Frontal Lobe Hyperconnectivity as a Biomarker for Executive Function in Fragile X Syndrome

Joy Li[1], Rui Liu, PhD[2], Lauren M. Schmitt, PhD[3,4], Ernest V. Pedapati, MD[2,5,6]

[1]University of Cincinnati College of Medicine (UCCOM); [2]Division of Psychiatry, Cincinnati Children's Hospital Medical Center (CCHMC); [3]Developmental and Behavioral Pediatrics, CCHMC; [4]Department of Pediatrics, UCCOM; [5]Division of Neurology, CCHMC; [6]Department of Psychiatry and Behavioral Neuroscience, UCCOM

Introduction

Fragile X Syndrome (FXS) is the leading inherited monogenetic cause of Autism Spectrum Disorder and intellectual disability. Executive function (EF), necessary for adaptive goal-oriented behavior and associated with frontal lobe activity, is impaired in individuals with FXS. Yet, little is known how alterations in frontal neural activity is related to EF deficits in FXS.

Hypothesis

Individuals with FXS will show decreased alpha and increased gamma band activity in the frontal lobe during rest compared to controls and this hyperconnectivity will correlate with the severity of EF deficits in FXS.

Methods

Sixty-one participants with FXS and 71 age- and sex-matched TDC completed a five-minute resting EEG recording and KiTAP, a measure testing multiple aspects of EF. EEG data was preprocessed and phase connectivity values for each gyrus paring in the frontal and prefrontal regions for the alpha (10-12.5 Hz) and gamma (30-55 Hz) bands were calculated. Linear mixed-effect models were generated with fixed factors of group, sex, and gyrus. Spearman's correlations between KiTAP variables for each subtask and the dwpli connectivity valves were calculated.

Results

The linear mixed-effect model showed significant group x sex x gyrus interactions for both alpha and gamma bands. Individuals with FXS demonstrated increased gamma band connectivity across gyri and hemispheres compared to TDC. In contrast, reduced alpha band activity were observed in FXS relative to TDC. No significant group x sex interactions emerged. Increased error rates on EF tasks were associated with increased gamma band connectivity within left frontal and prefrontal regions but reduced alpha band connectivity within right frontal regions

Conclusions

Results extend previous findings of frontal alpha and gamma activity differences between FXS and TDC, implicating hyper-connectivity within frontal brain regions. We also report relationships between frontal hyper-connectivity and performance-based data in FXS. Together, these findings suggest increased connectivity within high frequency bands may impair EF performance whereas increased connectivity within lower frequency bands may provide compensatory support for EF, thus providing insight into future directions for treatment intervention.

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