A longitudinal fMRI investigation of the development of sentential and lexical aspects of language processing in normal children

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Introduction

The cortical substrates supporting language have been shown to change during the normal course of child development using fMRI [1]. Though language development begins much earlier than children can cooperate with the demands of fMRI, we have successfully performed fMRI studies of language in children as young as 5 years of age. In this report we summarize the findings of a longitudinal study in a group of children who have been studied annually for five years using fMRI of a selected set of language paradigms designed to tap early and later developing lexical and sentential aspects of language. Key cortical areas that are activated during these language paradigms and that correlate with age in the developing longitudinal cohort of children will be discussed. The findings in the longitudinal cohort are analyzed in the context of results in a much large cross sectional cohort of children spanning the age range of 5-18 years, using the same language paradigms.

Methods

Subjects were 5, 6, or 7 years old at the inception of the study in the summer of 2000 and were scanned longitudinally, once per year, until the completion of the study in 2004. Therefore, five data sets were potentially available from each subject for each task. Data were acquired on a Bruker 3T Medspec system. fMRI-EPI scan parameters were: TR/TE = 3000/38 ms, matrix = 64 X 64, bandwidth = 125 kHz, FOV = 25.6 X 25.6 cm, slice thickness = 5 mm. The fMRI paradigms involved early- and later-developing, sentential and lexical language skills as outlined in Figure 1.

	Sentential	**Lexical**
Early-developing	*Syntactic Prosody*	*Word-Picture Matching*
Later-developing	*Story processing*	*Verb Generation*

Figure 1. Schematic diagram showing the developmental and theoretical framework for the four fMRI language paradigms selected for this study. Rows group the tasks developmentally and columns group tasks by language domain.

All paradigms employed a 30 second on-off block design except syntactic prosody, where the active epochs were 45 seconds each to allow for presentation of a target sentence. The tasks have been described in detail elsewhere [2]. The verb generation task involves the covert generation of nouns in response to a verb; the story processing task involves passive listening to stories; the word-picture matching tasks involves the subject matching a visually presented picture to an aurally presented noun; and the prosody task involves the subject matching a target sentence to sentences low-pass filtered such that only the prosody (inflection) is audible.

The data was processed using the CCHIPS/IDL [3] software developed in our laboratory. Motion was retrospectively corrected using a pyramid coregistration algorithm [4]; only those frames with a voxel displacement < 2 mm were used for subsequent analysis. If there were not at least 15 usable frames in the active and resting epochs (discarding the 1st three after the transition in order to allow the hemodynamic response to reach baseline), the entire dataset was discarded. The data was then transformed into the Talairach reference frame, previously validated for subjects in this age range [5], and percent-change BOLD activation maps were constructed for each scanning session for each task. Subsequent analysis was restricted to those voxels with $Z > 3$ ($p < 0.003$, double-tailed) using a voxelwise random-effects analysis for significant cortical activation. For each subject and task for which at least three datasets were available, maps of the slope of percent activation versus subject age were computed. In order to control for task performance for the prosody and word-picture matching tasks, only those datasets were used where task performance was better than chance at a $p < 0.05$ level. An additional subjectwise random-effects analysis was performed in order to find regions with significant slope of activation as a function of subject age (Figure 2); regions were significant at a corrected $p < 0.05$.

Results and Discussion

For the sentential tasks (Figure 2, left), the regions detected with significant increases of cortical activation as a function of age were the posterior aspect of the left superior temporal gyrus (BA 22) for the syntactic prosody task, and the superior temporal gyrus bilaterally (BA 22, 41 & 42) for the story processing task. These results are consistent with previous findings from behavioral data that syntactic interpretation, while classified as an early-developing skill, nevertheless does undergo development in early childhood [6], especially with regard to interpretation of sentence structure. For the lexical tasks (Figure 2, right), activation increases are shown primarily in Broca's area (BA 44) (both tasks) as well its right hemisphere homologue for the verb generation task. In addition, activation increases are seen in visual association areas in the left hemisphere, including the precuneus (BA 7; both tasks) and the inferior temporal gyrus (BA 37; verb generation task). While not reaching statistical significance, an exploratory analysis performed on the data from the word-picture matching task revealed an activation decrease with subject age in the left inferior temporal/fusiform gyrus (BA 37). Hence it is possible that the changes in cortical activation from the word-picture matching task to some extent represent a shift in processing strategy.

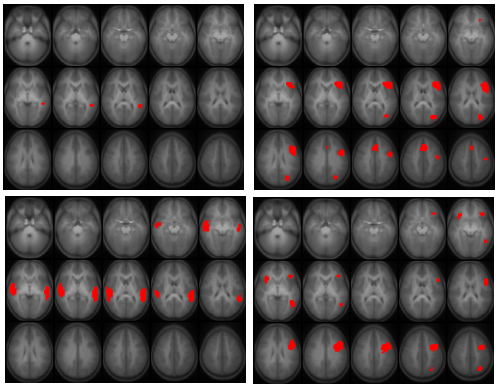

Figure 2. Regions with significant slope of cortical activation as a function of subject age in cortical activation for language tasks (top left; syntactic prosody, N = 13; top right; word-picture matching, N = 21; bottom left; story processing, N = 23; bottom right; silent verb generation, N = 21). The tasks are grouped by early- versus late-developing language skills (bottom and top rows, respectively) and sentential versus lexical aspects of language processing (left and right columns, respectively). Images in radiological orientation. All regions significant at corrected $p < 0.05$.

Conclusion

This longitudinal fMRI study evaluating language development in healthy children shows changes in BOLD signal intensity in the typical language areas (Broca's and Wernicke's), contralateral homologues, and visual association areas that are associated with increased age and improving language skills. This study shows the feasibility of performing long-term longitudinal imaging studies on normal children and provides direct neuroimaging evidence that improvement in language skills in children is associated with cortical plasticity. Correlations between brain activation and age in the longitudinal cohort are consistent with similar findings in a larger cross sectional cohort spanning a 5-18 year age range.

References

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