38. DISTINCT THEORY OF MIND DEFICIT PROFILES IN SCHIZOPHRENIA AND AUTISM: A META-ANALYSIS OF PUBLISHED RESEARCH

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Background: Theory of mind (ToM) is an aspect of social cognition which refers in part to the capacity to perceive and understand other people's mental state. Deficits in these mentalizing processes are commonly observed in both schizophrenia and Autism Spectrum Disorder (ASD), and are thus evident in disorders with very different symptoms and clinical presentations. The aim of this study was to conduct a meta-analysis of all published data examining ToM deficits in schizophrenia and autism in order to determine whether these two disorders have distinct deficit profiles across multiple domains of ToM. We additionally aimed to explore the relationship between clinical symptoms and phase of illness on ToM deficits in schizophrenia.
Methods: A literature search identified 74 eligible studies in schizophrenia involving 3555 cases and 22 studies in ASD involving 810 cases, as of August 2016. Meta-analyses were conducted to calculate the pooled effect size of deficits for each patient group in each ToM domain.
Results: As expected, significant theory of mind deficits were observed in both schizophrenia and ASD. Strikingly, the most significantly impaired ToM domain in schizophrenia was understanding verbal intention (g = −1.33) followed by indirect speech (g = −1.09), second-order false belief (g = −0.89), faux-pas −0.88), emotional ToM (g = −0.76) and first-order false belief (g = −0.61). Understanding visual intention was not significantly impaired. In ASD, the most impaired domain was understanding indirect speech (g = −1.40), followed by faux-pas (g = −1.27), emotional ToM (g = −0.75), and understanding false belief (g = −0.467). Intention inferencing was not significantly impaired in ASD (g = −0.01). Planned meta-regression analyses revealed that positive symptoms significantly modulated the magnitude of deficit across several ToM domains in schizophrenia.
Conclusion: Common symptoms of schizophrenia, such as paranoia and persecutory ideas, chime with the greatest observed ToM deficit observed here, which was understanding verbal intention, which was not impaired in ASD. Conversely, understanding meaning in speech was most impaired in ASD, but this was less impaired in schizophrenia. This study reveals that schizophrenia and ASD populations have distinct ToM deficit profiles. Understanding differences in ToM deficit profiles can help differentiate the clinical phenotypes of these disorders in a way that might enhance the identification of disorder-specific behavioral markers and the development of explanatory models and new treatments.

39. HEIGHTENED PHONOLOGICAL PRIMING DURING AMBIGUITY: MODELING AUDITORY HALLUCINATIONS IN SCHIZOPHRENIA

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Background: The mechanism of auditory hallucinations has been avidly pursued for decades although its formation remains largely cryptic. Another domain of clinical symptoms in schizophrenia is reduced working memory, for which the "phonological loop" is the elementary component. The phonological loop is a subvocal rehearsal of verbal information to support working memory for holding information while other information is manipulated. We hypothesize that auditory hallucinations and working memory deficit in schizophrenia share a common deficit in the phonological loop operation, especially when the phonological loop is heavily taxed.
Methods: We created a new active phonological priming paradigm to examine whether an abnormal phonological association to ambiguity may be an underlying mechanism of auditory hallucinations in schizophrenia, and tested it in 31 schizophrenia patient (SZ) and 20 healthy control (HC) participants. Using a set of pseudo-words to introduce semantically ambiguous stimuli yet requiring verbally generated semantic words to be linked to the otherwise ambiguous input, the paradigm obligates a phonological association and forces activation of the phonological loop. Once verbally primed, participants then rated their familiarity to each pseudo-word auditory stimulus, by comparing to real-word auditory stimulus. "Errors" are measured by rating of the familiarity to the pseudo- versus real words. Auditory hallucinations were assessed by the Psychotic Symptom Rating Scales - Auditory Hallucinations Scale.
Results: SZ did not show a significant increase in familiarity of real words after priming (P = .96); where HC were prone to "error" after the priming to the real words (P = .01). Conversely, with pseudo-words, SZ were prone to phonological priming of ambiguous stimuli and experienced a significant increase in their rating of familiarity to the otherwise meaningless pseudo-words (P = .006), whereas HC did not (P = .10). More severe auditory hallucinations correlated highly with increased familiarity to ambiguous stimuli after active phonological priming (r = .58, P = .001).
Conclusion: The paradigm aims to generate behavioral readouts of priming effects to both familiar words and ambiguous pseudo-words under passive vs. active association conditions. The results indicate that schizophrenia patients are specifically vulnerable to active association to ambiguous stimuli and this vulnerability is associated with more severe auditory hallucinations.

40. EXPLORATION NOT PERSEVERATION: COMPUTATIONAL MODELING OF PROBABILISTIC REVERSAL LEARNING IMPAIRMENTS IN PSYCHOSIS

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Background: Computational psychiatry applying algorithms for basic behavioral phenomena to understand how these parameters changed with symptoms across psychotic diagnoses. Rule generation and selection is a critical function for daily life and impairments in this construct have been associated with the negative symptoms of psychosis (Gold, et al., 2008). The current study used trial-by-trial decisions by people with schizophrenia (SZ), schizoaffective disorder (SA) and bipolar disorder (BP) on a probabilistic reversal learning (pRL) task to model five parameters: beliefs about the correct category, exploratory choices, motoric repetitions, attentional lapses and random responding.
Methods: 225 participants in the multisite CNTRaCS consortium (Henderson, et al., 2012) completed the pRL: SZ (n = 65), SA (n = 54), BP (n = 50) and demographically similar controls (n = 56). In the pRL, participants select 1 of 2 abstract images using a button press, after which they are told if their choice was correct. The task was probabilistic because one of the items was positively reinforced 80% of the time (and 20% of the time they were falsely told it was wrong), and the alternative item had the opposite contingency. After meeting the initial acquisition criterion of selecting the positively reinforced item on 10 trials, the reinforced item changed in favor of the alternative item. This simple design allowed us to

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.
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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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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