GLOBAL RESEARCH IMMERSION PROGRAM FOR YOUNG SCIENTISTS

Correlating MRI-quantified Regional Neural Flexibility to Neurodevelopmental Metrics

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Introduction

Neural Flexibility in Infantile Neurodevelopment: Neural flexibility (NF) is a measure of how often a brain region changes its allegiance from one functional group to another. NF is reflective of the brain's ability to adapt to new information and dynamically problem solve.

Diffusion-weighted MRI for Quantification of NF: Non-invasive imaging technique for measurement of tissue water molecule displacement over time allowing differentiation of white and gray matter tissue microarchitectures.

Eye-tracking for Assessing Visual Attention in Toddlerhood: Non-invasive technology that offers highly detailed temporal and spatial resolution on a child's direction of gaze. It can be mostly automated to generate scalable metrics for individual variations in visual attention during early development. Eye-tracking tasks that include social elements (such as people and faces) can be studied in the context of autism to understand how this diagnosis affects the results.

Hypothesis: We hypothesize that the **NF** of infants is positively correlated with sum-of-scaled **language** and **cognitive ability** values.

Methods

1. Data Acquisition

Figure 1 MRI machine for image acquisition

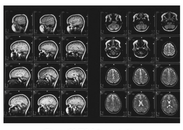

Figure 2 MRI data acquisition interface

Participants: 134 children from the Developing Human Connectome Project (dHCP) and the Baby Connectome Project (BCP) databases

Equipment: 3T Diffusion-Weighted MRI (Siemens MAGNETOM Prisma *syngo* MR XA30)

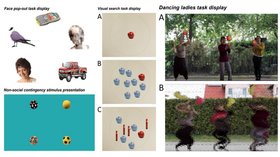

Figure 3 Eye-tracking tasks interfaces

Eye-tracking: 471 children from the Developing Human Connectome Project (dHCP), aged 18-month, data from 8 tasks

Equipment: Tobii TX-300 (Tobii AB, Sweden), sampling rate of 120Hz, stimuli were presented on Apple Macbook Pro 23" screen

2. Data Preprocessing

- Preprocessing used FSL and MATLAB based on a wavelet-based pipeline for motion correction. Data from failed scans with severe motion artifacts (i.e. spike % > 5) were excluded from analyses.
- T1-weighted and T2-weighted images utilized to obtain tissue segmentation results, to mitigate the effects of age-dependent gray matter contrast on the accuracy of registration.

3. Neural Flexibility Regional Calculations

- rsfMRI data was coregistered with the MMI atlas (210 cortex ROIs).
- Averaged voxel time series in each region.
- Captured interregional functional connectivity of each sliding window to remove weak and random connections.
- Computed the *p* value for each correlation coefficient. Only correlations with p <0.05 (significant) were retained as the connections can be thought of as significant.
- Neural flexibility (NF) was calculated using both *k*-means++ clustering and the GenLouvain community detection and the Munkres optimization algorithm, we ultimately used k-means for faster calculation.

$$\Delta Q = \frac{\sum_C + k_i^C}{2m} - \left(\frac{\sum_{\hat{C}} + k_i}{2m}\right)^2 - \left[\frac{\sum_C}{2m} - \left(\frac{\sum_{\hat{C}}}{2m}\right)^2 - \left(\frac{k_i}{2m}\right)^2\right]$$

Equation 1 Generalized Louvain equation for network modularity optimization

4. Correlative Comparison and Analysis

- ROI-wise correlative comparisons performed between NF and language/cognitive parameters. Visualization using Human Connectome Project (HCP) Workbench.

Results

1. Indications of regional association between neural flexibility quotients and language, cognition and social parameters

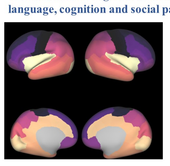

Figure 4 HCP Workbench visualization of regional NF association with language parameters

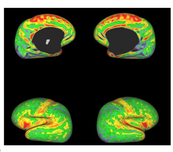

Figure 5 Graph of Association in 1 particular brain region - with equation of line + 95% CI

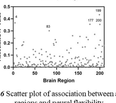

Figure 6 Scatter plot of association between all brain regions and neural flexibility

2. Identified associations between eye-tracking performance/autism test scores and regional neural flexibility

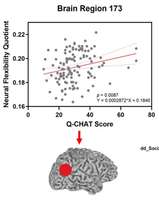

Figure 7 Association between NF and Q-CHAT Score in region 173 (right temporo-parietal junction (lateral sulcus, Wernicke's region))

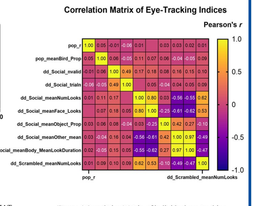

Figure 8 Correlation Matrix of individual eye-tracking indices. *dd* = Dancing ladies task, *pop* = Face pop-out task

3. Emerging patterns of association between autism test scores and eye tracking functions (n=471)

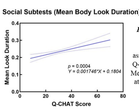

Figure 9a Linear regression demonstrating association between Q-CHAT Score and Mean Look Duration at body in Dancing ladies task

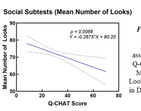

Figure 9b Linear regression demonstrating association between Q-CHAT Score and Mean Number of Looks (social context) in Dancing ladies task

Application of Quantitative Checklist for Autism in Toddlers (Q-CHAT) demonstrated primarily correlations to those eye-tracking tasks that included social elements, namely, Dancing ladies task. Variables that showed the mean number of looks in social context correlated negatively with high Q-CHAT scores, indicating the problems of the autistic group maintaining attention in such context. On the contrary, the mean look duration to bodies increased with higher Q-CHAT scores, demonstrating shift of gaze from faces to bodies, avoiding eye contact.

Limitations & Solutions

Limitations	Detail	Solutions
1. Sample Size Representativeness	Sample size was especially small for the BCP dataset (n < 50)	Using k-means clustering as a proxy for runtime reduction through dimensionality reduction, alongside hardware with greater computational effectiveness, allows for testing more subjects in parallel
2. Environmental and genetic factors	Neurodevelopment is influenced by numerous additional factors which may not have been accounted for, including maternal factors	More comprehensive data required for these factors, with additional statistical control for these variables within analysis. At an extreme, accompanying GWAS studies may also be obtained, ensuring PCA control of population stratification and genomic inflation factor controls
3. Eye-tracking interface accuracy	There may be additional factors as distractors in eye-tracking which are not accounted for	Greater control of surrounding conditions when performing eye-tracking tests

Conclusions & Future Directions

- Strong correlation identified almost exclusively to social subtests of all eye-tracking tests with Q-CHAT score, necessitating further confirmation via expansion of sample size to n ≥ 979
- Reduce NF calculation code complexity for runtime efficiency increase to allow for running of entire dHCP and BCP datasets, largely increasing sample size, compounded with utilization of more stringent FDR correction parameters such as the Benjamini-Hochberg-Yekutieli (BHY) procedure, comparing with simple Bonferroni correction for additional control
- Further correlation required between different MRI features such as T1 and T2-weighting for further elucidation of gray and white matter differences
- Directly test for correlations between regional NF and autism sub-measures
- Further analyses of individual brain region function may be critical in understanding highly-flexible brain regions and their correlation to language / cognitive measures

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