Understanding Neural Mechanisms of Cognitive Control in Neurodevelopmental Disorders

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SPECIFIC AIMS

Cognitive control deficits are a core feature of many neurodevelopmental disorders, yet the underlying neural mechanisms remain poorly understood. This knowledge gap hampers the development of targeted interventions and biomarkers for early diagnosis. The goal of this research is to characterize the neural mechanisms of cognitive control across typical development and in neurodevelopmental disorders, specifically attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD).

We will pursue the following specific aims:

Aim 1: Characterize developmental trajectories of neural circuits supporting cognitive control
Hypothesis: Cognitive control networks show protracted developmental trajectories that differ between typically developing children and those with ADHD or ASD.

We will use multimodal neuroimaging (fMRI-EEG) to map developmental changes in neural activation and connectivity during cognitive control tasks across ages 7-18 years in all three groups.

Aim 2: Identify disorder-specific neural signatures of cognitive control deficits
Hypothesis: ADHD and ASD are associated with distinct patterns of neural dysfunction during cognitive control tasks, despite behavioral similarities.

We will apply machine learning techniques to identify disorder-specific neural signatures that differentiate ADHD and ASD from typical development and from each other.

Aim 3: Determine the relationship between neural network dynamics and individual differences in cognitive control abilities
Hypothesis: Individual differences in cognitive control abilities are better predicted by neural network dynamics than by diagnostic category.

We will use computational modeling to characterize the relationship between neural network dynamics and performance on cognitive control tasks, accounting for both within- and between-group variability.

This research will significantly advance our understanding of the neural basis of cognitive control in typical and atypical development, with implications for the development of personalized interventions and objective biomarkers for neurodevelopmental disorders.

RESEARCH STRATEGY

Significance

Despite significant advances in understanding the neural basis of cognitive control, there remains a critical gap in our knowledge of how these processes develop and function in individuals with neurodevelopmental disorders. This project addresses this gap by investigating the neural mechanisms underlying cognitive control processes in three distinct populations: typically developing children, children with attention deficit hyperactivity disorder (ADHD), and children with autism spectrum disorder (ASD).

Our preliminary data indicate significant differences in neural activation patterns during cognitive control tasks between these groups, suggesting distinct neurodevelopmental trajectories that may inform targeted interventions.

Innovation

This proposal is innovative in several ways:

1. It employs a novel multimodal neuroimaging approach combining functional magnetic resonance imaging (fMRI) with electroencephalography (EEG) to capture both the spatial and temporal dynamics of neural activity during cognitive control tasks.
2. It utilizes advanced computational modeling techniques to characterize individual differences in neural network dynamics, moving beyond group-level analyses to capture heterogeneity within diagnostic categories.
3. It incorporates a developmental perspective by examining age-related changes in cognitive control networks across a wide age range (7-18 years), allowing for the identification of critical periods for intervention.

Approach

Participants: We will recruit 60 typically developing children, 60 children with ADHD, and 60 children with ASD, aged 7-18 years. Groups will be matched on age, sex, and IQ. All participants will undergo comprehensive clinical assessment.

Procedures: Participants will complete a battery of cognitive control tasks during simultaneous fMRI-EEG recording. Tasks include the Stop Signal Task, Flanker Task, and Task-Switching paradigm, all adapted for the developmental population.

Analysis: We will employ both traditional univariate analyses and advanced multivariate pattern analysis to identify neural signatures of cognitive control. Dynamic causal modeling will be used to characterize effective connectivity between brain regions. Machine learning approaches will be applied to predict individual differences in cognitive control abilities from neural data.

Expected Outcomes: This research will yield a comprehensive understanding of the neural mechanisms underlying cognitive control in typical development and neurodevelopmental disorders. Findings will inform the development of targeted interventions and contribute to the identification of biomarkers for early diagnosis and treatment monitoring.

BIBLIOGRAPHY & REFERENCES CITED

Bibliography

BUDGET & JUSTIFICATION

This five-year R01 project requires the following resources to accomplish the proposed aims:

PERSONNEL

Principal Investigator (Dr. Jane Smith, 25% effort): Dr. Smith will provide overall scientific leadership for the project, oversee all aspects of study design, data collection, analysis, and dissemination. She will supervise research staff and ensure adherence to timelines and research protocols.

Co-Investigator (Dr. Robert Johnson, 15% effort): Dr. Johnson will contribute expertise in neuroimaging methods and analysis, assist with fMRI protocol development, and supervise the neuroimaging data processing pipeline.

Co-Investigator (Dr. Sarah Williams, 10% effort): Dr. Williams will contribute expertise in developmental psychopathology, assist with clinical assessments, and help interpret findings in the context of neurodevelopmental disorders.

Postdoctoral Researchers (2 FTE): Two postdoctoral researchers will coordinate data collection, implement preprocessing and analysis pipelines, conduct statistical analyses, and prepare manuscripts and presentations.

Research Assistants (2 FTE): Two research assistants will recruit and schedule participants, administer cognitive and clinical assessments, assist with neuroimaging data collection, and manage research databases.

MRI Technician (25% effort): A certified MRI technician will operate the MRI scanner during data collection and ensure high-quality neuroimaging data.

EQUIPMENT

EEG System Upgrade ($75,000, Year 1 only): Funds are requested to upgrade the existing EEG system to enable simultaneous fMRI-EEG recording. This includes MRI-compatible caps, amplifiers, and software.

Computing Cluster Expansion ($50,000, Year 1 only): Additional computing nodes are needed for the intensive computational modeling and machine learning analyses proposed in Aims 2 and 3.

SUPPLIES

Neuroimaging Supplies ($15,000/year): Includes MRI-compatible response devices, head cushions, disposable EEG electrodes, and participant monitoring equipment.

Computing Supplies ($10,000/year): Storage media, backup systems, software licenses, and computing peripherals.

Office Supplies ($5,000/year): General office supplies, printing costs for assessment materials, and participant recruitment materials.

TRAVEL

Conference Travel ($15,000/year): Funds for PI, co-investigators, and postdocs to attend and present at 2-3 major conferences per year (e.g., Organization for Human Brain Mapping, Society for Neuroscience, Cognitive Neuroscience Society).

Collaboration Travel ($5,000/year): Travel for PI and key personnel to meet with collaborators for specialized training and data analysis.

PARTICIPANT COSTS

Participant Compensation ($60,000/year): Compensation for 180 participants (60 per group) at $250 per participant for approximately 6 hours of testing (includes neuroimaging, cognitive assessments, and clinical interviews) plus travel expenses. Additional funds for follow-up testing in years 3-5.

Participant Recruitment ($10,000/year): Advertising costs, community outreach materials, and screening expenses.

OTHER DIRECT COSTS

MRI Scanner Time ($120,000/year): 300 hours of scanner time per year at $400/hour for participant scanning and pilot testing.

Publication Costs ($10,000/year): Open access publication fees for approximately 4-5 manuscripts per year.

Research Computing Services ($15,000/year): High-performance computing resources and technical support for computational modeling and large-scale data analysis.

BUDGET JUSTIFICATION SUMMARY

The requested budget is appropriate and necessary to complete the proposed research. Personnel costs reflect the interdisciplinary expertise required for this complex project involving clinical populations, advanced neuroimaging methods, and sophisticated computational analyses. Equipment costs are essential for the simultaneous fMRI-EEG recording central to our approach. Participant costs reflect the comprehensive assessments and the need to adequately compensate families for their substantial time commitment. Neuroimaging costs are based on current rates at our institution's imaging center. This budget has been carefully planned to ensure the most efficient use of resources while enabling the successful completion of all aims.