Recent neurobiological research has studied functional resting connectivity of specific brain regions and brain networks for their insight into the disease condition. Whole-brain analysis is a data-driven technique that can be used to systematically examine the connectivity of major intrinsic networks, also called resting state networks (RSNs), of the diseased CRPS brain compared to the healthy state.

One previous study has employed this method on pediatric CRPS patients, but the authors acknowledged that a limitation of their work was low patient number [1]. Our project had the following specific aim: to extend previous research on whole brain connectivity analysis of pediatric CRPS patients compared to healthy controls by studying a larger pediatric patient population.

Notably, there were abnormalities in networks such as the salience, default mode, sensorimotor, and frontoparietal networks. Within the salience network, pediatric CRPS patients had decreased connectivity in the anterior cingulate compared to controls. Aberrant connectivity in the anterior cingulate may correspond with abnormal detection and responses to salient stimuli [2].

RSNs identified in pediatric patients with CRPS (red-yellow) in comparison with RSNs in the healthy subjects (green-light green).

Introduction

Methods

Forty-two pediatric subjects were included for this project (21 CRPS patients (13.4 ± 0.6 years (mean ± SEM)) and 21 controls (13.6 ± 0.6 years (mean ± SEM)). Healthy controls were tightly matched to the CRPS patients regarding sex, age, and scanning interval.

The Oxford Center for Functional MRI of the Brain’s Software Library (FSL) was used to analyze the imaging data. Differences in resting state network connectivity in CRPS patients were compared with resting state networks of healthy controls using dual regression. RSNs were investigated for CRPS patients and healthy subjects using Multivariate Exploratory Linear Optimized Decomposition into Independent Components version 3.0. Eleven functional networks were identified. Each component was spatially correlated with Pearson Correlation with adult networks available from FSL.

Results

The current study demonstrates significant alterations in the intrinsic brain networks of pediatric patients suffering from CRPS compared to the healthy pediatric brain.

Figure 1: RSNs of children with CRPS are superimposed on RSNs from healthy adults, which show high correspondence with RSNs of healthy children [1], for visual comparison with healthy RSN activity. There were abnormalities in networks such as the salience, default mode, sensorimotor, and frontoparietal networks. Within the salience network, pediatric CRPS patients had decreased connectivity in the anterior cingulate compared to controls. Aberrant connectivity in the anterior cingulate may correspond with abnormal detection and responses to salient stimuli [2].

Figures

Discussion

Pediatric patients with CRPS demonstrated widespread changes in resting state connectivity compared to healthy pediatric controls. Regions of abnormally increased connectivity and abnormally decreased connectivity may underlie positive CRPS symptoms, such as spontaneous and evoked pain, and negative CRPS symptoms, such as fear and altered cognition, respectively [2].

The modern advent of advanced neuroimaging technology has provided an unprecedented level of objectivity in the study of pain. Traditionally, pain has been a challenging area of research because pain is a subjective experience; each person responds differently to painful stimuli and can report varying experiences to the same stimulus [3]. The lack of a standardized laboratory test to quantify a patient’s pain levels leads to the difficulty of studying chronic pain [3]. Neuroimaging provides the opportunity to study pain more objectively compared to previous methods and to investigate comprehensively the mental, emotional, and sensorimotor aspects of pain with one tool.

Ultimately, this project elucidates the intrinsic brain networks in CRPS patients and contributes to our understanding of abnormal functional brain activity underlying the CRPS disorder and chronic pain state.

Conclusion

Our study indicates significant differences in brain network connectivities due to CRPS disease effects. It suggests that alterations in RSNs in pediatric patients with CRPS may help define a brain phenotype that represents the disease state. These brain markers have important potential clinical applications: monitoring changes in emotional, sensory, and modulatory pain circuits; measuring severity of pain over time; and providing more objective markers of treatment efficacy [4, 5].

Future studies should be conducted to determine whether abnormalities in intrinsic brain activity can help us identify potential therapy targets, guide personalized treatment choices, and improve treatment outcomes for pediatric patients with CRPS.

References