Investigating the relationship between white-matter brain connectivity and orthographic-phonological letter integration ability in pre-reading children

As a member of Northwestern's Developmental Cognitive Neuroscience (DCN) Lab, under Dr. James Booth, I have learned to analyze brain pathways and regions in relation to reading ability. I also work closely with a post-doctorate scholar, Margaret Gullick, on this project. My independent contribution is my experience with Diffusion Tensor Imaging (DTI), a new approach that analyzes the brain connectivity of white matter pathways between brain regions, as opposed to the activity of grey-matter regions (fMRI). I am one of the few people at Northwestern trained to perform and understand this new analysis, and my work would be an asset to the university.

Research Question

How is letter-sound integration ability in pre-readers related to the strength of connectivity in the arcuate fasciculus?

Background + Literature Review

To become literate, a reader must integrate the letter sounds they hear (phonology) with the letter shapes they see (orthography); difficulty with this integration has been hypothesized to be the major deficit in dyslexia (1,2). Previous research has identified brain areas that functionally support crossmodal or multi-modal letter identification (3-6), and more recent work has begun to specify related white matter tracts (7-9). The main track I will focus on is the arcuate fasciculus (AF), a pathway suggested to be involved with this audio-visual integration (7). Individuals with dyslexia demonstrate decreased connectivity along this tract (10-16). However, no studies have experimentally linked connectivity directly to integration ability in children or adults.

My current research in the DCN Lab investigates how performance on an audio-visual integration reading task is related to AF connectivity in a large sample of children with a range of reading abilities. We have found a significant connectivity-ability relationship specific to the crossmodal integration condition, wherein increased integrative performance is positively correlated with increased connectivity in the AF. This relationship was not found for the unimodal conditions. Although integration performance and connectivity have a significant relationship, the direction of causality remains unknown: Is this stronger connectivity a product of the participants' advanced ability to integrate, or does the increased connectivity exist prior to any reading instruction, leaving the child at a predisposition to integrate more effectively? I will address this question by targeting integration skills and AF connectivity in pre-readers.

Little is known about the relationship between brain structure and integration ability during this early period. Examining reading-related skills in pre-readers is a new and promising approach to investigate reading development and disorders. Pre-reader studies of disordered reading are feasible given the high heritability of dyslexia: over 40% of individuals with a first-degree relative with dyslexia (FH+) have been diagnosed (17), versus 5-10% of individuals with no family history (FH-) (18).

My goal for this project is to relate performance specifically on a crossmodal integration task to the strength of connectivity in the AF. I propose to address this question by testing FH+ and FH- 5-year-olds to assess AF connectivity prior to reading instruction. If high-risk children demonstrate decreased connectivity before instruction, these brain differences may be a causal factor of future reading deficits. Finding a specific relationship between connectivity and behavioral integration across all children will reveal factors that may impact future reading ability by suggesting that children are pre-disposed in their ability to perform on crucial reading skills. This design will thus provide a more tangible definition of reading disorders by recognizing neural predispositions or behavioral impairments.

By the end of the summer, through DTI data collection and analysis, I expect to have a more nuanced understanding of how the AF connectivity relates to integrative processing in pre-readers, and to determine whether a relationship between connectivity and ability exists with performance, and with dyslexia risk. With this knowledge, longitudinal studies can be conducted to examine the predictive ability of white matter connectivity on future reading performance.

Methodology

Participants will include 20 5-year-olds, either FH- or FH+, who have not yet entered kindergarten. Participants must be right-handed and may not have atypical developmental histories (e.g. history of a neurological disorder, premature birth, etc).

A standardized testing session will be administered to assess phonological and orthographic awareness (NIH Toolbox Oral Reading Recognition task, Letter Identification, Comprehensive Test of Phonological Processing) and general intelligence (Kaufman Brief Intelligence Test). In a second session, participants will undergo a "mock scan" in the DCN Lab to acclimate to an MRI environment. Then, an MRI scanning session, including DTI scans, will occur at the NU medical center using a Siemens TRIO 3T MRI scanner, adhering to all safety precautions. Lastly, participants will perform the integration task.

The integration task is a cross-modal letter-matching task. In the crossmodal condition, participants must determine if each letter in a series, alternating between visual and auditory presentations, matches its predecessor. Each letter will be presented for 1 second, followed by a 250msec pause. Unimodal (visual or auditory) letter-matching tasks will serve as control level responses. There will be two three-minute runs of each modality. Crossmodal versus unimodal task accuracy will be recorded as a measure of integration ability. Behaviorally, it is expected that FH+ children will demonstrate lower crossmodal task accuracy than FH- children, indicating a deficit in integration ability even before instruction.

Diffusion images will be processed using FSL to determine fractional anisotropy (FA), which reflects the degree to which a water molecule can diffuse in each direction within the brain. Higher FA values reflect greater directionality along a white-matter tract, indicating greater connectivity. The arcuate fasciculus (AF) will be identified using a standard anatomical mask. We will examine the relationship between an individual's FA at each point along the arcuate fasciculus, FH group membership, and integrative task performance using multiple regressions. We expect FH group membership to predict FA, where FH+ children will show lower connectivity. We also expect crossmodal task performance to predict FA along the AF.

Preparation

I have been an active member of the DCN Lab since October 2012. I have learned how to process DTI data using FSL, including quality control, preprocessing and group-level statistics. I have been trained to administer standardized testing sessions with 5-year-olds, and will administer my own sessions this spring. Last, I am certified through the CITI training modules to work with human subjects and have become MRI-safety trained at the NU medical school.

This summer, I will administer my own MRI scanning sessions and continue to administer standardized test sessions to participants, and conduct DTI data analysis. I can apply my strong background with DTI to specific questions and analysis and draw more informative conclusions.

Conclusion

Conducting this experiment will allow me to master the application of DTI analysis to experimentation. I expect to determine the relationship between connectivity in the AF and pre-reading integrative performance. These results will give significant insight into the fundamental deficit underlying dyslexia and address the impact of genetic predisposition on the ability to perform integrative reading skills.

My experience with such structural brain imaging techniques and neuroscience research design will promote my eventual goal of becoming a neurologist. My passion is to better understand human nature by studying the mental and physical health of others, and continuing my research at the DCN Lab with this novel experiment will undoubtedly promote that.

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