Correlation of Cognitive Training Gains and Resting State Functional Connectivity

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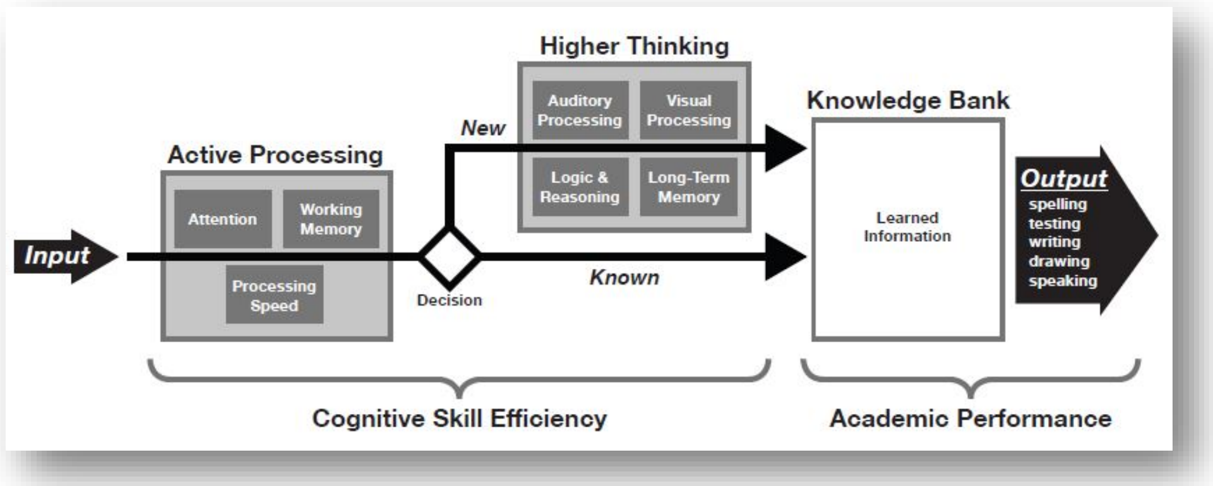
INTRODUCTION

Cognitive training programs improve cognitive ability by strengthening individual cognitive skills essential to learning. LearningRx cognitive training programs are grounded in Cattel-Horn-Carrol theory of intelligence and target the training of 7 primary skills and 25 subskills, including attention, working memory, processing speed, auditory processing, visual processing, logic and reasoning, and long-term memory.



Training is through repeated engagement in game-like mental tasks over a 60-90 hours. Throughout training intensity progresses by increasing cognitive load, use of a metronome and timer, and incorporating distractions. ThinkRx, the foundational training program, is typically delivered by a clinician using a one-on-one training model. A digital version of ThinkRx, called Brainskills, is used to scale the intervention in schools and learning centers. The comprehensiveness and intensity of the LearningRx training programs, and the one-on-one delivery of ThinkRx, make them unique from other cognitive training programs.

In a randomized control study the ThinkRx and Brainskills cognitive training programs were implemented in a school setting. Training efficacy was assessed using neuropsychological testing and measures related to school attitude and performance (Hill et al., 2016). For insight into training-induced performance changes, neuroimaging with functional MRI was performed.

Study Objective

The **primary objective** of this work was to identify changes in resting state functional connectivity associated with cognitive training.

The **secondary objective** was to identify changes in resting state functional connectivity that correlated with changes in cognitive construct measures.

The hypothesis is that intensive, multi-faceted cognitive training will drive brain plasticity evidenced by changes in resting state functional connectivity and a correlation of changes to performance measures.

METHODS

Study Design

- 225 high school students were randomly assigned to one of three groups:
  60 hours Cognitive Training with ThinkRx, 60 hours Cognitive Training with Brainskills, or Control.
- 30 of the 225 students were randomly assigned to have functional MRI exams before and after training:
  Cognitive Training with ThinkRx (n=11); Cognitive Training with Brainskills (n=12); and Control (n=7).
- For connectivity analyses cognitive training groups were combined giving two groups:
  Cognitive Training (n=23); and Control (n=7).

Neuropsychological Testing

Pre and post testing of cognitive constructs was conducted using Gibson Test of Cognitive Skills (V1), including Processing Speed, Logic & Reasoning, Visual Processing, Working Memory, Long-term Memory, Verbal Memory, Auditory Memory, Auditory Segmenting, and Auditory Dropping.

Image Acquisition

MR imaging was performed on a 1.5T GE MR scanner. Connectivity analyses were performed using a high-resolution T1-weighted anatomical image and a single 5-minute EPI-BOLD resting state acquisition (TR=3s).

Image Processing and Analysis

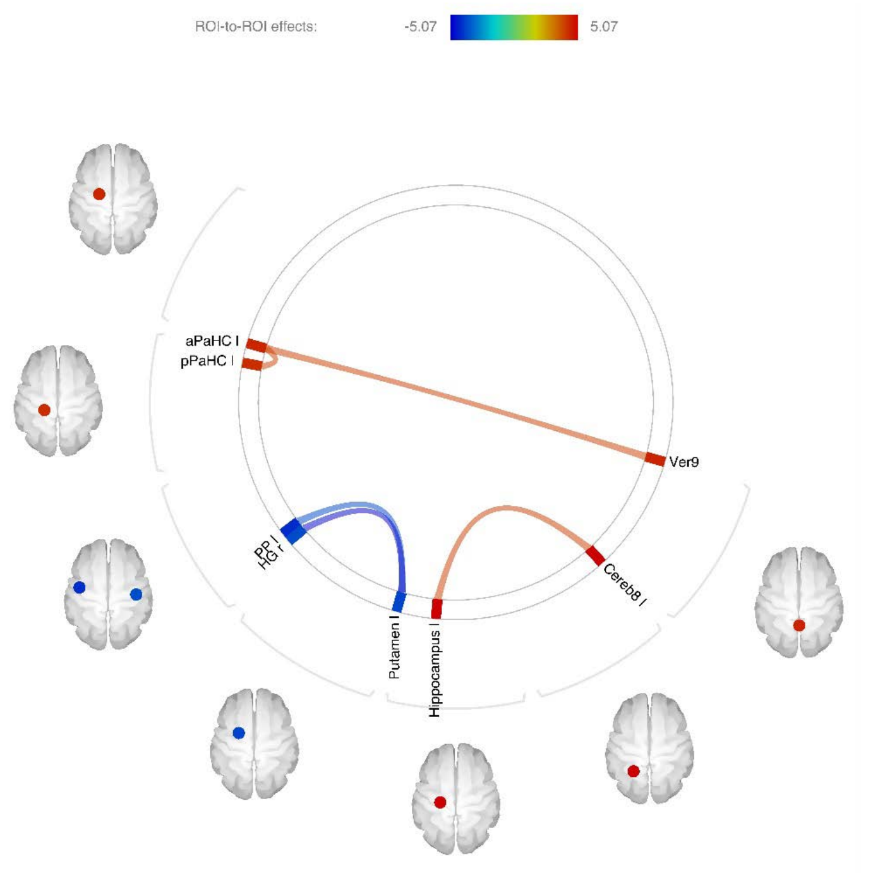
Preprocessing (slice timing, motion correction, artifact reduction and scrubbing, co-registration, spatial normalization, and smoothing), CompCor correction, and first and second level ROI to ROI analyses were performed using SPM12 and the CONN toolbox.

Repeated measures ANOVA with one within-subject factor (rest post > rest pre) and one between-subject factor (treatment > control) was used to identify the effect of cognitive training.

Correlation analyses using pre vs post connectivity and each cognitive construct change score were used to identify the simple effect of each cognitive construct on connectivity.

RESULTS

Overall Effect of Cognitive Training



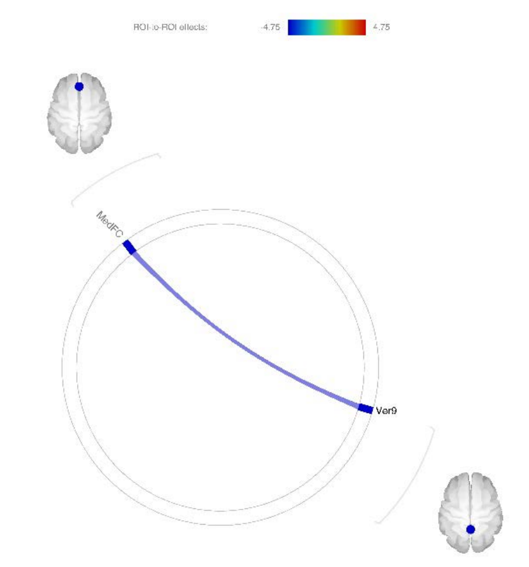
Treatment vs control, pre to post changes

p-FDR corrected < 0.05

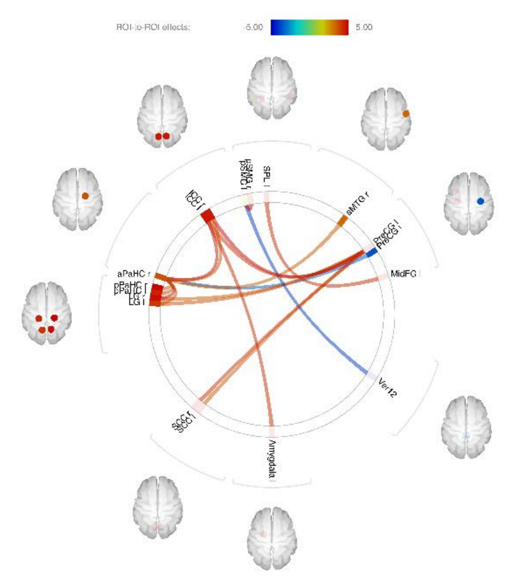
	T(28)	p-FDR
Parahippocampal Gyrus, anterior left Vermis 9	4.08	0.028
Parahippocampal Gyrus, anterior left Parahippocampal Gyrus, posterior left	4	0.028
Hippocampus left Cerebelum 8 Left	4.09	0.045
Putamen left Heschl's Gyrus Right	-5.07	0.0031
Putamen left Planum Polare Left	-3.8	0.0478

Correlation of Treatment Group Changes in Connectivity to Changes in Cognitive Test Scores

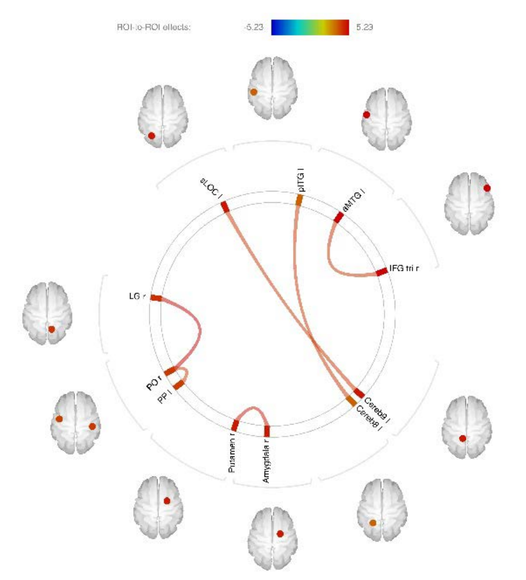
Processing Speed



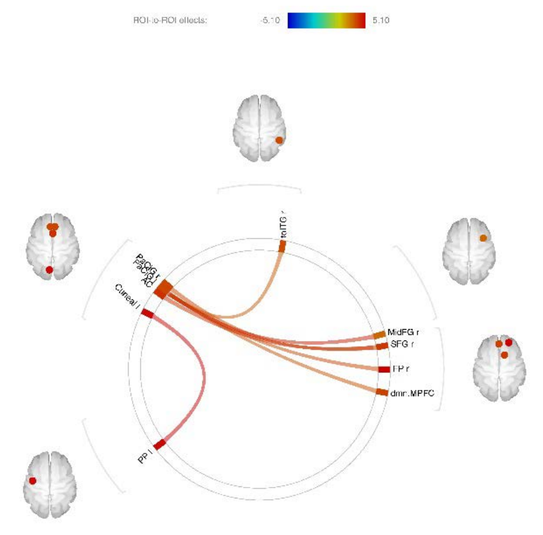
Logic & Reasoning



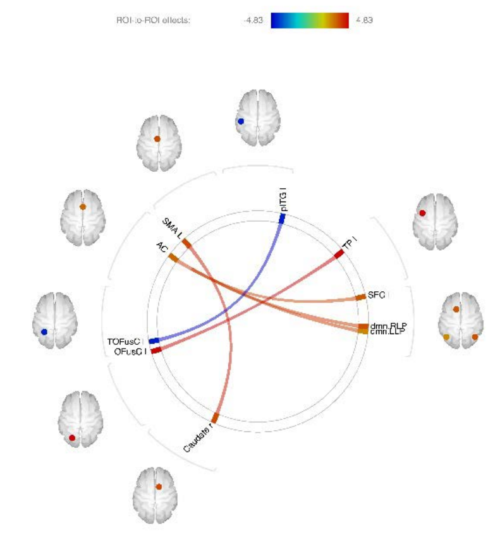
Visual Processing



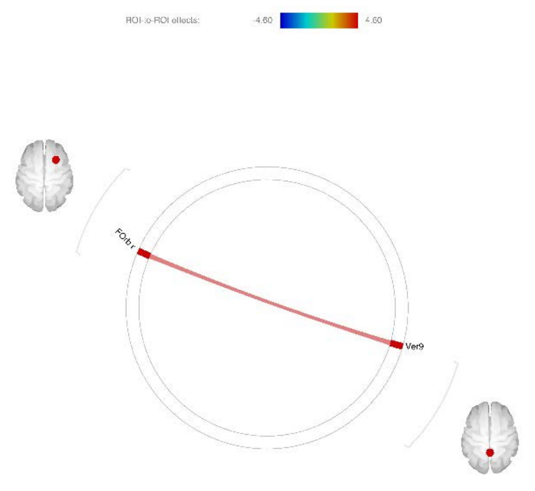
Working Memory



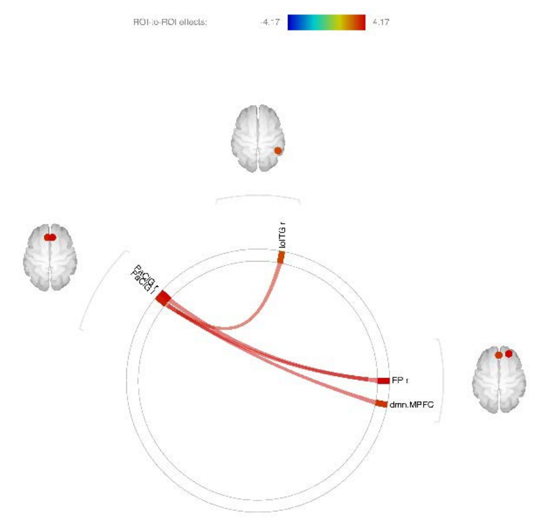
Long Term Memory



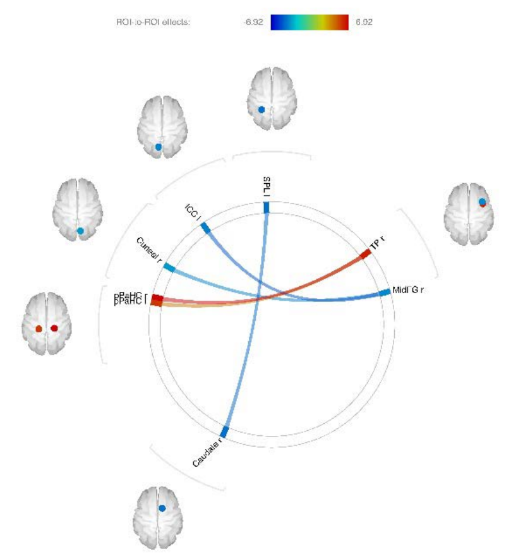
Visual Memory



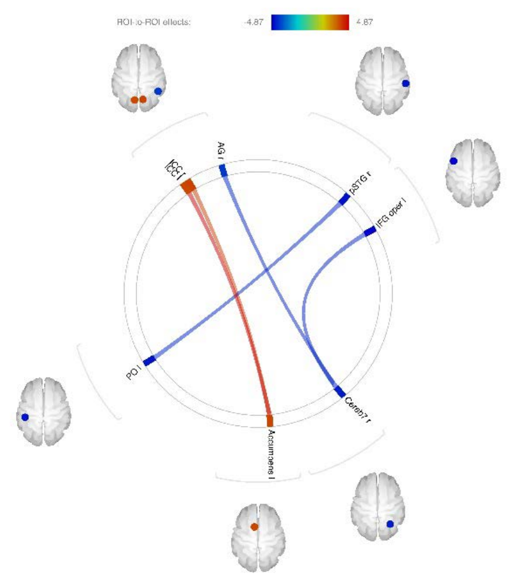
Auditory Memory



Auditory Dropping



Auditory Segmenting



All connectivity maps p-FDR corrected < 0.05

DISCUSSION

Cognitive training was associated with changes in connectivity between several regions that have key roles in cognitive processing including, the parahippocampus (paHC), auditory areas of the temporal lobe, putamen, and cerebellum.

Many functions have been ascribed to the paHC, but recent findings suggest that the common underlying role of the paHC is in processing information with contextual associations. Contextual associations are a unifying element underlying many higher-level cognitive processes that the paHC has been associated with, and that are trained in cognitive training, such as visual processing, memory encoding and memory retrieval (Aminoff, 2013).

In addition to their roles in motor function, the putamen and cerebellum are actively involved in cognitive processes. The putamen contributes to functions such as episodic memory, cognitive control, and learning. The cerebellum contributes to functions such as memory, language, associative learning, and sequencing (Buckner, 2013; Popa, et al., 2014).

Heschl's gyrus (HG) and the planum polare (PP) are areas in the temporal lobe associated with auditory processing. HG is part of the primary auditory cortex. The left PP coincides with Wernicke's area and has a critical role in language function (Shapleske, et al., 1999).

Cognitive training induced changes in connectivity correlated with performance change scores on each of the 9 cognitive construct measures.

CONCLUSIONS

- Multi-faceted, intense cognitive training resulted in significant changes in resting state functional connectivity between key brain regions associated with cognitive processes including, visual processing, auditory processing, and memory.
- Training-induced changes in brain connectivity correlated with performance measure changes supporting the hypothesis that cognitive training can drive brain plasticity. As performance measures for each cognitive construct were distinct from training tasks, these findings provide support for a transfer effect of LearningRx cognitive training.

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