Effect of prenatal alcohol exposure on brain activation during arithmetic task

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Introduction

Prenatal alcohol exposure (PAE) is known to be associated with structural dysmorphologies, including diminished growth and microcephaly [1]. Specifically, alterations of the parietal and temporal lobes of the left hemisphere, as well as hypoperfusion in the parieto-occipital region, are reported [2]. However, the relationship between teratogenic brain effects and behavior is still unclear. The current study examines the effects of prenatal alcohol exposure on performance and brain activation during a basic arithmetic task.

Methods

Image Acquisition: The fMRI experiments were conducted on a 3T Siemens Trio scanner. Single-shot T2*-weighted EPI images were acquired, consisting of 34 contiguous axial slices of with 3mm slice thickness. Pulse sequence parameters were TR/TE/FA/FOV of 3000ms/32ms/90°/22cm. The total scan time was 5 minutes 6 seconds, with 102 time points collected.

Experimental Design: Seven PAE subjects and 7 healthy individuals between 19-23 years old were recruited for the study from a longitudinal cohort. PAE subjects were characterized as prenatally exposed to alcohol based on repeated physical examination for growth retardation and dysmorphia, IQ testing, and by screening of the maternal population for alcohol use [3]. Control subjects were from a population of matching socio-economic status. All participants (and guardians, if necessary) gave written consent. The block-design paradigm consisted of alternating between a control task (lasting 2 time points) and an arithmetic task (lasting 8 time points). For the arithmetic task [4], the subjects were asked to subtract a number from eleven, and were given two possible answers for each question. Subjects were asked to choose the correct answer by pressing the left or right button on a button response box (www.curdes.com). Paradigm presentation and response collection was done using Eprime (www.pstnet.com). In the control task, subjects were asked to match a letter with one of two other letters, choosing the correct match in a similar fashion as described above.

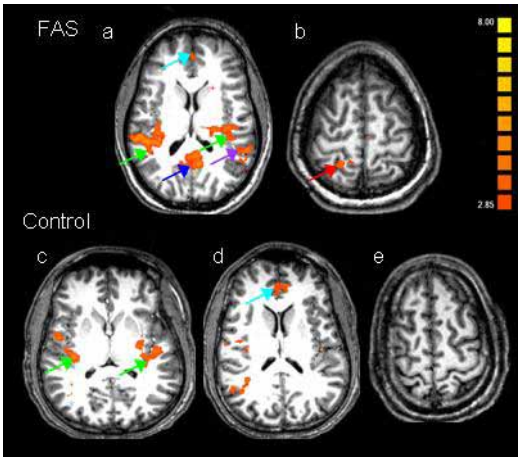
fMRI Data analysis: Preprocessing and Talairach transformation of the data were performed using BrainVoyager (www.brainvoyager.com). Individual brain activation maps were obtained. Regions of interest were defined as containing voxel clusters with a significance threshold of $p<0.005$ and a contiguity threshold of at least 300 connecting voxels. Multi-subject general linear models of brain activation were also formed for controls and PAE subjects from the individual volume time courses.

Results

Multi-subject activation maps for PAE and control subjects are shown in Figure 1. Significant activation is present in the temporal, prefrontal, posterior cingulate, angular gyrus, and superior/intra-parietal regions in PAE subjects. Control subjects, on the other hand, demonstrated significant activation in the temporal and prefrontal regions, but not in the parietal or posterior cingulate regions. Table 1 shows the significant differences in activation between PAE and control subjects. Regions of interest were analyzed by cluster size, using a Brodmann Area overlay for anatomical reference. Note that in addition to the regions displayed in Figure 1, PAE subjects also showed activation in the motor cortices (Table 1). Performance on the arithmetic task was not significantly different between the two experimental groups (percent correct: PAE=87.5±11.8; control=88.6±5.7; p= 0.83 by t-test).

Conclusion

While behavior performance on the arithmetic task was the same, brain activation was higher and more widespread in PAE subjects than in control subjects. It is established that normally the prefrontal and parietal regions of the brain are most responsible for arithmetic task performance [5]. Therefore, this difference between the PAE and control groups suggests that in order to have the same level of performance on an arithmetic task as a control subject, a PAE subject must utilize more neurons in the parietal and prefrontal regions. Furthermore, PAE subjects appear to require neuronal recruitment from other regions of the brain during such a task. Further study will examine if the degree of alcohol exposure is reflected in brain activation.



egion of Interest	Brodmann Area	Cluster size (voxel #)		Paired t-test (p-value)
		PAE	Controls	
L Temporal lobe	41, 42	843	541	0.26
R Temporal lobe	41, 42	240	270	0.39
Prefrontal cortex	11,12	175	152	0.44
Parietal lobe	7	472	47	0.0066[a]
Posterior cingulate	23,31	413	0	0.033[a]
Angular gyrus	39	50	0	0.18
Motor cortex	4	142	0	0.049[a]

Table 1. Brain activation in PAE and control subjects during arithmetic task. Activation threshold was $p<0.005$, with a cluster threshold of at least 300 connecting voxels. [a]Significant difference between PAE and control ($p<0.05$).

Figure 1. Group activation maps of PAE and control subjects (transverse sections). a) PAE subject group map (z=13) showing activation in the right and left temporal lobes (green arrows), posterior cingulate (dark blue arrow), angular gyrus (purple arrow), and prefrontal cortex (light blue arrow). b) PAE subject group map (z=59) showing activation in the superior and intraparietal lobes (red arrow). c-e) Control subject group maps (z=7, 17, 59, respectively) showing activation in the right and left temporal lobes (green) and prefrontal cortex (light blue). Activation threshold was $p<0.005$, with a cluster threshold of at least 300 connecting voxels.

References

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