18.2 MOBILE-ASSISTED COGNITIVE BEHAVIOR THERAPY FOR NEGATIVE SYMPTOMS (MCBTN) IN SCHIZOPHRENIA

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Background: The generic cognitive model (CBT) can be applied to the treatment of negative symptoms in schizophrenia. Defeatist attitudes (e.g., "Why bother trying, I always fail") contribute to amotivation and asociality and ultimately poor functioning in schizophrenia. Prior CBT clinical trials targeting defeatist attitudes have found that improvement in defeatist attitudes is associated with improvement in negative symptoms in schizophrenia.

Methods: Using an experimental therapeutics approach (R61/R33), we tested a novel intervention for negative symptoms in schizophrenia called, Mobile-assisted CBT for Negative symptoms (mCBTn). mCBTn is an integration of CBT-informed components targeting defeatist attitudes from our Cognitive-Behavioral Social Skills Training (CBSST) group therapy and mobile smartphone interventions ("CBT2go" app) from our prior clinical trials research. We report here on the R61 phase, which was an open trial of mCBTn in 31 participants with schizophrenia with persistent moderate-to-severe negative symptoms. Weekly 90-min sessions of group CBT plus the CBT2go iPhone app targeted defeatist attitudes, pleasure savoring, and behavioral activation/goal setting. The primary aim was to test whether mCBTn can reduce severity of the treatment target: defeatist performance attitudes.

Results: We recruited and assessed 67 participants; however, only 31 participants started the intervention, because 36 (54%) of participants did not meet the strict persistent negative symptoms entry criteria. After starting treatment, however, retention rates were excellent, especially for this negative symptom population: 87%, 84% and 79% at the 12-, 18- and 24-week assessments, respectively. Significant improvements were found on the Defeatist Performance Attitudes Scale with medium to large effect sizes (DPAS; Week 12 d=.4, p=.034; Week 18 d=.7, p<.001; Week 24 d=.9, p=.002). Negative symptoms (CAINS Motivation and Pleasure) also showed significant reduction with large effect sizes at all assessment points (Week 12 d=.6, p=.048; Week 18 d=.8, p=.007; Week 24, d=.7, p=.014), and positive symptoms also showed significant reduction by week 24 (p=.014, d=.5). The large effect sizes for DPAS and CAINS MAP by week 18 suggest an 18-week intervention might be sufficient to produce meaningful improvements, which is faster than in our prior CBSST trials of group therapy alone.

Conclusions: This preliminary open trial of mCBTn suggests that mobile apps can strengthen psychotherapy and targeting defeatist attitudes in participants with schizophrenia with persistent negative symptoms can lead to improvement in motivation and pleasure negative symptoms.

18.3 IMPROVING COMMUNITY ENGAGEMENT IN VETERANS WITH SCHIZOPHRENIA: QUALITATIVE DATA ANALYSIS FROM AN ONGOING TREATMENT TRIAL

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Background: Negative symptoms predict poor outcome in schizophrenia; however there is no recommended evidence-based treatment. Enhancing community functioning and promoting recovery in Veterans with schizophrenia is a VHA priority.

Methods: This presentation will review the sample, methods, and preliminary qualitative findings from an in-progress, VA-funded trial to evaluate a behavioral intervention to increase community engagement – Engaging in Community Roles and Experiences (EnCoRE) – in Veterans with schizophrenia who receive mental health services at three VA Medical Centers. EnCoRE includes motivational, cognitive, and behavioral skills training strategies aimed at increasing intrinsic motivation to engage in community activities, reduce negative expectancies, and perform skillfully in social situations. To date, 72 Veterans with schizophrenia have enrolled and 56 have completed study assessments. Participants completed post-assessment qualitative interviews about their experiences in EnCoRE, aspects of the program they perceived as more or less helpful, what they found challenging about becoming more active, and other reflections or suggestions about the intervention.

Results: Interviews were analyzed in 3 phases employing constant comparison of data units with others and data with emerging themes and examining meaning across interviews via focused cross-interview coding to organize themes, variations and interrelationships among the ideas, views, and experiences of the sample. We also examined relationships among using different components of the program and reports of engaging in community activities with intervention engagement and attendance. Participants who attended more frequently reported greater use of EnCoRE skills and strategies to increase participation in community/family activities. Participants reported benefits of specific components – especially detailed Action Planning - and offered suggestions for improvement. Participants reported that the group format, in which they felt that they were accountable to other Veterans, helped them feel more motivated to accomplish the goals they set in each group meeting.

Conclusions: Veterans with schizophrenia are receptive to a behavioral program to improve community functioning. Features such as focused content with in-depth planning for implementation, small group size, and having other Veterans to help and learn from can help Veterans with schizophrenia participate in new community activities. [Source of funding: VA RR&D (Bennett, PI)]

18.4 GROUP-AUGMENTED MOTIVATIONAL INTERVIEWING + CBT FOR NEGATIVE SYMPTOMS

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Background: Motivational difficulties, primarily motivational negative symptoms are a primary determinant of functional impairments in schizophrenia. There are currently no evidence-based treatments uniquely designed to target negative symptoms. Some studies have shown that CBT may be efficacious for improving motivational negative symptoms; however, engaging in structured CBT exercises requires a high level of motivation. Further, motivation often vacillates over the course of CBT, which impedes efforts to implement structured CBT exercises. Our team recently developed an integrated Motivational Interviewing (MI) + CBT intervention for motivational negative symptoms in Veterans with schizophrenia that focuses on attaining functional recovery-related goals.

Methods: Currently, 80 Veterans with schizophrenia and moderate to high negative symptoms have been randomized to three months of either group-based MI + CBT for negative symptoms or a Mindfulness Skills Training group. Participants completed comprehensive assessments of cognition, symptoms, motivation, community functioning, and defeatist beliefs at baseline, at the completion of three-month intervention, and at three-month follow-up. Quantitative data will be presented regarding the feasibility, tolerability, and efficacy of the treatment.
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?

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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 dissociative 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 habitation 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.

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.