A Brief Intensive Learning Intervention Affects Resting State Connectivity and Neuropsychological Test Performance

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Gregory M. Rose and Audreyana C. Jagger-Rickels

Departments of Anatomy and Physiology, Southern Illinois University School of Medicine, Department of Psychology, Southern Illinois University, and VA Boston Healthcare System

Introduction

- Cognitive training represents a potentially valuable tool for treating conditions that are unresponsive to drug therapy, or for which no clearly effective therapy has been developed.
- The present study evaluated the effects of a 6-week period of intensive training on a single task designed to strengthen the integration and synthesis of information.
- The study population consisted of students with learning disabilities, ranging in age from 10-19.
- Resting state functional connectivity in networks (Default Mode, Dorsal Attention, Salience, and Frontoparietal Control) thought to be involved in information processing was evaluated using fMRI.
- Formal neuropsychological testing was performed using components of the Woodcock-Johnson IV battery.

Materials and Methods

Participants

Participants (n = 49) were male and female students in the Cognitive Intensive Program (CIP) held during the summers of 2017-2019 at the Arrowsmith School in Toronto, Ontario, Canada. The average age was 13.4 years old (SD = 2.4). Informed consent was obtained from parents of participants under 18 years old, as well as child assent. Students aged 18 or older gave informed consent.

Training

Arrowsmith Symbol Relations Task

The training exercise consisted of the Arrowsmith Symbol Relations Task, a computer-based sustained visual-spatial processing task of progressively increasing difficulty. Subjects are presented with an analog clock face, initially showing only one hand. The subject uses a keyboard to enter a value for the hour shown. Feedback on the computer screen indicates whether the response is correct or incorrect. If the response was incorrect, the subject continues to respond until the correct response is entered. After this, a new clock face is shown. Once subjects reach a criterion of 90% accuracy over a series of consecutive responses, an additional hand is added to the clock face (e.g., hours and minutes). This process continues until up to 10 hands have been added to the clock differentiated by a combination of thickness, length, and color. Students in the CIP work 30 to 40 minutes per session on this task with a break and up to five hours per day, five days per week, for six weeks. Subjects are assigned a level of proficiency (1-12) based upon an assessment of their accuracy at the various levels of the task.

Magnetic Resonance Imaging

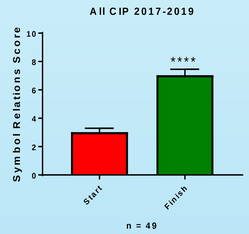
Resting-state fMRI images were collected at the beginning and end of the six-week program using a Siemens 3T scanner with 20-channel head coil at the Toronto Hospital for Sick Children. Structural scans were obtained using the Siemens default MPRAGE protocol. During the subsequent 8-minute resting-state functional scan (TR = 4 sec, TE = 30 msec; 120 volumes) participants were told to keep their eyes open to view a cross hair on a screen and to think of nothing in particular. The scans were pre-processed and analyzed using the CONN toolbox (version 17f; www.nitrc.org/projects/conn, RRID:SCR_009550).

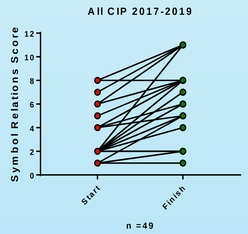
Neuropsychological Testing

Assessments were performed at the beginning and end of the program, and were administered by a professional psychometrist. Testing consisted of elements from the Woodcock-Johnson IV batteries for Cognitive Abilities and Achievement. The data are expressed as W scores to accommodate expected age differences in ability.

Results

Symbol Relations Training

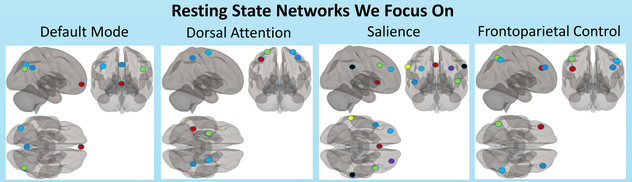




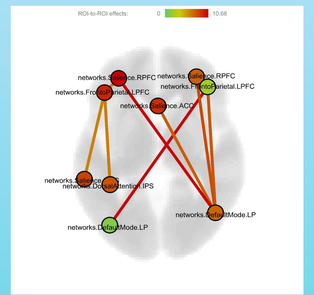
Overall, intensive training resulted in significant improvement in the Symbol Relations task (left). However individual performance varied considerably (right). Multiple identical scores explain the reduced number of points in the right-hand plot.

Imaging

Resting State Networks We Focus On

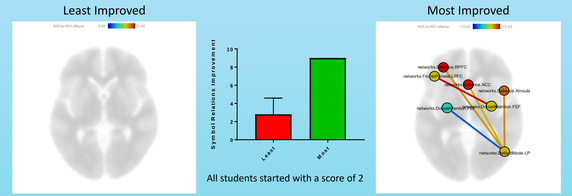


Symbol Relations Training Strengthens Network Connectivity



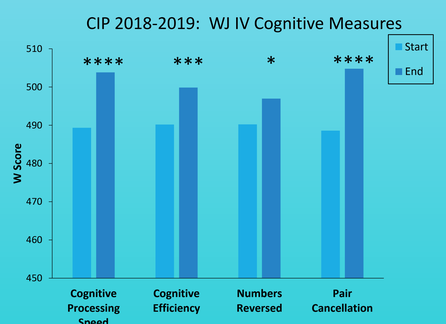
Axial view of changes in resting state network connectivity after Symbol Relations training in 22 subjects who gave permission to be imaged. Warmer colors indicate relatively stronger increases in connectivity between network components (p-FDR values range from < 0.02 - < 0.05). Changes are proportional to Symbol Relations improvement. Most of the sites are within or between the Salience and Default Mode networks, although sites in the Dorsal Attention and Frontoparietal Control networks are also involved.

Network Changes Require Performance Improvement



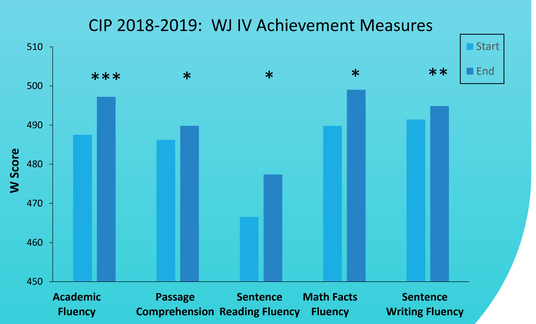
Analysis of subgroups (n =5 per group) who showed either the least or the most improvement in Symbol Relations performance showed that no changes in network connectivity were seen in subjects who made minimal progress., in contrast to the changes seen in subjects who made maximal progress.

Neuropsychological Testing



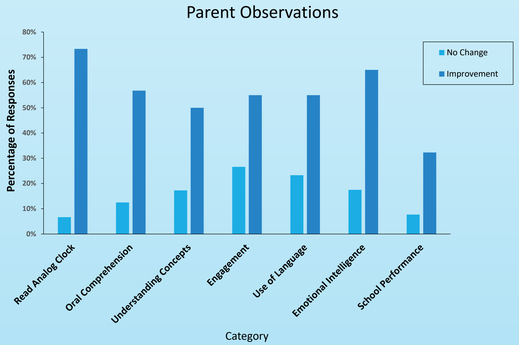
*p < 0.05,***p < 0.001, **** p < 0.0001, paired t-tests (n = 27)

Woodcock Johnson testing of the 2018 and 2019 cohorts revealed significant improvements in several measures of cognition, including the categories of cognitive efficiency, processing speed and working memory. Additional tests given in only one year showed significant improvements in fluid reasoning, visual-auditory learning, and vocabulary, but these data need to be replicated. WJ Achievement measures, developed to predict academic performance, were significantly improved in all areas evaluated.



*p < 0.05, ** p < 0.01, ***p < 0.001, paired t-tests (n = 27)

"Real World" Consequences of Symbol Relations Training



To begin to determine whether Symbol Relations training affected function in every day life, parents were asked to respond to a 50-item questionnaire given approximately three weeks after the beginning of the school year. Responses are grouped into broad categories. Functional decline was not seen in any area. As expected, the ability to read an analog clock face showed greatest improvement. Interestingly, substantial improvements were also seen across the categories evaluated. Scores for "Not a Concern" or "Can't Tell" were not included, so percentages do not add up to 100%. "Can't Tell" comprised approximately 50% of School Performance responses, as might be expected early in the academic year. The survey will be repeated at the end of the school year.

Summary

- A six-week period of intensive training in the Symbol Relations task causes changes in the strength of resting state networks thought to be involved in cognitive processing.
- The increases in functional connectivity are proportional to the degree of improvement in the Symbol Relations task. Most of the changes are between nodes in the Default Mode and Salience networks.
- Neuropsychological testing showed group level improvements in a broad range of cognitive and achievement measures. Only improvements in Pair Cancellation were found to be significantly related to Symbol Relations improvement (data not shown).
- Preliminary data suggest that everyday activities are also improved after Symbol Relations training. Studies are in progress to determine if these effects are lasting.

Acknowledgements

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Arrowsmith PROGRAM Strengthening Learning Capacities