

**Results:** Results indicate a significant treatment effect with significantly reduced motivational negative symptom scores among those in the MI+CBT intervention following treatment ( $F = 6.5, p = .01$ ) and at three-month follow-up ( $F = 3.9, p = .03$ ). Participants in the MI+CBT group showed significant improvement on a measure of readiness for change ( $F = 10, p < .01$ ). We have not observed significant change on community functioning or defeatist beliefs in the data so far.

**Conclusions:** The findings suggest a recovery-oriented group that targets intrinsic motivation as well as cognitive and behavioral techniques for goal achievement can significantly improve negative symptoms. Implications for translating clinical changes to community functioning will be discussed.

## 19. RELATIONAL MEMORY DEFICITS IN SCHIZOPHRENIA: WHAT IS WRONG WITH THE HIPPOCAMPUS AND FRONTAL LOBE?

Stephan Heckers

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Humans constantly integrate new information about their environment with prior experiences in order to successfully navigate the world. The ability to flexibly integrate information into cohesive relational memories is particularly affected in many patients with schizophrenia. Deficits in hippocampal and prefrontal cortex function have been implicated as the neural basis of the relational memory deficits, although the contribution of each region to relational memory function remains unclear. As memory deficits are linked with significantly poorer outcomes in schizophrenia, behavioral and neurobiological findings provide targets for meaningful interventions. The speakers in this symposium will present competing cognitive neuroscience models to explain relational memory impairment in schizophrenia.

Alison Preston will present results discussing how hippocampus and prefrontal cortex work in concert to create integrated memories that relate information acquired during different episodes. Data from high-resolution fMRI studies will provide a mechanistic account of the component processes that support formation of integrated, relational memories as well as how those processes may be impacted in schizophrenia. She will further discuss how alterations in relational memory processing impact higher-order cognitive processes such as reasoning.

Daniel Ragland will demonstrate how cognitive neuroscience approaches for understanding functional neuroanatomy of episodic memory can be used to discover when prefrontal and/or hippocampal deficits may or may not be disruptive to performance in people with schizophrenia. Behavioral and imaging studies will employ verbal and non-verbal lists and scene memory paradigms utilizing eye-tracking methods to demonstrate the dissociable contributions of dorsolateral and ventrolateral prefrontal cortex, and anterior and posterior portions of the hippocampus.

Martin Lepage will present results from a brief intervention targeting the self-initiation of semantic strategies relational memory which significantly improved performance in schizophrenia. Moreover, he will present functional and structural brain imaging results that collectively suggest an important role of the left dorsolateral prefrontal (DLPFC) region for the implementation of strategies that lead to improvement in relational memory performance.

Suzanne Avery will present recent findings demonstrating deficits in hippocampal habituation and associated relational memory dysfunction in the early stages of psychotic illness. These results build on previous work demonstrating profound relational memory and hippocampal deficits in the chronic stages of schizophrenia, suggesting that hippocampal and relational memory dysfunction in the early stages of illness are followed by progressive changes in the chronic stage.

Chair/Discussant Stephan Heckers will discuss the emerging findings and competing cognitive neuroscience models in the context of the extant literature on hippocampal dysfunction in schizophrenia.

## 19.1 HIPPOCAMPAL AND PREFRONTAL MECHANISMS UNDERLYING RELATIONAL MEMORY FORMATION AND REASONING

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**Background:** Everyday behaviors require a high degree of flexibility, in which prior experience is applied to inform behavior in new situations. Such flexibility is thought to be supported by memory integration, a process whereby related experiences become interconnected in the brain through recruitment of overlapping neural populations. Integrating information acquired at different times allows memory to extend beyond direct experience by representing unobserved relationships between elements of different events. Integrated knowledge may then be flexibly deployed to promote higher-level cognitive functions such as reasoning. Across a series of functional magnetic resonance imaging (fMRI) studies in healthy young adults, we show that integrating related information in memory is mediated by interactions between the anterior hippocampus and medial prefrontal cortex. Furthermore, we will discuss evidence about how aberrant function of the hippocampal circuit in schizophrenia may impact memory integration mechanisms, leading to impairments in both memory and reasoning.

**Methods:** Healthy young adults participants performed an associative inference task in which they learned about overlapping image pairs (AB, BC) followed by an inference test tapping their knowledge for the indirect relationships among pairs. Using a combination of high-resolution fMRI and multivariate statistical analyses, we examined how three component processes underlying memory integration supported learning of the overlapping experiences and inferential memory judgments. First, we used multivariate brain decoding techniques to test whether reinstatement of overlapping information (A items) facilitated or interfered with new learning (BC pair memory) and inference (AC decisions). Second, we tested the hypothesis that hippocampal novelty signals detecting deviations between present experience (BC pairs) and reinstated memories (AB pairs) would promote integration. Third, we used representational similarity analyses to test whether indirectly related memory elements (A and C items) are assimilated within hippocampus and medial prefrontal cortex. In a separate high-resolution fMRI study, we further tested how schizophrenia impacts hippocampal novelty signals essential for memory integration.

**Results:** We found that memory reinstatement during new learning had a facilitative effect on memory and reasoning performance in healthy young adults. Co-activation of the anterior hippocampus and medial prefrontal cortex was observed during encoding of overlapping experiences, with novelty responses within the network predicting subsequent reasoning performance. Novelty responding in individuals with schizophrenia in a separate study was aberrant, suggesting one potential mechanism for impaired associative inference behavior in the disorder. In healthy young adults, representational similarity further evinced integration of indirectly related memory elements within anterior hippocampus and medial prefrontal cortex.

**Conclusions:** Collectively, these data indicate that the anterior hippocampus and medial prefrontal cortex work in concert to assimilate new experiences into reinstated memory content, resulting in superior learning and reasoning performance. Our data further indicate that hippocampal novelty signals may be critical for initiating memory integration when new events deviate from reinstated memory-based predictions. Aberrant novelty processing in hippocampus may therefore underlie deficits in memory-based reasoning tasks observed in schizophrenia.