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Increased left prefrontal activation during an auditory language task in adolescents born preterm at high-risk

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Abstract

Although individuals born preterm are at risk for cognitive dysfunction, few studies have examined functional brain reorganization in these individuals. We used magnetoencephalography (MEG) to examine cortical reorganization related to preterm birth. Thirty-one adolescents systemically selected from a longitudinal study on child development based on gestational age, birth weight and medical complications (full term, low-risk preterm, high-risk preterm) performed real-word and non-word auditory rhyme tasks during MEG recording. Equivalent current dipoles were localized every 4ms during the 50ms to 250ms period following the onset of the auditory stimulus. The association between the number of dipoles (NODs) and birth group, language task, latency and phonological skills was examined. Adolescents born preterm at high-risk demonstrated a greater NODs in the left Broca's and prefrontal areas combined, left cingulate gyrus and left superior temporal gyrus and a fewer NODs in the right superior temporal gyrus as compared to those born preterm at low-risk and term. A greater NODs in the left Broca's and prefrontal areas combined and fewer NODs in the left cingulate gyrus was associated with better phonological skills only in adolescents born preterm at high-risk. These results suggest that the language networks are reorganized in adolescents born preterm at high-risk. Increased prefrontal activity has also been seen in adolescents born preterm during a reading task and in young adults with a history of dyslexia who are well compensated for their disorder. We suggest that this increased prefrontal activation may represent increased top-down control of weak posterior language networks.

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Keywords

Cortical reorganization; Preterm birth; Speech Perception; Magnetoencephalography

1. Introduction

Children born preterm have a unique pattern of cognitive deficits, including difficulties with executive function, visuospatial skills and early language development (Frye et al., 2009a). To better understand the relation between brain activation and both preterm birth and reading ability, we recently examined brain activation using magnetoencephalograph (MEG) during adolescence (Frye et al., 2009b). Participants for our MEG study were selected from a large-cohort of children born term and preterm whose development was followed from birth (See Frye et al., 2009a). In this cohort, children born preterm were divided into low-risk and high-risk groups based on medical complications during the neonatal period and all groups were divided into poor, average and good readers (See Frye et al., 2009a). During the MEG scan, adolescents read sequential presented real words or non-words and indicated if they rhymed. During the real-word rhyme task, when all groups performed adequately, adolescents born preterm at high-risk demonstrated a greater number of dipoles (NODs) in the left Broca's and prefrontal areas combined (B/PFA) as compared to those born preterm at low-risk and at term. Results from the non-word rhyme task provided evidence that this overactivation of B/PFA may represent compensatory reorganization of brain networks. During the non-word rhyme task performance was adequate for the good and average readers, but subpar for the poor readers. For adolescents born preterm at high-risk, only good and average readers, but not poor readers, demonstrated greater NODs in the left B/PFA. Thus, for adolescents born preterm at high-risk, overactivation of the B/PFA was only observed when adolescents performed adequately on the rhyme tasks. This suggests that prefrontal overactivation is important in the cognitive processes related to reading and may represent recruitment of compensatory neural systems.

Although the data from our previous MEG study is interesting, overactivation of the prefrontal area is at odds with studies measuring brain activation by functional magnetic resonance imaging (fMRI). Two fMRI studies compared individuals born preterm to those born term using a passive auditory listening tasks with semantic and phonological conditions. Neither of these studies found any increase in prefrontal activation (as compared to resting baseline) in individuals born preterm during the phonological condition (Ment et al., 2006; Peterson et al., 2002).

The discrepancy between our previous MEG study and fMRI studies could be due to language modality (i.e., visual v. auditory), methodology (fMRI v. MEG) or task (active discrimination v. passive listening). In this study we used MEG to examine functional brain activation during two auditory phonological rhyme tasks that paralleled the reading task we used in our previous MEG study to ensure that our findings were not simply due to the language modality used and to better understand the prefrontal overactivation in preterm children born at high-risk. We hypothesized that, like the reading task, increased prefrontal MEG activation (i.e., NODs) will be demonstrated in adolescents born prematurely at high-risk during the auditory phonological tasks. Our hypothesis is that this increased prefrontal activity represents top-down activation of phonological language networks. This is based on our recent study which demonstrated that top-down activation of the temporoparietal region from the inferior frontal region in dyslexic readers was positively correlated with performance (Frye et al., 2008a). Given our hypothesis, overactivation of the B/PFA would have to occur during the early response window (i.e., stimulus perception). This time course would be consistent with our previous MEG study on reading in adolescents born preterm and at term (Frye et al., 2009b).

2. Results

Participant Characteristics

Neither the number of males nor females, age, Stanford-Binet quantitative skills scores nor phonological skills were significantly different across birth groups. Birth weight and gestational age were significantly difference across birth groups [$F(2,22)=222.91$, $p<.0001$ and $F(2,22)=132.05$, $p<.0001$, respectively] (Table 1).

Auditory Rhyme Task

Neither sensitivity nor bias significantly differed across birth groups for both the real-word or non-word tasks.

The NODs in the left B/PFA was found to be different across birth groups [$\chi^2(2)=8.05$, $p<.05$] but not tasks. The NODs was found to be greater for the high-risk group as compared to the other birth groups [$\chi^2(1)=7.71$, $p<.01$] but was not found to be different between the adolescents born at term and preterm at low-risk (Fig 1). Time course analysis demonstrated no difference between the two time latencies. The NODs in the left B/PFA was significantly related to performance on Word Attack (WA) on the Woodcock-Johnson-III (WJ3) and accuracy (ACC) on the Gray Oral Reading Test (GORT) but both of these relationships were different across birth groups [WA: $\chi^2(2)=11.28$, $p<.01$; ACC: $\chi^2(2)=8.83$, $p=.01$]. The relationship between WA and NODs was different for adolescents born preterm at high-risk as compared to the other birth groups [$\chi^2(1)=9.65$, $p<.01$] while the relationship was not different between the adolescents born term and preterm at low-risk. Individual analyses demonstrated that better performance on WA was related to fewer NODs in the B/PFA for adolescents born at term and pre-term at low-risk [$\chi^2(1)=4.10$, $p<.05$] while better performance on WA was related to a greater NODs in the B/PFA for adolescents born pre-term at high-risk [$\chi^2(1)=6.64$, $p<.01$] (Figure 2A). The relationship between ACC and NODs was different for adolescents born preterm at high-risk as compared to the other birth groups [$\chi^2(1)=4.57$, $p<.05$] while the relationship was not different between the adolescents born term and preterm at low-risk. Individual analyses demonstrated that better ACC was related to a greater NODs in the B/PFA for adolescents born pre-term at high-risk [$\chi^2(1)=4.40$, $p<.01$] while ACC was not significantly related to NODs in the B/PFA for adolescents born at term and pre-term at low-risk (Figure 2B).

The NODs in the left cingulate gyrus was found to be different across birth groups [$\chi^2(2)=6.80$, $p<.05$] but not tasks. The NOD was found to be greater for the high-risk group as compared to the other birth groups [$\chi^2(1)=6.80$, $p<.01$] but was not found to be different between the adolescents born at term and preterm at low-risk (Fig 1). Time course analysis demonstrated no difference between the two time latencies. The NODs in the left cingulate gyrus was significantly related to performance on the segmenting word (SW) and segmenting non-word (SN) tests on the Comprehensive Test of Phonological Processing (CTOPP) but both of these relationships were different across birth groups [SW: $\chi^2(2)=8.83$, $p=.01$; SN: $\chi^2(2)=11.28$, $p<.01$] but not tasks. The relationship between NODs and both SW and SN was different for adolescents born preterm at high-risk as compared to the other birth groups [SW: $\chi^2(1)=12.41$, $p<.001$; SN: $\chi^2(1)=8.10$, $p<.01$] while these relationships were not different between the adolescents born term and preterm at low-risk. Individual analyses demonstrated that better SW or SN performance was related to a fewer NODs in the cingulate gyrus for adolescents born pre-term at high-risk [SW: $\chi^2(1)=18.11$, $p<.0001$; SN: $\chi^2(1)=14.21$, $p<.001$] while SW or SN was not significantly related to NODs in the cingulate gyrus for adolescents born at term and pre-term at low-risk (Figure 2C,D).

The NODs in the left and right superior temporal/Hesch's gyrus combined (STG) was different across birth groups [Left: $\chi^2(2)=8.95$, $p=.01$; Right: $\chi^2(2)=7.33$, $p<.05$] but not tasks. In the left STG the NODs was greater for the high-risk group as compared to the other birth groups [$\chi^2(1)=8.17$, $p<.01$] (Fig 1) while in the right STG the NOD was greater for adolescents born at term and preterm at low-risk as compared those born preterm at high-risk [$\chi^2(1)=6.56$, $p=.01$] (Fig 1). The number of dipoles did not differ between the adolescents born at term and preterm at low-risk for either the left or right STG. Time course analysis demonstrated no difference between the two time latencies. NODs in the left or right STG were not related to phonological skill.

Dipole Localization

Dipole location did not differ across birth groups or tasks. As an example of dipole localization we present case examples in Fig 3 for term and high-risk participants. Note that the dipoles in B/PFA are all located in the inferior frontal area and in the cingulate area are all located in the posterior cingulate gyrus.

Dipole Amplitude

Dipole amplitude did not differ across birth groups or tasks.

3. Discussion

This is the first study to examine neuromagnetic responses to auditory language stimuli in adolescents born preterm without obvious brain injury. In this study we examined cortical activation using MEG in adolescents born at term and preterm at high and low medical risk during auditory real-word and non-word rhyme tasks. The cohort of participants selected for this study paralleled our previous MEG study that examined reading. The participants in both studies demonstrated a wide range of reading, intelligence and executive function skills, thereby representing the full range of cognitive abilities in adolescents with normal intelligence. This study confirms our previous MEG findings of overactivation of the left B/PFA in adolescents born preterm at high-risk compared to those born preterm at low-risk and term during phonological tasks. This study also demonstrates differences in activation of the left and right STG and the left cingulate gyrus between the adolescents born preterm at high-risk compared to those born preterm at low-risk and term. We will discuss these findings in detail below.

Prefrontal activation in adolescents born preterm at high-risk

The results of the current study are consistent with our previous MEG study on this same cohort of adolescents that examined reading. Our previous study (Frye et al., 2009b) demonstrated an increase in the NODs in the left B/PFA during both a real-word and non-word reading-based phonological rhyme task for adolescents born preterm at high-risk as compared to adolescents born term or preterm at low-risk (Frye et al., 2009b). However, within the adolescents born preterm at high-risk, the NOD was significantly different across reading groups for the non-word rhyme task. Adolescents born preterm at high-risk who were also poor readers, unlike the average and good readers, did not demonstrate this increased in B/PFA NODs on the non-word reading task. Since adolescents born preterm at high-risk who were also poor readers performed significantly poorer than the other reading groups on the non-word but not the real word task, this suggested that the increase in the left B/PFA NODs in the adolescents born preterm at high-risk may be related to performance. The current study provides further support to the notion that the activation of the left B/PFA is related to performance and suggests that this activity may be compensatory.

Like our previous MEG study (Frye et al., 2009b), the left B/PFA demonstrated an increase in the NODs for the adolescents born preterm at high-risk as compared to those born term or preterm at low-risk. This was true for both the real-word and non-word auditory-based phonological task. In the current study we examined the relationship between the NOD in the B/PFA and individual performance on tests of phonological ability. The NODs was related to WA and ACC performance such that better performance on these orthographically-based phonological tasks was related a greater NODs in the B/PFA for adolescents born preterm at high-risk but not adolescents born at term or preterm at low-risk. These results lend support to the idea that adolescents born preterm at high-risk tend to overactivate B/PFA and that this overactivation is most likely compensatory in nature.

Diffusion tensor imaging studies have demonstrated abnormal microstructure in white matter pathways connecting the frontal lobes with the parietal, temporal and occipital areas in children born preterm (Cheong et al., 2009; Constable et al., 2008; Frye et al., 2010; Skranes et al., 2007). This pattern of white matter changes is particularly interesting since dyslexia has been linked to similar microstructure abnormalities. For example, abnormal microstructure has been demonstrated in the major fasciculi connecting anterior and posterior language areas (Klingberg et al., 2000), specifically the superior longitudinal fasciculus (Rollins et al., 2009) and the inferior fronto-occipital fasciculus (Odegard et al., 2009; Rollins et al., 2009), in dyslexia. Interestingly fMRI studies have also suggested that overactivation of the prefrontal regions may be compensatory in full-term individuals with dyslexia (Pugh et al., 2000a; Shaywitz et al., 2003). Recently we used Granger causality analysis to demonstrate that greater directional neuromagnetic connectivity from the left inferior frontal area to the left temporoparietal area was correlated with better performance on a non-word rhyme reading task for dyslexic, but not typical, readers (Frye et al., 2008a). This suggests that the increased prefrontal activation seen in dyslexia associated with reading may represent greater top-down activation of the language areas. The similarities in activation of the frontal brain areas between adolescents born preterm at high-risk and dyslexic readers suggest that similar mechanisms of neural reorganization may exist for dyslexia and those born preterm at high-risk.

Like the current study, fMRI studies have also compared brain activation between individuals born preterm as compared to those born term. These fMRI studies did not find an increase in prefrontal activation during the phonological condition of a listening task in older children and young adolescents (Ment et al., 2006; Peterson et al., 2002). However, these studies used a passive task which did not require manipulation or discrimination of phonological information. The difference in prefrontal activation between the current MEG study and the previous fMRI studies could be a result of the differences in the experimental paradigm, the classification of the participants into low-risk and high-risk groups, or the age of the participants. Further studies will be required to understand the association between neural reorganization in children born preterm and these factors.

Cingulate and Temporal activation in adolescents born preterm

In the current study, adolescents born preterm at high-risk demonstrated greater left STG and left cingulate gyrus activation and lesser right STG activation as compared to adolescents born preterm at low-risk and term. Interestingly, young adolescents born preterm with normal MRI scans have also demonstrated an increase in fMRI activation in the left STG and posterior cingulate gyrus during the phonological condition of a passive listening task while term children demonstrated deactivation in these areas (Ment et al., 2006). However, such increased fMRI activation was not seen in older children born preterm during a similar task (Peterson et al., 2002). Thus, the few studies available suggest that this pattern of exaggerated left lateralization of STG activity and left cingulate gyrus activity may develop with age.

Unlike previous studies, we attempted to better define the relation between these patterns of cortical activation and individual performance on phonological skill. Activation in the STG was not related to phonological skill but greater left cingulate gyrus activation was associated with poorer auditory phonological performance only for adolescents born preterm at high-risk. Dipole localization demonstrated that cingulate activation was localized to the posterior cingulate gyrus. Several functional imaging studies have linked posterior cingulate gyrus activation during auditory language tasks to language comprehension (Vannest et al., 2009; Whitney C, et al. 2009). This may suggest that the high-risk participants that performed poorly were trying to understand the auditory stimuli rather than analyzing the phonological content of the stimuli. Such a finding would be consistent with the fMRI study from Ment et al. (2006) who suggested that the preterm participants engaged semantic networks rather than phonological brain networks during the phonological condition of their listening task.

Recent MEG studies suggest that the early processing of phonological stimuli occur in both the left and right posterior STG (Frye et al., 2007; Frye et al., 2008b). This suggests that the exaggerated left lateralization of the STG activation is clearly abnormal in adolescents born preterm at high-risk. This extreme pattern of hemispheric lateralization could result from poor interactions between the left and right STG. A lack of interactions between the left and right STG could result from the well documented corpus callosum abnormalities found in infants, children and adolescents born preterm (Nagy, 2009). Atypical function of the phonological brain network in adolescents born preterm is consistent with developmental behavioral studies that documents subtle phonological deficits in children born preterm (Sansavini et al., 2007). Deficits in phonological processing in individuals born preterm could explain a reliance on semantic word processing during language tasks. Further studies will be needed to confirm this notion and investigate the implications of dysfunction of the phonological processing network in individuals born preterm.

Conclusion

This study demonstrates that adolescents born preterm at high-risk with normal anatomic MRI scans demonstrate different patterns of neuromagnetic activation as compared to adolescents born at term and preterm at low-risk during an auditory phonological rhyme task. Most significantly, adolescents born preterm at high-risk appear to overactivate the left prefrontal area and this activation appears to be associated with better orthographic-based phonological skill. The same pattern of prefrontal overactivation was also been reported in adolescents born preterm at high-risk during a phonological reading task in our previous study (Frye et al., 2009b). The prefrontal cortex is important for the top-down tuning and modulation of posterior brain areas, the encoding and retrieving of information to and from memory and maintaining working memory and the phonological loop (Abe and Hanakawa, 2009; Abe et al., 2007; Muller and Knight, 2006). Dipole localization (Figure 3) suggests that the B/PFA dipoles were located to the inferior frontal area. The inferior frontal area is believed to play a critical role in top-down regulation of posterior language networks (Aron and Poldrack, 2005; Bitan et al., 2009; Pugh et al., 2000b). Considering the STG has been shown to demonstrate abnormal morphology in children born preterm, it is possible that increased prefrontal activity could represent increased regulation of incompletely developed posterior language areas (Martinussen et al., 2005). Further studies will be needed to address the significance of the patterns of reorganization found in children born preterm at high-risk.

4. Experimental Procedure

Participants in the Longitudinal Study

The participants were selected from a longitudinal cohort of 360 children recruited from three hospitals in the Houston area. Term children had no significant prenatal, perinatal or neonatal

complications. Children born preterm had a gestational age ≤ 36 weeks and a birth weight ≤ 1600 g and were demographically similar to those born term. The high-risk cohort had more severe neonatal complications, primarily bronchopulmonary dysplasia, as compared to the low-risk cohort (See Tables SI and SII in Frye et al., 2010). Participants were excluded if they had nervous system abnormalities, symptomatic syphilis, short bowel syndrome, positive HIV antibody, the mother was <16 years of age or tested positive for drugs at the time of the child's birth or if English was not the primary language at home. Most participants were African-American (63.0%) with fewer being of Caucasian (20.1%) and Hispanic (15.0%) ethnicity. The sample contained predominately lower social economic status (SES) participants. There were slightly more females than males. Quality of schooling, SES, gender and ethnicity were not different across birth groups.

Selection of adolescents for the current study

Sixteen (5%) of the original cohort were excluded due to *Stanford-Binet 4th Ed.* quantitative skill scores below 85 during the 3rd, 5th or 7th grades. This subscale was used due to its relatively low language load. Another 91 participants (25%) were excluded due to attrition, leaving a total of 253 participants. We selected at least ten participants from each birth group evenly distributed across gender (Table 1). Of the selected participants, many had braces which were contraindicated for MRI and MEG scanning. Of the other selected, 9 declined to participate, one demonstrated ventriculomegaly, one could not perform the tasks, one had unilateral deafness, and technical problems arose with two. The final sample contained 11 participants born at term, 10 participants born preterm at low-risk and 10 participants born preterm at high-risk.

Right-handedness was confirmed by a laterality index as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971) score greater than 50 (Dragovic, 2004). After description of the study, written informed consent was obtained in accordance with our Institutional Review Board regulations. Participants were tested on phonological skills and underwent an MEG and MRI scan as described below.

Phonological Awareness Skill Assessment

Both auditory and orthographic-based phonological skills were assessed. Auditory phonological skill was assessed using the CTOPP Phoneme Reversal (PR), SW and SN subtests. These three subtests require segmenting and manipulation of real-words and non-words. Orthographic sublexical decoding skill was measured with WJ3 WA and GORT ACC. Table 1 provides performance for these skills for each birth group and the intercorrelations between these subtests. As expected, auditory phonological skills have higher intercorrelations with each other than orthographic-based phonological skills, and vis-a-versa.

MEG Language Task

Thirty-one participants performed two six minute auditory rhyme tasks separated by 3 minutes. The tasks required the participant to determine if two consecutively presented words rhymed. The first task presented high frequency non-exception (42%) or exception (58%) real-words. Non-exceptions words are orthographically decoded using regular phonological rules; examples include 'tint', 'hint', 'lint', and 'mint.' Exception words require non-regular phonological rules that must be memorized. The exception word that corresponds to the preceding example is 'pint.' The second task presented non-pseudohomophone pronounceable letter strings (i.e., non-word) which were matched to the real words by creating words with similar length and unconstrained bigram frequency. Each word was delivered binaurally through two 5-m-long plastic tubes terminating in ear inserts at an intensity of 80 dB at the participant's outer ear. The auditory word stimuli were produced by a native female English speaker with a flat intonation (duration between 321 and 848 ms; mean 535 ms). The words were digitized

with a sampling rate of 22,000 Hz and 16-bit resolution. Sequential words were separated by a 500ms interstimulus interval. The participant responded using a response pad. The intertrial interval lasted from 2 to 3 seconds. A cross was displayed in the center of a screen and the participant was requested to fixate on the cross and to inhibit eye movements and blinking during the auditory stimulus presentation. Each task contained 68 trials with words rhyming in half of the trials. Tasks were controlled by PresentationTM (Neurobehavioral Systems, Albany, CA).

Performance Measurements

A signal detection paradigm was used to obtain a measurement of performance without response bias. Rhyme trials were considered signal+noise trials while non-rhyme trials were considered noise trials. Sensitivity (d') was calculated from the hit and false alarm rates assuming an equal variance model (i.e., $z(\text{Hit Rate}) - z(\text{False Alarm Rate})$).

MEG Data Acquisition

Recordings were made in a magnetically shielded room with a WH3600 (4D Neuroimaging, San Diego, CA) whole-head neuromagnetometer that consisted of 248 axial gradiometers in a cryogenic dewar. The signal was continuously sampled at 500Hz and filtered on-line with a bandpass filter between 0.1 and 50 Hz. Event-related fields (ERFs) were extracted and averaged after removing trials during which eye movement or blink occurred. The averaged epochs were digitally lowpass filtered at 20 Hz.

Magnetic Resonance Imaging (MRI)

Two sets of structural T1 MRIs were acquired for each participant using a 3T Siemens Sonata scanner (Malvern, PA). The best quality of the two images was used for dipole localization. All scans were reviewed by a board-certified radiologist and/or neurologist. Adolescents with any cortical or significant subcortical abnormality were excluded.

Magnetic Source Imaging

A detailed account of the magnetic source imaging is provided elsewhere (Frye et al., 2009c; Papanicolaou et al., 1999). The intracranial sources of the average ERFs were modeled as single equivalent current dipoles (ECDs). An ECD was fitted at successive 4ms intervals using a non-linear fitting algorithm. The algorithm was applied to an automatically selected group of 34–38 magnetometers that included both magnetic flux extrema. ECD solutions were considered satisfactory if the predicted and observed magnetic field distribution correlated with $r > 0.90$. The ECDs were coregistered with the structural MRI (Papanicolaou et al., 1999).

Cortical Regions of Interest

We selected regions of interest (ROI) implicated in auditory language processing. These areas included the Cingulate gyrus, Broca's and prefrontal areas combined (B/PFA), the frontal and supplementary motor areas combined, the middle temporal gyrus (MTG), superior temporal and Heschl's gyri combined (STG) and the supramarginal and angular gyri combined. Areas were combined due to their proximity and coactivation.

Statistical Analysis

Participant characteristics, scores on cognitive and phonological tasks and performance during the MEG tasks were analyzed using an analysis of variance as implemented by the 'genmod' procedure in SAS 9.1 (SAS Institute Inc., Cary, NC). A dipole represents the maximal brain activation over a 4ms period and NODs is the number of 4ms periods in a particular ROI over a 100ms period (Papanicolaou et al., 2006). Since the NODs measure was quite skewed, it was

analyzed using a log link function and a negative binomial distribution (Papanicolaou et al., 2006; Zeger and Liang, 1986). For this model to be valid the mean NODs across participants needed to be ≥ 2 for any particular ROI. B/PFA, CG, STG and MTG reached this criterion.

We conducted a three stage analysis. First, we identified whether the NODs differed in a particular ROI across risk level (full term, low-risk premature, high-risk premature) and task from 50ms to 250ms following the onset of the stimulus. ROIs were examined separately for each hemisphere. Second, a detailed time course analysis was conducted for analyses in which NODs differed across an effect. In the time course analysis we determined if the NODs differed across the first and second 100ms periods. Third, we examined the relation between NODs and phonological skill for analyses in which NODs differed across an effect. Models were simplified by eliminating non-significant interactions and effects. Orthogonal contrasts were used for planned post-hoc comparison for birth risk and its interaction. We compared high-risk vs the other groups and low-risk vs full term. An alpha of 0.05 was used for the first two stages and for the orthogonal contrasts. An alpha of 0.01 was used for the third analysis to control for the multiple comparisons of the same dependent variable with analyses of each phonological skill. This simplification procedure and correction for multiple comparisons has been used in our previous neuroimaging and behavioral studies (Frye et al., 2009a,b,2010). Significant interactions with birth risk were analyzed within each level of the birth groups identified to differ by the contrasts. Finally, we examined whether the average dipole location and amplitude differed across risk group and task. Examples of dipole localization on participant MRIs are provided.

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Figure 1.

Mean number of dipoles for selected regions of interest averaged across both auditory language tasks. The left Broca's and prefrontal area, left cingulate and left superior temporal gyrus demonstrate greater number of dipoles in adolescents born preterm at high-risk as compared to those born term and preterm at low-risk. The right superior temporal gyrus demonstrated greater activation for adolescents born term and preterm at low-risk as compared to adolescents born preterm at high-risk. Note that error bars are not included in the graphs since these data are derived from a discrete distribution in which the mean and variance are directly related to each other. (* indicates a significant difference between the birth groups).

Figure 2.

The relationship between phonological skill and number of dipoles estimated by the non-linear model. (A,B) A greater number of dipoles in the left Broca's/prefrontal area combined was associated with better performance on word attack from the Woodcock-Johnson-III and accuracy from the gray oral reading test only for the adolescents born preterm at high-risk. (C,D) A greater number of dipoles in the left cingulate gyrus was associated with poorer performance on the segmenting word and segmenting non-word subtests of the comprehensive test of phonological processing.

Figure 3.

Examples of dipole localization for adolescents born term and preterm at high-risk. Only the regions of interest with significant differences between birth groups are shown. Data from the real-word auditory rhyme task was used for this example (Pink = Broca's/prefrontal area, blue = cingulate gyrus, green= superior temporal gyrus).

Table 1

Participant characteristics. Number of male and female participants and mean (standard error) age, Stanford-Binet quantitative skills score, birth weight and gestational age across birth groups. Significant differences between groups are indicated.

	Full-Term	Low Risk	High Risk	All Birth Groups
Male:Female	7:4	5:5	5:5	17:14
Age	16.6 (.14)	16.4 (.17)	16.2 (.22)	16.4 (.11)
Birth Weight	3491 (110)	1306 (55) *	907 (75) *,**	1952 (216)
Gestational Age	40.0 (0.0)	31.2 (0.7) *	29.7 (1.2) *,**	33.3 (1.0)
Cognitive Characteristics	Full-Term	Low Risk	High Risk	All Birth Groups
Quantitative skills	98.3 (1.5)	95.3 (2.0)	97.4 (3.6)	97.1 (1.4)
Segmenting Words	8.18 (.74)	7.00 (.63)	8.44 (.52)	7.87 (.38)
Segmenting Non-words	7.64 (.53)	5.80 (.97)	8.11 (.90)	7.17 (.48)
Phoneme Reversal	8.09 (1.0)	7.80 (.33)	8.78 (1.1)	8.20 (.57)
Word Attack	95.91 (3.0)	96.69 (5.4)	99.56 (3.4)	97.26 (2.3)
GORT Accuracy	8.55 (1.1)	10.10 (1.4)	10.56 (1.4)	9.67 (.74)
Correlations	Segmenting Non-words	Phoneme Reversal	Word Attack	GORT Accuracy
Segmenting Words	0.69 [†]	0.77 [†]	0.47 [†]	0.47 [†]
Segmenting Non-words		0.79 [†]	0.57 [†]	0.61 [†]
Phoneme Reversal			0.78 [†]	0.79 [†]
Word Attack				0.84 [†]

* Significantly different ($p < 0.001$) than full-term;

** Significantly difference ($p < 0.01$) than low-risk

[†] $p < 0.01$