Data-driven Cognitive and Neuroimaging Clusters in Persistent Dyslexia

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Introduction

- **Developmental dyslexia (dD)** is a neurodevlopmental disorder characterized by difficulties in reading despite adequate intelligence and education
- **Aims**:
  - Identify the cognitive and correspondent neuroanatomical signatures of dD in a well-characterized cohort of children with persistent dyslexia despite intervention
  - Increase **precision** and **efficiency** in **characterizing learning profiles** by using data-driven methods
- **Hypothesis**: Deviation from typical neurodevelopment in specific brain regions will be associated with corresponding performance on cognitive measures, providing insight into subtypes of dyslexia

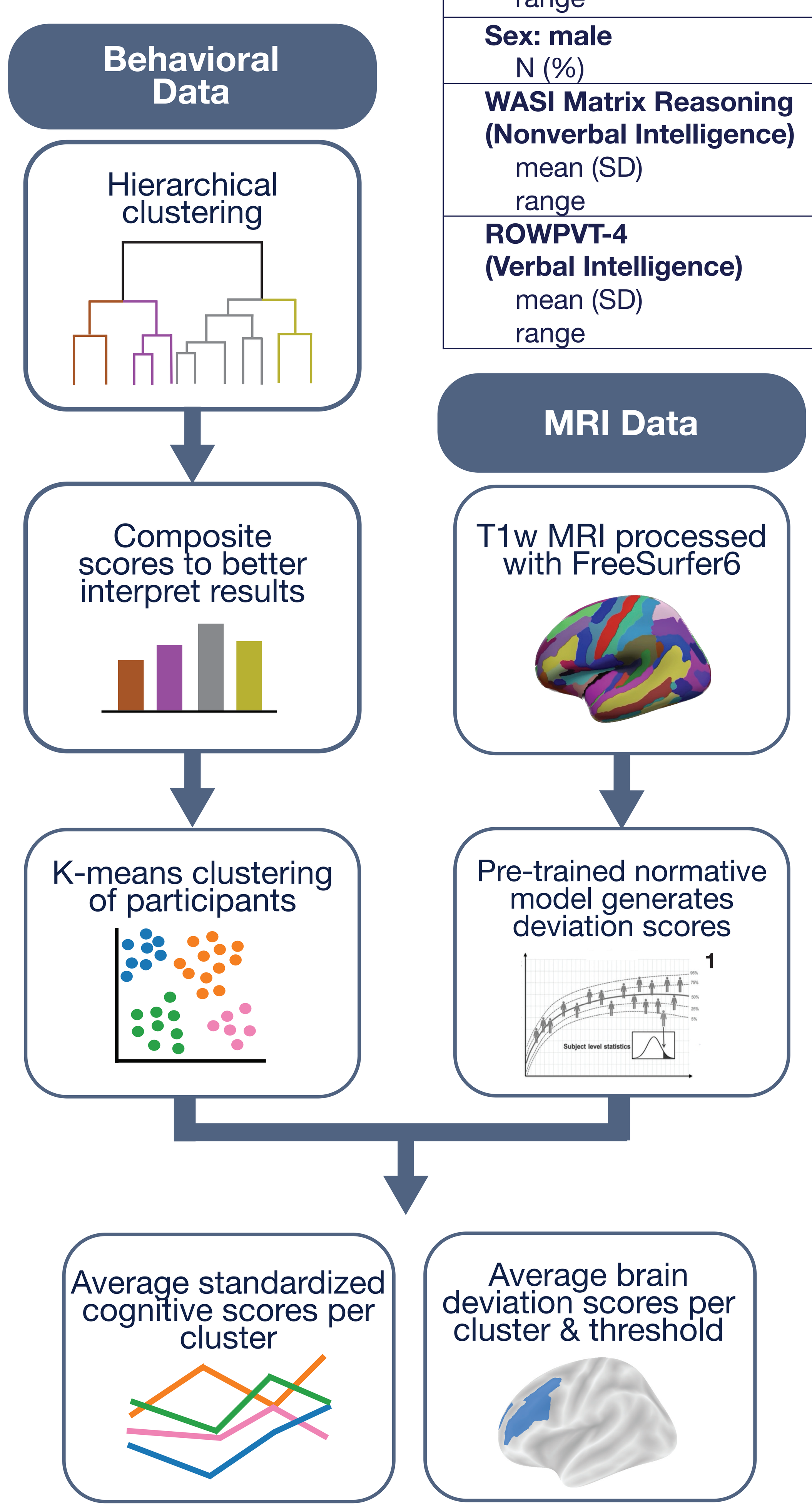
Methods

Study Sample

- Participants (*n*=102) received a comprehensive battery (15+ hours) of neuropsychological, academic, and language tests and MRI (3T Siemens Prisma) by an interdisciplinary team at the UCSF Dyslexia Center
- Children were referred with dD diagnosis and also diagnosed with dD by our team of trained neurologists and neurospsychologists
- Exclusion criteria: clinically significant MRI contraindications or WASI Matrix Reasoning < 9th percentile

Sample Characteristics (*n* = 102)	
Age	
mean (SD)	11.07 (1.74)
range	8 - 14
Sex: male	
N (%)	61 (58.80%)
WASI Matrix Reasoning (Nonverbal Intelligence)	
mean (SD)	60.68 (24.08)
range	12-97
ROWPVT-4 (Verbal Intelligence)	
mean (SD)	72.91 (23.89)
range	13-99

Table 1



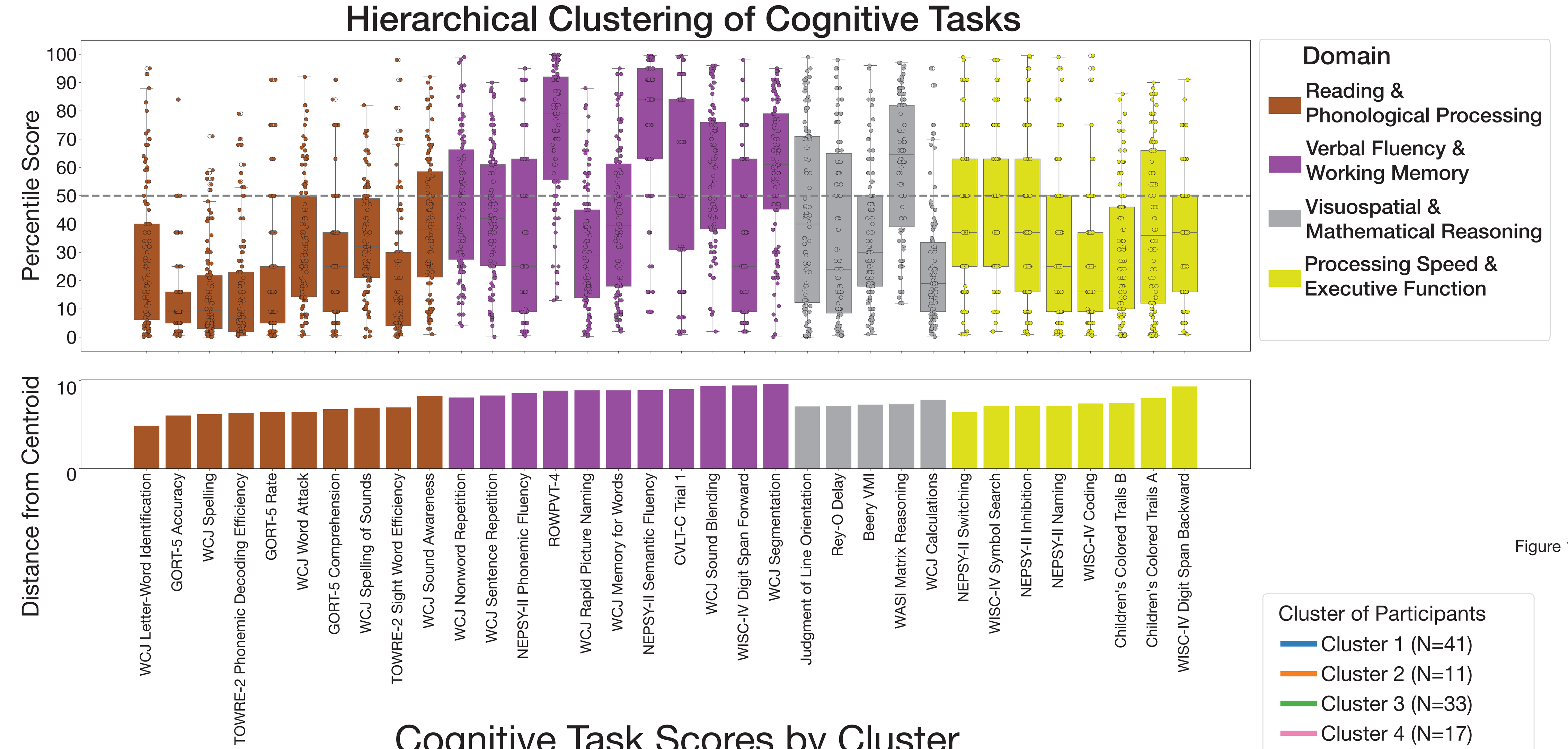
MRI data quality checked and standardized in BIDS

Normative Modeling

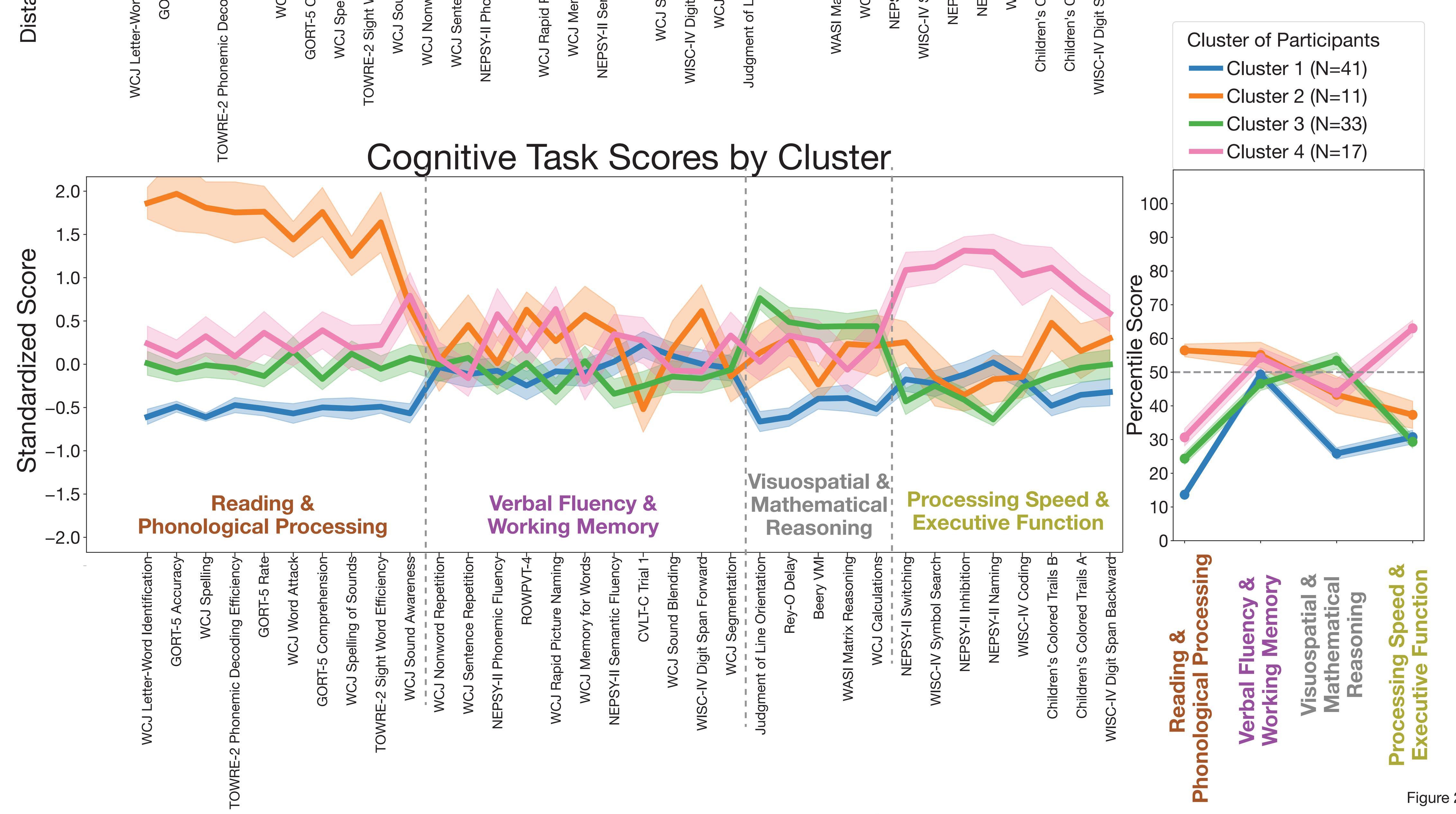
- Open source warped Bayesian linear regression normative model **(82 sites; N=58,536; ages 2-100)**[1] to generate brain deviation scores which account for: age, sex, and MRI site effects
- **Measures**: Cortical area and thickness (Destrieux atlas[2]) and subcortical volume (Aseg atlas[3])

Results

Hierarchical Clustering of Cognitive Tasks



Cognitive Task Scores by Cluster



Average Deviation Scores

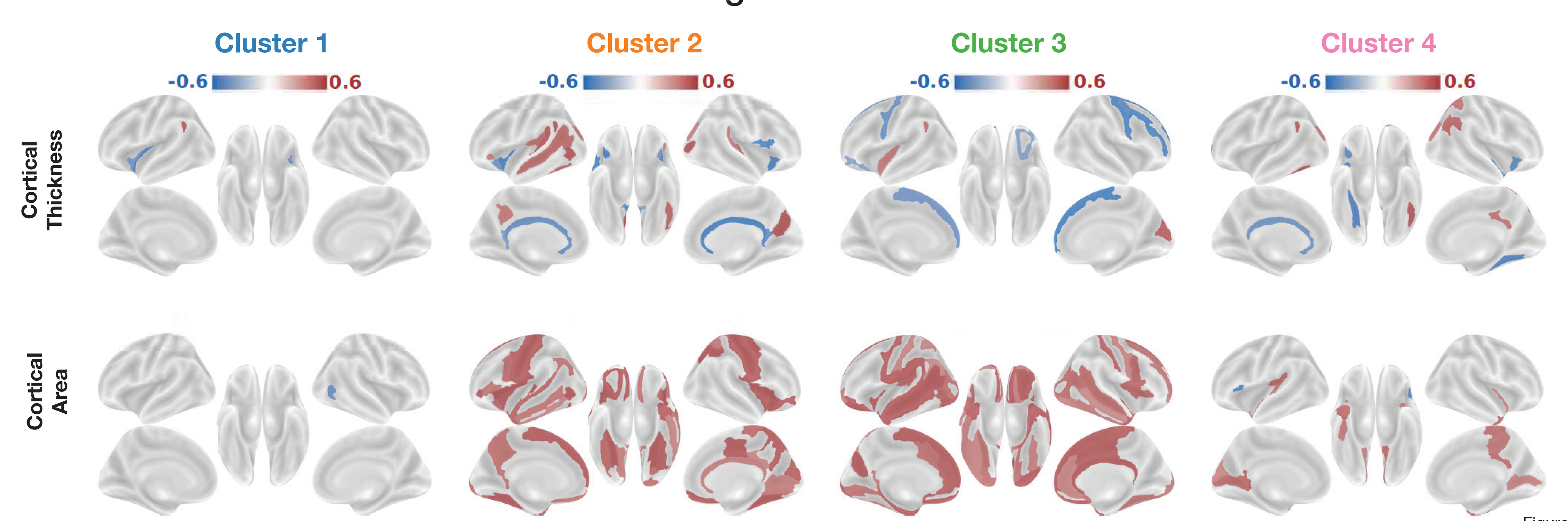


Figure 1: Percentile scores for cognitive tasks. Cognitive tasks are arranged according to their hierarchically clustered groups and their distance from respective cluster centroids. Task clusters are partially independent (-0.02<r<0.38).

Figure 2: K-means (*k*=4) clustering of participants using standardized cognitive scores. Average score per cluster with SEM shading is plotted.

Figure 3: Average deviation scores for each cluster, thresholded by the 85th percentile. No regions survived |*z*|>1.96 (*p*<0.05) thresholding.

Discussion

Interpreting Dyslexia Phenotypes

- **Cluster 1**: most distinct phonological and visuospatial & math difficulties
  - Highest proportion diagnosed with co-occurring **dyscalculia** (34.2%)
- **Cluster 2**: relatively stronger performance in reading and phonological tasks potentially indicates better compensatory strategies or ADHD driving the deficits (72.7% with **ADHD**)
- **Cluster 3**: average performance in all domains, except relative strength in visuospatial & mathematical reasoning
  - Second lowest proportion diagnosed with co-occurring **dyscalculia** (15.2%); lowest is cluster 4 with 11.8%
- **Cluster 4**: average performance in all domains, except relative strength in processing speed & executive function
  - Lowest proportion diagnosed with co-occurring **ADHD** (29.4%)

Neuroimaging Relationships - Exploratory

- **Cluster 1**: Majority brain deviations close to zero and do not survive thresholding
- **Cluster 2**: Higher thickness in left temporal language regions; higher area in bilateral central sulcus and surrounding regions; higher area bilateral fusiform gyrus; higher thickness in left occipitotemporal region
- **Cluster 3**: Widespread higher area notably in bilateral temporal regions; lower thickness in middle frontal and precentral gyri
- **Cluster 4**: Higher area in right angular gyrus and superior parietal lobule; higher thickness in left occipitotemporal region
- Higher thickness in Jensen's sulcus consistent across clusters

Summary

- Findings highlight the importance of visuospatial, mathematical, working memory, and executive function abilities in dD, beyond traditional reading measures
- Results suggest heterogeneity in dD manifestations, emphasizing the need for personalized assessment and intervention

Future Research

- Focus on identifying dD subtypes based on cognitive profiles and their corresponding neurodevelopmental trajectories
- Incorporate other neuroimaging modalities, i.e. DTI and fMRI
- Include subjects from diverse geographical regions and socioeconomic backgrounds

Acknowledgments

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