New Neuroscience Based Cognitive Paradigms for Biomarker Research in Schizophrenia

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Background: Cognitive neuroscience has seen an explosion of technical advances and new knowledge regarding the neural basis of cognition. This presentation will overview of the results of the *Cognitive Neuroscience Task Reliability & Clinical Applications (CNTRACs) Consortium* work developing imaging biomarkers for three of the cognitive tasks developed by the consortium: Goal Maintenance (Dot Probe Expectancy Task; DPX), Episodic Memory (Relational and Item Specific Encoding Task; RISE), and Visual Integration (Jittered Orientation Visual Integration Task: JOVI).

Methods: The CNTRaCs Consortium conducted a five-site imaging study, with a demographically matched sample of 55 patients with schizophrenia, and 50 healthy controls. Participants completed a behavioral practice session within one week of their baseline scan, and then completed a baseline scan session followed by a retest scan within 28 days. Three of the scanners were Siemen's Tim TRIOs using a 12 channel headcoil, one was a Siemen's Allegra using an 8 channel headcoil, and one was a Phillips Achieva using a 12 channel head coil. Each imaging session including high resolution T1 imaging based on ADNI sequences, a T2 acquisition (to aid in co-registration), two sets of field maps, and 11 BOLD runs using an EPI sequence. Participants completed 4 runs of the DPX, 3 runs of the JOVI, and 4 runs for the RISE (1 during encoding, 2 during item recognition and 1 during relational recognition). Order of task administration was counterbalanced across participants and all participants took a break half way through the session. fMRI data were pre-processed using standard procedures with the FMRI Expert Analysis Tool (FEAT) in the FMRIB Software Library (FSL version 4.1). Statistical analysis was performed using the general linear model in FEAT, with research site added as a co-variate.

Results: For the RISE, controls had greater activation than patients in medial temporal lobe regions (right hippocampus and parahippocampal gyrus) when successfully retrieving objects that had undergone relational encoding. In addition, when participants made errors following relational encoding controls showed greater activation than patients in a set of bilateral prefrontal regions (inferior and middle frontal gyrus, anterior cingulate gyrus) often associated with error detection. Conversely, in the item encoding condition, there were no group differences observed in medial temporal or prefrontal activation during either successful or unsuccessful item recognition. For the DPX, controls had greater activation than patients in dorsolateral prefrontal cortex in the comparison of cues signifying greater versus lesser need for goal maintenance. For the JOVI, all participants showed linear increases in activation in visual, frontal and parietal regions as demands on visual integration increased and patients showed altered activation in superior parietal and inferior frontal regions. There were few site differences that interacted with group, and minimal differences in QA indices across sites. Analyses of test-retest reliability are ongoing.

Discussion: These results illustrate the successful development and implementation of imaging biomarkers paradigms of tasks developed as part of the CNTRaCs Consortium, and provide evidence for the validity of these paradigms as measures of the neural systems associated with specific cognitive processes. These results also illustrate the sensitivity of these measures to identifying neural changes associated with cognition impairment in schizophrenia and pave the way for their use as outcome and predictor measures in studies focused on evaluating treatments to enhance cognitive function in psychosis.