Interhemispheric transmission in adults prenatally exposed to alcohol

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Introduction

Alteration of the corpus callosum (CC), including thinning, shrinking, and agenesis, is one of the most prominent effects of prenatal alcohol exposure (PAE) [1]. Improper development and damage to the CC have been known to cause hemispheric disconnection syndrome [2]. Furthermore, deficiency in interhemispheric transfer of somatosensory information has been reported in children with heavy PAE [3]. The effects of PAE on brain activation during interhemispheric transmission have not been previously examined.

Methods

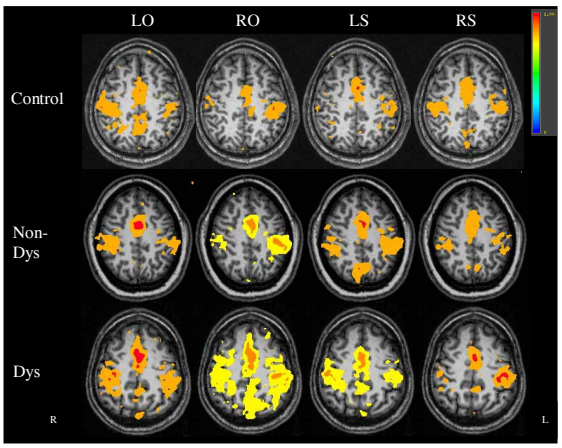
Image Acquisition: The fMRI experiments were performed on a 3T Siemens Trio scanner. An EPI-BOLD sequence was used to acquire 120 axial images (30, 4mm thick slices) in each run, with an in-plane resolution of 3.44 mm×3.44 mm. Sequence parameters were TR/TE/FA/FOV of 2000ms/35ms/90º/22 cm.

Experimental design: Seven dysmorphic PAE subjects, 7 non-dysmorphic PAE subjects, and 7 healthy individuals between 20-24 years old were recruited for the study from a longitudinal cohort. PAE subjects were characterized as prenatally exposed to alcohol and/or dysmorphic based on pre-screening during pregnancy of the maternal population for alcohol use [4]. Control subjects were from a population of matching socio-economic status. All participants gave written consent. Tactile stimulation was applied using MRI-compatible piezo-electric buzzers (www.piezo.com) controlled through an analog output board (www.ni.com) using a MATLAB control script (www.mathworks.com). Stimuli were triggered from the scanner using a TTL line to achieve time-locking of events. A buzzer was placed on each hand, and a button box (www.curdes.com) was used to collect responses in Presentation (www.neurobs.com). Two conditions were used, each in a separate scan (24 trials, 10s ISI, l/r balanced); in the "same" condition, participants were asked to press a button with the hand ipsilateral to the vibrotactile sitmulus, and in the "opposite" condition, they responded with the hand contralateral to the stimulus.

fMRI Data Analysis: Data preprocessing was performed in AFNI (http://afni.nimh.nih.gov/afni/) and included slice-timing correction, motion correction, spatial smoothing (using a 5mm FWHM), and Talairach transformation. Given the stimulus function, we first estimated the impulse response function (IRF) for each voxel. The IRF was then convolved with the stimulus time series to yield the estimated response. The final activation maps were generated by a multiple linear regression analysis evaluating the goodness of the fit. Activation was defined as voxel clusters with a significance threshold of $p<0.05$.

Results

Group activation maps for the PAE and control subjects are shown in Figure 1. Significant activation clusters are found in the primary motor and premotor areas. Table 1 indicates the regions with significantly more activation in dysmorphic PAE subjects as compared with controls, including right and left primary motor regions during the right hand response to opposite side stimulation (RO), right premotor area during RO condition, and left premotor area during both "opposite" conditions. No significant difference was seen in any area between the control and non-dysmorphic PAE group, nor between groups during any of the "same" conditions. Accuracy was 100% for all groups, and reaction time was also not significantly different between groups with the exception of the RS condition between dysmorphic PAE and control subjects ($p=0.007$ by group t-test).



	Activation volume for LO (mm^3)		p-value	Activation volume for RO (mm^3)		p-value
ROI	**Controls**	**Dys-PAE**		**Controls**	**Dys-PAE**	
L Primary Motor	3270	2878	0.41	3098	5967	**0.010***
R Primary Motor	3602	4349	0.34	2244	4817	**0.048***
L Premotor	1535	3220	**0.04***	1134	3632	**0.016***
R Premotor	1873	2810	0.26	1917	4328	**0.029***

Table 1. Activation volumes in regions of interest during LO (left hand response to opposite side stimulation) and RO (right hand response to opposite side stimulation) tasks. P-values are from group t-tests comparing controls and dysmorphic PAE (Dys-PAE) subjects. * indicates a significant difference in activation volume.

Figure 1. Group-averaged activation maps of non/dysmorphic PAE and control subjects (transverse sections). LO (left hand response to opposite side stimulation), RO (right hand to opposite side), LS (left hand response to same side stimulation), and RS (right hand to same side) denote task condition. Multi-subject maps (z=46S) showing activation in the right and left primary motor areas and anterior cingulate. Activation threshold was $p<0.05$.

Conclusion

While all groups had similar activation during tasks requiring ipsilateral brain activation for somatosensation and motor control ("same" condition), the dysmorphic PAE group had greater activation during tasks requiring interhemispheric transfer of information ("opposite" condition). Increased activation in the right and left primary motor areas during the RO task demonstrates that dysmorphic PAE individuals need more neuronal activation to perform the hand-localization task when interhemispheric transfer is needed as compared with non-dysmorphic PAE and healthy individuals. Additionally, this dysmorphic group appears to require extra activation from the premotor regions as compared with the other two groups when performing tasks requiring interhemispheric transmission, regardless of which hand is responding. Altered development of the CC in the dysmorphic group may be responsible for the additional neuronal requirements by motor centers in each hemisphere during interhemispheric transmission. Correlation analysis between white matter differences in the CC and functional differences will further reveal the relationship between heavy prenatal alcohol exposure and hemispheric disconnection.

References: [1] Riley, E.P., et al. Alcohol Clin Exp Res. 1995 Oct; 19(5):1198-202. [2] Benavidez, D.A., et al. Cortex. 1999 Jun;35(3):315-36. [3] Roebuck T.M. Alcohol Clin Exp Res. 2002 Dec;26(12):1863-71. [4] Coles, C.D., et al. Alcohol Clin Exp Res. 2002 Feb;26(2):263-71.

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