Functional MRI of Fetal Alcohol Syndrome

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Synopsis

Functional Magnetic Resonance Imaging (fMRI) was used to assess differences between Fetal Alcohol Syndrome (FAS) or Alcohol Related Neurological Disorders (ARND) diagnosed individuals (adult and child) and controls. The results were correlated with standard psychological tests. In general, activations were decreased in regions of the brain associated with working memory, attention and executive function (frontal lobe and cingulate) in FAS subjects. Greater latency and incorrect responses were observed during fMRI tasks for FAS individuals, especially FAS children, compared to controls. FMRI may be a useful tool to assist in diagnosis of FAS/ARND.

Introduction

FAS and ARND are the single most important causes of mental retardation in North America. In order to design possible interventions, it is necessary to characterize and understand the effects of alcohol on the central nervous system (CNS). Presently, a diagnosis for FAS is commonly made on the basis of four criteria: growth deficiency, facial appearance, history of maternal alcohol consumption, and CNS damage. While the first three criteria are roughly consistent in FAS patients, CNS damage presents itself in various forms that are difficult to diagnose. Moreover, despite these criteria, FAS is largely undiagnosed, or misdiagnosed. We hypothesize that the development of novel fMRI and anatomical neuroimaging methods will allow for accurate and less subjective diagnosis of FAS/ARND.

Methods

Brain function and anatomy were assessed through a series of imaging experiments preceded by three psychological experiments designed to correlate with the neuroimaging data. Functional imaging studies were conducted on 8 FAS (4 children (age 7-12) and 4 adults) and healthy control subjects (n=8) on a 1.5 T Sigma GE MRI system using a GE volume coil. FMRI tasks required the subject to indicate (by pressing a button on a keypad) one of four possible spatial locations of a lit circle, viewed through MR compatible goggles. The first task requires the subject to press a button at the circle’s present position while continuous presentation of subsequent locations is being shown. These conditions place increasingly greater demands on spatial working memory and attention. Experiments were acquired in which 3 activation states were alternated with 4 rest periods and a total of 56 images acquired for each experiment. FMRI data were acquired using a single shot, gradient echo, echo planar imaging (EPI) sequence with a matrix size of 64 x 64, field of view of 24 cm, TE of 50 ms, TR of 2 s, and 21 contiguous 5 mm thick slices oriented parallel to the anterior-posterior commissure (AC-PC) line. FMRI data were analyzed using SPM99 (Statistical Parametric Mapping) (1) by co-registering the images and normalizing them to either a pediatric brain template (2), or to the MNI (Montreal Neurological Institute) brain template, for adult volunteers (3). Several standard psychological tests were also administered and correlated to the fMRI results.

Results

Consistent activations were observed at p < 0.001 in regions of the brain associated with working memory and attention, namely dorsolateral prefrontal cortex (DPFC, bilateral), and visual cortex in healthy volunteers. Both child and adult FAS subjects showed significantly reduced areas of activation than the control subjects as well as increased response times and frequently no responses were recorded. Two of the four FAS adults performed well and the other two significantly more poorly in terms of incorrect or no response. The average latency of response for all tasks is shown in the figure below. Reduced or even absence of functional activation was observed in the DPFC as well as the visual cortex of the FAS population compared to controls.

Discussion and Conclusions

The four fMRI tasks involve visual stimulation, saccadic eye movement, finger movement, working memory, procedural learning, and attention. As FAS is characterized by diverse behavioural and physical effects it is difficult to predict performance. Common deficits appear, however, such as difficulty maintaining attention, problems with working memory and executive function and trouble with impulsivity. The decrease in DPFC activity can be attributed to either inattention to the task, or trouble with executive and frontal lobe function. The DPFC is important in working memory and as such, less activation may be expected in fMRI studies in patients compared to controls. Attention and response selection have been attributed to the anterior cingulate gyrus, and has also demonstrated less activation in the FAS group, particularly in the more difficult memory and attention tasks (i.e. 1-back and 2-back). While fMRI results from adult subjects were quite varied, in general, FAS children tended to perform the tasks much worse. FMRI may be a useful tool in assistance of diagnosis of Fetal Alcohol Syndrome.

References

2. Wilke, M., Schmithorst, W. K., and Holland, S. K. 2002; Proc. ISMRM.