Examining Associations Between Functional Brain Activation and Behavior in Adolescents With a History of Prenatal Drug Exposure

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BACKGROUND

Prenatal Drug Exposure (PDE) and Development in Childhood

Previous research examining outcomes in children with a history of PDE has yielded mixed results. In most global domains, such as physical growth or IQ, the effects of prenatal drug exposure on development do not appear to be greater than those observed with other teratogens or more powerful than other known environmental risk factors (e.g., poverty; Frank et al 2001). However, reports examining specific cognitive domains, such as executive functioning or visual-spatial skills, have reported deleterious effects of PDE. For example, one study of 4-year-old children documented impairments in visual-spatial abilities, as measured by the Weschler Preschool and Primary Scales of Intelligence-Revised, in exposed children despite the fact that IQ scores were similar to the non-exposed comparison group (Singer et al., 2004). Other studies of school-aged children have reported impaired performance on tests of visuospatial working memory (Schroder et al., 2004, Mayes et al., 2006). However, it remains unclear whether these effects persist into adolescence.

Adolescence

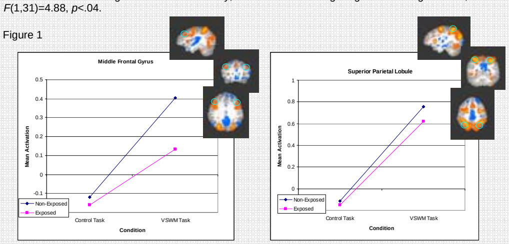
As the brain develops improvements are observed in performance on tasks involving visuospatial working memory (Kwon et al., 2002). Studies using fMRI in typically developing children suggest that changes in the underlying neural circuitry (especially in the frontal and parietal regions) account for these behavioral improvements (Schweinsburg et al., 2005, Scherf et al., 2006).

Recent neuroimaging studies have also reported differences in both brain structure and function associated with PDE. Structural differences include reductions in caudate volume (Avants et al., 2007) and decreases in overall brain volume (Rivkin et al., 2008). Functional imaging studies have revealed an overall decrease in cerebral blood flow during rest associated with PDE (Rao et al., 2007).

Previous Findings from our Laboratory

Recently, our laboratory reported differences in functional brain activation during a visual spatial working memory (VSWM) task in adolescents with a history PDE compared to non-exposed adolescents (DeBoer et al., 2008). Across exposure groups, both the middle frontal gyrus (MFG) and superior parietal lobule (SPL) showed significant bilateral activations during performance of the VSWM task (see Figure 1). Posthoc analyses of these regions of interest (ROIs) revealed that the non-exposed group recruited the MFG to a greater extent bilaterally, even after controlling for gender and age effects, $F(1,31)=4.88$, $p<.04$.

Figure 1



CURRENT STUDY

The aim of the current study was to examine the relationship between the pattern of neural activation and behavioral performance on standardized neuropsychological assessments. This exploratory analysis examined these associations collapsed across the exposed and non-exposed groups. Recruitment for the study is ongoing and future analyses are expected to examine whether these associations differ between adolescents with and without a history of PDE.

METHODS

Participants

Participants included 20 adolescents with a history of PDE and 15 non-exposed adolescents from a comparison group drawn from the same community. All participants were between 12 and 15 years of age (Table 1). The current study used previously collected imaging data (i.e., DeBoer et al., 2008) and data collected on the same subjects as part of a larger longitudinal study investigating effects of PDE in adolescence.

Table 1

	Prenatal Drug-Exposed Group (N=20)	Comparison Group (N=15)
Age Mean (SD)	14.3 years (1.0 year)	13.5 years (1.1 years)
Gender	10 male, 10 female	4 male, 11 female
IQ: WASI Mean (SD)	91.25 (11.58)	94.2 (12.27)

Neuropsychological Assessments

Judgment of Line Orientation (JLO): a visuospatial processing task that assesses the ability to determine the correct orientation of short line segments.

Conners Continuous Performance Test (CPT): a test of attention that requires one to maintain vigilance and react to the presence of a specific stimulus within a set of continuously presented distracters.

Stroop Test: a test of inhibitory control that requires one to say the names of colors printed in a different color ink.

Analyses

Analyses of covariance (with age and gender as covariates) were used to assess differences in performance between the two exposure groups on the neuropsychological assessments.

Partial correlations (with age entered as a covariate) were used to assess the relationship between neuropsychological performance and brain activation in frontal and parietal regions.

RESULTS

Group Differences

There was a main effect of exposure on CPT response style. Responses in the exposed group were relatively more "risky" than in the nonexposed group, $F(1,31)=6.66$, $p<.01$.

There were no significant exposure group differences on the JLO or Stroop task (Table 2).

Table 2

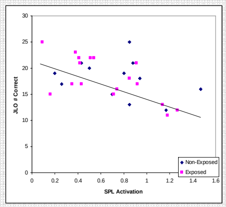
Assessment	Variable	Exposed Mean (SD) N=20	Non-Exposed Mean (SD) N=15	Group Difference
STROOP "Switching" Condition	Color Naming Scaled	9.80 (3.04)	9.67 (2.74)	ns
	Word Reading Scaled	9.20 (3.04)	9.27 (3.45)	ns
	Color Word Naming Scaled	9.30 (2.72)	9.87 (3.68)	ns
	Interference Scaled	10.65 (3.25)	10.67 (2.72)	ns
CPT	Commission T-Score	50.24 (7.55)	51.35 (13.26)	ns
	Omission T-Score	49.42 (9.02)	54.74 (19.73)	ns
	Average Reaction Time	363.82 (36.13)	384.35 (58.93)	ns
	Response Style	47.49 (4.50)	55.71 (12.70)	$p<.05$
JLO	# Correct (Note N=17 PDE, 13 Non)	18.06 (4.15)	17.46 (4.01)	ns

Associations between ROI Activation and Neuropsychological Assessments

There was a significant negative correlation between activation in the SPL* during the VSWM task and performance on the JLO, r (35) = -.57, $p<.01$.

More accurate performance was associated with less activation (Fig 2).

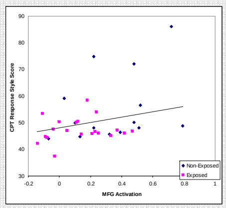
Figure 2



There was a significant positive association between activation in the MFG * during the VSWM task and CPT response style, r (34)=.37, $p<.05$ (one outlier was excluded).

Greater activation was associated with less "risky" response style (Fig. 3).

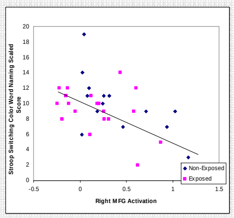
Figure 3



There was a significant negative correlation between activation in the right MFG during the VSWM task and Stroop Switching Color Naming Scaled Score, r (34)= -.47, $p<.05$, Stroop Switching Word Reading Scaled Score, r (34)= -.37, $p<.05$, Stroop Switching Color Word Naming Scaled Score, r (34)= -.47 (Fig 4), $p<.05$, and Stroop Interference Scaled Score, r (34) = -.42, $p<.05$.

Better performance (e.g., faster response times) was associated with less activation.

Figure 4



* Collapsed across hemispheres as correlations were similar for both.

SUMMARY

Although no significant differences were found between exposure groups in behavioral performance on the fMRI VSWM task, there were significant differences in neural activation. This finding suggests that there may be differences between the groups in the underlying neural circuitry used in during the task.

In order to investigate the possible behavioral consequences of these differences, we compared performance between the two groups on neuropsychological assessments and conducted correlational analyses between performance on these measures and functional brain activity in regions previously established to play a role in those tasks (Schweinsburg et al., 2005, Scherf et al., 2006).

Results showed that adolescents with a history of PDE had a more "risky" response style compared to non-exposed adolescents on the CPT. Moreover, these differences in performance were significantly related to MFG activation during the VSWM task.

Additionally, although there were no group differences in inhibitory control (as measured by Stroop) or visual spatial abilities (as measured by JLO), performance on these tasks were correlated with MFG activity and SPL activity respectively.

CONCLUSION

Adolescents with and without PDE show frontoparietal activation associated with VSWM task performance. However, non-exposed adolescents show greater activity in the MFG.

Although there were few overall between-group differences in performance on neuropsychological measures of visuospatial abilities and executive functioning, these differences in brain activation during the VSWM task were correlated with task performance. This finding suggests that the observed differences in neural activation may impact behavioral outcomes.

A limitation of neuropsychological tests is that performance cannot be directly attributed to a specific brain region or pathway, but rather this must be inferred. Neuroimaging helps to address this limitation by demonstrating that performance is linked to activity in specific brain regions. Using both methodologies in combination may prove to be a powerful way to link PDE to neurocognitive task performance and to identify the neural substrates associated with specific outcomes.

Data collection is ongoing and future research in our laboratory will examine whether there are differences in the associations between brain activation and behavior between individuals with and without PDE. In addition, we will also begin to examine the impact of environmental variables known to moderate the effects of PDE such as maternal education, socioeconomic status and prenatal exposure to other substances such as alcohol and cigarettes, which commonly co-occur with prenatal drug exposure.

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