ALTERATIONS IN FUNCTIONAL CONNECTIVITY DURING EXECUTIVE CONTROL IN ADOLESCENTS WITH HISTORIES OF HEAVY PRENATAL ALCOHOL EXPOSURE

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BACKGROUND

- Posner & Petersen (1990) suggest that the attention system is comprised of three distinct networks: alerting, orienting, and executive control. The Attention Network Test (ANT) measures the efficiency of these networks in a single task (Fan et al. 2002).
- Previously we showed that while there were no significant behavioral differences between alcohol exposed (AE) and control (CON) adolescents in the alerting and orienting networks, groups did differ in terms of blood-oxygenated level dependent (BOLD) response corresponding to these networks (AE<CON in alerting and AE>CON for orienting).
- The AE group showed reduced behavioral performance in the executive control network but no difference in BOLD response relative to the CON group.
- To further explore the neural correlates of executive control deficits following heavy prenatal alcohol exposure, this study examined functional connectivity of the executive control network, hypothesizing that atypical functional connectivity in this network may explain the behavioral differences.

METHOD

Subjects
- Two groups, (N's =18) of adolescents ages 12-16 (M=14.91, SD=1.34) participated in the study: Heavy prenatal alcohol exposure (AE) and non-exposed controls (CON).

Image acquisition and data analyses
- fMRI data was collected on a 3T GE Signa Excite scanner with an 8-channel head coil.
- Subjects performed an adapted version of the ANT (Fan et al. 2005; **Fig 1**.) while undergoing fMRI.
- Functional images were processed and analyzed using AFNI.
- For each participant, contrast images were calculated to estimate brain activity of the alerting, orienting, and **executive control** networks.
  - *The executive control contrast was defined as the difference between BOLD response to the incongruent versus congruent target conditions*.

Fig 1. Experimental paradigm: modified version of the Attention Network Test
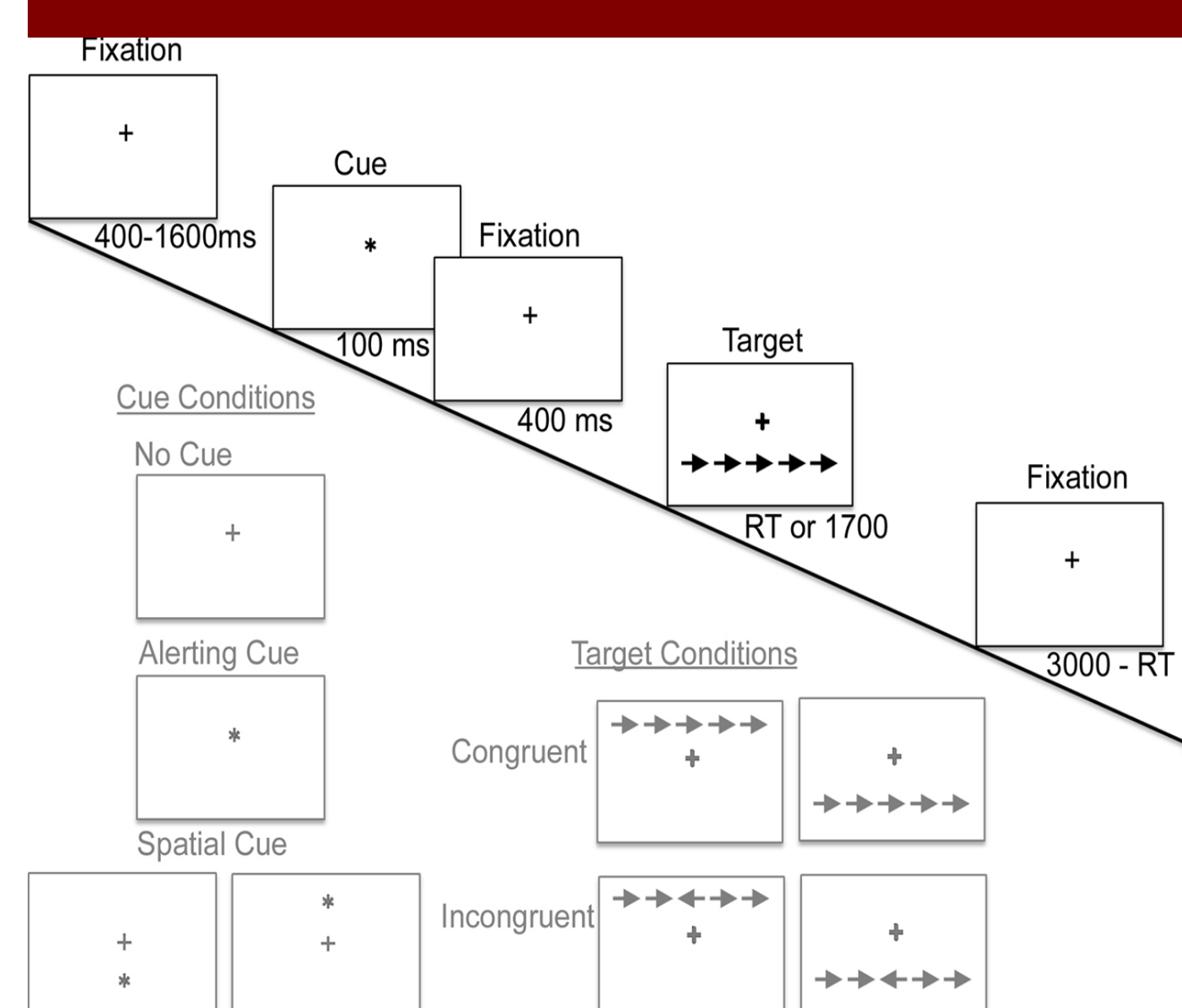
- Seed regions were created based upon activation clusters for the executive control contrast.
- Functional connectivity analyses were conducted using generalized psychophysiological interaction (gPPI), with left and right middle frontal gyrus (MFG) as seeds.
- The resulting gPPI parameter estimates were then taken to the group level, to examine differences in functional connectivity between groups.
- Monte-Carlo simulations indicated that clusters larger than 38 voxels at a threshold of p<.05 (with a peak voxel of p<.05) were considered significant.

RESULTS

Demographic Data
- Groups were similar on sex, race, ethnicity, handedness, SES, and age (ps>.05), although the AE group had lower FSIQ than the CON group [t(33)=-4.11, p<.001] (**Table 1**).

Group differences in MFG functional connectivity during executive control
- The AE group showed greater functional connectivity between the left MFG seed and clusters in the right anterior cingulate cortex, bilateral posterior cingulate cortex extending into the cuneus, and left fusiform extending laterally into middle temporal gyrus (**Table 2**; **Fig 2**).
- The AE group showed greater functional connectivity between the right MFG seed and clusters in the bilateral anterior cingulate cortex and adjacent medial frontal cortex, left cingulate gyrus, and bilateral caudate. Decreased connectivity between the right MFG seed and a small cluster in the left postcentral gyrus and inferior parietal lobe was noted (**Table 2**; **Fig 3**).

Table 1. Demographic information by group

Variable	AE (n=18)	CON (n=18)
Age [M (SD)]	14.7 (1.2)	15.1 (1.5)
Sex [n (% Female)]	7 (38.9)	7 (38.9)
Race [n (% White)]	12 (66.7)	12 (66.7)
Ethnicity [n (% Hispanic)]	6 (33.3)	7 (38.9)
Handedness [n % Right)]	16 (88.9)	18 (100)
SES [M (SD)]	47.8 (11.4)	51.4 (11.3)
FSIQ [M (SD)] *	89.4 (12.2)	105.2 (10.5)
FAS Diagnosis [n (% FAS)]	5 (27.8)	0 (0)

Significant at p<.001

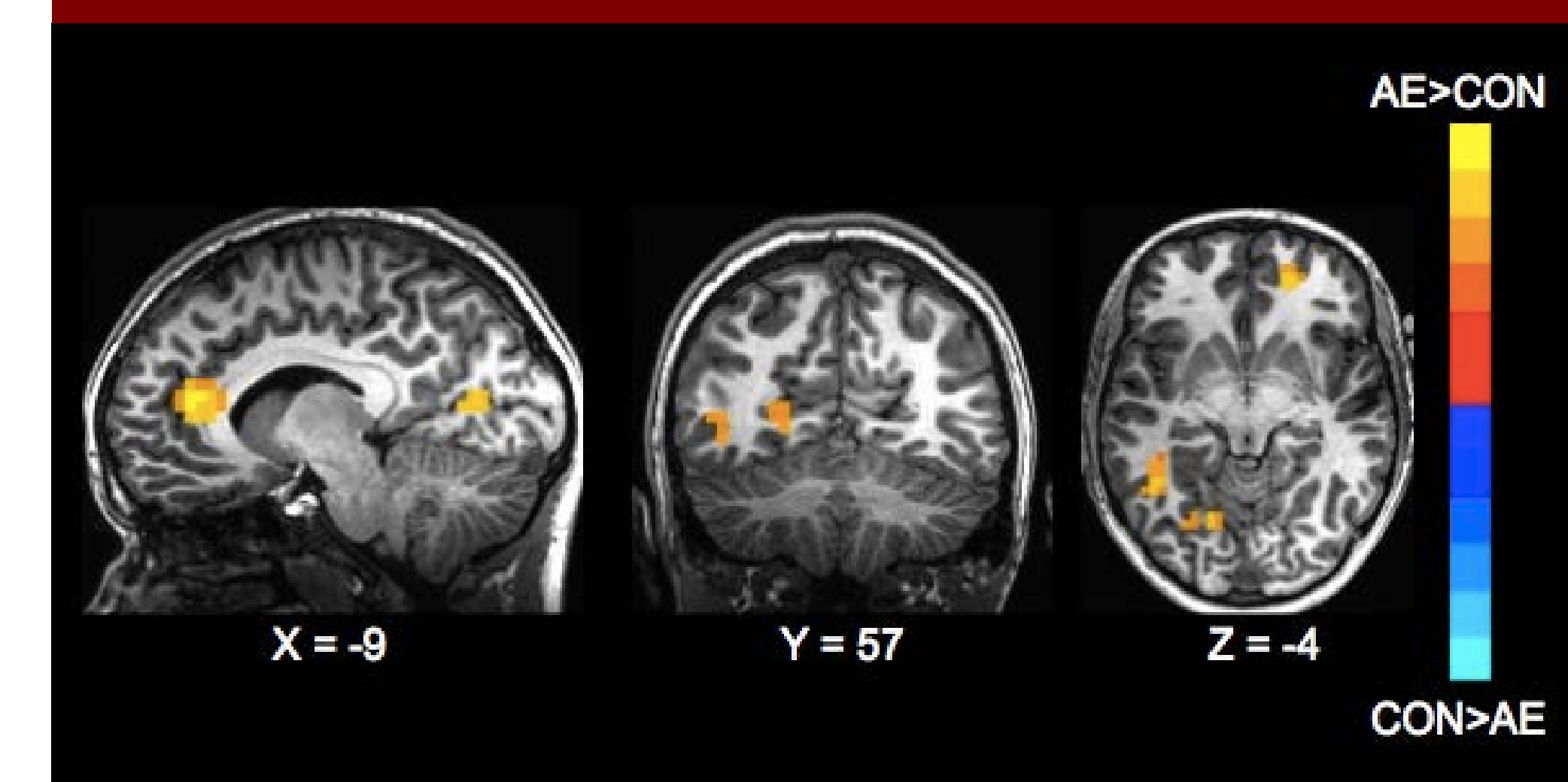Fig 2. Group differences in functional connectivity of left MFG

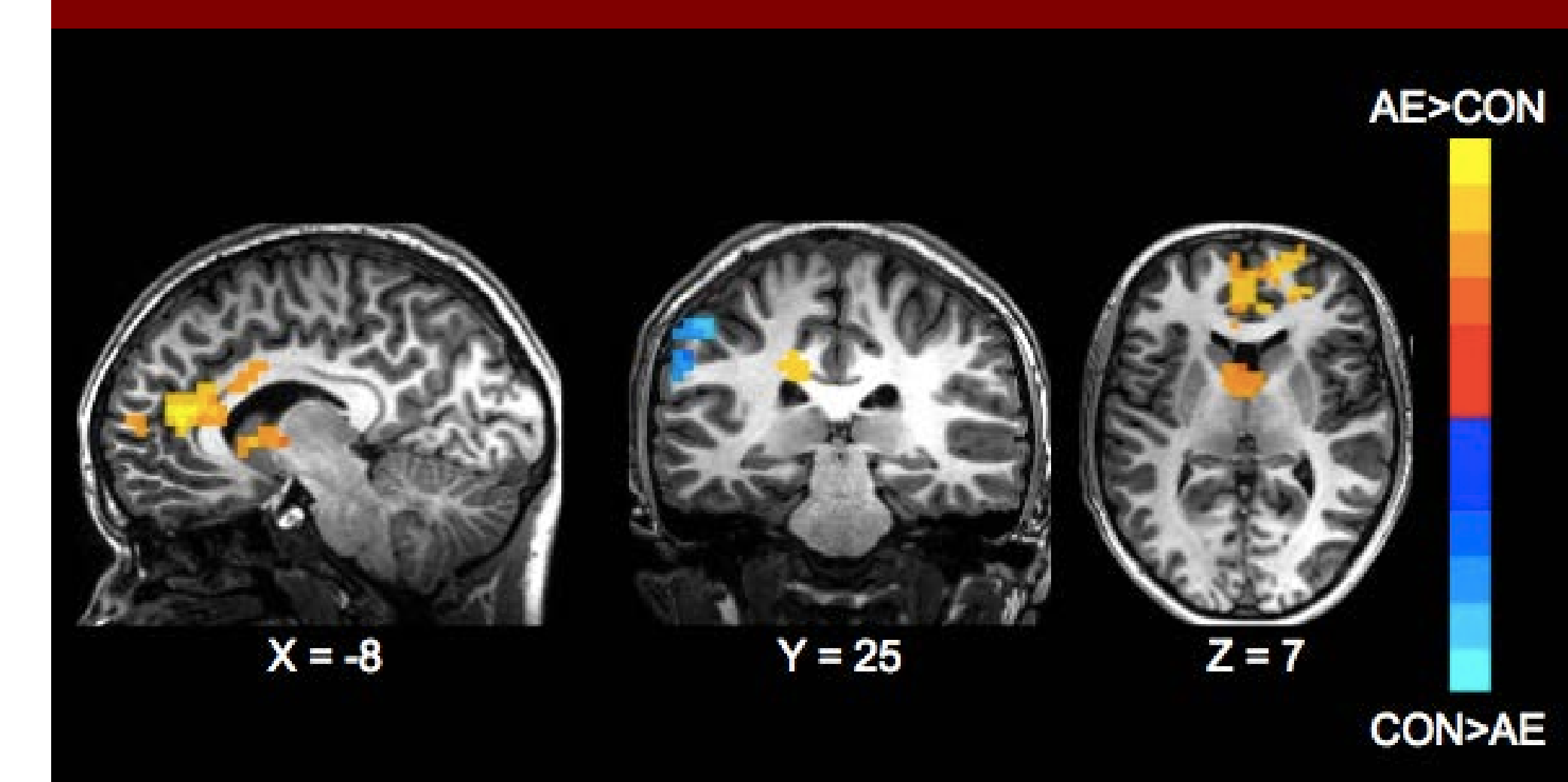Fig 3. Group differences in functional connectivity of the right MFG

Table 2. Clusters showing significant group differences in functional connectivity of the left and right MFG

Peak location	# Voxels	Talairach coordinates			t-value
		x	y	z	
L MFG seed					
R anterior cingulate cortex	128	-10	-39	16	3.77
R posterior cingulate cortex	121	-2	65	12	2.74
L fusiform gyrus	57	46	49	-8	2.48
R MFG seed					
R anterior cingulate cortex	212	-6	-39	16	2.95
L cingulate gyrus	52	18	29	28	2.97
L caudate	50	6	-11	4	3.63
L postcentral gyrus	38	50	33	-48	-2.62

Note. Positive t-value reflects AE > CON. BOLD = Blood oxygen level dependent; L = Left; R = Right.

DISCUSSION

- Increased connectivity with the cingulate, a region associated with motivation, cognition, and motor control, suggests that this region may play a critical role in executive control for alcohol-exposed individuals.
- Adolescents with prenatal alcohol exposure may require greater temporal synchrony to monitor behavior requiring executive control suggesting increased effort towards error detection.
- Reaction time differences between incongruent and congruent trials indicated decreased efficiency of the executive control network. Thus, greater temporal synchrony in this network may not be sufficient to improve the efficiency of error detection in the AE group.

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