MRI and Neuropsychological Outcomes of Cognitive Rehabilitation Training for Repetitive Sports Concussion

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Background and Prior Research: Repetitive concussions along with post-concussion syndrome are a growing concern for athletes, especially student athletes.
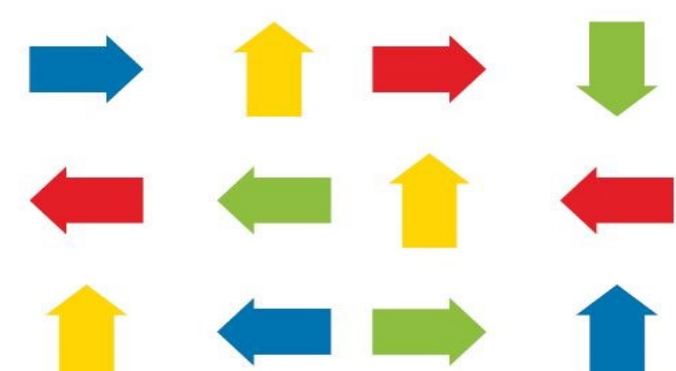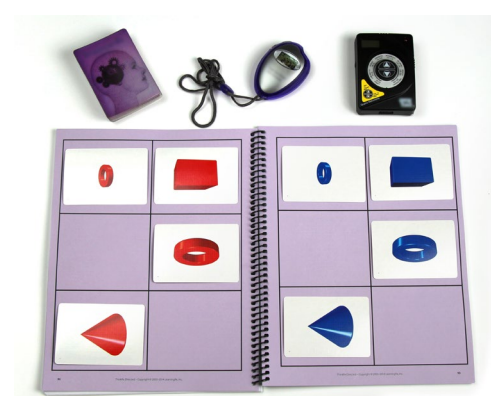
- Cognitive deficits typically involve memory, processing speed, attention, and reasoning skills, and may persist beyond the recovery period following these "mild" traumatic brain injuries (mTBI).
- Post-concussion symptoms may also add headache with noise and light sensitivity, dizziness, fatigue, irritability, insomnia, loss of concentration, slow reaction time, depression, and anxiety.
- Neuroimaging studies have reported abnormal brain connectivity, specifically in the Default Mode Network (DMN), the most robust resting state network.
- DMN neural correlates include the medial prefrontal cortex (MPFC), posterior cingulate cortex (PCC), and the left and right inferior parietal (warm colors in figure).
- Anticorrelated with the DMN are attention regions including left and right frontal poles and the left and right temporal (cool colors).
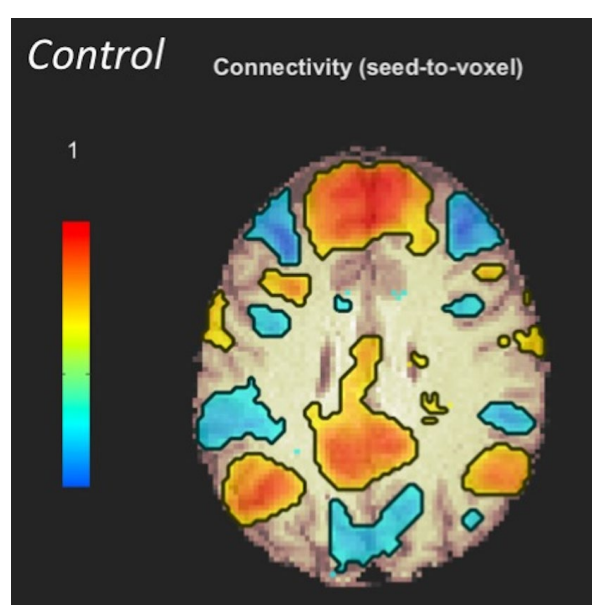- Reports of both hyper and hypo DMN connectivity have been reported in mTBI[1].

- We have reported significant improvements in cognitive constructs in multiple published studies on ThinkRx with diverse samples[2-4] including a large observational study of clients with mild to moderate TBI (n = 329)[5].
- Results included significant gains across all cognitive constructs.

Default Mode Network

Control — Connectivity (seed-to-voxel)

TBI Client Outcomes

ADULTS (Ages 18+), n = 190

CHILDREN (Ages 6-17), n = 139

ThinkRx Cognitive Training Intervention: ThinkRx (LearningRx®) is an intensive, one-on-one, clinician-delivered cognitive training program where multiple cognitive skills are remediated through repeated engagement in game-like but rigorous mental tasks.
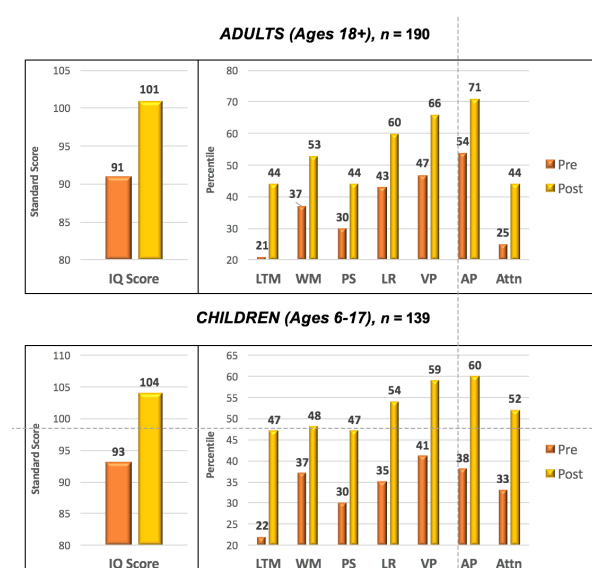- The key cognitive components of training include: working and long-term memory, processing speed, auditory and visual processing, logic and reasoning, and attention.
- A metronome, timer, and manipulatives are used to deliver intense, fast-paced tasks while providing dynamic feedback and motivation.
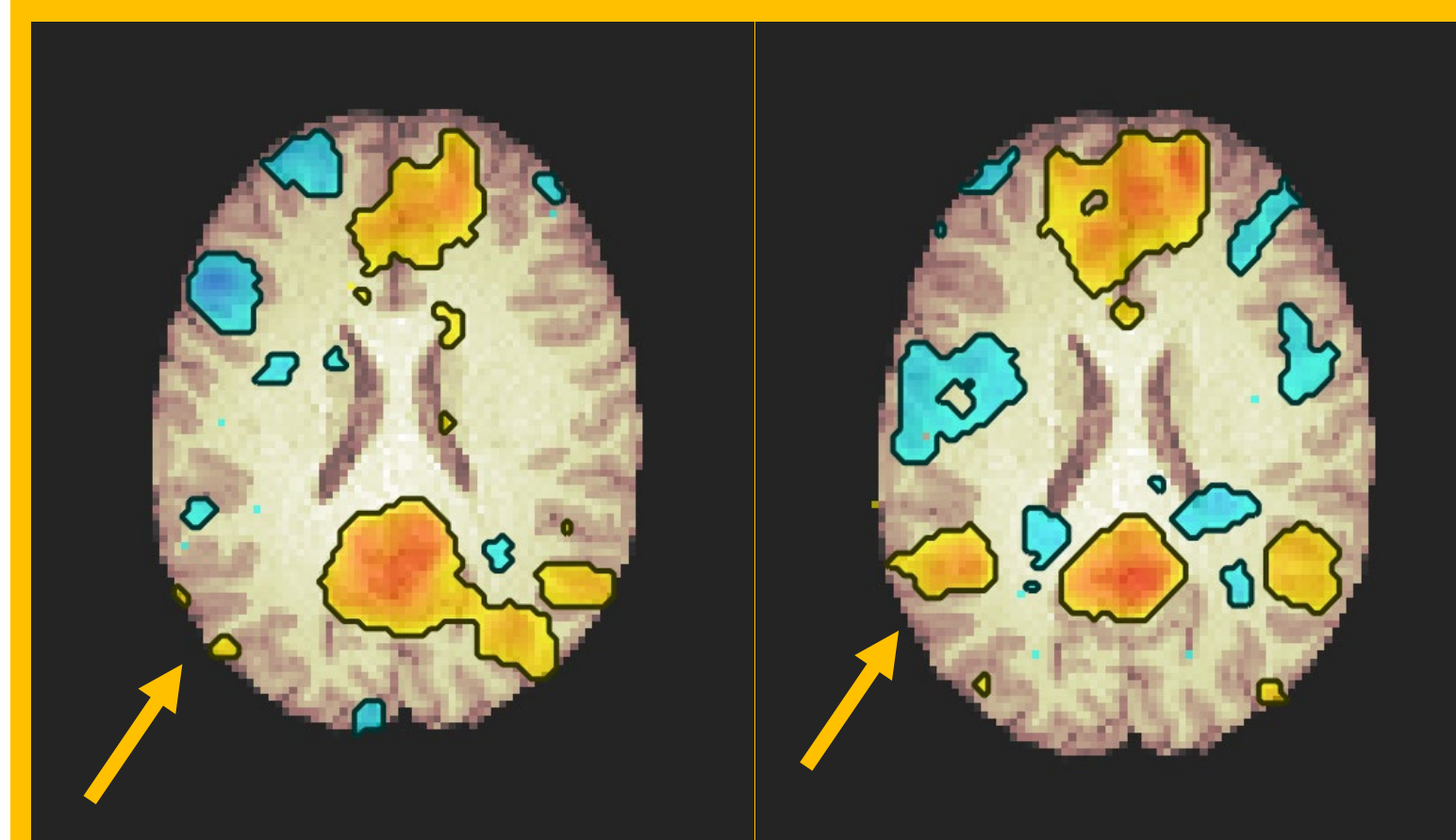- Training sessions are typically 90 minutes at least three days per week.

References:

[1]Zhou, Y., Milham, M. P., Lui, Y. W., Miles, L., Reaume, J., Sodickson, D. K., ... Ge, Y. (2012). Default-mode network disruption in mild traumatic brain injury. Radiology, 265(3), 882–892.
[2]Ledbetter, C., Moore, A.L., Mitchell, T. (2017). Cognitive effects of ThinkRx cognitive rehabilitation training for eleven soldiers with brain injury: A retrospective chart review. Frontiers in Psychology, 8(825).
[3]Carpenter, D., Ledbetter, C., & Moore, A.L. (2016). LearningRx cognitive training effects in children ages 8-14: A randomized controlled study. Applied Cognitive Psychology, 30(5), 815-826.
[4]Moore, A.L., Carpenter, D.M., Miller, T.M., & Ledbetter, C., (2019). ThinkRx Cognitive Training for Adults over Age 50: Clinician-Caregiver Partners in Delivery as Effective as Clinician-Only Delivery. Psychology and Neuroscience, 12(2), 291-306.
[5]Moore, A.L., Ledbetter, C., & Carpenter, D. (2018). Neuropsychological assessment outcomes following cognitive rehabilitation training for children and adults with traumatic brain injury. Presented at Society for Neuroscience, November 2018, San Diego, CA.

In a student athlete with a history of **repetitive concussions and post concussion syndrome,** cognitive rehabilitation with ThinkRx – an intense, clinician delivered, multi-faceted cognitive training program, resulted in **normalization of the default mode network (DMN)** and a **24 point increase in general intellectual ability score (IQ).**
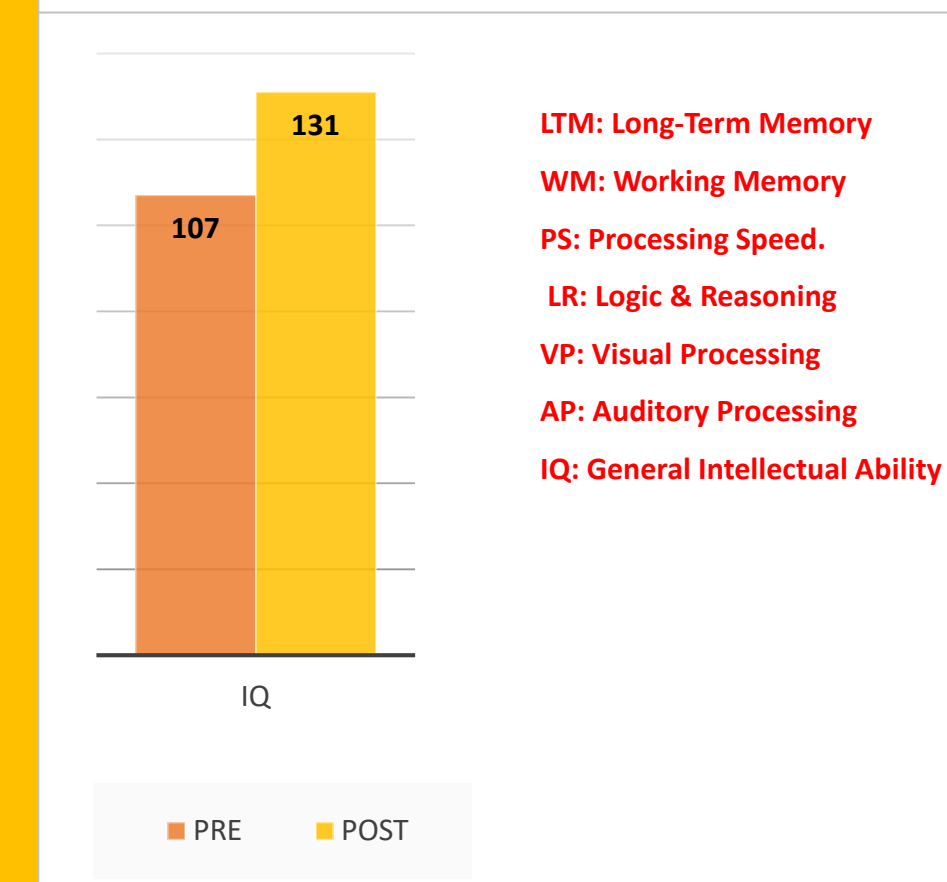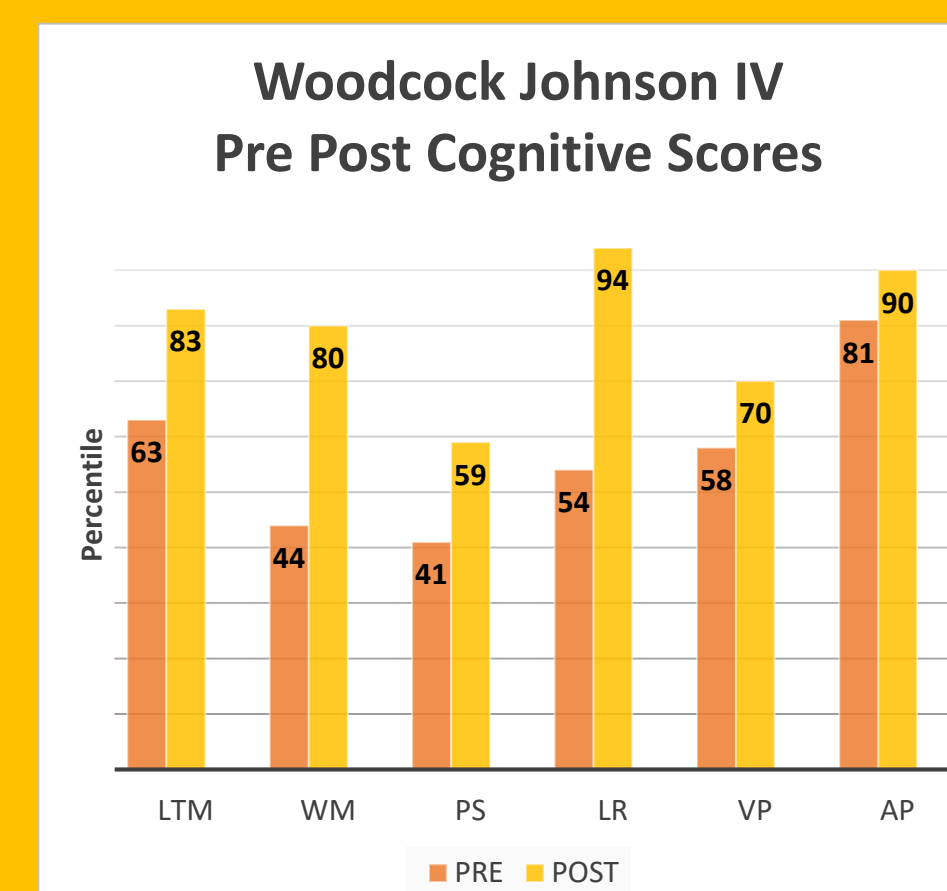

Pre
- **DMN: loss of MPFC connectivity with the left parietal node (arrow)**
- **Minimal anti-correlated activity (blue) with attention network**

Post
- **DMN: reintegration of left parietal node connectivity (arrow)**
- **Increased areas of anticorrelation (blue) with attention network**

Woodcock Johnson IV Pre Post Cognitive Scores

LTM: Long-Term Memory
WM: Working Memory
PS: Processing Speed.
LR: Logic & Reasoning
VP: Visual Processing
AP: Auditory Processing
IQ: General Intellectual Ability

Objective: Using an interventional single case study pre-post trial design, cognitive and neuroimaging changes following cognitive rehabilitation training were evaluated in a student-athlete with repetitive concussions and post-concussion syndrome.

Patient: 20-year-old male who was a high-school athlete. He suffered 5 concussions and was suffering from post-concussion syndrome 12-months post-injury.

Intervention: The ThinkRx cognitive training program was delivered as 40 training sessions each lasting 90 minutes over five months.

Outcome Measures & Methods: Training-induced changes were assessed using MRI imaging and neuropsychological assessments including the Woodcock Johnson IV.

- Brain connectivity was assessed using resting-state functional MRI of the Default Mode Network. Imaging was performed on a Seimens 3T Ingenia MR System, with 240 images acquired during the resting state (TR=3sec). Image analysis was performed using SPM and the CONN toolbox.
- Neuropsychological assessment was completed using full scale IQ and individual cognitive constructs measured by the Woodcock Johnson IV. Executive functioning was measured by the Comprehensive Executive Function Inventory. Emotional competency was measured by the Patient Competency Rating Scale for TBI.

Results:
- Dramatic normalization of the Default Mode Network with normalized increased connectivity between the left parietal node and the medial prefrontal cortex.
- Full scale IQ score improved by 24 points along with gains in all individual constructs, including large jumps from the 54th to 94th percentile in logic and reasoning, 44th to 80th percentile in working memory, and 63rd to 83rd percentile in long-term memory test.
- Executive function (EF) improved by 30 points. Improvements in executive functioning were noted across skills as reported by both the patient and his parents. The patient rated all of his executive functioning skills as "low" or "very low" prior to cognitive training. After training, all EF skills were in the average range for his age, including ratings on attention.
- Self-reported impairment in emotional competency decreased from moderate to mild, and parent-reported impairment in emotional competency decreased from mild to none.
- After training, the patient returned to school, was able to actively participate in conversations again, reported that 'brain fog' had lifted, and had a hopeful outlook for his future.

Conclusions: The improvements across outcome measures suggest the use of a comprehensive, clinician-delivered one-on-one cognitive rehabilitation training program may be a viable option for remediating the cognitive and neural deficits associated with post-concussion syndrome in an otherwise healthy young athlete.

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