Microstructure in the posterior parietal cortex supports working memory function in 9-10-year-old children

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Introduction

- Research on the nature and limits of working memory (WM) operations points to the fundamental importance of WM in determining the limits of our cognition.
- Cognitive neuroscience of WM has been extensively studied in adult research. However, it has been more challenging to specify the mechanisms through which WM matures across development.

∴ This poses further limits on our understanding of developmental disorders that manifest WM deficits, such as Attention-Deficit Hyperactivity-Disorder (ADHD).

∴ An impaired WM function is commonly observed in ADHD (e.g. Karalunas et al., 2017). However, the specificity of these deficits at a mechanistic level, as well as their underlying neurobiology are still lacking.

Goal: Evaluate individual differences in microstructure and neural activation patterns in regions that support WM. How do they further modulate ADHD-related effects in working memory?

Study Approach

- Leveraged the Adolescent Brain Cognitive Development (ABCD) Study (https://abcdstudy.org), a large scale (over 11000 participants) national consortium that entails 21 data collection sites in the US.
- The ABCD study aims to follow neurodevelopment throughout adolescence and into young adulthood, monitoring brain development of a large number of children (ages 9-10) for a ten-year period (Barch et al., 2017; Casey et al., 2018; Garavan et al., 2018).

Working Memory Measures

1. NIH toolbox List Sorting Working Memory Task. Participants use their WM resources to sequence task stimuli based on category membership and perceptual characteristics. Included in the neurocognitive battery of the ABCD study.

2. N-Back Task. Participants view pictures and indicate whether a picture is a "match" or "mismatch". Included in the imaging protocol of the ABCD study.
   - 2-back: Stimulus matches the picture two trials back.
   - 0-back: Stimulus matches the same target of current trial.

Study Approach cont.

Neural Measures:

1. Neurite Density Measures. For both tasks, we tracked the relationship between microstructure patterns in the prefrontal and posterior parietal cortices and WM performance.

2. Functional MRI Measures. For the n-back task, we were also able to track the relationship between magnitude of neural activation in the prefrontal and posterior parietal cortices and WM performance.

Diagnostic Category:

Derived from the Kiddie Schedule of Affective Disorders and Schizophrenia for DSM-5 (KSADS-5) included in the mental health assessments of the ABCD study (Barch et al., 2017).

Data Analyses:

- Prior to analyses, brain measures centered around ABCD site to account for variability in scanner measurement across the different sites.
- Linear mixed-effects models (using the lmer function in R) to evaluate the contribution of target regions to working memory performance.
- Recommended covariates by the ABCD study included in the models (demographic variables as fixed effects, family and ABCD site as random effects).
- Missing Data Approach. Data analyses replicated adapting two approaches:
  - Multiple Data imputation. 20 imputation sets constructed using MICE software in R (van Buuren & Grothuis-Oudshoorn, 2011).
  - Exclusion of participants with missing data.

References

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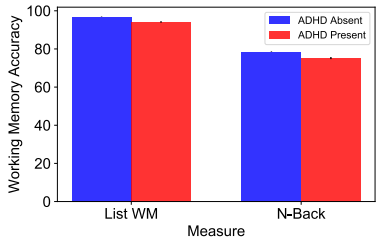
Results

Behavioral Data



- Participants with ADHD exhibit lower accuracy in both the list sorting working memory task, and the n-back task.

Results cont.

Regions that predict WM

1. Neurite Density Measures

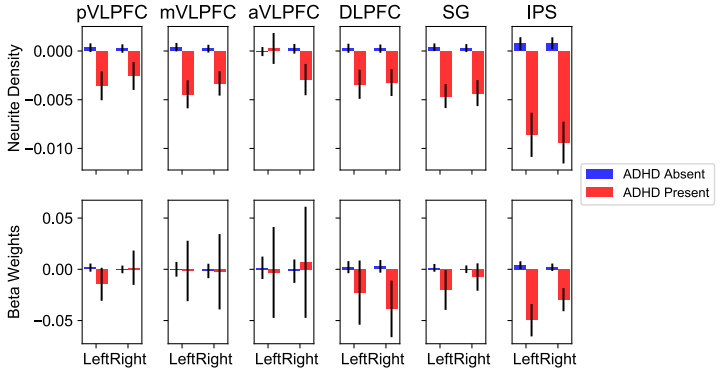
List Sorting WM task
Bilateral intraparietal sulci (IPS)
Bilateral anterior ventrolateral prefrontal cortex (VLPFC).

N-Back task
Bilateral IPS

2. Functional MRI Measures

N-Back task
Bilateral IPS
Bilateral dorsolateral prefrontal cortex (DLPC)
Bilateral supramarginal gyrus (SG)
Right anterior VLPFC
Right mid VLPFC

Target Regions



Regions that predict ADHD

- Both data analyses approaches converged on the further importance of the intraparietal sulcus region of the posterior parietal cortex in predicting diagnostic category.
- Among the regions that contribute to WM, data implicate the IPS to be a potential key contributor to ADHD-related deficits in working memory.

Summary

- The rich measures of the ABCD study allowed us to concurrently evaluate structural and functional measures from a large number of participants at an age range where rapid working memory development is known to take place (e.g. see Cowan, 2016 for a review).
- Consistent with prior WM literature, both neurite density and functional MRI measures point to the important contribution of the ventrolateral prefrontal and posterior parietal cortices.
- The data further pinpointed the intraparietal sulcus as a key region potentially responsible for modulating ADHD related effects in working memory performance.