Functional alteration and asymmetry in salience network of children and youth with prenatal alcohol exposure

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Introduction

Fetal alcohol spectrum disorder (FASD) is a diagnostic term used to describe the entire spectrum of conditions associated with prenatal alcohol exposure (Cook et al., 2016). Prenatal alcohol exposure is known as causing structural damages to the brain such as decreased grey and white matter volume, cortical thickness, and cortical surface area (Moor, Migliorini, Infante, & Riley, 2014). Individuals with FASD often exhibit neurocognitive deficits including poor attention, learning, language skills, visual-spatial abilities, memory, speech, and sensorimotor deficits such as a poor motor coordination (Nguyen et al., 2017; Long, Little, Beaulieu, & Lebel, 2017). Moreover, they exhibit high comorbidity to other neurological, psychiatric, and neurodevelopmental disorders such as ADHD, anxiety, depression, autism, conduct disorder, bipolar disorder, and others (Zhou et al. 2018).

A group of brain regions called salience network is located at the interface of the cognitive and physiological systems to guide various cognitive processes (Menon, 2015). Previous studies identified that functional alteration, which is an alteration of connected brain activities during a specific task or resting, in the salience network can cause cognitive deficits and neurological disorders (Menon, 2015; Stern, Fitzgerald, Welsh, Abelson, & Taylor, 2012; Zhao et al., 2017; Liu et al., 2018; Toyomaki & Murohashi, 2013). However, the functional alteration of this network in individuals with FASD is still unclear. Therefore, the purpose of this project was investigating the functional alteration and brain asymmetry of salience network in children and youth with FASD by using resting-state functional magnetic resonance imaging (rs-fMRI) to reveal how the brain mechanism is fundamentally different compared to healthy controls.

Method

A total of 186 participants were recruited from the Kids Brain Health Network FASD study across universities in Canada (University of Alberta, Queen's University, University of Manitoba, and University of British Columbia). After exclusion of data, rs-fMRI data of 59 children and youth with FASD and 50 typically developing controls (5-18 years) remained. In this project, the regions of salience network such as bilateral anterior insula, dorsal anterior cingulate cortex, amygdala, ventral striatum, and ventral tegmental area were chosen as seed regions. Based on each seed region, functional connectivity (FC) maps were generated for control and FASD group to reveal which connected region showed significant brain activity difference between the two groups. After functional connectivity analysis, the asymmetry analysis was performed by using the formula called Asymmetry Index, which is equal to FC of left seed region minus FC of right seed region. Two-sample t-tests between groups and multiple correction were performed on both FC and asymmetry analysis. Age, sex, handedness, site of recruitment, and frame-wise displacement were used as covariates.

Results/Discussion

As a result, the bilateral insula showed significant co-activation with occipital regions such as calcarine sulcus, lingual gyrus, and cuneus (Figure 1). The control group showed co-activation of insula and those occipital regions, while the FASD group showed negative correlation of activities, which represents that the insula and occipital regions did not activate together (Figure 2). However, as the age increased, the co-activation of insula and occipital regions decreased for the control group on both left/right side of the insula. On the other hand, as the age increased, the significant co-activation of the right insula and precuneus in the FASD group was detected (Figure 3).

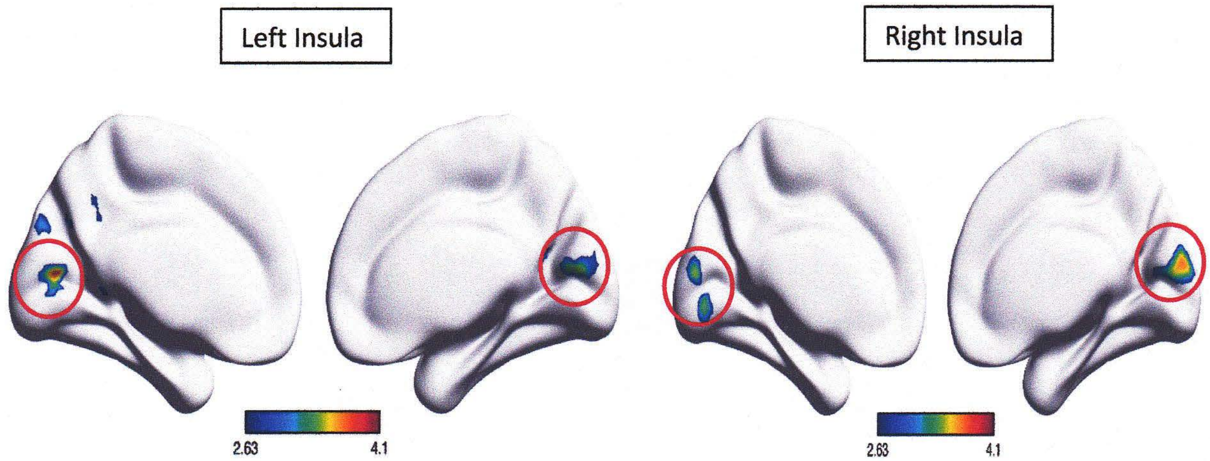

Figure 1. Occipital regions (calcarine sulcus, lingual gyrus, and cuneus) that showed significant connectivity (activity) to the bilateral insula.

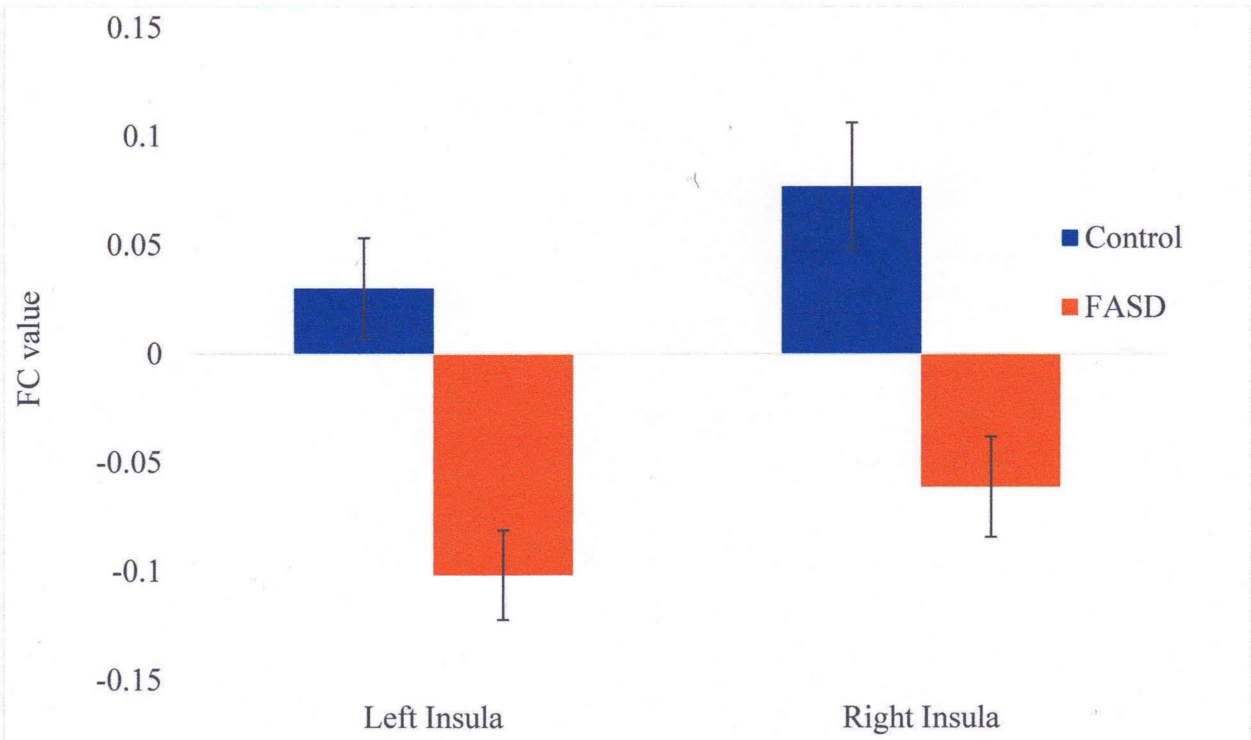

Figure 2. Positive correlation of brain activities of the bilateral insula and occipital regions for the control group, while the FASD group showed negative correlation of brain activities.

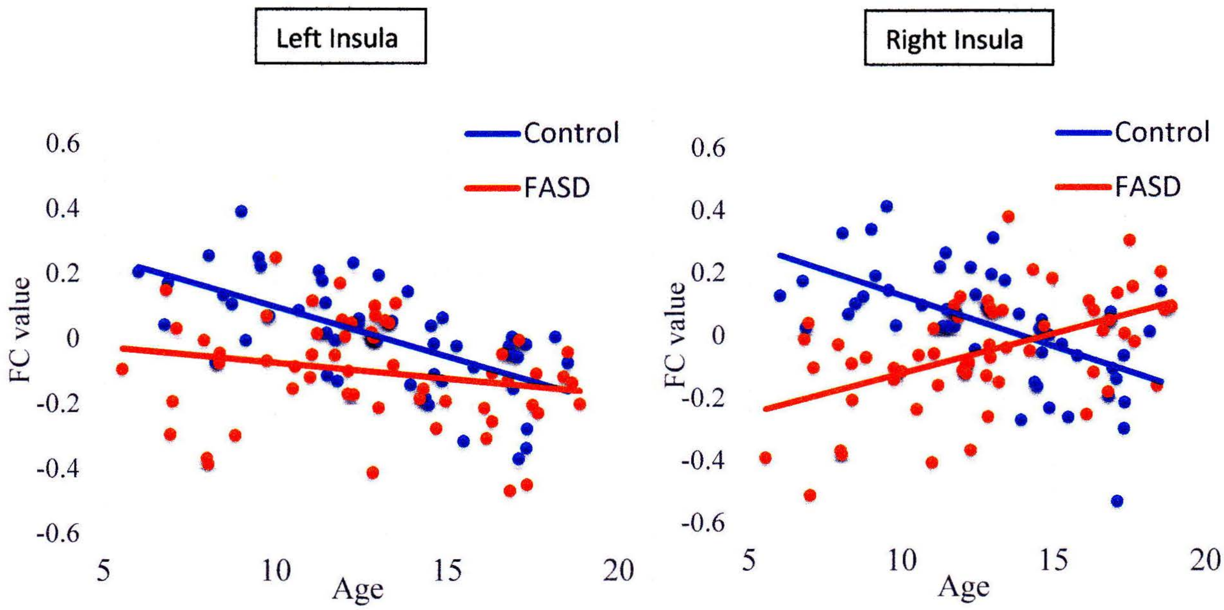

Figure 3. Negative correlation between age and connectivity from left/right insula to the same occipital regions for the control. Positive correlation between age and connectivity from right insula to precuneus was detected on the FASD group.

Although asymmetry analysis did not pass the multiple correction, a total of 6 regions such as middle temporal gyrus, cerebellum, cuneus, lingual gyrus, supplementary motor area, and middle occipital gyrus showed significant asymmetry to the insula with the two-sample t-tests. The FASD group showed a greater extent of asymmetry on most of the regions than the control group (Figure 4). Specifically, the cerebellum showed the significant ipsilateral connectivity to the insula while the cuneus, lingual gyrus, and supplementary motor area showed the significant contralateral connectivity to the insula for the FASD group. On the other hand, the control group showed the significant asymmetry on the middle temporal gyrus and middle occipital gyrus.

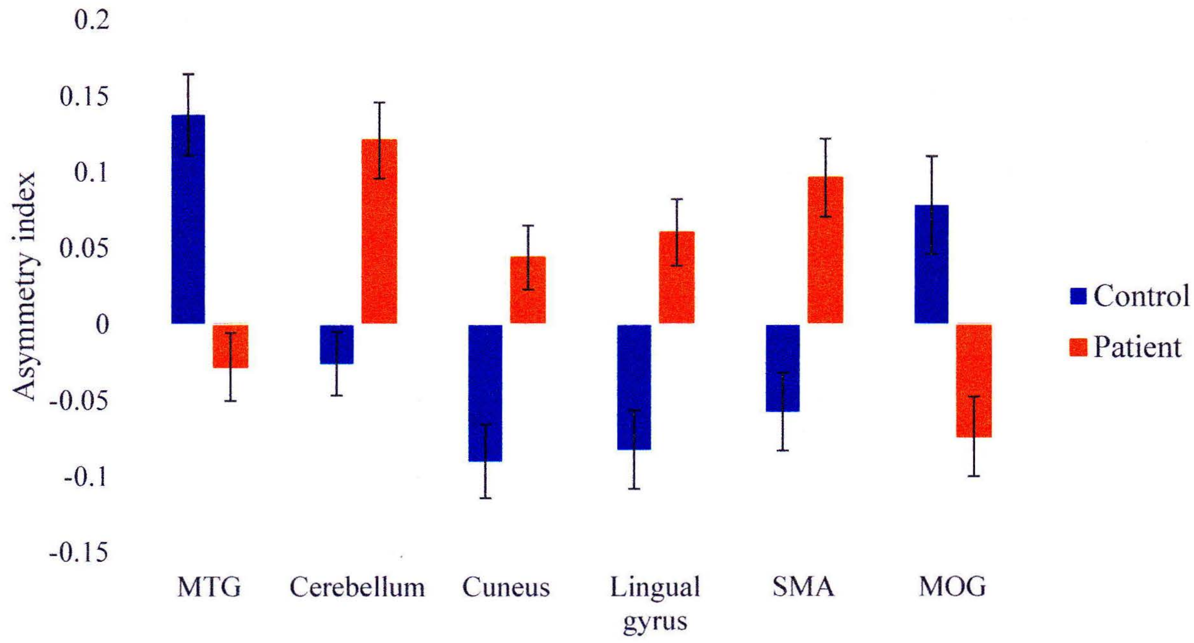

Figure 4. Overall asymmetry difference between control and FASD group on middle temporal gyrus, cerebellum, cuneus, lingual gyrus, supplementary motor area, and middle occipital gyrus.

Overall, the opposite brain activation and asymmetry patterns shown by FASD group indicate that they possess fundamentally different brain mechanisms to perform cognitive functions. The functions associated with the insula and highlighted regions in this study such as visual perception, memory, word recognition, understanding meaning of words, self-awareness, and social behavior such as facial emotion recognition might be altered in FASD group (Cavanna & Trimble, 2006; Davey et al., 2016; Ghaziri et al., 2017; Hoffman, Pobric, Drakesmith, & Ralph, 2012; Lalli et al., 2006; Onitsuka et al., 2004). The altered activity pattern in the insula and the occipital regions from the FASD group was similar to the patterns shown by Alzheimer's disease and ADHD patients (Liu et al., 2018; Zhao et al., 2017). Moreover, the increasing activation of the insula and the precuneus in the FASD group was similar to the pattern observed from obsessive-compulsive disorder patients (Stern et al., 2012).

What I gained from this experience

In summary, this project revealed that functional alteration of the salience network might be responsible for the disorders and cognitive deficits associated with FASD. By learning more about fMRI technique, I realized that producing just one fine brain image to yield a better result takes various important steps such as using imaging programs, pre-processing procedures, and coding of programs for analysis. Moreover, it was important that I learned more about what is FASD and the critical impact of prenatal alcohol exposure on individuals. This knowledge will help me to build mature judgments and perspectives on every aspect of health-care career in the future. Lastly, I learned that imaging technique such as fMRI has a potential to be used to predict symptoms of disease in the future and help in targeting new treatment option by examining the damages in the brain.