Exploring the Effects of Congenital Heart Disease on Brain MRI Registration

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Abstract

Congenital Heart Disease (CHD) patients can have neurocognitive abnormalities. To study differences between CHD and control neurodevelopment, we observed patterns between CHD and control brain MRI registration similarity measures between a fetal and neonatal scan. Our study found patients with CHD have deviations from neurodevelopmental trends. We observed that CHD similarity scores had weaker correlations with fetal age and time duration between the scans than control similarity scores.

Introduction

Congenital Heart Disease (CHD) is a birth defect characterized by structural heart abnormalities, and has been shown to be associated with downstream neurodevelopmental problems[1]. Brain image registration is the process of geometrically aligning one image onto another and is a common step in neuroimaging analyses performed to compare images. The registration correlation ratio measures how similar two images are during the registration process. This study aims to explore how neurodevelopment differs between CHDs and controls by comparing registration performance across fetal and neonatal time points between CHDs and controls. We hypothesize that differences in registration between CHD and control can be indicative of abnormal brain growth.

Methods

To remove non-brain tissue, both fetal and neonatal images were skullstripped. The fetal brains were then linearly registered onto the neonatal image using FSL's FLIRT algorithm[2]. The FLIRT registration's cost function, the correlation ratio, was used as a similarity score to quantify the similarity of the brain between time points. We recorded the subjects and their correlation ratio values, along with their ages at scanning, and the time duration between the two scans. We then analyzed how their age at the time of scanning and the time duration between the two scans correlated with the similarity score using Pearson Correlation Coefficients. Finally, a Mann-Whitney U was performed to examine the differences between the CHD and Control distributions.

Results

69 subjects were included in this study. Two subjects were excluded due to their neonatal age being greater than one year at scan time. Of the remaining 67 subjects, there were 19 CHD and 48 control subjects. According to the Mann-Whitney U, the difference between the CHDs and the controls in relation to their similarity score was not statistically significant. In the controls, the time duration between the two scans had a strong, negative correlation with the similarity score, as the Pearson $r = -0.53$ with a p-value < 0.01. In the CHDs, the time duration between the two scans did not have a statistically significant correlation. In the controls, the fetal gestational age (GA) had a strong, positive correlation with the similarity score, as the Pearson $r = 0.61$ with a p-value < 0.01. In the CHDs, the fetal GA did not have a statistically significant correlation with the similarity score (Fig. 1).

Discussion

For the control group, the similarity measure between the fetal and neonatal scan had a positive correlation to the fetal GA and negative correlation to the time duration between the scans. In contrast, for the CHD group, the similarity measure between the scans did not have statistically significant correlations to the fetal GA and time duration. The fetal brain develops faster than the neonatal brain, which may explain the increased similarity between older fetal brains and their neonatal counterparts in controls. Similarly, there are substantial structural brain changes over time during neurodevelopment which can explain why the similarity decreased across longer time durations within controls. In contrast, the characteristic high variability in neurodevelopment among CHD patients can explain why CHD similarity scores did not have a significant correlation across time[3]. While these results require further validation with more data, they offer a data driven comparison of structural neurodevelopment over time in CHDs and control patients. Future studies will control for variables such as scan time and demographics as these can differ between CHD and controls due to social determinants of health and difficulties in study recruitment.

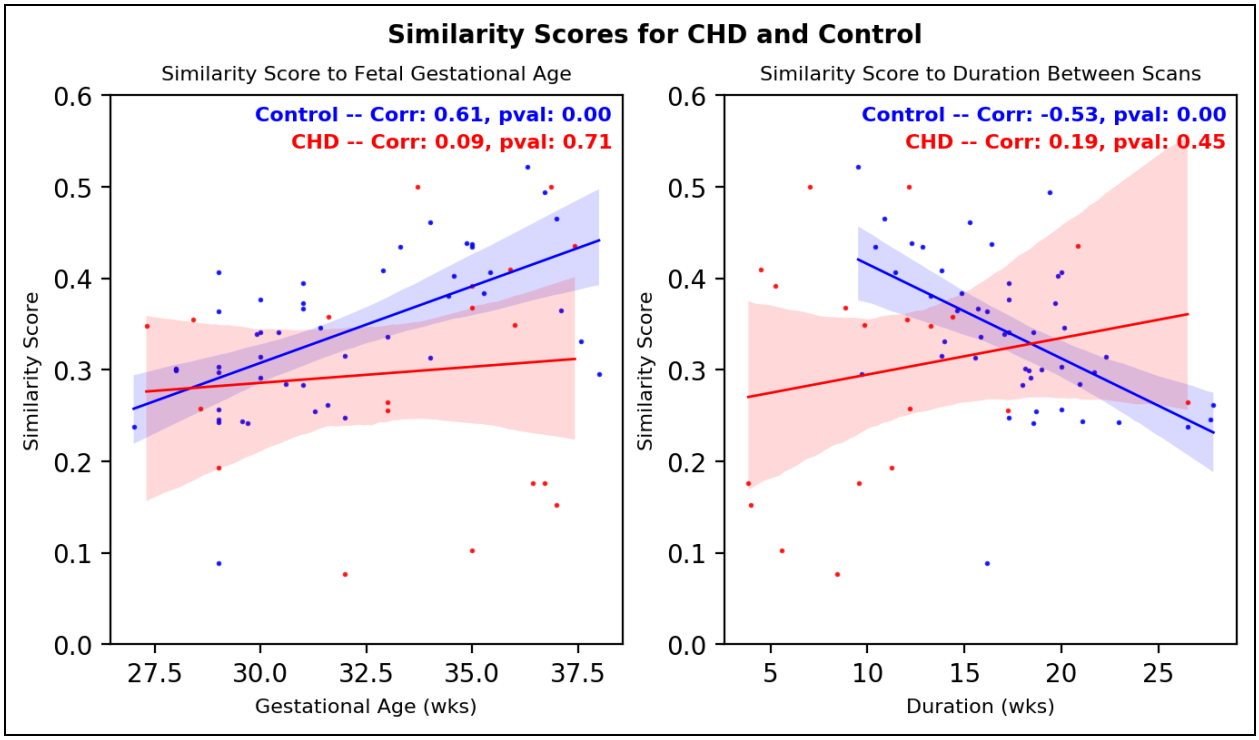

Figure 1. Control patients display a positive correlation between similarity score and fetal gestational age and a negative correlation between similarity score and duration between scans. There were no statistically significant correlations among CHD patients. The shaded region represents the 95% confidence interval. CHD patients show larger confidence intervals than control subjects.

References

1. Panigrahy A, Lee V, Ceschin R, Zuccoli G, Beluk N, Khalifa O, Votava-Smith JK, DeBrunner M, Munoz R, Domnina Y, Morell V, Wearden P, Sanchez De Toledo J, Devine W, Zahid M, Lo CW. Brain Dysplasia Associated with Ciliary Dysfunction in Infants with Congenital Heart Disease. J Pediatr. 2016 Nov;178:141-148.e1. doi: 10.1016/j.jpeds.2016.07.041. Epub 2016 Aug 26. PMID: 27574995; PMCID: PMC5085835.
2. Jenkinson, M., Bannister, P., Brady, J. M. and Smith, S. M. Improved Optimisation for the Robust and Accurate Linear Registration and Motion Correction of Brain Images. NeuroImage, 17(2), 825-841, 2002.
3. Morton PD, Ishibashi N, Jonas RA. Neurodevelopmental Abnormalities and Congenital Heart Disease: Insights Into Altered Brain Maturation. Circ Res. 2017 Mar 17;120(6):960-977. doi: 10.1161/CIRCRESAHA.116.309048. PMID: 28302742; PMCID: PMC5409515.