a place of mind
THE UNIVERSITY OF BRITISH COLUMBIA

ARROWSMITH BRAIN IMAGING STUDY: END OF YEAR 1 UPDATE AND FUTURE PLANS

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OVERVIEW

Learning disabilities affect one in 10 Canadians, compromising their ability to acquire the fundamental skills of reading, writing, and mathematics. The challenges associated with learning disabilities may extend beyond school to other domains such as social skills, seriously hindering a child's ability to reach their full potential in life.

Recent advances in neuroimaging and neuroscience have led to an enormous growth in the understanding of the brain's capability to change, which is termed neuroplasticity. Given this new understanding of the dynamic nature of the brain, there is now acute interest in learning to exploit it to refine learningi based interventions to optimize outcomes and enhance function. One such learningi based intervention is the Arrowsmith Program, which was designed to identify and strengthen deficient cognitive functions that are thought to be a source of specific learning disabilities in children. Enhancing our understanding of what brain functions and structures are affected by interventions such as the Arrowsmith Program is critical to determining their effectiveness and refining their utility.

The University of British Columbia (UBC) partnered with the Vancouver-based Eaton Arrowsmith School to advance our mutual interest in exploring the scientific validity of neuroplasticity in youth. The research team is led by Dr. **Lara Boyd**, PT, PhD, Professor of Physical Therapy and Canada Research Chair in the Neurobiology of Motor Learning. The study represents an essential first step in expanding our understanding of how neuroplastic change may be operationalized in children with learning disabilities and what types of change are stimulated by the Arrowsmith Program. The seed funding provided by the Eaton Foundation was successfully leveraged to secure additional funding for a much larger pilot study, which will provide the preliminary data needed to design a large-scale assessment of the Arrowsmith Program's impact on brain plasticity. The published findings are also expected to catalyze future work in this area, which may lead to the development of novel educational interventions that optimally stimulate learning in children.

The team will continue to increase the size of the control group, add testing of social and emotional development associated with the intervention, fund a full time post-doctoral fellow and continue to follow children in the Arrowsmith group and matched controls through their second year of the program. This type of longer term follow up and analysis is critical as changes in the brains and behaviour of these children will undoubtedly continue to occur over the second year. More children are interested in participating in the study, but funding must be secured to allow them to enroll. The results of the expanded pilot study are expected to come out in Spring 2017.

EXPERIMENTAL OVERVIEW

No brain imaging data that characterizes the impact of the Arrowsmith Program has been published to date, and this is the first brain imaging study to explore the impact of the Arrowsmith Program. The aims of the pilot study are:

1) To provide information regarding the feasibility of brain imaging in this population, and
2) To generate preliminary data to power and motivate future studies of the Arrowsmith Program with larger scope.

The first aim has already been accomplished; brain imaging is feasible in this population. The second aim will be accomplished once the larger control groups are recruited and tested.

To begin to assess how the Arrowsmith Program may alter the brain, we employing a multiple time point design to capture neuroplastic change associated with training in children with a learning disability. Each child enrolled will already have a diagnosis of learning disability. Educational psychologists confirm the diagnosis and administer a battery of educational and cognitive tests. Multiple forms of imaging take place, including structural (T1 anatomy, myelin water imaging) and functional (resting and taski based functional MRI).

Initially, we set out to test 20 children: 10 from the Arrowsmith Program and 10 matched typically developing controls. By leveraging the seed funding provided by the Eaton Foundation, we have nearly tripled the number of children enrolled in the study. At this time (Fall 2015), 56 participants have been enrolled. Given the variability in how children learn and develop, the ability to enroll a larger sample has significantly increased our power to detect differences. This is a tremendously exciting development. We are now planning to study a total of 90 children from three groups: 1) children with learning disabilities who are enrolled in the Arrowsmith program, 2) children with learning disabilities who are enrolled in other educational programs, and 3) typically developing children who are matched for age and sex.

So far, we have tested (or are in the midst of testing) 32 children from the Arrowsmith Program. These children and their families have come from Eaton Arrowsmith schools in Vancouver, White Rock, Victoria, and Seattle/Redmond, Washington. We have also 14 children with learning disabilities who are not in the Arrowsmith Program and 10 children who are typically developing and do not have a learning disability. Our focus moving forward is to locate and enroll more children in the two control groups.

INTERVENTION

Children in the Arrowsmith Program continue with their regular education, which includes the engagement of the student in six 40-minute blocks of Arrowsmith cognitive exercises, five days per week. Children in the control group are necessary to control for the effects of development and educational exposure. Control participants will be matched for age, gender, handedness, years of education, and type of learning disability. A typically developing control group was added to the study to factor in the effects of development on the measures. Recruitment of the controls is off by one year from that of the Arrowsmith group by design; this allows for careful matching across the three groups.

For each group, three brain imaging time points took place, separated by one year. Cognitive testing was completed at the beginning of the study (in the fall) and again at the end of the school year (in June), as a delay is required between many of the tests being employed. During the study, all children completed their normal coursework as assigned. Each child will be scanned three times (at the beginning, middle, and end of the school year).

KEY FINDINGS TO DATE

At this point, the research team has performed interim analyses on the first 40 study participants (28 from Arrowsmith, 15 learning disabled controls, and 7 typically developing controls). In our examination of baseline data across our whole sample, we have discovered a strong relationship between myelination in the corpus callosum and reading ability (Fig. 1). This finding is important as it supports other work that suggested that callosal integrity is important for word attack. Our data extend these past findings and demonstrate a specific neurobiological substrate. Understanding the brain-behaviour relationships that are key to academic achievement during development illustrates biomarkers that may be shifted with interventions and can also serve as therapeutic targets.

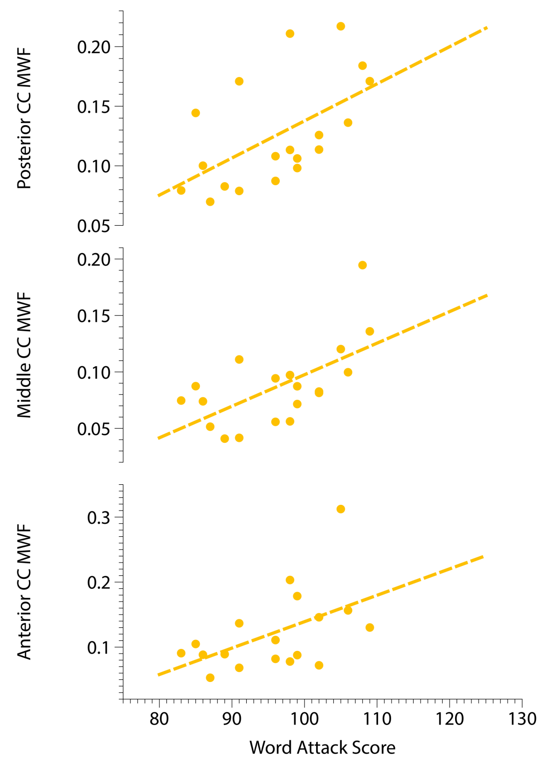

Fig.1. Relationship between corpus callosum myelin water fraction and word attack score.

We have also considered how the size of certain brain regions may relate to educational ability. This approach relies on the ability to understand the morphometrics of the brain. Here we discovered that a larger right insular cortex is evident in children with higher math ability (above a normalized score of 100), as measured by the Woodcock-Johnson III test (Fig. 2). This finding is very interesting in light of our functional MRI findings (see below) that indicate the insula is activated during one of the signature Arrowsmith cognitive exercises, the clocks task. Although these data are preliminary, they suggest that improvement on clocks may alter insular structure and function, and that perhaps these alterations in brain may promote changes in math ability.

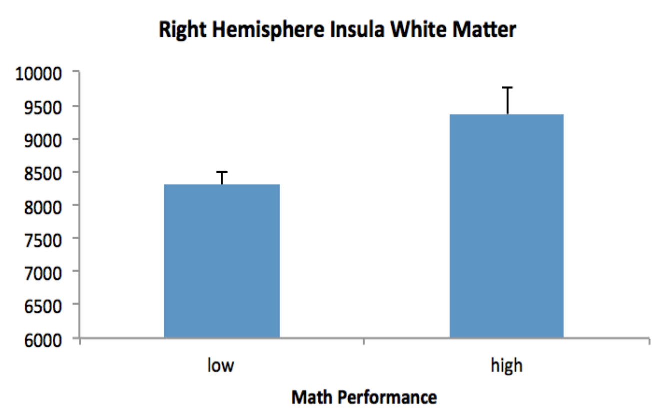

Fig. 2. The right insula is larger in children with higher math performance scores (as measured by the Woodcock-Johnson III).

We also conducted analyses of brain function during the clock task. In this work, we note that a unique network is activated in association with increased proficiency with this task (Fig. 3). Notably, the children with learning disability in the Arrowsmith group demonstrate significant activity in the insular cortex while performing the task when time points 1 and 2 are contrasted.

Finally, we have considered the effect of the program on resting state brain activation. Interestingly, we note very low amounts of activity in the prefrontal cortex at time point 1 in children with learning disability (Fig 4A). However, after just three months in the Arrowsmith Program, this activity has shifted such that a small yet notable prefrontal region of activity is emerging (Fig 4B). This is much more similar to normal and suggests that the Arrowsmith Program may be helping to facilitate a more normal resting state pattern of brain activity. A full analysis of all data will be required to confirm this finding, yet our early data are highly encouraging.

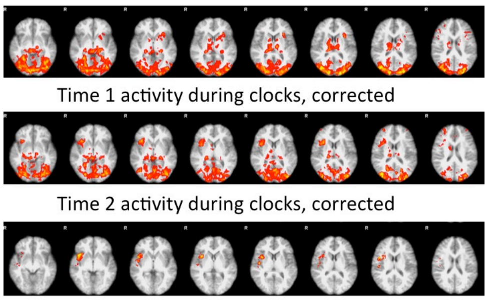

Fig. 3: Functional MRI data during clocks task at time points 1 and 2. The unique network is shown in the lowest panel.

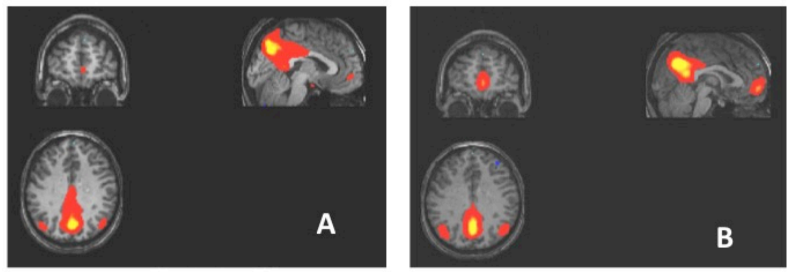

Fig. 4: Resting state functional MRI data from time points 1 and 2. Note the emergence of a frontal network at time point 2.

We have already been able to present and publish in abstract form data from time point 1 that characterizes the relationships between brain function and educational ability (Lakhani et al. (2015) Organization for Human Brain Mapping). These results show that myelination increases with age and confirms past work in this field. The presentation of this work catalyzed a new method where structural and segmented brain data could be merged to generate highly specific cortical maps. After working to optimize this approach for the past three months, we recently completed a full re-analysis of our data. We are presently interpreting these results. It is important to note that this work catalyzed both a unique approach to understanding how learning disability affects the brain and also a new method that we are applying in other work considering stroke and diabetes. As such, it has had a large impact on the neuroimaging field in general.

FUTURE PLANS

Additional funding will enable us to continue recruiting children to the study until the goal of 90 participants in the intervention group and two control groups is achieved, as well as to continue following the children in the intervention group through their second year of the Arrowsmith Program. The additional study participants will be invaluable in generating enough power to detect significant differences among the children, and these data will be crucial in determining the long-term impact of the Arrowsmith Program on children who have received this training.

A new aim in our research plan is to build a more complete picture of how the Arrowsmith Program impacts social and emotional health in children. To accomplish this goal, we are now collaborating with Dr. Kim Schonert-Reichl, an expert in indexing social and emotional health in children (Schonert-Reichl, K.A. et al. *Developmental Psychology*, 2015, 51:52-66). Dr. Schonert-Reichl was originally a teacher, has a PhD in Education and directs the Human Early Learning Partnership at UBC. She and Dr. Boyd are collaborating to consider the question of how varied educational interventions impact social and emotional health, as well as patterns of neuroplastic change. This collaboration arose in response to the subjective observation of large amounts of change in the affect of the children who are participating in the Arrowsmith Program. We suspect that new successes associated with this program are impacting the overall emotional well-being of the children who are enrolled in the Arrowsmith intervention. If so, this would be a critical discovery.

School is the first place where many children are exposed to a larger social world beyond the family, and it is during school years that children gradually acquire the social skills necessary to succeed in a complex world. Growing up without essential social and emotional skills such as compassion and empathy can lead to lifelong mental illness. By 2020, it is estimated that mental illness will represent one of the leading health care cost in the world. Further, children with learning disabilities are at higher risk for developing mental illness as adults, and suffer from greater rates of depression and anxiety as compared to their peers. Thus, a program that facilitates social and emotional health in children with learning disabilities has to potential to mitigate the development of serious mental illness and profoundly impact lives.

The addition of Dr. Schonert-Reichl's testing will not significantly increase either the testing burden on children or the costs associated with the study. Her battery of tests is computerized, can be completed in 1-hour sessions, and includes child self-report of: empathy, perspective taking, optimism, self-control, anxiety, social responsibility, and depressive symptoms (Schonert-Reichl et al., 2015). Our plan is to add this to our existing battery of testing in an effort to consider how the social and emotional health of children who are in the Arrowsmith Program compares to both children with learning disabilities in other programs and typically developing children.

As we work to complete the pilot study and prepare for the largei scale assessment of the Arrowsmith program's impact on brain plasticity, we will also explore opportunities for interdisciplinary collaboration with the Faculty of Medicine's Human Early Learning Partnership (HELP). Current and future studies will advance knowledge in both education and neuroscience to further enhance the Arrowsmith Program and other educational interventions that stimulate learning in children and support them in reaching their full potential.