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Neuroimaging Outcomes of a Cognitive Rehabilitation Training Program

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Cognitive training has shown promise in the remediation of cognitive skill deficits resulting from injury or neuropathology. It is presumed that intensive cognitive training can drive neuroplasticity and thus is the mechanism underlying associated gains. MRI is a noninvasive technique by which the manifestation of changes in neuroplasticity can be assessed, and while most MRI studies assessing cognitive training outcomes are group studies, MRI techniques may be sensitive enough to assess effects of a robust cognitive training program, such as ThinkRx, at the single subject level.

ThinkRx (LearningRx) is an intensive, 60+hour, one-on-one, clinician-delivered cognitive training program based on the Cattell-Horn-Carroll theory of cognitive abilities, and targets multiple cognitive skills including attention, working memory, processing speed, logic and reasoning, auditory processing, and visual processing. Observational results in a traumatic brain injury (TBI) population (n=273) found a mean increase of 10 points in intelligence quotient score, and a retrospective chart review of 11 soldiers with brain injury found a mean increase of 23 points, as well as reliable and clinically significant change.

To investigate if aberrant brain connectivity and changes in brain connectivity (a neuroimaging marker of neuroplasticity), were evident prior to and after completion of a robust cognitive training program, a series of case studies were carried out in subjects with varying degrees of traumatic brain injuries (n=5) and cognitive impairment (n=5). An MRI image acquisition protocol optimized for single subject imaging and sensitive enough to allow for repeat visualization of the resting-state default mode network (DMN) was developed on a 3T Siemens Skyra MR system and included acquisition of the following: a T1-weighted sequence for high-resolution anatomical imaging, a diffusion-weighted sequence for identification of white matter fiber tracts, and an echo planar imaging blood oxygen-level dependent sequence (repetition

time=3 seconds, 240 acquisitions, scan time= 12 minutes) for assessment of resting-state brain connectivity. MR exams were acquired on all subjects prior to and upon completion of the cognitive training program. MRI data were processed and analyzed using FreeSurfer and the CONN toolbox.

In addition to MR exams, all subjects completed pre/post neuropsychological testing (WJ-IV) and condition-specific rating scales. For all cases and a control subject, the DMN was visualized and within network connectivity quantified. Pretraining scans of the more severely impaired cases revealed varying degrees of aberrant DMN connectivity, including hyperconnectivity, hypoconnectivity, and a loss of anticorrelated (or negative) connectivity. Pretraining scans of the less impaired cases did not suggest the involvement of the DMN nor vastly abnormal brain connectivity. As such, pre-/postscans of the more homogeneous least impaired cases were analyzed at the group level.

For all cases, neuropsychological testing and qualitative outcomes measures increased, supporting that the robustness of the training program held for each imaged case study. Normalization of DMN connectivity, including decreased hyperconnectivity and reoccurrence of anticorrelated activity, was evident in the most severe TBI case. At the group level, significant training-induced changes in neural connectivity were identified. Two of the notable changes included (1) a significant (p-FDR=.002) increase in anticorrelated activity between the posterior cingulate and the left anterior temporal fusiform, and (2) a significant increase (p-FDR=.007) in language network connectivity specifically between the right frontal gyrus and the left supramarginal gyrus.

In conclusion, quantitative and qualitative gains across subjects suggest that ThinkRx is a robust cognitive rehabilitative training program. Further, these results support the hypothesis that MRI can be used to visualize default mode network connectivity, even at the single subject level, and to quantify changes in resting-state brain connectivity at both the single subject and group level.

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