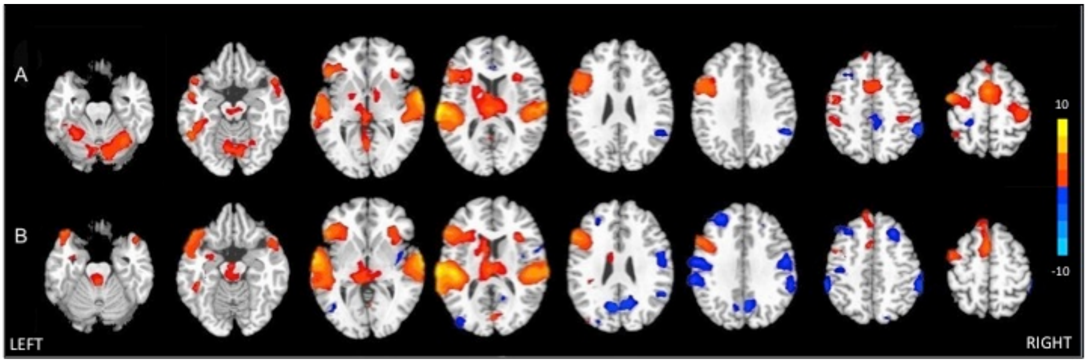

Figure 1: Significant clusters of activation effects for the contrast lexical-semantic decision vs. reverse speech within the: (A) Adult group, and (B) Child group.

Similar to the adults, children showed a large activation cluster that extended from the left middle and superior temporal gyri to the left inferior frontal gyrus (Table 5; Figure 1B). A cluster in the right hemisphere peaked in superior temporal gyrus, extending to the temporal pole, middle temporal gyrus, insula, and inferior frontal gyrus. Children further showed activation in left superior and medial frontal regions (including SMA), left inferior temporal gyrus and cuneus, as well as lingual and fusiform gyri bilaterally. Outside cerebral cortex, activation was seen in bilateral thalamus and cerebellum. Deactivations were observed in bilateral inferior parietal lobules, extending into pericentral cortex and supramarginal gyri, bilateral middle frontal gyri, right precuneus and cuneus, as well as left middle occipital gyrus.

Table 4: Significant clusters ($t \geq 4.033$; $p < .001$; cluster corrected $p < .05$) detected in the adult group for the contrast lexical-semantic decision vs. reverse speech. Subregions of large clusters are listed as the percentage of total cluster volume. Subregions are contiguous areas of cluster activation that extend beyond the peak activation (Eickhoff et al., 2007).

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates x	 y	 z	Volume (μl)	T-score
Activations					
L superior temporal gyrus (BA 22)	-56	-14	6	64098	15.96
L inferior frontal gyrus [p. triangularis] (14.5%)					
L superior temporal gyrus (13.9%)					
L middle temporal gyrus (10.6%)					
L precentral gyrus (8.2%)					
L thalamus (6.1%)					
R superior temporal gyrus (BA 22)	58	-8	2	16767	13.02
R superior temporal gyrus (61.8%)					
R temporal pole (9.8%)					
R middle temporal gyrus (9.4%)					
R Heschls gyrus (7.2%)					
R rolandic operculum (6.0%)					
L medial frontal gyrus (BA 6)	-8	-2	60	14067	11.91
L SMA (53.5%)					
R SMA (27.8%)					
R middle cingulate cortex (5.8%)					
R cerebellum	8	-70	-16	14040	9.05
R cerebellum (41.4%)					
cerebellar vermis 6 (10.6%)					
L cerebellum (10.1%)					
cerebellar vermis 4/5 (5.3%)					
R precentral gyrus (BA 4)	34	-22	50	6048	8.24
R precentral gyrus (58.8%)					
R postcentral gyrus (31.3%)					
L cerebellum	-26	-46	-18	5103	8.30
L inferior temporal gyrus (42.6%)					
L cerebellum (32.5%)					
L fusiform gyrus (16%)					
R insula (BA 13)	28	20	6	2214	7.74
L superior medial gyrus (BA 8)	-2	28	50	1485	5.69
L superior medial gyrus (77.8%)					
L superior frontal gyrus (8.2%)					
L inferior parietal lobule (BA 40)	-46	-32	44	1188	6.25
L inferior parietal lobule (68.9%)					
L postcentral gyrus (21%)					
Deactivations					
R inferior parietal lobule (BA 40)	56	-44	42	3294	-7.76
R supramarginal gyrus (46.4%)					
R inferior parietal lobule (32.8%)					
R angular gyrus (14.9%)					
R precuneus (BA 7)	8	-34	42	945	-5.36
R middle cingulate cortex (81.7%)					
L middle cingulate cortex (10.2%)					
L anterior cingulate cortex (BA 24)	-4	34	6	945	-4.88
L anterior cingulate cortex (84.4%)					
R anterior cingulate cortex (10.1%)					
L postcentral gyrus (BA 3)	-22	-34	54	675	-6.22
L middle frontal gyrus (BA 8)	-22	16	48	594	-5.83

Table 5: Significant clusters ($t \geq 4.033$; $p < .001$; cluster corrected $p < .05$) detected in the child group for the contrast lexical-semantic decision vs. reverse speech.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates			Volume (μl)	T-score
	x	y	z		
Activations					
L superior temporal gyrus (BA 22)	-50	-32	6	57672	12.25
L inferior frontal gyrus [p. triangularis] (17.3%)					
L superior temporal gyrus (16.6%)					
L middle temporal gyrus (15.1%)					
L inferior frontal gyrus [p. orbitalis] (9%)					
L temporal pole (5.7%)					
R superior temporal gyrus (BA 41/42)	56	-16	8	24867	11.33
R superior temporal gyrus (48.1%)					
R temporal pole (8.9%)					
R inferior frontal gyrus [p. orbitalis] (7.5%)					
R insula (6.6%)					
R middle temporal gyrus (5.9%)					
R Hechls gyrus (5.1%)					
L thalamus	-8	-14	18	19872	8.28
L thalamus (21.1%)					
L caudate nucleus (9.4%)					
R thalamus (8.7%)					
L superior frontal gyrus (BA 6)	-4	4	50	6696	8.63
L medial frontal gyrus (42.7%)					
L SMA (41.1%)					
L superior frontal gyrus (12.9%)					
Vermis	-2	-58	-4	2214	4.59
R lingual gyrus (7.7%)					
L lingual gyrus (5.1%)					
R insula (BA 13)	32	20	12	2160	6.56
R insula (64.2%)					
R inferior frontal gyrus (13.6%)					
L cuneus	-2	-94	8	2079	4.97
L cuneus (64.5%)					
L calcarine gyrus (26.1%)					
L parahippocampal gyrus (BA 34)	-26	-2	-16	1512	5.07
L inferior temporal gyrus (48.2%)					
L amygdala (16.4%)					
L fusiform gyrus (8.1%)					
R fusiform gyrus (BA 36)	32	-4	-28	675	5.15
R fusiform gyrus (86%)					
R inferior temporal gyrus (7.1%)					
Deactivations					
R inferior partietal lobule (BA 40)	58	-38	48	11853	-7.55
R supramarginal gyrus (33.5%)					
R postcentral gyrus (17.4%)					
R inferior parietal lobule (8.7%)					
R precentral gyrus (7.6%)					
L precentral gyrus (BA 4)	-56	-10	32	9747	-8.56
L postcentral gyrus (26.9%)					
L supramarginal gyrus (17.3%)					
L inferior parietal lobule (16.4%)					
L precentral gyrus (6%)					
L middle occipital gyrus (BA 19)	-38	-76	8	3105	-6.16
R middle frontal gyrus (BA 8)	26	26	42	2079	-6.12
R middle frontal gyrus (77.6%)					
R superior frontal gyrus (22.3%)					
L middle frontal gyrus (BA 8)	-32	26	38	1890	-5.59
R precuneus (BA 7)	16	-76	38	675	-5.57
R precuneus (54.6%)					
R superior occipital gyrus (19.7%)					
R cuneus (12.8%)					

Morphosyntactic tag judgment (TAG) task v. control condition (reversed speech). Adults showed significant activation in left supplementary motor area (SMA), left IFG, bilateral MTG, bilateral insula, bilateral thalamus, and bilateral caudate nucleus for the TAG task (Table 6; Figure 2A). Deactivations were found in left anterior and middle cingulate cortex, left middle frontal gyrus (MFG), left cuneus, bilateral superior frontal gyrus (SFG), and right STG.

Similar to adults, children showed enhanced brain responses in the left SMA, and left MTG (Table 7; Figure 2B). Deactivations were observed in the left rolandic operculum, left MFG, left insula, right Heschl's gyrus, right precuneus, right anterior cingulate cortex, right supramarginal gyrus, and right mid-orbital gyrus.

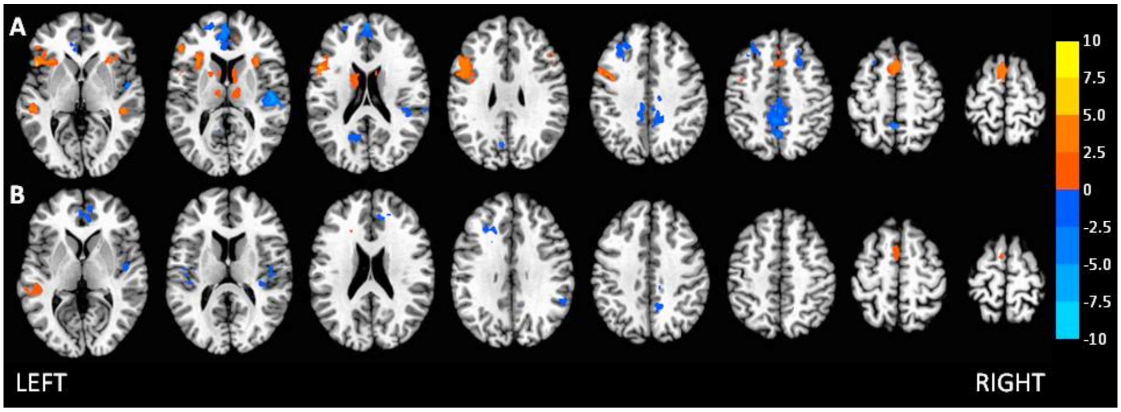

Figure 2: Significant clusters of activation effects for the contrast morphosyntactic tag judgment vs. reverse speech within the: (A) Adult group, and (B) Child group.

Table 6: Significant clusters ($t \geq 4.118$; $p < .001$; cluster corrected $p < .05$) detected in the adult group for the contrast morphosyntactic tag judgment vs. reverse speech.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI)				
	x	*y*	*z*	Volume (µl)	T-score
L superior frontal gyrus (BA 6)	-8	8	56	2862	7.61
L SMA (71.9%)					
R SMA (15.6%)					
L Superior Medial Gyrus (8.4%)					
R Superior Medial Gyrus (3.1%)					
L middle frontal gyrus (BA 9)	-44	14	26	4563	7.56
L Inferior Frontal Gyrus (p. Triangularis) (45.5%)					
L Inferior Frontal Gyrus (p. Opercularis) (36.9%)					
L Precentral Gyrus (17.0%)					
R superior temporal gyrus	44	-32	2	405	7.44
R Middle Temporal Gyrus (50.3%)					
R Superior Temporal Gyrus (24.7%)					
L insula	-28	22	12	2268	6.96
L Insula Lobe (59.6%)					
L Inferior Frontal Gyrus (p. Triangularis) (23.7%)					
L Inferior Frontal Gyrus (p. Orbitalis) (11.6%)					
L Thalamus	-10	-14	12	621	6.62
L inferior frontal gyrus (BA 46)	-46	32	12	621	6.33
L Inferior Frontal Gyrus (p. Triangularis) (91.0%)					
L Inferior Frontal Gyrus (p. Orbitalis) (9.0%)					
R insula	32	20	8	972	6.11
R Insula (68.4%)					
R Putamen (4.8%)					
R Thalamus	8	-16	14	486	5.99
L Caudate	-14	4	18	1053	5.96
L Caudate (78.2%)					
L Putamen (7.7%)					
L superior temporal gyrus (BA 21)	-50	-26	2	486	5.91
L Middle Temporal Gyrus (97.0%)					
R Caudate Nucleus	10	-2	12	540	5.74
L superior temporal gyrus (BA 38)	-50	-2	-6	351	5.41
L Middle Temporal Gyrus (63.9%)					
L Superior Temporal Gyrus (36.1%)					
R middle frontal gyrus (BA 9)	44	20	30	486	5.34
R Inferior Frontal Gyrus (p. Triangularis) (76.3%)					
R Middle Frontal Gyrus (9.9%)					
R Inferior Frontal Gyrus (p. Opercularis) (4.7%)					
Deactivations					
L medial frontal gyrus (BA 9)	-4	44	14	3375	-10.55
L Anterior Cingulate Cortex (48.3%)					
L Superior Medial Gyrus (24.4%)					
R Anterior Cingulate Cortex (9.2%)					
R Superior Medial Gyrus (5.3%)					
R Mid Orbital Gyrus (4.1%)					
L cingulate (BA 31)	-4	-38	42	5940	-8.30
L Middle Cingulate Cortex (36.9%)					
R Middle Cingulate Cortex (26.6%)					
R Precuneus (17.6%)					
L Precuneus (16.5%)					
R transverse temporal gyrus (BA 41)	46	-22	12	2592	-7.84
R Superior Temporal Gyrus (57.3%)					
R Heschls Gyrus (28.5%)					
R Insula Lobe (6.6%)					
R Rolandic Operculum (5.6%)					
L middle frontal gyrus (BA 9)	-32	22	38	2349	-7.10
L Middle Frontal Gyrus (83.0%)					
L Superior Frontal Gyrus (16.9%)					
R superior frontal gyrus (BA 8)	22	14	44	702	-6.83
R Superior Frontal Gyrus (73.8%)					
R Middle Frontal Gyrus (26.2%)					
L superior frontal gyrus (BA 10)	-22	52	18	810	-6.71
L Superior Frontal Gyrus (69.8%)					
L Middle Frontal Gyrus (18.9%)					
L Superior Medial Gyrus (6.5%)					
L Superior Orbital Gyrus (4.8%)					
L precuneus	-10	-62	20	1080	-6.55
L Cuneus (63.2%)					
L Precuneus (29.4%)					
L Calcarine Gyrus (4.2%)					

Table 7: Significant clusters ($t \geq 4.118$; $p < .001$; cluster corrected $p < .05$) detected in the child group for the contrast morphosyntactic tag judgment vs. reverse speech.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI)			Volume (µl)	T-score
	x	*y*	*z*		
L medial frontal gyrus (BA 6)	-2	2	54	648	5.82
Left SMA (99.1%)					
L superior temporal gyrus (BA 41)	-44	-32	6	891	5.36
Left Middle Temporal Gyrus (81.8%)					
Left Superior Temporal Gyrus (10.9%)					
<u>Deactivations</u>					
R insula (BA 13)	44	-14	8	1863	-6.02
Right Heschls Gyrus (39.2%)					
Right Insula Lobe (23.2%)					
Right Rolandic Operculum (18.2%)					
Right Superior Temporal Gyrus (17.0%)					
R precuneus (BA 7)	16	-68	32	1026	-5.59
Right Precuneus (54.5%)					
Right Cuneus (25.7%)					
Left Precuneus (13.8%)					
Right Middle Cingulate Cortex (4.2%)					
R precuneus (BA 7)	14	-50	38	702	-5.90
Right Precuneus					
R inferior parietal lobule	50	-44	26	405	-5.03
Right SupraMarginal Gyrus (87.6%)					
Right Angular Gyrus (12.4%)					
L insula (BA 13)	-34	-14	14	891	-4.79
Left Rolandic Operculum (59.1%)					
Left Insula Lobe (23.8%)					
Left Heschls Gyrus (6.2%)					
Left Superior Temporal Gyrus (5.2%)					
R medial frontal	10	46	18	513	-4.80
Right Anterior Cingulate Cortex (91.3%)					
Right Superior Medial Gyrus (3.1%)					
	-26	26	30	540	-4.75
Left Middle Frontal Gyrus					
R medial frontal gyrus (BA 10)	8	50	6	378	-4.77
Right Mid Orbital Gyrus (51.5%)					
Right Anterior Cingulate Cortex (45.8%)					
L insula	-38	-10	8	324	-4.42
Left Insula Lobe (40.0%)					
Left Putamen (21.7%)					

Hemodynamic response latency. The group-averaged hemodynamic response time courses were examined for latency differences between adults and children. Peak activated voxels for the lexical-semantic decision (LSD) task were selected from within the left IFG and MTG for each group and independent sample t-tests indicated that the time courses were not significantly different between groups for either region (Figure 3). Peak activated voxels in the left IFG for the morphosyntactic tag judgment (TAG) task were also selected for each group. Again, the hemodynamic response for the two groups differed only in their intensity and not in their latency (Figure 4).

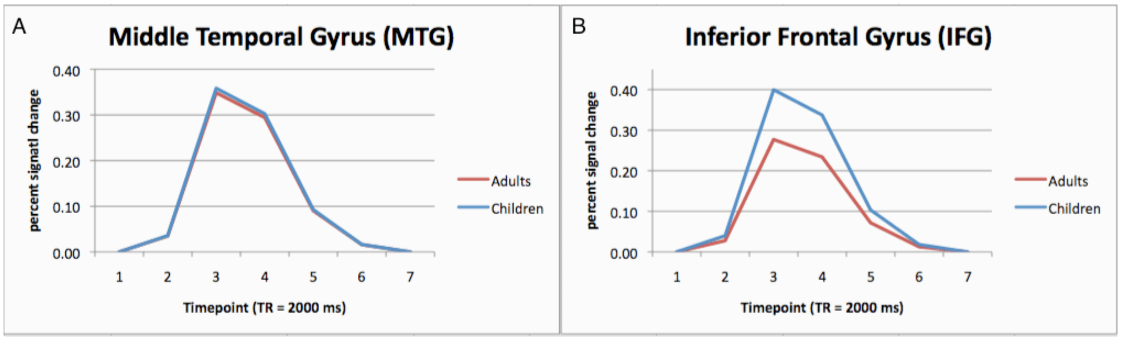

Figure 3: Hemodynamic response time courses for LSD; peak voxels in (A) left MTG and (B) left IFG. Independent sample t-tests for each timepoint indicated that the time courses were not significantly different between groups for either MTG or IFG.

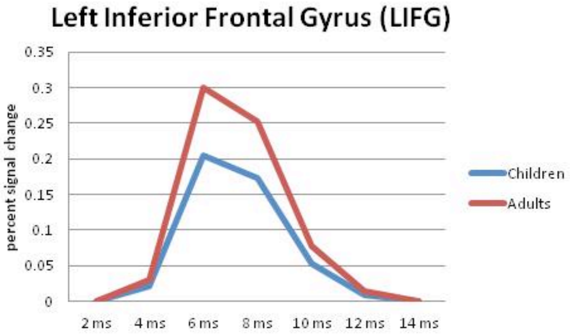

Figure 4: Hemodynamic response time courses for TAG in left IFG. Independent sample t-tests for each timepoint indicated that the time courses were not significantly different between groups.

Cross-sectional comparison of adults and children. Two-sample independent t-tests were used for a whole-brain, between-group analysis comparing adults and children for each of the two tasks. The Adult group (n=15) was compared to pooled data from the first time point for the two groups of children (i.e., Young and Older; n=30). The following contrasts are illustrated in Figure 5 with full cluster listings in Tables 8 and 9.

Lexical-semantic decision (LSD) task. Adults showed greater activation than children in bilateral inferior parietal lobe, and middle and superior temporal gyrus (Table 8; Figure 5A). Greater left hemisphere activation was also seen for the adults in the pre- and postcentral, inferior frontal, and supramarginal gyri, insula, superior parietal lobe, lingual and heschl's gyri, caudate, putamen, and middle occipital gyrus. Finally, right hemisphere activity in the fusiform gyrus and cerebellum was also greater in the adults. Children showed greater activation than adults in the left superior medial frontal gyrus and SMA. Greater bilateral activation was seen in the precuneus, cingulate and insula extending into the rolandic operculum, superior temporal and Heschl's gyri.

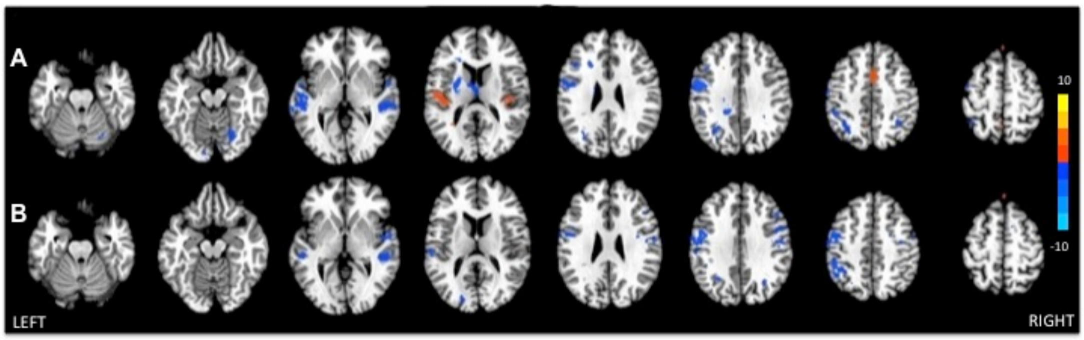

Figure 5: Significant clusters of between-group effects showing greater activation in the adults (blue) and the children (red) for (A) lexical-semantic decision and (B) morphosyntactic tag judgment.

Morphosyntactic tag judgment (TAG) task. Adults showed greater activation than children in bilateral pre- and postcentral gyrus, inferior parietal, middle and superior temporal, and superior occipital gyri (Table 9; Figure 5B). Greater activation in the adults was also observed in the right inferior and middle frontal gyri, angular gyrus, insula, and left middle occipital gyrus.

Table 8: Significant clusters ($t \geq 2.016$; $p < .05$; cluster corrected $p < .05$) detected in the between-group comparison of adults and children for lexical-semantic decision.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI)				
	x	*y*	*z*	Volume (μl)	T-score
Greater in Adults					
Left precentral gyrus (BA 6)	55.5	1.5	29.5	8721	-4.43
L precentral gyrus (27.5%)					
L putamen (12.0%)					
L postcentral gyrus (10.3%)					
L caudate nucleus (8.1%)					
L inferior frontal gyrus (p. opercularis) (2.6%)					
L superior temporal gyrus (BA 22/41)	52.5	16.5	5.5	5076	-3.83
L middle temporal gyrus (45.5%)					
L superior temporal gyrus (22.3%)					
L rolandic operculum (13.3%)					
L Heschl's gyrus (7.0%)					
L middle temporal gyrus	28.5	70.5	26.5	2430	-3.29
L inferior parietal lobule (57.1%)					
L middle occipital gyrus (18.5%)					
L superior parietal lobule (7.5%)					
L cingulate gyrus	19.5	-19.5	26.5	1782	-3.34
L inferior frontal gyrus (p. triangularis) (25.3%)					
L insula lobe (9.7%)					
L inferior parietal lobe	49.5	34.5	35.5	1458	-3.22
L inferior parietal lobule (81.5%)					
L supramarginal gyrus (16.9%)					
R superior temporal gyrus (BA 22)	-55.5	1.5	-0.5	1350	-3.89
R superior temporal gyrus (73.3%)					
R middle temporal gyrus (14.1%)					
R temporal pole (9.6%)					
R superior temporal gyrus (BA 22)	-46.5	28.5	-0.5	1269	-3.61
R middle temporal gyrus (68.6%)					
R superior temporal gyrus (14.4%)					
R declive	-22.5	67.5	-15.5	1107	-3.64
R cerebellum (77.4%)					
R fusiform gyrus (18.0%)					
L cingulate gyrus	16.5	37.5	32.5	837	-3.13
R inferior parietal lobe	-34.5	49.5	47.5	783	-3.55
R inferior parietal lobule (71.3%)					
L declive	10.5	79.5	-18.5	729	-3.02
L lingual gyrus (30.7%)					
L calcarine gyrus (22.1%)					
L cerebellum (21.6%)					
Greater in Children					
L insula	34.5	25.5	14.5	1161	3.28
L rolandic operculum (45.7%)					
L superior temporal gyrus (25.7%)					
L Heschl's gyrus (23.5%)					
R insula	-37.5	25.5	17.5	1053	3.47
R Heschl's gyrus (42.6%)					
R rolandic operculum (32.2%)					
R insula lobe (12.0%)					
R superior temporal gyrus (11.3%)					
L precuneus (BA 7)	1.5	55.5	47.5	864	3.27
L precuneus (76.5%)					
R precuneus (20.5%)					
R cingulate (BA 32)	-1.5	-10.5	41.5	783	3.24
R middle cingulate cortex (40.4%)					
L middle cingulate cortex (20.1%)					
L superior medial gyrus (19.4%)					
L SMA (17.4%)					

Table 9: Significant clusters ($t \geq 2.016$; $p < .05$; cluster corrected $p < .05$) detected in the between-group comparison of adults and children for morphosyntactic tag judgment.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI)				
	x	*y*	*z*	Volume (μl)	T-score
Greater in Adults					
R precentral gyrus (BA 6)	-37.5	10.5	32.5	4698	-3.70
R postcentral gyrus (23.8%)					
R precentral gyrus (22.8%)					
R inferior frontal gyrus (p. triangularis) (18.5%)					
R inferior frontal gyrus (p. opercularis) (9.9%)					
R middle frontal gyrus (4.9%)					
R superior frontal gyrus (3.5%)					
L precentral gyrus (BA 6)	46.5	1.5	44.5	4536	-3.49
L precentral gyrus (49.5%)					
L postcentral gyrus (35.1%)					
L inferior frontal gyrus (p. opercularis) (3.6%)					
L supramarginal gyrus (2.9%)					
L inferior parietal lobule (2.7%)					
L inferior parietal lobe	46.5	40.5	38.5	3375	-3.86
L inferior parietal lobule (86.2%)					
L superior parietal lobule (4.8%)					
L angular gyrus (3.7%)					
L middle occipital gyrus (2.0%)					
L superior temporal gyrus (BA 22)	49.5	16.5	5.5	1512	-4.40
L superior temporal gyrus (65.0%)					
L middle temporal gyrus (28.2%)					
R superior temporal gyrus	-55.5	4.5	5.5	1404	-4.06
R superior temporal gyrus (73.0%)					
R insula lobe (9.3%)					
R middle temporal gyrus (8.1%)					
R temporal pole (6.6%)					
R supramarginal gyrus	-31.5	49.5	35.5	1215	-3.38
R angular gyrus (42.8%)					
R inferior parietal lobule (14.6%)					
R superior occipital gyrus (12.3%)					
R middle occipital gyrus (6.6%)					
R middle temporal gyrus (BA 21)	-49.5	31.5	2.5	1053	-4.83
R middle temporal gyrus (70.3%)					
R superior temporal gyrus (15.0%)					
L cuneus	16.5	82.5	11.5	648	-3.21
L middle occipital gyrus (51.1%)					
L superior occipital gyrus (23.5%)					
R precentral gyrus	-37.5	-19.5	35.5	567	-3.40
R middle frontal gyrus (81.2%)					
R superior frontal gyrus (7.0%)					

Longitudinal analysis of time. Paired and independent two-sample t-tests were used for a whole-brain analysis of time point (1 and 2), groups of children (Young children and Older children), and language tasks (i.e., lexical-semantic decision and morphosyntactic tag judgment). The following results are illustrated in Figure 6 with full cluster listings in Tables 10 through 12.

Main effect of time. To determine which brain regions change as a function of time, a whole-brain analysis compared data from the first and second time points, acquired one year apart, across language tasks and across age groups. A paired t-test revealed significantly greater bilateral precuneus activation in the first time point. For the second time point, significantly greater activation was detected in left pre- and postcentral gyri, middle and superior temporal gyri, middle and superior occipital gyri, angular gyrus, and the left hippocampus and putamen (Table 10; Figure 6A).

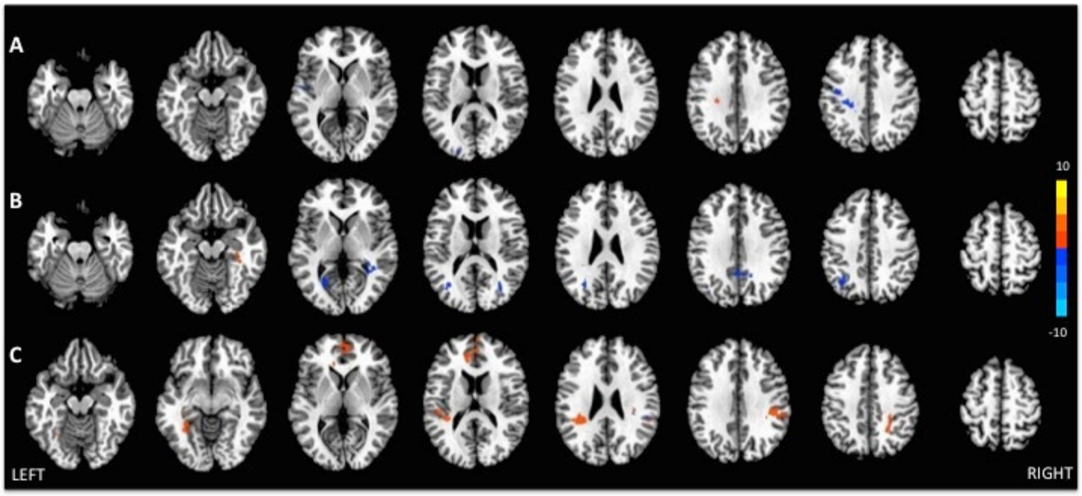

Figure 6: Significant clusters of (A) the main effect of time showing greater activation in time point 1 (red) compared to time point 2 (blue) across groups and across tasks, (B) the between-group comparison of change over time for the Young kids (red) and Older kids (blue) across tasks, and (C) the within-group comparison of change over time for TAG (red) and LSD (blue) across groups.

Table 10: Significant clusters ($t \geq 2.757$; $p < .01$; cluster corrected $p < .05$) detected in the analysis of time comparing the first and second time point across groups and across tasks.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI) *x*	 *y*	 *z*	Volume (μl)	T-score
Greater in first timepoint					
R Precuneus (BA 7)	4	-58	56	486	3.99
R precuneus (73.4%)					
L precuneus (15.4%)					
R superior parietal lobule (11.2%)					
Greater in second timepoint					
L cingulate gyrus (BA 31)	-26	-26	36	270	-4.04
L precentral gyrus (BA 6)	-38	-14	36	216	-4.56
L postcentral gyrus (46.3%)					
L precentral gyrus (38.8%)					
L insula (BA 13)	-44	-8	0	189	-3.21
L superior temporal gyrus (77.5%)					
L insula lobe (8.7%)					
L rolandic operculum (5.0%)					
L cuneus (BA 18)	-20	-92	12	162	-3.62
L middle occipital gyrus (88.2%)					
L superior occipital gyrus (11.8%)					

Interaction of time and age group. To determine if some brain regions experience more change (in any direction) over one year as a function of age group, a whole-brain analysis compared data from the Young children and Older children across language tasks. Greater change over time was seen in the Young children in the right parahippocampal and fusiform gyrus. Greater change over time was observed in the Older children in left lingual gyrus and bilaterally in the precuneus, cingulate and middle occipital gyrus (Table 11; Figure 6B).

Table 11: Significant clusters ($t \geq 2.757$; $p < .01$; cluster corrected $p < .05$) detected in the between-group comparison of change over time for the Young and Older children across tasks.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI)			Volume (µl)	T-score
	x	*y*	*z*		
Greater change in young kids					
R parahippocampal gyrus	32	-26	-12	216	4.08
R parahippocampal gyrus (53.2%)					
R fusiform gyrus (46.8%)					
Greater change in older kids					
L posterior cingulate	-26	-62	24	837	-4.17
L middle occipital gyrus (42.9%)					
L lingual gyrus	-22	-58	6	486	-3.84
L calcarine gyrus (55.6%)					
R cingulate gyrus	16	-52	30	378	-3.85
R precuneus (19.9%)					
L cingulate gyrus	-4	-50	30	324	-3.77
R precuneus (30.4%)					
R middle cingulate cortex (27.3%)					
L posterior cingulate cortex (26.7%)					
L precuneus (15.5%)					
L inferior parietal lobe (BA 39)	-34	-62	38	324	-4.13
L inferior parietal lobule (72.6%)					
L angular gyrus (25.4%)					
R caudate	32	-38	6	297	-3.75
R calcarine gyrus (6.4%)					
R middle occipital gyrus	32	-68	14	270	-4.72
R middle occipital gyrus (19.7%)					

Interaction of time and language task. To determine if some brain regions experience more change (in any direction) over one year as a function of language task, a whole-brain analysis compared data from the lexical-semantic decision task (LSD) and morphosyntactic tag judgment (TAG) across age groups. Greater change over time was seen in the TAG task than for LSD. Significant effects were found in the left medial frontal and superior temporal gyri along with left insula and bilateral anterior cingulated cortex. Left parahippocampal and fusiform gyri and right precuneus and supramarginal gyrus also had greater change in the TAG task over time (Table 12; Figure 6C).

Table 12: Significant clusters ($t \geq 2.046$; $p < .05$; cluster corrected $p < .05$) detected in the within-group comparison of change over time for the lexical-semantic decision (LSD) and morphosyntactic tag judgment (TAG) tasks across age groups.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI) *x*	 *y*	 *z*	Volume (μl)	T-score
Greater change in TAG task					
L medial frontal gyrus (BA 10)	-2	52	6	3537	3.94
L anterior cingulate cortex (15.9%)					
R mid orbital gyrus (9.8%)					
R anterior cingulate cortex (7.0%)					
L superior medial gyrus (6.8%)					
R superior medial gyrus (5.7%)					
L superior temporal gyrus (BA 41)	-44	-34	18	1593	3.35
L superior temporal gyrus (22.2%)					
L caudate	-22	8	20	837	2.99
L insula lobe (10.9%)					
L putamen (10.9%)					
L parahippocampal gyrus (BA 37)	-32	-44	-6	702	3.55
L fusiform gyrus (35.2%)					
L hippocampus (16.5%)					
L parahippocampal gyrus (15.7%)					
R precuneus	22	-50	38	567	4.06
R middle cingulate cortex (8.8%)					
R inferior parietal lobe (BA 40)	44	-32	30	540	3.33
R supramarginal gyrus (28.5%)					

Follow-up analysis of interactions and main-effects. Paired t-tests for each group (i.e., Young and Old children) for each task (i.e., LSD and TAG) were completed to determine the directionality of changes. Cross-sectional analysis via independent two-sample t-tests were also completed to provide additional information. The following results are illustrated in Figure 7 with full cluster listings in Tables 13 through 18.

Young children; lexical-semantic decision (LSD) task. Young children showed significantly greater activation for the LSD task when they were eight years old than when they were a year younger. Significant clusters were found in the left inferior, middle, and superior frontal gyri, anterior cingulate, angular gyrus, inferior parietal lobe, and left caudate. Significant right hemisphere effects was seen in the anterior cingulate gyrus, precuneus, and caudate. No inverse effects were found (Table 13; Figure 7A).

Older children; lexical-semantic decision (LSD) task. Older children displayed significantly greater right hemisphere activation at their first time point (i.e., age 9 years) with activation in the right inferior and middle frontal gyri (including pars triangularis) and right precentral gyrus. They also had greater left hemispheric activation in the left inferior frontal gyrus (pars opercularis) and middle frontal gyrus when compared to their activation patterns one year later. At their second time point (i.e., age 10), the Older children showed significantly more activation in the left precentral gyrus, insula, middle and superior temporal gyrus, and middle occipital gyrus, as well as right middle cingulate gyrus (Table 14; Figure 7B).

Cross-sectional analysis of lexical-semantic decision (LSD) task. Young children at their first time point (i.e., age 7 years) were compared to Older children at their second time point (i.e., age 10 years) in an independent two-sample t-test. The Young children displayed greater right-hemisphere activation in the right SMA, superior frontal gyrus, middle cingulate cortex, middle and superior temporal gyrus. The Older children demonstrated greater activation than their younger peers primarily in the left hemisphere. Significant clusters were found in the left pre- and postcentral gyri, middle and superior frontal gyri, insula, parietal lobe, precuneus, angular gyrus, middle and superior temporal gyri, hippocampus, and inferior and middle occipital gyri. Greater right hemispheric activation was found in the cingulate, caudate, and cerebellum (Table 15; Figure 7C).

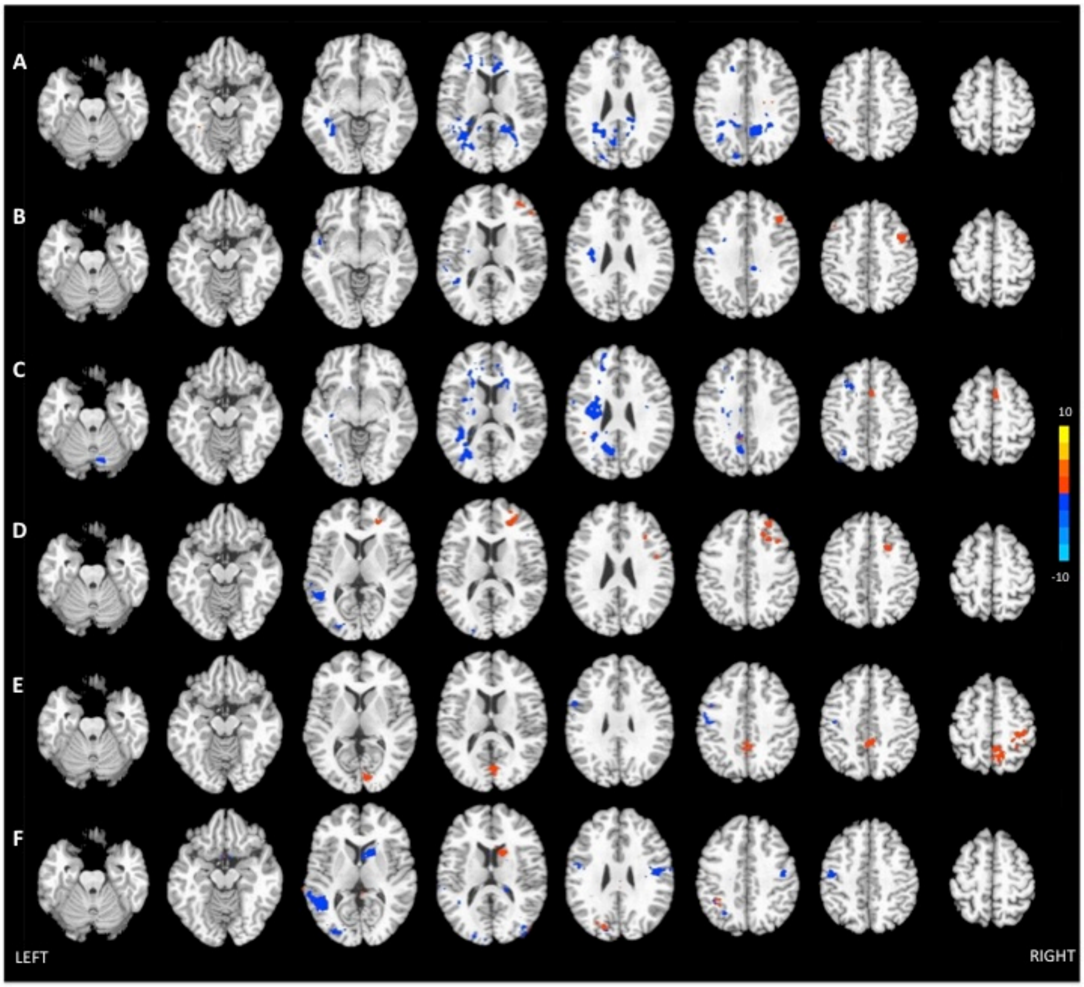

Figure 7: Significant clusters of activation effects for the lexical-semantic decision (LSD) task (A) longitudinally, within-group analysis of the Young children at age 7 (red) versus age 8 (blue), (B) longitudinally, within-group analysis of the Older children at age 9 (red) versus age 10 (blue), (C) cross-sectionally, between-group analysis of the Young children at age 7 (red) versus the Older children at age 10 (blue), and for the morphosyntactic tag judgment (TAG) task (D) longitudinally, within-group analysis of the Young children at age 7 (red) versus age 8 (blue), (E) longitudinally, within-group analysis of the Older children at age 9 (red) versus age 10 (blue), and (F) cross-sectionally, between-group analysis of the Young children at age 7 (red) versus the Older children at age 10 (blue).

Table 13: Significant clusters ($t \geq 2.146$; $p < .05$; cluster corrected $p < .05$) of activation effects for the longitudinal, within-group analysis comparing Young children at age 7 (red) versus age 8 (blue) for the lexical-semantic decision (LSD) task.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI) *x*	 *y*	 *z*	Volume (µl)	T-score
Greater activation in older kids (8-year-olds)					
R precuneus	-28	-52	12	18846	-6.55
R precuneus (8.0%)					
L medial frontal gyrus	-22	40	12	2430	-3.78
L anterior cingulate cortex (9.9%)					
L inferior frontal gyrus (p. triangularis) (9.0%)					
R caudate	16	22	14	1188	-3.21
R caudate nucleus (34.5%)					
R anterior cingulate cortex (30.1%)					
R anterior cingulate (BA 24)	4	26	12	1053	-4.37
R anterior cingulate cortex (33.7%)					
R thalamus	2	-2	6	972	-5.83
L caudate nucleus (2.3%)					
L angular gyrus (BA 39)	-32	-58	32	945	-4.51
L angular gyrus (56.0%)					
L inferior parietal lobule (37.4%)					
L middle frontal gyrus (BA 9)	-32	20	32	648	-4.35
L superior frontal gyrus (18.9%)					
L middle frontal gyrus (17.2%)					

Table 14: Significant clusters ($t \geq 2.146$; $p < .05$; cluster corrected $p < .05$) of activation effects for the longitudinal, within-group analysis comparing Older children at age 9 (red) versus age 10 (blue) for the lexical-semantic decision (LSD) task.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI)			Volume (μl)	T-score
	x	*y*	*z*		
Greater activation in older kids (10-year-olds)					
L insula (BA 13)	-44	-2	0	1971	-3.92
L superior temporal gyrus (80.3%)					
L middle temporal gyrus (10.3%)					
L temporal pole (7.7%)					
L insula	-28	-20	26	1566	-3.41
L insula lobe (7.0%)					
L precentral gyrus (6.0%)					
L superior temporal gyrus	-38	-44	12	837	-5.04
L middle temporal gyrus (78.1%)					
L middle occipital gyrus (6.1%)					
R cingulate (BA 23)	8	-32	30	540	-4.25
R middle cingulate cortex (38.1%)					
Greater activation in younger kids (9-year-olds)					
R inferior frontal gyrus (BA 46)	46	34	12	648	3.72
R middle frontal gyrus (54.4%)					
R inferior frontal gyrus (p. triangularis) (44.4%)					
R middle frontal gyrus (BA 9)	40	28	32	567	5.48
R middle frontal gyrus (75.1%)					
R inferior frontal gyrus (p. triangularis) (24.9%)					
L middle frontal gyrus (BA 9/8)	-34	22	38	567	3.72
L middle frontal gyrus (94.8%)					
L inferior frontal gyrus (p. opercularis) (4.0%)					
R middle frontal gyrus (BA 8)	44	8	42	540	3.44
R middle frontal gyrus (78.1%)					
R precentral gyrus (21.9%)					

Table 15: Significant clusters ($t \geq 2.046$; $p < .05$; cluster corrected $p < .05$) of activation effects for the cross-sectional, between-group analysis comparing Young children at age 7 (red) versus Older children at age 10 (blue) for the lexical-semantic decision (LSD) task.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI)			Volume (µl)	T-score
	x	*y*	*z*		
Greater activation in older kids (10-year-olds)					
L postcentral gyrus	-32	-20	26	13068	-3.96
L superior frontal gyrus (8.3%)					
L middle frontal gyrus (7.4%)					
L insula lobe (6.9%)					
L putamen (6.8%)					
L superior temporal gyrus	-32	-52	12	5535	-4.47
L middle occipital gyrus (6.3%)					
L middle temporal gyrus (5.4%)					
R caudate	10	14	8	2673	-3.55
R caudate nucleus (24.1%)					
R anterior cingulate cortex (18.5%)					
L precuneus (BA 7)	-4	-62	32	1701	-4.09
L precuneus (58.1%)					
L cuneus (22.9%)					
R precuneus (10.6%)					
R cerebellum	14	-70	-22	1161	-3.09
R cerebellum (64.1%)					
R cerebellum (VI) (22.0%)					
Cerebellar vermis (7) (10.0%)					
L precuneus (BA 39)	-32	-62	38	918	-3.93
L inferior parietal lobule (47.6%)					
L angular gyrus (30.9%)					
L superior parietal lobule (20.9%)					
R insula (BA 13)	34	-8	24	702	-3.32
R putamen (20.6%)					
R insula lobe (8.3%)					
R rolandic operculum (8.3%)					
L inferior occipital gyrus (BA 18)	-26	-88	-6	648	-3.73
L middle occipital gyrus (68.6%)					
L inferior occipital gyrus (21.3%)					
L precentral gyrus (BA 6)	-50	-2	30	621	-2.93
L precentral gyrus (55.0%)					
L postcentral gyrus (44.1%)					
L parahippocampal gyrus	-26	-16	-10	540	-3.30
L hippocampus (79.0%)					
Greater activation in younger kids (7-year-olds)					
R superior frontal gyrus (BA 6)	4	4	54	675	3.62
R SMA (62.4%)					
R middle cingulate cortex (22.0%)					
L SMA (11.0%)					
R superior temporal gyrus (BA 22)	50	-34	6	621	3.19
R middle temporal gyrus (56.9%)					
R superior temporal gyrus (40.2%)					

Young children; morphosyntactic tag judgment (TAG) task. Young children showed significantly greater right hemisphere activation for the TAG task when they were seven years old than they did a year later. Greater right hemisphere activation was seen in the inferior frontal gyrus (both pars triangularis and opercularis), middle and superior frontal gyri, and insula at their first time point. A year later, the same children showed greater activation in the left hemisphere – middle and superior occipital gyri and middle and superior temporal gyri than at time point 1 (Table 16; Figure 7D).

Table 16: Significant clusters ($t \geq 2.146$; $p < .05$; cluster corrected $p < .05$) of activation effects for the longitudinal, within-group analysis comparing Young children at age 7 (red) versus age 8 (blue) for the morphosyntactic tag judgment task.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI) *x*	 *y*	 *z*	Volume (µl)	T-score
Greater activation in older kids (8-year-olds)					
L cuneus	-14	-88	12	648	-3.00
L middle occipital gyrus (47.9%)					
L superior occipital gyrus (45.9%)					
L superior temporal gyrus (BA 42)	-56	-32	12	594	-3.85
L middle temporal gyrus (85.4%)					
L superior temporal gyrus (11.9%)					
Greater activation in younger kids (7-year-olds)					
R middle frontal gyrus (BA 8)	26	38	38	1188	5.89
R middle frontal gyrus (51.4%)					
R superior frontal gyrus (38.2%)					
R middle frontal gyrus	38	28	18	1161	4.48
R inferior frontal gyrus (p. triangularis) (35.5%)					
R inferior frontal gyrus (p. opercularis) (27.8%)					
R insula lobe (5.8%)					
R anterior cingulate	22	38	14	864	3.58
R superior frontal gyrus (29.3%)					
R middle frontal gyrus (11.4%)					

Older children; morphosyntactic tag judgment (TAG) task. At the first time point, 9-year-olds displayed significantly greater hemodynamics responses in bilateral postcentral gyrus, precuneus, superior parietal lobe and left middle cingulate, and lingual gyrus, than at the second time point one year later. Inverse effects (i.e., greater activation when 10 years old) were found in the left pre- and postcentral gyrus and the left inferior frontal gyrus (pars opercularis; Table 17; Figure 7E).

Table 17: Significant clusters ($t \geq 2.146$; $p < .05$; cluster corrected $p < .05$) of activation effects for the longitudinal, within-group analysis comparing Older children at age 9 (red) versus age 10 (blue) for the morphosyntactic tag judgment task.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI) *x*	 *y*	 *z*	Volume (µl)	T-score
Greater activation in older kids (10-year-olds)					
L precentral gyrus (BA 4)	-44	-16	38	1242	-4.03
L precentral gyrus (51.5%)					
L postcentral gyrus (34.5%)					
L inferior frontal gyrus (p.opercularis) (13.0%)					
Greater activation in younger kids (9-year-olds)					
R postcentral gyrus (BA 3/4)	14	-38	56	3780	4.65
R postcentral gyrus (37.1%)					
R precuneus (27.5%)					
R superior parietal lobule (25.7%)					
R precentral gyrus (5.5%)					
L cingulate gyrus (BA 31)	-2	-46	38	1188	3.84
R precuneus (35.1%)					
R middle cingulate cortex (32.1%)					
L middle cingulate cortex (21.1%)					
L precuneus (11.0%)					
L lingual gyrus	10	-82	2	972	3.90
R calcarine gyrus (79.1%)					
L calcarine gyrus (14.5%)					
L precuneus (BA 7)	-10	-58	62	891	3.44
L postcentral gyrus (36.9%)					
L precuneus (33.1%)					
L superior parietal lobule (26.9%)					

Cross-sectional analysis of morphosyntactic tag judgment (TAG) task.

Young children at their first time point (i.e., age 7 years) were compared to Older children at their second time point (i.e., age 10 years) in an independent two-sample t-test for the TAG task. There were no areas of activation that were significantly greater in the 7-year-olds than in the 10-year-olds. However, inverse effects (greater activation at age 10 than age 7) were seen bilaterally with significant clusters in pre- and postcentral gyri, cuneus and precuneus, and middle and superior occipital gyri. Left hemisphere activation was observed in the left inferior and superior parietal lobe, and middle and superior temporal gyri. Right cingulate and lingual gyri also had significantly more activation in the 10-year-olds when compared to the 7-year-olds (Table 18; Figure 7F).

Table 18: Significant clusters ($t \geq 2.046$; $p < .05$; cluster corrected $p < .05$) of activation effects for the cross-sectional, between-group analysis comparing Young children at age 7 (red) versus Older children at age 10 (blue) for the morphosyntactic tag judgment task.

Peak location (Brodmann area) Regions included in cluster (% volume of cluster)	Talairach coordinates (LPI)				
	x	*y*	*z*	Volume (μl)	T-score
Greater activation in older kids (10-year-olds)					
L middle temporal gyrus	-40	-46	8	2295	-3.85
L middle temporal gyrus (76.4%)					
L superior temporal gyrus (5.5%)					
L precentral gyrus	-38	-14	36	1944	-4.47
L precentral gyrus (37.2%)					
L postcentral gyrus (25.9%)					
R anterior cingulate	4	4	-4	1863	-3.60
R caudate nucleus (37.4%)					
R putamen (23.5%)					
R pallidum (8.9%)					
R olfactory cortex (7.2%)					
R precentral gyrus	44	-10	26	1377	-4.09
R postcentral gyrus (31.2%)					
R precentral gyrus (27.9%)					
R cuneus	20	-82	20	1026	-3.30
R middle occipital gyrus (50.7%)					
R superior occipital gyrus (44.7%)					
R thalamus	16	-32	14	918	-2.83
R posterior cingulate cortex (7.1%)					
R caudate nucleus (7.1%)					
R precuneus (4.2%)					
L precuneus	-20	-56	36	837	-3.35
L inferior parietal lobule (19.3%)					
L middle occipital gyrus (12.3%)					
L superior parietal lobule (11.2%)					
L angular gyrus (6.8%)					
L cuneus (BA 18)	-8	-92	18	756	-2.82
L middle occipital gyrus (70.0%)					
L superior occipital gyrus (14.6%)					
L cuneus (6.8%)					
R middle occipital gyrus	32	-74	6	702	-3.44
R lingual gyrus (8.4%)					
R calcarine gyrus (4.6%)					
R middle occipital gyrus (4.4%)					
L cuneus (BA 18)	-16	-74	20	567	-2.89
L middle occipital gyrus (49.9%)					
L superior occipital gyrus (42.1%)					
L cuneus (8.0%)					

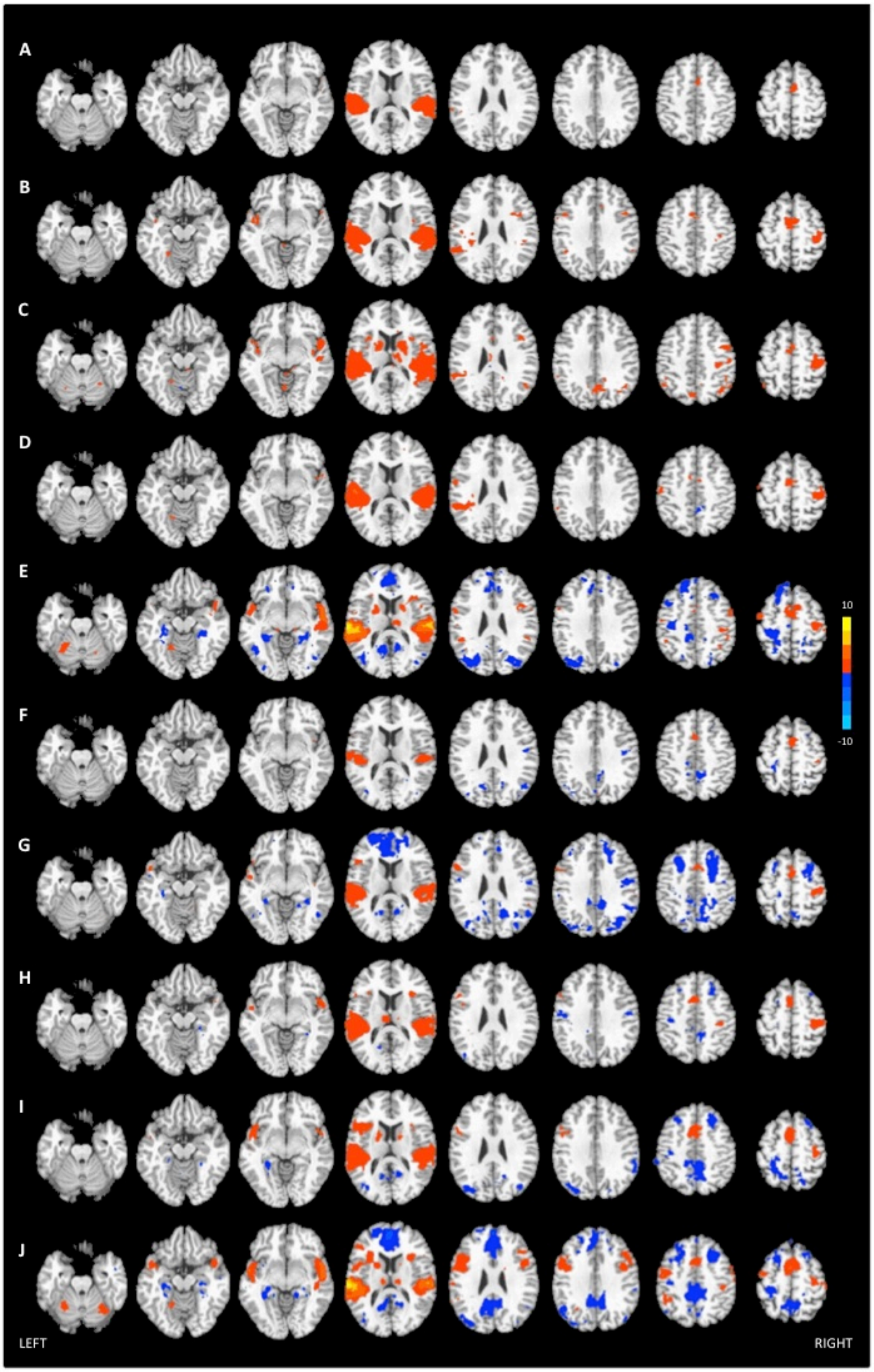

Figure 8: To aid in the discussion, significant ($t \geq 2.146$; $p < .05$; cluster corrected $p < .05$) within-group clusters of activation effects for LSD at age (A) 7, (B) 8, (C) 9, (D) 10, and (E) Adult, and for TAG at age (F) 7, (G) 8, (H) 9, (I) 10, and (J) Adult.

Discussion

While many of the seminal studies of language development took a longitudinal approach following single children from infancy into adulthood (R. Brown, 1973), the majority of neurolinguistic studies have relied on group comparison through cross-sectional methodology. These fMRI studies of language development have compared groups of children to adults and have demonstrated that even very young children, despite their immature language abilities, have left-dominant language networks quite similar to adults when performing a range of primarily passive listening, single-word and word-pair language tasks (Blumenfeld et al., 2006; Chou et al., 2006; Dehaene-Lambertz et al., 2002; Gaillard et al., 2000; Holland et al., 2001; Kotz et al., 2002; Schlaggar et al., 2002).

By the age of five years, most children show mastery of all vowels and most consonants, actively participate in conversations with adults (including asking and answering questions), narrate anecdotes, sight-read a few common words and comprehend simple stories (Nippold, 2007). Specifically relevant to our studies, semantic-skills of a 5-year-old include knowledge of at least 10,000 different words (Clark, 2003), understanding of some common idioms and concrete metaphors, and intentional humor through rhyming and misnaming objects (e.g., "You're a towel!") (McGhee, 1979; Nippold, 1985). Morphosyntactic skills at the age of 5 include mastery of Brown's 14 grammatical morphemes (including past tense, possessive, and plural), production of sentences with relative, adverbial, and nominal clauses, use of infinitives, gerunds, negation, past, present and future-tense verbs, and initial use of easy coordinate and subordinate conjunctions (Paul, 1981).

However, anyone who has spoken to a 5-year-old will readily attest to the fact that while their current language skills and the rate of language development in the preceding years are impressive, they clearly still differ from adults with respect to their level of overall linguistic abilities. During the next two decades, these young children will acquire at least 40,000 more words, develop knowledge of roots, prefixes, and suffixes, will learn to understand subtle differences between semantically similar words, increase the length of their discourse, use increasingly difficult conjunctions, and will learn to read proficiently (Nippold, 2007).

Whereas their basic command of language supports the expectation of overall similarity between language networks in young children and adults, the still apparent disparity in linguistic abilities supports the consistent finding that while the neural language networks are *similar*, they are not yet *the same*. So how do the immature cortical language networks “grow up”? Brown and colleagues (2005) have used that idiom to suggest that during development, certain regions (e.g., frontal cortex) “grow up” and become responsible for subserving language function while other regions (e.g., extrastriate cortex) are now “growing down” and are less utilized for language. Their findings support the theory of ‘progressive neural scaffolding’ (Petersen et al., 1998), which posits that in the process of learning, when performance is still immature, large sets of lower-level sensory brain regions are recruited for novel tasks. As novel tasks become learned, top-down support is provided through higher-level control mechanisms. This scaffolding model is not specific to language, but relates to domain-general mechanisms of learning.

The vast majority of neuroimaging studies of language development have utilized single-word paradigms. Single-word and word-pair paradigms are generally ‘non-ecological’, creating highly artificial task demands that differ dramatically from actual language use. With the exception of Szaflarski and colleagues (2006) who report on a *longitudinal*, single-word study, all other fMRI language research has used cross-sectional methodology. Cross-sectional designs are limited as they only capture development at a single point in time and thus the mechanisms by which these cognitive changes occur over time are still uncertain.

Our study, which combined longitudinal and cross-sectional assays, sought to answer three questions:

1.) Can the findings in support of ‘progressive neural scaffolding’ be replicated in a longitudinal study of sentence processing?
2.) What are the neural correlates of morphosyntactic development?
3.) What are the neural correlates of lexical-semantic development?

Longitudinal study design

There are many challenges in a longitudinal study. Notably, they tend to take longer and cost more than a cross-sectional design. Increased project time is self-explanatory; in one month, one could test children in several different age groups, each one year apart. A longitudinal design would require waiting for each of those years to pass. Attrition, a great concern in all studies, becomes particularly costly in imaging studies, as it is necessary to initially scan several more participants than your desired target sample size. Attrition may be equally challenging in studies of adults and children; however, *imaging* studies of children have a unique attrition factor, orthodontia. While we lost participants to parent factors (e.g., divorce, moving), and child factors (e.g., disinterest), we experienced more attrition due to the implantation of potentially ferromagnetic orthodontia (e.g., spacers, bridges, retainers, braces) than due to any other factor. Future studies would benefit from asking parents in advance of the likelihood that they may be pursuing orthodontic work for their children. That being said, many parents did not understand that ‘spacers,’ typically a precursor to more involved orthodontia such as braces, would exclude them from the study. However, as orthodontic work is common in pre-teenagers, and the majority of orthodontic work is no longer ferromagnetic, additional imaging techniques should be explored to reduce imaging artifacts.

The results of our mixed longitudinal cross-sectional design provides some preliminary evidence that in developmental imaging studies, the extra burden of longitudinal designs may be worthwhile. For one example, in the right frontal lobe, children showed significantly less activation at age 8 years than one year previous for the morphosyntactic tag judgment task. This within group finding of decreased right frontal activity with age was not seen in a cross-sectional analysis of these children at age 7 (i.e., first time point) compared to a group of ten-year-olds. However, we did not have an independent group of 8-year-olds so that we could directly compare a within group longitudinal design with a between-group cross-sectional design for the 7 to 8-year-old comparison. Future studies would benefit from an additional group of children in order to directly compare the two methodologies.

Task Comparisons

This project employed judgment tasks to examine the neural correlates of development for lexical-semantic and morphosyntactic language components. These were chosen as the two main language components with a protracted development that continues into adolescence. We hypothesized that children would have developed, but not yet fully mastered these skills. Our performance results support this hypothesis: Children performed distinctly above chance on both tasks, but adults performed significantly better, and children improved with age. More errors were seen with the morphosyntactic tag judgment task (TAG) than the lexical-semantic decision task (LSD), and the children also showed a greater improvement in performance over time for TAG. Congruent with this performance discrepancy, comparison of fMRI activation for the two tasks revealed that several regions showed significantly more change over time for TAG than LSD, whereas no inverse relationship was found. Specific regional results will be discussed below, organized with respect to brain regions.

Frontal cortex

Our sentence-embedded lexical-semantic decision task (LSD) yielded findings consistent with previous single-word and word-pair studies showing age-dependent activation increases in left lateral frontal cortex with localized clusters in *both* premotor cortex (BA 6; discussed below) and classical Broca's area (BA 44, 45). In the longitudinal analysis of time, Young children displayed increased involvement of left medial and superior frontal gyrus and left inferior frontal gyrus (pars triangularis) as they age from 7 to 8 years. In the cross-sectional analysis of age, 10-year-olds showed greater activation when compared to 7-year-olds in superior and middle frontal gyrus, extending into postcentral gyrus and insula. Finally, adults had greater activation in the pars opercularis of the left inferior frontal gyrus (BA 44) when compared to all children at the first time point. For the morphosyntactic tag judgment (TAG) task, Older children showed significant activation increases in left inferior frontal gyrus (pars opercularis) from age 9 to 10 years and adults had greater activation than children in left inferior frontal gyrus, both in pars opercularis (BA 44) and pars triangularis (BA 45).

Our findings of age-dependent increases in ‘top-down’ control mechanisms are consistent with a model of progressive neural scaffolding (Petersen et al., 1998) presented earlier, and replicate other studies of language processing (T. T. Brown et al., 2005; Schlaggar et al., 2002). However, while nearly all of our findings in the left frontal lobe showed age- or time-dependent gains (in cross-sectional and longitudinal analyses, respectively), pars opercularis in left IFG showed *decreased* activation with age for Older children for the LSD task, with inverse results for the TAG task.

The role of Broca’s area (i.e., the pars triangularis and pars opercularis) in sentence processing continues to be debated. Broca’s area has been implicated in syntactic processing (Grodzinsky, 2000), verbal working memory (Caplan, Alpert, & Waters, 1999; E. E. Smith & Jonides, 1999), and phonological recoding and rehearsal (Paulesu, Frith, & Frackowiak, 1993). Further, researchers have suggested several functions for the different subdivisions within Broca’s area (Bookheimer, 2002), with the pars opercularis being linked to articulatory rehearsal (Rogalsky, Matchin, &

Hickok, 2008) and supporting hierarchical syntactic structure building and reanalysis (Hirotani, Makuuchi, Rüschemeyer, & Friederici, 2011). While our findings may be seen as further support for specialization within Broca's area of the pars opercularis for morphosyntactic and the pars triangularis for semantic processing, we are cautious as conflicting data have also been reported (Kuperberg et al., 2003). Specialization may also be temporal. Older children saw a time-dependent decline in activation for the pars opercularis when completing the lexical-semantic task, thus this region was active for the task. Additional time points and exploration within individuals may help to elucidate potential temporal specialization for this region.

In contrast to the predominantly age- and time-dependent *increases* seen in the left frontal lobe, the *right* frontal lobe displayed only *decreases* in activation with age and time for *both* semantic and syntactic processing. This is consistent with Johnson's interactive specialization (IS) model (Johnson, 2001, 2003), which hypothesizes that during development, cortical regions may initially be involved in processing a range of tasks or stimuli, but become increasingly specialized for specific tasks or stimuli with maturation. This theory posits that localization, as frequently discussed in language development, is a result of specialization of cortical networks and pathways, possibly through selective pruning or inhibition of alternative pathways. Several other studies have observed decreasing activity in the right frontal lobe with age (T. T. Brown et al., 2005; Gaillard, 2004), and our findings suggest that activation in right-hemisphere homologues of Broca's area may be recruited in the learning of several aspects of language development without developing final specialization in lexicosemantic or morphosyntactic functions.

Premotor cortex

Time-dependent effects were seen in premotor cortex (BA 6) bilaterally for both the morphosyntactic tag judgment (TAG) and lexical-semantic decision (LSD) tasks. First, left pre- and postcentral gyri displayed increased activation with age for both tasks. Our analysis of time showed that greater change was seen in this region in the second time point. Cross-sectional analysis showed that 10-years-olds had significantly more activation than 7-year-olds in left premotor cortex for both tasks. Though no significant difference was seen between groups, the longitudinal analysis of time for the Older children (aging from 9 to 10 years) showed increased activation with age while the analysis for Younger children (aging from 7 to 8 years) did not reach significance for this region, possibly suggesting relatively late onset of recruitment of left premotor cortex for language. Conversely, activation in *right* premotor cortex decreased with time for the Older children for both language tasks.

Two studies by Schlaggar and colleagues (T. T. Brown et al., 2005; Schlaggar et al., 2002) previously reported concordant left-hemisphere effects (activity increasing with age) in similar regions. One of our research questions was whether effects in motor cortices may have been related to overt speech responses required in the above studies. Since we also found effects of greater activation with age in motor and premotor cortex (for a paradigm *without* speech response), it appears unlikely that such effects are selectively tied to overt speech. Note that our tasks also required a motor response, albeit a manual button press. Peak coordinates in BA 6 detected in our study were, however, not distinctly superior to those seen in the overt speech study by

Brown and colleagues (2005), as would be expected based on somatotopic organization (Hauk, Johnsrude, & Pulvermuller, 2004) if activation sites were linked to the response effector (hand vs. mouth and vocal tract).

It should be further considered that in the present study participants used their *left* hands for button presses. While responses by the non-dominant hand may be slightly more effortful, this allowed us to better segregate activation effects of motor-response (expected in the right hemisphere) from those related to lexical processing (predominantly expected in the left hemisphere). It is therefore unlikely that effects in motor and premotor cortex of the left hemisphere detected in our study were directly tied to button presses. One may argue that inhibition of a preferential response with the dominant hand could have still contributed to effects in motor cortex. However, it is hard to construe how this would have resulted in the group and time differences observed by us. While children might have found responding with the non-dominant hand (possibly while inhibiting a right-hand response) more difficult than adults, such a scenario would have resulted in greater activation in motor and premotor cortex (reflecting more effortful processing), which is the inverse of our actual finding. Further, the longitudinal analysis of children showed that the same children had additional involvement in the left premotor cortices as they aged where we would have expected activation to decrease with age if it were a matter of difficulty.

Conversely, activation seen in *right* pre- and post-central gyri may be related to the button press response with the left hand. However, this activation *decreased* with age for the older children as they age from 9 to 10 years in both the lexical-semantic and morphosyntactic tasks. Effects of time were not hypothesized for this motor response, nor were we anticipating differences between the Young and Older groups of children. While no significant differences between groups were seen for this region, we observed trending within group-results for the Young children that reached significance for the Older children. It is not clear why the motor response would decrease with age. It may be a reflection of increased non-dominant hand dexterity or fine motor skills as children age.

Based on existing findings, greater activity in left (pre)motor cortices with age is therefore probably not related to motor response, although it remains possible that it reflects developmental changes in covert speech processes that may have accompanied performance on our language tasks. These covert speech processes may include silent generation of the final clause of the stimuli before it is presented, (e.g., Something you sit on, is a *chair*; It is nice outside, *isn't it*) or "inner speech" (Wise et al., 1991). Covert speech processes may also involve visualization (e.g., of a chair or the weather outside); this is discussed in greater detail below when describing our occipital lobe findings. Our present results appear to suggest that such covert speech components are more pronounced with age. While this interpretation may seem counterintuitive, it is supported by concordant age-dependent effects in left premotor cortex (BA 6) detected in studies by Szaflarski and colleagues (2006; 2006), who used *covert* word generation. As mentioned above, Schlaggar, Petersen, and colleagues (T. T. Brown et al., 2005; Schlaggar et al., 2002) also found consistent age-dependent effects in (pre)motor cortex for word generation tasks using *overt* speech. In our view, a more general interpretation of the pattern of findings suggests that in language stimulus-response tasks younger children may direct more attentional resources to the perceptual part of the task – reflected by greater activity in extrastriate cortices as observed by Brown et al. (2005) – whereas older children and adults tend to be more response-oriented, reflected in greater activity in motor, premotor, and supplementary motor cortices. However, this interpretation remains tentative as no language fMRI study designed to isolate effects of motor planning, covert speech, or other factors that may contribute to age-dependent changes in premotor cortex is currently available, to our knowledge.

Insula, anterior cingulate gyrus, and caudate nucleus

Age- and time-dependent increases in left insula were found for both the lexical-semantic decision (LSD) task and the morphosyntactic tag judgment (TAG) task. The insula has been associated with coordination of speech articulation (Ackermann & Riecker, 2010) and has been seen in children during an overt verb generation task (Wood et al., 2004). However, recent studies have linked the insula to motor *planning*, rather than exclusively execution, which accounts for activation in tasks without overt speech (Price, 2010) such as ours.

The right anterior cingulate gyrus, extending into the caudate nucleus, showed age-related increases primarily for the LSD task. Booth and colleagues (Booth et al., 2003) found more anterior cingulate activation in adults than children for a selective attention task. In a task of semantic memory, anterior cingulate was associated with decision making while reconciling competing response alternatives (Grossman et al., 2002). Our task required holding a sentence in working memory (e.g., “Something you sit on…”), while waiting for the final clause (e.g., “…is a chair”), and making a decision as to which of two buttons to press (i.e., correct or incorrect). While the morphosyntactic tag judgment (TAG) task also required attention, working memory, decision making, and anticipation of the next item, our results indicate that there was no significant *change* in the anterior cingulate between time points or groups. Performance differences between the two tasks may account for the differences in cingulate activation with the near ceiling performance at the last time point for LSD suggesting it was an 'easier' task. Practice effects have been associated with decreased activation in the anterior cingulate and other frontal regions (Petersen et al., 1998), however both tasks were equally rehearsed and administered equally at all time points, making it unlikely that practice effects could account for the task-specific differences we detected. It is furthermore unlikely that practice effects would have confounded longitudinal analyses, given that time points were one year apart. Note that any such unlikely effects should have resulted in decreased anterior cingulate activity, based on Petersen (1998), whereas we observed the opposite effect of activity increases at time point 2.

Parietal lobe

Studies in adults, indicate a role of the left inferior parietal lobule (IPL) in both phonological (Hickok & Poeppel, 2000) and semantic processing(Kuperberg, Sitnikova, & Lakshmanan, 2008). Age-dependent activation increases for overt word generation in left IPL were found by Brown et al. (2005); Chou and colleagues (2006) further observed that activity in left IPL was stronger for semantically associated (compared to unrelated) words in children ages 9-15 years. Our results are consistent with previous findings as age- and time- dependent increases in activation were seen in the left IPL for the lexical-semantic decision (LSD) task. However, we also found increased activation with age in the left IPL for our morphosyntactic tag judgment (TAG) task. Our findings suggest that left IPL may not be uniquely involved in semantic functions, but may rather be associated with increased domain-general top-down control (Corbetta & Shulman, 2002) consistent with the theory of progressive neural scaffolding discussed previously. A comparison of groups revealed that Older children showed significantly more change in left IPL and angular gyrus over one year than Young children. This may suggest that the rate of maturation of a top-down network is not necessarily linear. Angular gyrus has been implicated in both semantic and goal-directed tasks as a part of the default network, with a recent study suggesting differentiation with the gyrus (Seghier, Fagan, & Price). We only found significant change with age in the angular gyrus for the semantic task.

Age-related changes in the *right* parietal lobe were greater for the morphosyntactic tag judgment (TAG) task than the lexical-semantic decision (LSD) task with activation *decreasing* with age for the Older children. Brown et al. (2005) also found age-related decreases in the right parietal lobe, though for a single-word semantic task. This finding supports the hypothesis that when a task is new or unlearned, a wide network of cortical regions may be recruited. As a task becomes learned and mastered, it is increasingly processed in a more efficiently sculpted or 'pruned' network.

Temporal lobe

Our study found age- and time-dependent increases in activation in left middle (MTG) and superior temporal gyri (STG) for both the lexical-semantic decision (LSD) and morphosyntactic tag judgment (TAG) tasks. A comparison of tasks showed that significantly more change was seen for the TAG task, and a comparison of time points revealed greater activation at the second time point within the temporal lobe. Previous studies found age-dependent increases of activation in left MTG, which was attributed to increasing richness and complexity of semantic representations (Blumenfeld et al., 2006; Chou et al., 2006). Syntactic processing has also been associated with activation in STG (Grodzinsky & Friederici, 2006). As *both* our semantic and syntactic tasks had significant changes over time in *both* MTG and STG, this region may be illustrating that the neurological process of *developing* a language is fundamentally different than the neurological process of *maintaining* a language.

In the left parahippocampal and fusiform gyri, significantly more change over time was detected for the TAG task than the LSD task. A closer look at these regions shows that for the TAG task, activation in the left parahippocampal and fusiform gyri *decreased* with development (though not significantly) whereas that same region showed statistically significant bilateral *increases* with age for LSD. Parahippocampal activation has been previously identified for an auditory semantic decision task (J.R. Binder et al., 1997) that also utilized a left-hand button press response. Bilateral parahippocampal gyri have also been associated with the default mode network discussed previously (Fair et al., 2008) and the relatively flat and deactivating responses seen in our morphosynactic task for this region may reflect the emerging default network. Additionally, the parahippocampal gyri has been associated with visualizing objects, as seen in a study comparing faces, watches and objects (Haist, Lee, & Stiles, 2010). Our semantic task described concrete nouns (e.g., "Something you sit on is a chair") and participants may have been more likely to mentally imagine the statements throughout the task (see discussion below on mental imagery). Finally, Mueller and colleagues (2002) found activation in bilateral parahippocampal gyri to be associated with later stages of learning and higher levels of performance. This is consistent with the present findings of age- and time-dependent increases in bilateral activation for 10-year-olds who had improved performance over their younger peers.

Occipital lobe

Some previous single-word and word-pair studies have shown greater activation in non-perisylvian sensory cortices (in particular extrastriate cortex) in children compared to adults (T. T. Brown et al., 2005; Schlaggar et al., 2002), arguably related to progressive neural scaffolding (as discussed above) and 'bottom-up' language development emerging from sensorimotor abilities. This finding was not replicated in our sentence-embedded paradigm. In fact, we found inverse results with age- and time-dependent *increases* in bilateral middle and superior occipital gyri for both the lexical-semantic decision (LSD) and morphosyntactic tag judgment (TAG) tasks. More activation was seen at the second time point, when compared to the first, across age groups, and Older children saw more change in extrastriate cortex over one year than Young children.

When examining these significant age- and time- dependent changes, we observe that the majority of these findings are driven by regions that initially show slight deactivation relative to baseline and later statistically ‘flatten.’ These deactivations themselves are not statistically significant, rather the change between time points is significant. It is not entirely clear what these negative values in the within-group activation maps represent. Deactivated regions have been associated with a default network, i.e., a brain system that is active during task-free periods and is considered to relate to self-reflective processing (Fair et al., 2008; Fransson, 2005; Greicius, Supekar, Menon, & Dougherty, 2009). Occipital regions are, however, not typically associated with the adult default network. The age-dependent decreases in the occipital lobe described by Brown et al. (2005) may relate to their use of overt speech paradigms, which typically result in overall more activation in children as compared to adults and thus more findings that appear to decrease with age (Palmer et al., 2001), or their use of visual stimuli for some trials. Laurienti et al (Laurienti et al., 2002) proposed a cross-modal inhibitory process based on findings of deactivation in visual cortex during auditory stimulation, and deactivation of auditory cortex during visual stimulation, in adults. This finding has recently been replicated in children (S. Sanchez and R.A. Mueller, personal communication) and encourages thoughtful consideration of task modality in designing and interpreting language paradigms.

Another consideration for the findings of age- and time- dependent increases in the middle and superior occipital lobe is the use of mental imagery. Our tasks contained descriptions of concrete nouns (e.g., “Something you wear on your head is a hat”; “The boy bakes a cake, doesn’t he?”). Covert speech processes may involve visualization (e.g., of a hat, or of a cake) that may result in activation in middle and superior occipital cortex. This hypothesis would suggest an increase in mental imagery during language processing with age. Just and colleagues (Just, Newman, Keller, McEleney, & Carpenter, 2004) found increased activation in left extrastriate cortex for a high imagery sentence comprehension task when compared to a low imagery task. Similar to a single-word task of mental imagery (D'Esposito et al., 1997), concrete nouns were associated with increased activation outside of the occipital lobe in left intraparietal sulcus and left inferior temporal gyrus (BA 37) when compared to abstract nouns. There are methodological differences from our study, such as explicitly telling subjects to use mental imagery during concrete trials and not during abstract trials, in additional to concrete trials requiring mental manipulation (e.g., The letter *W* rotated 180 degrees … looks like the letter *M*). In a PET study with a paradigm similar to our LSD task (Mellet, Tzourio, Denis, & Mazoyer, 1998), participants read definitions of abstract words (e.g., grammar, theory) and concrete words (e.g., bottle, lion). Activation was detected in the left fusiform gyrus extending into middle occipital gyrus for concrete words compared to abstract words. Similar to most mental imagery studies, participants were explicitly encouraged to produce visual images. Additional studies are needed to test the hypothesis of increased mental imagery with age.

Two regions with consistently robust findings in the present study are the precuneus and cuneus (Greicius et al., 2009). Both regions showed increased activation with age and time in the left hemisphere. The cuneus has been associated with both semantic (Balsamo et al., 2002) and syntactic (Booth et al., 2000) processing in children. Our findings are consistent with age- and time-dependent increases in *both* the lexical-semantic and morphosyntactic tasks for this region. The precuneus, however, was primarily found to be related to increased development for the lexical-semantic task. When compared to baseline, both regions initially showed deactivation that flattened and became positive with age and time.

We had hypothesized that negative age-related effects would be seen in sensorimotor regions, such as bilateral extrastriate and occipitoparietal cortices. Instead, we found increased activation with age and time for these regions. Inspection of percent signal change within each age group and within each time point for this region suggests that age-related increases in visual cortices may not be nonlinear. For example, when examining signal change from age 7 and 8 (in Young children) to age 9 and 10 years (in Older children), there was overall increase across the entire time span, but signal decrease between ages 7 and 8 years. While these changes did not reach significance, they invite a discussion on the possible nonlinearity of development over this age range. For example, neurocognitive development may be quadratic, taking a U- or an inverse U-shape suggesting that some regions increase in activation, coming online for a limited amount of time to subserve development and then regress. A discussion of how we could test for these nonlinear relationships is included below in Future Directions. However, our finding must be viewed with caution because age comparisons were only partly longitudinal.

Finally, we found a cluster of activation in the left posterior cingulate extending into the lingual gyrus that showed significantly more change for the Older children than the Young children. Further inspection of these results indicated that for both tasks, the Older children experienced a *decrease* in activation for that region. However, while no within-group effects were statistically significant, there was a trend of *increasing* activation with between ages 7 and 9 years. This region may be another illustration of nonlinear development, discussed previously, where a region may come online during a period of development, and then regress when no longer needed for the task, though this conclusion is premature.

In the right lingual gyrus, we found decreased activation with age only in the Older children for the morphosyntactic tag judgment (TAG) task. These findings are not consistent with the results of a longitudinal study from Szarflarski, Holland and colleagues (2006), the only other longitudinal fMRI study of language development that we know of, which found increased activation with age in the right lingual gyrus. Fundamental differences between fMRI paradigms may account for divergent results. Szaflarski and colleagues employed a 30-second block-designed task with covert single-word verb generation to a noun, with a bilateral finger tapping control task. Our task was an event-related design with a full sentence judgment task with overt response via button-press allowing performance monitoring.

This latter study is another example of a general problem in the fMRI literature on language development. Since a wide variety of paradigm designs (e.g., single-word vs. sentence, generation vs. judgment) has been implemented in these studies, it can not always be determined whether seemingly inconsistent results are due to differences in task design or true maturational effects. The literature would benefit from future studies that delineated the roles of these different task variables by manipulating them one at a time.

Performance

The adults in our study had significantly fewer errors than the children. The Older children were more accurate than the Young children for the lexical-semantic decision (LSD) task at both time points while there were no significant differences between the two groups for the morphosyntactic tag judgment (TAG) task at either time point. The developmental imaging literature commonly handles performance discrepancies between groups (primarily adults and children) in a number of ways: Some studies use paradigms that do not allow performance measures (e.g., covert generation of verbs to nouns), while others use tasks that are sufficiently easy for both children and adults to perform at ceiling. Yet others that detect performance discrepancies for harder tasks may either include only correct trials in analyses, while others use all trials in modeling their hemodynamic response (HDR), as we did in the present study.

Brown and colleagues (2005) only included correct trials when analyzing the HDR for their overt speech tasks, but also used overall performance to match a subset of their participants for a group comparison (adults vs. children) of selected regions of interest. The regions that were significantly different between performance-matched groups were labeled as age-dependent regions, whereas regions that were exclusively activated in an unmatched subset were labeled as performance-dependent regions.

A weakness of only using correct trials when analyzing the HDR is that adults will tend to have a greater number of data points than children (in Brown's study discussed above, the poorest performing child would have 36 data points while the highest performing adult would have nearly double, 61). Another constraint is the way in which one defines and conceptualizes performance errors. In Brown's verb generation task, responses to the stimulus 'CAR' may be an incorrect verb 'jump', a noun 'trip', or silence (no response). While all three are incorrect, it can be argued that the participants are attempting to solve the task and that the cognitive resources they are used in generating an error are similar or identical to those used for a correct response, implying that associated activity patterns are important in understanding their development. Even when a participant does not respond to a stimulus, it may reflect lack of attention to the task, but it may also be due to slower response times.

In the present study, we used all trials and included a performance regressor to account for variance uniquely due to performance in the GLM. We also completed performance-adjusted between-group comparisons (adults vs. children) comparing the lowest performing adults to the highest performing children for both tasks. We found similar results to the comparison of full samples for both tasks, highlighting that effects for the full samples were probably not driven by differences in performance.

Summary

The present experiment is the first fMRI study of language development that tested two linguistic domains (i.e., lexical semantics and morphosyntax), utilized sentence-embedded paradigms with button press responses, and executed within-group *and* between-group analyses in a mixed longitudinal and cross-sectional design. We found that both the lexical-semantic and morphosyntactic judgment tasks were associated with left lateralized fronto-temporal networks that were very similar to those seen in adults.

Our study sought to answer three questions. First, could the cross-sectional findings from single-word studies supporting ‘progressive neural scaffolding’ be replicated in a longitudinal study of sentence processing? Our findings are consistent with a model of age-dependent increases in ‘top-down’ control mechanisms during language processing as we saw age- and time- dependent increases in left frontal and parietal networks. However, we did not find evidence of language development emerging from sensorimotor abilities. In fact, we found inverse results with age- and time-dependent *increases* in bilateral middle and superior occipital gyri for both tasks. We were also able to replicate age- and time-dependent decreases in right-hemisphere homologues in the frontal, parietal, and temporal lobes consistent with the model of interactive specialization (Johnson, 2001, 2003).

Second, we describe the neural correlates of morphosyntactic development. Performance on our morphosyntactic task was significantly worse than performance on our lexical-semantic task, possibly suggesting that syntactic skills, or the meta-linguistic judgment of morphosyntactic correctness (grammaticality), have a more protracted development than lexical-semantic skills. This greater immaturity likely led to our findings of more change over time for compared to the lexical-semantic task. The left fronto-temporal network, parahippocampal gyri, and right parietal lobe all experienced greater change over one year for the morphosyntactic task than the lexical-semantic task. In addition to the regions described in the preceding two paragraphs, development in morphosyntax was also associated with increases in left inferior frontal pars opercularis and right middle occipital gyrus, and decreases in the left parietal lobe. Finally, we describe the neural correlates of lexical-semantic judgment development. In addition to the time- dependent increases in the fronto-temporal network described above, we also saw the left inferior frontal pars triangularis, premotor cortex, middle occipital and parahippocampal gyri increase in activity with time.

Limitations and Future Directions

Three primary limitations in the present study inform our recommendations for future directions: variability among children, assumed linearity of development, and meta-linguistic development. First, behavior and cognition in children have a wide range of normal variability. For logistical reasons, not all children in a group were exactly the same age (e.g., the youngest child in the group of 7-year olds was 7.14 years and the oldest in this group was 7.99). However, even perfect matching for chronological age would not ensure matching for maturational age, especially in groups including both girls and boys. This variability means that group analysis can give an incomplete picture. Brown's 13 grammatical morphemes (1973) are an excellent example of how typical development may take a set course but have a variable rate. Brown and colleagues found that while children may begin to correctly use morphemes (e.g., plural, past tense) at various ages, the *sequence* in which they develop the grammatical morphemes is the same across children. This is even seen in studies of perinatal stroke (Stiles, Reilly, Levine, Trauner, & Nass, 2012) where language milestones follow the same sequence, even though they have a delayed onset and may need to be subserved by different brain regions. We hypothesize that the same may be true for the cortical networks supporting language. While the initial and end stage (adulthood) may present with similar cortical maps for language, and the mechanisms underlying development may be the same, the onset and rate of neural development may be variable. Our longitudinal analysis removed some variability with each child serving as their own control, but was available for only some age comparisons, whereas others relied on cross-sectional contrasts (Young children vs. Older children vs. Adults). A longitudinal analysis with more than two time points would allow for a rich within-individual analysis of neurocognitive development.

More longitudinal time points would also provide the ability to look for nonlinear development. U-shaped (or inverse U-shaped) effects over time are seen in both physical and cognitive learning. One example from language development involves learning to form and use the past tense. Children have an extended period of correct performance on irregular verbs (e.g., he ate) before they begin making errors and overgeneralizing (e.g., he eated) (Marcus et al., 1992). The neurological underpinnings of language development may likewise be nonlinear. Future studies would benefit from multiple time points with regression analysis approaches to characterize the course and rate of changes in regional neurological activity over development.

One weakness of our paradigms is that they require metalinguistic competence, or "the ability to reflect upon and to analyze language as an entity itself" (Nippold, 2007). While metalinguistic competence is present by age 6 or 7 (Gombert, 1992), well within our age range, full development of metalinguistic skills is protracted, continuing into adulthood. In trying to isolate lexical-semantics and morphosyntax within a task that is measurable and ecologically valid (e.g., sentence imbedded), the use of a metalinguistic paradigm mandates caution in the interpretation of activation findings and age-related changes. Continued creativity and discussion is needed for future paradigm designs.

Conclusion

A better understanding of developmental changes in the brain organization for language may broaden our understanding of cognitive development, elucidate the causes of atypical development, and could potentially inform our diagnosis, treatment, and prevention of neurodevelopmental disorders. Consistent with the neurolinguistic literature, our results evidenced a broad network of brain regions involved in the development of language. Developmental changes were seen in brain regions spanning both hemispheres, in all four lobes, and in both positive and negative directions. Our study was not able to determine if any of these brain regions were *essential* for language development, only validating that they were indeed involved in language development. As acquiring language is a whole-brain endeavor, it is less surprising that a wide range of neurodevelopment disorders have coincident or concomitant language impairment. Conversely, this lack of predetermined focal specialization, coupled with the brain's early plasticity, allows language to develop even in cases of extreme neuronal disruption such as an early hemispherectomy.

While our study was novel in examining two linguistic domains in a mixed longitudinal and cross-sectional design, it suffered from the familiar flaw of being unable to disentangle the complicated relationship between behavioral development (e.g., higher accuracy, faster reaction time, lower effort) and neuronal development. Neuronal change was seen in the absence of measurable performance differences between our two time points. However, performance does not drive neuronal change - time and experience do, and improved performance is not the only purpose, nor result, of neuronal development. While language is a rich, complex task, arguably one that defines us as humans, it is not the *only* task of the human brain. Assuming that the brain is developing towards increased efficiency, said development is not just in service of the task being studied; hence the messiness in clearly defining the brain-behavior relationship. Our study presents a broad neuronal network for typical language development. A comparison with future longitudinal studies of atypical development will hopefully aid in the search for the causes and treatments of numerous developmental disorders, even those where language is not the primary casualty.

References

Ackermann, H., & Riecker, A. (2010). The contribution(s) of the insula to speech production: a review of the clinical and functional imaging literature. *Brain Struct Funct, 214*(5-6), 419-433.

Anglin, J. M. (1993). Vocabulary development: A morphological analysis. *Monogr Soc Res Child Dev, 58*(10).

Balsamo, L. M., Xu, B., Grandin, C. B., Petrella, J. R., Braniecki, S. H., Elliott, T. K., & Gaillard, W. D. (2002). A functional magnetic resonance imaging study of left hemisphere language dominance in children. *Arch Neurol, 59*(7), 1168-1174.

Barrett, M. (1995). Early lexical development. In P. Fletcher & B. MacWhinney (Eds.), *The handbook of child language* (pp. 362-392). Oxford: Blackwell.

Bates, E., Thal, D., Finlay, B., & Clancy, B. (2003). Early language development and its neural correlates. In I. Rapin & S. Segalowitz (Eds.), *Handbook of Neuropsychology: Child Neurology* (2nd ed., Vol. 8, pp. 525-592). Amsterdam: Elsevier.

Bell, N. L., Lassiter, K. S., Matthews, T. D., & Hutchinson, M. B. (2001). Comparison of the Peabody Picture Vocabulary Test-Third Edition and Wechsler Adult Intelligence Scale-Third Edition with university students. *J Clin Psychol, 57*(3), 417-422.

Ben-Shachar, M., Hendler, T., Kahn, I., Ben-Bashat, D., & Grodzinsky, Y. (2003). The neural reality of syntactic transformations: evidence from functional magnetic resonance imaging. *Psychol Sci, 14*(5), 433-440.

Benedict, H. (1979). Early lexical development: comprehension and production. *J Child Lang, 6*(2), 183-200.

Berko, J. (1958). The child's learning of English morphology. *Word, 14*, 150-177.

Binder, J. R. (1997). Neuroanatomy of language processing studied with functional MRI. *Clin Neurosci, 4*(2), 87-94.

Binder, J. R., Frost, J. A., Hammeke, T. A., Cox, R. W., Rao, S. M., & Prieto, T. (1997). Human brain language areas identified by functional magnetic resonance imaging. *Journal of Neuroscience, 17*, 353-362.

Bitan, T., Burman, D. D., Lu, D., Cone, N. E., Gitelman, D. R., Mesulam, M. M., & Booth, J. R. (2006). Weaker top-down modulation from the left inferior frontal gyrus in children. *Neuroimage, 33*(3), 991-998.

Bitan, T., Cheon, J., Lu, D., Burman, D. D., & Booth, J. R. (2009). Developmental increase in top-down and bottom-up processing in a phonological task: an effective connectivity, fMRI study. *J Cogn Neurosci, 21*(6), 1135-1145.

Bitan, T., Cheon, J., Lu, D., Burman, D. D., Gitelman, D. R., Mesulam, M. M., & Booth, J. R. (2007). Developmental changes in activation and effective connectivity in phonological processing. *Neuroimage, 38*(3), 564-575.

Blumenfeld, H. K., Booth, J. R., & Burman, D. D. (2006). Differential prefrontal-temporal neural correlates of semantic processing in children. *Brain Lang, 99*(3), 226-235.

Bookheimer, S. (2002). Functional MRI of language: new approaches to understanding the cortical organization of semantic processing. *Annu Rev Neurosci, 25*, 151-188.

Booth, J. R., Burman, D. B., Harasaki, Y., Van Santen, F., Gitelman, D. R., Parrish, T. B., & Mesulam, M. M. (2000). The development of orthographic, phonologic, semantic ad syntactic representationsin reading: analytic versus automatic processing. *Neuroimage, 11*(5), S293.

Booth, J. R., Burman, D. D., Meyer, J. R., Lei, Z., Trommer, B. L., Davenport, N. D., . . . Mesulam, M. M. (2003). Neural development of selective attention and response inhibition. *Neuroimage, 20*(2), 737-751.

Booth, J. R., Mehdiratta, N., Burman, D. D., & Bitan, T. (2008). Developmental increases in effective connectivity to brain regions involved in phonological processing during tasks with orthographic demands. *Brain Res, 1189*, 78-89.

Bowerman, M. (1976). Semantic factors in the acquisition of rules for word use and sentence construction. In D. M. Morehead & A. E. Morehead (Eds.), *Normal and deficient child language*. Baltimore: University Park Press.

Bowerman, M. (1979). The acquisition of complex sentences. In P. Fletcher & M. Garman (Eds.), *Language acquisition* (pp. 285-306). Cambridge, UK: Cambridge University Press.

Brauer, J., & Friederici, A. D. (2007). Functional neural networks of semantic and syntactic processes in the developing brain. *J Cogn Neurosci, 19*(10), 1609-1623.

Brauer, J., Neumann, J., & Friederici, A. D. (2008). Temporal dynamics of perisylvian activation during language processing in children and adults. *Neuroimage, 41*(4), 1484-1492.

Brown, R. (1973). *A First Language: The Early Stages*. Cambridge, Mass: Harvard University Press.

Brown, T. T., Lugar, H. M., Coalson, R. S., Miezin, F. M., Petersen, S. E., & Schlaggar, B. L. (2005). Developmental changes in human cerebral functional organization for word generation. *Cereb Cortex, 15*(3), 275-290.

Caplan, D., Alpert, N., & Waters, G. (1999). PET studies of syntactic processing with auditory sentence presentation. *Neuroimage, 9*, 343-351.

Carlisle, J., & Nomanbhoy, D. (1993). Phonological and morphological awareness in first graders. *Applied Psycholinguistics, 14*, 177-195.

Caselli, M. C., & Casadio, P. (1995). *Il primo vocabolario del bambino. Guida all'uso del questionario MacArthur per la valutazione della comunicazione e del linguaggio nei primi anni di vita*. Milano: Franco Angeli.

Chomsky, N. (1965). *Aspects of the Theory of Syntax*. Cambridge (Mass.): MIT Press.

Chou, T. L., Booth, J. R., Burman, D. D., Bitan, T., Bigio, J. D., Lu, D., & Cone, N. E. (2006). Developmental changes in the neural correlates of semantic processing. *Neuroimage, 29*(4), 1141-1149.

Clark, E. V. (2003). *First language acquisition*. Cambridge, UK: Cambridge University Press.

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci, 3*(3), 201-215.

Cox, R. W. (1996). AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Comput Biomed Res, 29*(3), 162-173.

D'Esposito, M., Detre, J. A., Aguirre, G. K., Stallcup, M., Alsop, D. C., Tippet, L. J., & Farah, M. J. (1997). A functional MRI study of mental image generation. *Neuropsychologia, 35*(5), 725-730.

Dapretto, M., & Bookheimer, S. Y. (1999). Form and content: dissociating syntax and semantics in sentence comprehension. *Neuron, 24*(2), 427-432.

De Villiers, J. G., & De Villiers, P. A. (1973). A cross-sectional study of the acquisition of grammatical morphemes in child speech. *Journal of Psycholinguistic Research, 2*, 267-278.

DeCasper, A. J., & Fifer, W. P. (1980). Of human bonding: newborns prefer their mothers' voices. *Science, 208*(4448), 1174-1176.

DeCasper, A. J., & Spence, M. J. (1986). Prenatal maternal speech influences newborns' perception of speech sounds. *Infant Behavior and Development, 9*(2), 133-150.

Dehaene-Lambertz, G., Dehaene, S., & Hertz-Pannier, L. (2002). Functional neuroimaging of speech perception in infants. *Science, 298*(5600), 2013-2015.

Démonet, J. F., Thierry, G., & Cardebat, D. (2005). Renewal of the neurophysiology of language: functional neuroimaging. *Physiol Rev, 85*(1), 49-95.

Dennis, M. (1980). Capacity and strategy for syntactic comprehension after left or right hemidecortication. *Brain Lang, 10*(2), 287-317.

Dennis, M. (1982). The Acquisition of Tag Questions. *Child Dev, 53*(5), 1254-1257.

Derwing, B. (1976). Morpheme recognition and the learning of rules for derivational morphology. *Canadian Journal of Linguistics, 21*(1), 38-66.

Echols, L. D., West, R. F., Stanovich, K. E., & Zehr, K. S. (1996). Using children's literacy activities to predict growth in verbal cognitive skills: A longitudinal investigation. *Journal of Educational Psychology, 88*, 296-304.

Fair, D. A., Cohen, A. L., Dosenbach, N. U., Church, J. A., Miezin, F. M., Barch, D. M., . . . Schlaggar, B. L. (2008). The maturing architecture of the brain's default network. *Proc Natl Acad Sci U S A, 105*(10), 4028-4032.

Fenson, L., Dale, P. S., Reznick, J. S., Bates, E., Thal, D. J., & Pethick, S. J. (1994). Variability in early communicative development. *Monogr Soc Res Child Dev, 59*(5), 1-173; discussion 174-185.

Fiebach, C. J., Schlesewsky, M., & Friederici, A. D. (2001). Syntactic working memory and the establishment of filler-gap dependencies: insights from ERPs and fMRI. *J Psycholinguist Res, 30*(3), 321-338.

Fiez, J. A. (1997). Phonology, semantics, and the role of the left inferior prefrontal cortex [editorial]. *Human Brain Mapping, 5*(2), 79-83.

Flores d'Arcais, G. B. (1978). Levels of semantic knowledge in children's use of connectives. In A. Sinclair, R. J. Jarvella & W. J. Levelt (Eds.), *The child's conception of language* (pp. 133-153). New York: Springer-Verlag.

Fransson, P. (2005). Spontaneous low-frequency BOLD signal fluctuations: an fMRI investigation of the resting-state default mode of brain function hypothesis. *Hum Brain Mapp, 26*(1), 15-29.

Fried-Oken, M. (1984). *The development of naming skills in normal and language deficient children*. doctoral dissertation. Boston University, Boston.

Friederici, A. D. (2002). Towards a neural basis of auditory sentence processing. *Trends Cogn Sci, 6*(2), 78-84.

Friederici, A. D. (2004). *The Neural Basis of Syntactic Processes* (3rd ed.). Cambridge, MA: The MIT Press.

Friederici, A. D., Bahlmann, J., Heim, S., Schubotz, R. I., & Anwander, A. (2006). The brain differentiates human and non-human grammars: functional localization and structural connectivity. *Proc Natl Acad Sci U S A, 103*(7), 2458-2463.

Friederici, A. D., Ruschemeyer, S. A., Hahne, A., & Fiebach, C. J. (2003). The role of left inferior frontal and superior temporal cortex in sentence comprehension: localizing syntactic and semantic processes. *Cereb Cortex, 13*(2), 170-177.

Gaillard, W. D. (2004). Functional MR imaging of language, memory, and sensorimotor cortex. *Neuroimaging Clin N Am, 14*(3), 471-485.

Gaillard, W. D., Berl, M. M., Moore, E. N., Ritzl, E. K., Rosenberger, L. R., Weinstein, S. L., . . . Theodore, W. H. (2007). Atypical language in lesional and nonlesional complex partial epilepsy. *Neurology, 69*(18), 1761-1771.

Gaillard, W. D., Hertz-Pannier, L., Mott, S. H., Barnett, A. S., LeBihan, D., & Theodore, W. H. (2000). Functional anatomy of cognitive development: fMRI of verbal fluency in children and adults. *Neurology, 54*(1), 180-185.

Gaillard, W. D., Sachs, B. C., Whitnah, J. R., Ahmad, Z., Balsamo, L. M., Petrella, J. R., . . . Grandin, C. B. (2003). Developmental aspects of language processing: fMRI of verbal fluency in children and adults. *Hum Brain Mapp, 18*(3), 176-185.

Giedd, J. N., Blumenthal, J., Jeffries, N. O., Castellanos, F. X., Liu, H., Zijdenbos, A., . . . Rapoport, J. L. (1999). Brain development during childhood and adolescence: a longitudinal MRI study. *Nat Neurosci, 2*(10), 861-863.

Gombert, J. E. (1992). *Metalinguistic development*. Chicago: University of Chicago Press.

Greicius, M. D., Supekar, K., Menon, V., & Dougherty, R. F. (2009). Resting-state functional connectivity reflects structural connectivity in the default mode network. *Cereb Cortex, 19*(1), 72-78.

Grodzinsky, Y. (2000). The neurology of syntax: language use without Broca's area. *Behav Brain Sci, 23*(1), 1-21; discussion 21-71.

Grodzinsky, Y., & Friederici, A. D. (2006). Neuroimaging of syntax and syntactic processing. *Curr Opin Neurobiol, 16*(2), 240-246.

Grossman, M., Smith, E. E., Koenig, P., Glosser, G., DeVita, C., Moore, P., & McMillan, C. (2002). The neural basis for categorization in semantic memory. *Neuroimage, 17*(3), 1549-1561.

Grunwell, P. (1986). Aspects of phonological development in later childhood. In K. Durkin (Ed.), *Language development in the school years* (pp. 34-56). Cambridge, MA: Brookline.

Haist, F., Lee, K., & Stiles, J. (2010). Individuating faces and common objects produces equal responses in putative face-processing areas in the ventral occipitotemporal cortex. *Front Hum Neurosci, 4*, 181.

Hauk, O., Johnsrude, I., & Pulvermuller, F. (2004). Somatotopic representation of action words in human motor and premotor cortex. *Neuron, 41*(2), 301-307.

Heim, S. (2005). The structure and dynamics of normal language processing: insights from neuroimaging. *Acta Neurobiol Exp (Wars), 65*(1), 95-116.

Hickok, G., & Poeppel, D. (2000). Towards a functional neuroanatomy of speech perception. *Trends in Cognitive Sciences, 4*(4), 131-138.

Hirotani, M., Makuuchi, M., Rüschemeyer, S.-A., & Friederici, A. D. (2011). Who was the agent? The neural correlates of reanalysis processes during sentence comprehension. *Human Brain Mapping, 32*(11), 1775-1787.

Holland, S. K., Plante, E., Weber Byars, A., Strawsburg, R. H., Schmithorst, V. J., & Ball, W. S., Jr. (2001). Normal fMRI Brain Activation Patterns in Children Performing a Verb Generation Task. *Neuroimage, 14*(4), 837-843.

Holland, S. K., Vannest, J., Mecoli, M., Jacola, L. M., Tillema, J. M., Karunanayaka, P. R., . . . Byars, A. W. (2007). Functional MRI of language lateralization during development in children. *Int J Audiol, 46*(9), 533-551.

Hwang, K., Palmer, E. D., Basho, S., Zadra, J. R., & Müller, R.-A. (2009). Category specific activations during word generation reflect experiential sensorimotor modalities. *Neuroimage*, in press.

Ingram, D. (1989). *First language acquisition: Method, description, and explanation.* Cambridge, UK: Cambridge University Press.

Johnson, M. H. (2001). Functional brain development in humans. *Nat Rev Neurosci, 2*(7), 475-483.

Johnson, M. H. (2003). Development of human brain functions. *Biol Psychiatry, 54*(12), 1312-1316.

Just, M. A., Newman, S. D., Keller, T. A., McEleney, A., & Carpenter, P. A. (2004). Imagery in sentence comprehension: an fMRI study. *Neuroimage, 21*(1), 112-124.

Kaan, E., & Swaab, T. Y. (2002). The brain circuitry of syntactic comprehension. *Trends Cogn Sci, 6*(8), 350-356.

Kandel, E. R., Jessell, T. M., & Sanes, J. R. (2000). Sensory experience and the fine tuning of synaptic connections. In E. R. Kandel, J. H. Schwartz & T. M. Jessell (Eds.), *Principles of Neural Science* (4th ed., pp. 1115-1130). New York: Elsevier.

Karmiloff-Smith, A. (1986). Some fundamental aspects of language development after age 5. In P. Fletcher & A. M. Garman (Eds.), *Language acquisition* (2nd ed., pp. 455-474). Cambridge, UK: Cambridge University Press.

Katz, E. W., & Brent, S. B. (1968). Understanding connectives. *Journal of Verbal Learning and Verbal Behavior, 7*, 501-509.

Knecht, S., Drager, B., Deppe, M., Bobe, L., Lohmann, H., Floel, A., . . . Henningsen, H. (2000). Handedness and hemispheric language dominance in healthy humans. *Brain, 123 Pt 12*, 2512-2518.

Kotz, S. A., Cappa, S. F., von Cramon, D. Y., & Friederici, A. D. (2002). Modulation of the lexical-semantic network by auditory semantic priming: an event-related functional MRI study. *Neuroimage, 17*(4), 1761-1772.

Kuperberg, G. R., Holcomb, P. J., Sitnikova, T., Greve, D., Dale, A. M., & Caplan, D. (2003). Distinct patterns of neural modulation during the processing of conceptual and syntactic anomalies. *J Cogn Neurosci, 15*(2), 272-293.

Kuperberg, G. R., Sitnikova, T., & Lakshmanan, B. M. (2008). Neuroanatomical distinctions within the semantic system during sentence comprehension: evidence from functional magnetic resonance imaging. *Neuroimage, 40*(1), 367-388.

Laurienti, P. J., Burdette, J. H., Wallace, M. T., Yen, Y. F., Field, A. S., & Stein, B. E. (2002). Deactivation of sensory-specific cortex by cross-modal stimuli. *J Cogn Neurosci, 14*(3), 420-429.

Loban, W. (1976). Language development: Kindergarten through grade twelve. Urbana, IL: National Council of Teachers of English.

Mandel, D. R., Jusczyk, P., & Pisoni, D. B. (1995). Infants' recognition of the sound patterns of their own names. *Psychological Science, 6*, 314-317.

Marcus, G. F., Pinker, S., Ullman, M., Hollander, M., Rosen, T. J., & Xu, F. (1992). Overregularization in language acquisition. *Monogr Soc Res Child Dev, 57*(4), 1-182.

Martin, A. (2007). The representation of object concepts in the brain. *Annu Rev Psychol, 58*, 25-45.

McGhee, P. E. (1979). *Humor: Its origin and development*. San Francisco: Freeman.

McGrath, C. O., & Kunze, L. H. (1973). Development of phrase structure rules involved in tag questions elicited from children. *J Speech Hear Res, 16*(3), 498-512.

Mehler, J., Jusczyk, P., Lambertz, G., Halsted, N., Bertoncini, J., & Amiel-Tison, C. (1988). A precursor of language acquisition in young infants. *Cognition, 29*(2), 143-178.

Mellet, E., Tzourio, N., Denis, M., & Mazoyer, B. (1998). Cortical anatomy of mental imagery of concrete nouns based on their dictionary definition. *Neuroreport, 9*(5), 803-808.

Moore, E. N., Palmer, E. D., Luna, M., Ramsier, F., Brueseke, L. A., Rubio, M. A., . . . Müller, R.-A. (2007). *Developmental changes in morphosyntactic judgments of tag grammaticality.* Paper presented at the 35th Annual International Neuropsychological Society Conference, Portland, OR.

Moore-Parks, E. N., Burns, E. L., Bazzill, R., Levy, S., Posada, V., & Muller, R. A. (2010). An fMRI study of sentence-embedded lexical-semantic decision in children and adults. *Brain Lang, 114*(2), 90-100.

Müller, R.-A. (1996). Innateness, autonomy, universality? Neurobiological approaches to language. *Behavioral and Brain Sciences, 19*(4), 611-631.

Muller, R. A., Kleinhans, N., Pierce, K., Kemmotsu, N., & Courchesne, E. (2002). Functional MRI of motor sequence acquisition: effects of learning stage and performance. *Brain Research. Cognitive Brain Research, 14*(2), 277-293.

Muzik, O., Chugani, D. C., Juhasz, C., Shen, C., & Chugani, H. T. (2000). Statistical parametric mapping: assessment of application in children. *Neuroimage, 12*(5), 538-549.

Nagy, W. E., Diakidoy, I., & Anderson, R. (1993). The acquisition of morphology: Learning the contribution of suffixes to the meanings of derivatives. *Journal of Reading Behavior, 25*(2), 155-171.

Nagy, W. E., & Herman, P. A. (1987). Breadth and depth of vocabulary knowledge: Implications for acquisition and instruction. In M. G. McKeown & M. E. Curtis (Eds.), *The nature of vocabulary acquisition*. Hillsdale, NJ: Erlbaum.

Nagy, W. E., Herman, P. A., & Anderson, R. C. (1985). Learning words from context. *Reading Research Quarterly, 22*, 233-253.

Nagy, W. E., & Scott, J. A. (2000). Vocabulary processes. In M. L. Kamil, P. B. Mosenthal & R. Barr (Eds.), *Handbook of reading research* (Vol. 3, pp. 269-284). Mahwah, NJ: Erlbaum.

Newman, A. J., Pancheva, R., Ozawa, K., Neville, H. J., & Ullman, M. T. (2001). An event-related fMRI study of syntactic and semantic violations. *J Psycholinguist Res, 30*(3), 339-364.

Newman, S. D., Just, M. A., Keller, T. A., Roth, J., & Carpenter, P. A. (2003). Differential effects of syntactic and semantic processing on the subregions of Broca's area. *Brain Res Cogn Brain Res, 16*(2), 297-307.

Nippold, M. A. (1985). Comprehension of figurative language in youth. *Topics in Language Disorders, 5*(3), 1-20.

Nippold, M. A. (1992). The nature of normal and disordered word finiding in children and adolescents. *Topics in Language Disorders, 13*(1), 1-14.

Nippold, M. A. (2007). *Later language development: School-age children, adolescents, and young adults* (3rd ed.). Austin, TX: PRO-ED, Inc.

Palmer, E. D., Rosen, H. J., Ojemann, J. G., Buckner, R. L., Kelley, W. M., & Petersen, S. E. (2001). An event-related fMRI study of overt and covert word stem completion. *Neuroimage, 14*(1 Pt 1), 182-193.

Paul, R. (1981). Analyzing complex sentence development. In J. F. Miller (Ed.), *Assessing language production in children: Experimental procedures* (pp. 36-40). Baltimore: University Park Press.

Paulesu, E., Frith, C. D., & Frackowiak, R. S. (1993). The neural correlates of the verbal component of working memory. *Nature, 362*(6418), 342-345.

Paus, T. (2005). Mapping brain maturation and cognitive development during adolescence. *Trends Cogn Sci, 9*(2), 60-68.

Petersen, S. E., van Mier, H., Fiez, J. A., & Raichle, M. E. (1998). The effects of practice on the functional anatomy of task performance. *Proc Natl Acad Sci U S A, 95*(3), 853-860.

Petitto, L. A., & Marentette, P. F. (1991). Babbling in the manual mode: evidence for the ontogeny of language. *Science, 251*(5000), 1493-1496.

Preece, A. (1987). The range of narrative forms conversationally produced by young children. *J Child Lang, 14*(2), 353-373.

Price, C. J. (2010). The anatomy of language: a review of 100 fMRI studies published in 2009. *Ann N Y Acad Sci, 1191*, 62-88.

Pruessmann, K. P., Weiger, M., Scheidegger, M. B., & Boesiger, P. (1999). SENSE: sensitivity encoding for fast MRI. *Magn Reson Med, 42*(5), 952-962.

Quartz, S. R., & Sejnowski, T. J. (1997). The neural basis of cognitive development: a constructivist manifesto. *Behav Brain Sci, 20*(4), 537-556; discussion 556-596.

Rakic, P., Ang, E. S. B. C., & Breunig, J. (2004). Setting the stage for cognition: Genesis of the primate cerebral cortex. In M. S. Gazzaniga (Ed.), *The Cognitive Neurosciences* (3rd ed., pp. 33-49). Cambridge (Mass.): MIT Press.

Reilly, J. S., Bates, E. A., & Marchman, V. A. (1998). Narrative discourse in children with early focal brain injury. *Brain Lang, 61*(3), 335-375.

Rogalsky, C., Matchin, W., & Hickok, G. (2008). Broca's area, sentence comprehension, and working memory: an fMRI Study. *Front Hum Neurosci, 2*, 14.

Rubio, M. A., Basho, S., Johnson, C. C., Sennett, S., Little, H., Wulfeck, B., . . . Muller, R. A. (2004). Hemodynamic effects of morphosyntactic operations and polarity reversal in a tag judgment task. *Neuroimage, (suppl.):S24 (MO91).*

Rubio, M. A., Sennett, S., Basho, S., Johnson, C. C., Little, H., Mahazeri, Y., . . . Müller, R. A. (2004). Hemodynamic response during judgment of morphosyntactic integrity in tag questions. *Journal of Cognitive Neuroscience, (suppl.):210 (F92).*

Ruff, I., Blumstein, S. E., Myers, E. B., & Hutchison, E. (2008). Recruitment of anterior and posterior structures in lexical-semantic processing: an fMRI study comparing implicit and explicit tasks. *Brain Lang, 105*(1), 41-49.

Sachs, J., & Truswell, L. (1978). Comprehension of 2-word instructions by children in the 1-word stage. *Journal of Child Language, 5*, 17-24.

Schlaggar, B. L., Brown, T. T., Lugar, H. M., Visscher, K. M., Miezin, F. M., & Petersen, S. E. (2002). Functional neuroanatomical differences between adults and school-age children in the processing of single words. *Science, 296*(5572), 1476-1479.

Schmithorst, V. J., Holland, S. K., & Plante, E. (2007). Development of effective connectivity for narrative comprehension in children. *Neuroreport, 18*(14), 1411-1415.

Scott, C. M. (1988). Spoken and written syntax. In M. A. Nippold (Ed.), *Later language development: Ages nine through nineteen* (pp. 49-95). Austin, TX: PRO-ED.

Seghier, M. L., Fagan, E., & Price, C. J. (2010). Functional subdivisions in the left angular gyrus where the semantic system meets and diverges from the default network. *J Neurosci, 30*(50), 16809-16817.

Smith, E. E., & Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science, 283*(5408), 1657-1661.

Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E. J., Johansen-Berg, H., . . . Matthews, P. M. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *NeuroImage, 23*(S1), 208-219.

Stanovich, K. E., & Cunningham, A. E. (1992). Studying the consequences of literacy within a literate society: the cognitive correlates of print exposure. *Mem Cognit, 20*(1), 51-68.

Stiles, J., Reilly, J., Levine, S., Trauner, D., & Nass, R. (2012). *Neural Plasticity and Cognitive Development*. New York: Oxford University Press.

Szaflarski, J. P., Holland, S. K., Schmithorst, V. J., & Byars, A. W. (2006). fMRI study of language lateralization in children and adults. *Hum Brain Mapp, 27*(3), 202-212.

Szaflarski, J. P., Schmithorst, V. J., Altaye, M., Byars, A. W., Ret, J., Plante, E., & Holland, S. K. (2006). A longitudinal functional magnetic resonance imaging study of language development in children 5 to 11 years old. *Ann Neurol, 59*(5), 796-807.

Talairach, J., & Tournoux, P. (1988). *Co-Planar Stereotaxic Atlas of the Human Brain*. Stuttgart: Georg Thieme.

Tettamanti, M., Alkadhi, H., Moro, A., Perani, D., Kollias, S., & Weniger, D. (2002). Neural correlates for the acquisition of natural language syntax. *Neuroimage, 17*(2), 700-709.

Tyler, A., & Nagy, W. E. (1989). The acquisition of English derivational morphology. *Journal of Memory & Language, 28*, 649-667.

Ullman, M. T. (2001). The neural basis of lexicon and grammar in first and second language: the declarative/procedural model. *Bilingualism: Language and Cognition, 4*(1), 105-122.

van Kleeck, A. (1994). Metalinguistic development. In G. P. Wallach & K. G. Butler (Eds.), *Language learning disabilities in school-age children and adolescents: Some principles and applications* (pp. 53-98). New York: Macmillan.

Vannest, J., Karunanayaka, P. R., Schmithorst, V. J., Szaflarski, J. P., & Holland, S. K. (2009). Language networks in children: evidence from functional MRI studies. *AJR Am J Roentgenol, 192*(5), 1190-1196.

Weckerly, J., Contreras, R., Wulfeck, B., Bellugi, U., & Reilly, J. (1998). *Tags are tricky, aren't they? The acquisition of tag questions in children with language impairment.* Paper presented at the Boston University Child Language Conference.

Weckerly, J., Wulfeck, B., & Reilly, J. (2004). The development of morphosyntactic ability in atypical populations: The acquisition of tag questions in children with early focal lesions and children with specific language impairment. *Brain and Language, 88*, 190-201.

Wing, C. S., & Scholnick, E. K. (1981). Children's comprehension of pragmatic concepts expressed in "because", "although', "if' and "unless'. *J Child Lang, 8*(2), 347-365.

Wise, R., Chollet, F., Hadar, U., Friston, K., Hoffner, E., & Frackowiak, R. (1991). Distribution of cortical neural networks involved in word comprehension and word retrieval. *Brain, 114 (Pt 4)*, 1803-1817.

Wood, A. G., Harvey, A. S., Wellard, R. M., Abbott, D. F., Anderson, V., Kean, M., . . . Jackson, G. D. (2004). Language cortex activation in normal children. *Neurology, 63*(6), 1035-1044.

Woolrich, M. W., Jbabdi, S., Patenaude, B., Chappell, M., Makni, S., Behrens, T., . . . Smith, S. M. (2009). Bayesian analysis of neuroimaging data in FSL. *Neuroimage, 45*(1 Suppl), S173-186.