

12-month follow-up. Similar results were obtained when data were clustered following clinical decision rules.

Conclusion: Despite extensive neuropsychological investigations within CHR cohorts, this is one of the first studies to investigate NP clustering profiles as a contributor to heterogeneity in outcome. Our results indicate that the four NP profiles vary substantially in their outcome, underscoring the relevance of cognitive functioning in the prediction of illness progression. Our findings may tentatively suggest that individualized cognitive profiling should be explored in clinical settings, and my point to important directions for personalized treatment.

43. COGNITIVE FUNCTIONING IN FIRST-EPISODE PSYCHOSIS: X000B_ COMPARISON OF A 2-YEAR COORDINATED SPECIALTY CARE PROGRAM TO COMMUNITY CARE

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Background: Significant cognitive impairment is already seen in first-episode psychosis (FEP) and degree of impairment is a moderator of long-term outcomes. Does specialized FEP treatment improve cognitive functioning? The NIMH sponsored RAISE-ETP study allows comparison of NAVIGATE, a coordinated specialty care intervention designed for FEP, to Community Care (CC) in a randomized clinical trial. (RCT)

Methods: The RCT was conducted at 34 sites in the United States. Seventeen sites were randomly assigned to provide NAVIGATE and 17 to provide CC. Four hundred four consenting participants age 15 to 45 years old, experiencing an FEP and had not received more than 6 months of antipsychotic medication entered the study. Treatment and assessment continued for up to two years. The Brief Assessment of Cognition in Schizophrenia (BACS) was administered at baseline, one and two years. Age and sex adjusted T-scores for the BACS Composite and six sub-tests (Verbal Memory, Digit Sequencing, Verbal Fluency, Token Motor, Symbol Coding and Tower of London) were calculated. Generalized estimating equations (GEEs) were applied to compare change in treatments between baseline, months 12 and 24 adjusting for within and between site variation.

Results: The NAVIGATE and CC groups included 221 and 181 participants. The Group X Visit interactions was a statistically significant predictor of change in: Verbal Memory, Verbal Fluency, Symbol Coding, Tower of London and the Composite ($P < .001$ for all). For the NAVIGATE group, there was significant improvement at Month 12 and Month 24 for Verbal Memory, Digit Sequencing, Tower of London, and the Composite. For the CC group, there was a significant improvement at Month 12 and Month 24 for the Composite; and only at month 24 for the Tower of London.

Conclusion: The results of this analysis suggest that NAVIGATE resulted in greater improvement in cognitive functioning in both an overall score and for specific components than did CC. NAVIGATE is a multi-component intervention, guided by manuals and supervision by a central team. NAVIGATE includes psychopharmacological treatment with antipsychotics and other psychotropic medications using an internet based decision support system, an individual psychotherapy called Individual Resiliency Training, family psychoeducation and supported employment and education. The role of individual components cannot be readily determined and further analyses will evaluate the effect of moderator variables such as duration of untreated psychosis, symptomatology and functioning at study entry. To date, pharmacologic treatments to improve cognition have not demonstrated efficacy. Cognitive remediation strategies, notably Cognitive Enhancement Therapy pioneered by Gerard Hogarty, has shown efficacy in

FEP patients but to the best of our knowledge, this is the first RCT to show an effect of a broad FEP focused intervention on cognitive functioning.

44. TRANSDIAGNOSTIC RELATIONS BETWEEN FUNCTIONAL BRAIN NETWORK INTEGRITY AND COGNITION

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Background: Cognitive impairment occurs across the psychosis spectrum; however, it is unknown whether these shared manifestations of cognitive dysfunction also reflect shared neurobiological mechanisms, or whether the source of impairment differs. The current study aims to determine whether the general cognitive deficit observed across psychotic disorders is similarly associated with functional integrity of two brain networks widely implicated in supporting many cognitive domains.

Methods: 201 healthy controls, 143 schizophrenia, 103 schizoaffective, and 129 bipolar disorder with psychosis patients from the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP1) consortium were included in the analyses. All participants underwent cognitive testing and a resting-state fMRI scan. Network integrity was measured through estimations of global and local efficiency of the whole brain, cingulo-opercular network (CON), frontoparietal network (FPN), and auditory network (AUD). Group differences in network measures, relationships between cognition and network measures, and mediation models were tested.

Results: Schizophrenia and psychotic bipolar patients showed significantly reduced CON global efficiency compared to healthy controls ($P_s < .01$). All psychotic disorders had significantly reduced CON local efficiency ($P_s < .03$), but the clinical groups did not differ from one another. CON global efficiency was significantly associated with general cognitive ability across all groups ($\beta = .109$, $P = .003$), and significantly mediated the relationship between psychotic disorder status and general cognition ($P < .05$).

Conclusion: These findings provide evidence for a role of reduced CON efficiency in the general cognitive deficits observed across the psychosis spectrum. They also support the hypothesis that a shared neurobiological mechanism underlies the dimension of cognitive impairment in psychotic disorders.

45. IMPACT OF THEORY OF MIND ABILITIES AND NEGATIVE SYMPTOMS IN SCHIZOPHRENIA DURING REAL SOCIAL INTERACTIONS

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Background: There is a recognized need to understand the determinants of social functioning in people with schizophrenia. While several factors such as cognitive or social cognitive deficits or negative symptoms are linked to social functioning, we know little about the impact of these symptoms during real social interactions.

Methods: We developed new social collaboration tasks based on the social communication paradigm. Participants were asked to collaborate

with another person to reorder sequences of images. For each trial of the task, participants were presented with a series of 6 images forming a story and were asked to tell the story to a confederate, who had the same 6 images in a random order. The confederate was asked to place her set of images in order based on the narrative produced by the participant. She was trained to provide feedback to signal eventual misunderstandings. A first study included 25 patients with schizophrenia and 22 healthy controls who presented 6 sequences of images from different movie scenes. A second study included 21 patients with schizophrenia and 22 healthy controls who presented 9 sequences of cartoon images. Patients also completed a theory of mind task and an evaluation of their symptoms with the PANSS (5-factor version). Naive research assistants then rated the audio recordings regarding how easy it was to place the card in order from the produced stories, how interesting each story was, and how expressive the voice was.

Results: In both studies, patients were judged to make the collaborative task more difficult than healthy controls (Study 1: $t(45) = 2.5$, $P = .015$; Study 2 $t(41) = 2.0$, $P = .05$). Patients' stories were perceived as less interesting (Study 1: $t(45) = 3.0$, $P = .004$; Study 2: $t(41) = 3.1$, $P = .003$) and their voices were perceived as less expressive (Study 1: $t(45) = 4.0$, $P < .001$; Study 2 $t(41) = 3.1$, $P = .004$). In patients, the perceived difficulty was correlated with theory of mind abilities in both studies (Study 1: $r = .49$, $P = .01$; Study 2: $r = .63$, $P = .002$). In contrast, the expressiveness and the interest of the story were strongly linked together (Study 1: $r = .80$, $P < .001$; Study 2: $r = .90$, $P < .001$) and both significantly correlated with patient's negative symptoms as assessed with the PANSS (study 1: $r = -.42$, $P = .04$ for expressiveness and $r = .44$, $P = .03$ for interest; Study 2: $r = -.62$, $P = .003$ for expressiveness and $r = -.60$, $P = .004$ for interest).

Conclusion: These results suggest that during the same social interaction, theory of mind deficits and negative symptoms can affect distinct aspects of the interaction. Theory of mind deficits seem to hinder the success of collaborative interactions whereas the lack of expressiveness (and more globally negative symptoms) seem to impact how interesting patients are perceived during social interactions.

46. EFFORT, AVOLITION, AND FUNCTION IN SCHIZOPHRENIA: ANALYSIS OF BEHAVIORAL AND NEUROIMAGING DATA WITH RELATIONSHIPS TO REAL-WORLD FUNCTION

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Background: Many schizophrenia (SZ) patients experience negative symptoms such as reductions in motivational drive. Recent work has suggested that abnormal effort-based decision-making may be a key contributory mechanism to such motivational deficits. However, the neural correlates of effort-based decision-making deficits in SZ as well as relationships to real-world functioning are unclear.

Methods: To test this hypothesis about effort-based decision-making, we utilized a novel paradigm. Prior to scanning, participants (30 SZ; 30 CN) experienced increasingly difficult versions of a cognitively demanding task. Then participants made decisions about repeating difficult levels for increased reward or an easy level for less reward. Easy version offers were stepwise titrated until an indifference point was reached. Next, during fMRI scanning, participants made choices between repeating hard/easy levels for more or less reward. In addition, to analyze relationships between effort-based decision-making and real-world function participants completed a weeklong ecological momentary assessment protocol. Four times/day subjects completed a short cell phone survey stating their current activities and interest/enjoyment with these activities.

Results: Patients required greater amounts of money to choose to perform cognitively demanding tasks compared to CNs. This effect was largest for high negative symptom patients and held even when accounting for behavioral performance. Analysis of daily reports of emotional experience revealed that patients who showed the greatest effort avoidance also reported the least enjoyment/interest in their daily activities, suggesting that deficits in experimentally derived effort-based decision-making may be linked to real-world emotional functioning. Finally, we hypothesize that brain regions highly implicated in the allocation of effort, as well as representations of subjective value, such as the anterior cingulate cortex, ventromedial prefrontal cortex, and ventral striatum will show blunted activation patterns for SZ patients compared to CN during effort-based decisions, suggesting specific neural correlates for aberrant choice behavior.

Conclusion: Our results suggest that abnormal effort-based decision-making may be a contributory mechanism to motivational impairment and is related to real-world function in those with SZ. Such findings have important implications to the etiology of abnormalities in goal-oriented behavior in SZ.

47. EFFECT OF ANTIPSYCHOTIC MEDICATION ON HIPPOCAMPAL FUNCTION AND NEUROCHEMISTRY: A LONGITUDINAL STUDY IN PATIENTS WITH SCHIZOPHRENIA

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Background: Our prior studies with PET and 15O have shown associations between hippocampal function and treatment response to antipsychotic drugs (APDs). In addition, we found elevated hippocampal glutamate in unmedicated patients with schizophrenia (SZ) but not in medicated. Here, we use a longitudinal design to evaluate the relationship between glutamate and function of the hippocampus in SZ in relation to treatment response to APDs.

Methods: 34 SZ were scanned while unmedicated and after 6 weeks of APD. 23 matched healthy controls were also scanned twice six weeks apart. Imaging was done on a 3T head-only scanner equipped with a circularly polarized transmit/receive head coil. A high-resolution structural scan was acquired using the 3D T1-weighted magnetization-prepared rapid acquisition gradient-echo sequence (TR/TE/TI = 2300/3.93/1100ms; flip angle = 12°; 256 × 256 matrix; and 1mm isotropic voxels). Eyes open resting-state fMRI (rsfMRI) was acquired using the gradient recalled echo-planar-imaging sequence (TR/TE = 2000/30ms, flip angle = 70°, field of view = 192mm³, 6mm slice thickness, 1mm gap, 30 axial slices, 225 acquisitions). rsfMRI data were preprocessed and analyzed using CONN toolbox and SPM12. Resting-state magnetic resonance spectroscopy was collected with a voxel prescribed in the left hippocampus (2.7 × 1.5 × 1cm) using the PRESS sequence optimized for glutamate (TR/TE = 2000/80ms, spectral bandwidth = 1024 points, 640 averages) and analyzed in jMRUI. A median split was used to separate SZ into treatment responders and non-responders (calculated as percent change in BPRS positive symptoms).

Results: Before treatment, those who subsequently responded to treatment were characterized by significantly elevated glutamate levels compared to both healthy controls and nonresponders. Treatment responders but not non-responders or healthy controls glutamate levels significantly decreased over the 6-week course of treatment. Additionally, treatment responders demonstrated reduced hippocampal blood oxygen-level-dependent (BOLD) fMRI signal compared to healthy controls and nonresponders.

Conclusion: Before treatment, both hippocampal glutamate levels and hippocampal BOLD signal appear to differentiate good treatment responders from poor treatment responders.