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42. Heterogeneity of Neuropsychological Profiles in the Prodrome to Psychosis: An Examination of the Association Between Cognition and Clinical Outcomes in NAPLS-1

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examine differences on these five learning-based parameters to examine reward-based learning across psychotic diagnoses.

Results: All patient groups were more impaired for the initial acquisition than controls, however there were no group differences to obtain subsequent criteria, or in perseverations or false-feedback switches. Patients' difficulty on the task derived from an excess of win-switch trials, or spontaneous switches (Kruskal-Wallis $\chi^2(3) = 12.71, P < .001, SZ, SA, BP > C$), and was correlated with total symptoms ($\rho = .20, P = .017$), but not symptom factor scores. The computational model including both belief about the correct category and exploratory choices fit the data most parsimoniously, excluding the other parameters. Of these two, patient deficits in all groups were associated with more errors due to exploratory choices ($\chi^2(3) = 13.509, P = 0.004^*$; SZ, SA, BP > C). The exploratory choice parameter correlated with negative and positive symptom factors, and with the total number of symptoms.

Conclusion: Consistent with previous research, we found patients with schizophrenia to be impaired on pRL. This impairment was not specific to schizophrenia and predominated in all patients in the initial acquisition stage. A computational model of rule selection and exploration predicted participant performance and showed patients' rule selection capacity was unimpaired whereas they appeared to explore reward contingencies more than controls. This capacity was relevant to an array of symptoms across psychotic diagnoses.

41. COGNITIVE DISENGAGEMENT AND TASK SWITCHING IN PATIENTS WITH SCHIZOPHRENIA

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Background: Schizophrenia is associated with impaired cognition as a core feature (1) and also with amotivation (2) and reductions or abnormalities in willingness to expend effort (3, 4). It remains unclear whether reduced effort is responsible for any of the observed cognitive deficit, as we do not generally assess continuous effort during testing.

Methods: In the current study, we use a novel paradigm to test whether disengagement of effort is greater during cognitive performance in individuals with first-episode psychosis (FEP) compared with healthy community members. We used a novel task called the Cognitive Effort and DisEngagement (CEDE), which increases in difficulty and requires task-switching, a function with a well-documented link with cognitive effort (5). Participants had the option to skip any trial without penalty. No additional monetary incentives were used. Skips were used as an index of effort disengagement. We also used a self-report measure of amotivation.

Results: FEP patients had lower overall accuracy on the task-switching task ($P = .030$), but they also made significantly more skips ($P = .018$). When only examining trials with attempted answers, FEP patients still had reduced accuracy, but it did not reach significance ($P = .348$), and the effect size was reduced by 80%. Groups did not differ significantly in number of incorrect responses ($P = .547$). Self-reported amotivation significantly predicted skips in the entire sample ($B = .41, P = .023$) and separately among individuals with FEP ($B = .64, P = .035$).

Conclusion: Disengagement of effort is likely to account for a portion of cognitive test performance among individuals with psychosis. The present results call into question the degree to which observed performance deficits in FEP are caused by true reductions in ability versus lack of motivation and sustained effort. This is an optimistic possibility, as effort is a more pliable phenomenon and may be more easily augmented with intervention than cognitive ability.

1. Elvevag B, Goldberg TE. Cognitive impairment in schizophrenia is the core of the disorder. *Critical Reviews™ in Neurobiology* 2000;14(1).

2. Strauss GP, Waltz JA, Gold JM. A review of reward processing and motivational impairment in schizophrenia. *Schizophrenia bulletin* 2014;40(Suppl 2):S107-S116.

3. Gold JM, Strauss GP, Waltz JA, Robinson BM, Brown JK, Frank MJ. Negative symptoms of schizophrenia are associated with abnormal effort-cost computations. *Biological psychiatry* 2013;74(2):130-136.

4. Gard DE, Sanchez AH, Cooper K, Fisher M, Garrett C, Vinogradov S. Do people with schizophrenia have difficulty anticipating pleasure, engaging in effortful behavior, or both? *Journal of abnormal psychology* 2014;123(4):771.

5. Rubinstein JS, Meyer DE, Evans JE. Executive control of cognitive processes in task switching. *Journal of Experimental Psychology: Human Perception and Performance* 2001;27(4):763.

42. HETEROGENEITY OF NEUROPSYCHOLOGICAL PROFILES IN THE PRODROME TO PSYCHOSIS: AN EXAMINATION OF THE ASSOCIATION BETWEEN COGNITION AND CLINICAL OUTCOMES IN NAPLS-1

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Background: The vast majority of studies of neuropsychological (NP) functioning in Clinical High Risk (CHR) cohorts have examined group averages, possibly concealing a range of subgroups ranging from very impaired to high functioning. Our objective was to assess NP profiles and to explore associations with conversion to psychosis, functional and diagnostic outcome.

Methods: Data were acquired from individuals (mean age 18.4, SD = 4.6) participating in the longitudinal North American Prodrome Longitudinal Study-I (NAPLS-I), a multi-site consortium following individuals at CHR for developing psychosis for up to 2½ years. By applying the Hierarchical Clustering Ward's method including 8 different neuropsychological tests, we clustered data of 166 CHR individuals, 49 persons with a family history of psychosis without prodromal symptoms, and 109 healthy controls. We then tested whether cluster profiles with more severe NP impairments were associated with higher conversion rates, lower social and role functioning scores, and/or more chronic diagnostic outcomes compared to the lesser-impaired profiles. To examine clinical utility, analyses were repeated after data were clustered based on clinical decision rules that were established by clinical experts in the field.

Results: Four distinctive profile clusters best described the level of NP performance in our CHR cohort: Severely Impaired (n = 33); Clearly Abnormal (n = 82); Borderline (n = 145) and Normal (n = 64). The Severely Impaired cluster largely distinguished itself from the rest of the clusters by larger deviations on processing speed and memory tasks. We found compelling differences in outcome between cluster profiles. Importantly, those assigned to the most impaired profile had a conversion rate of 42.4%, had a 40% chance of developing a diagnosis in the schizophrenia spectrum (as compared to 24.4% in the Clearly impaired, 7.4 % in the Borderline impaired and 2.9% in the Normal functioning group), and had significantly worse social ($P < .001$) and role ($P < .001$) functioning scores at baseline and

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