DIFFERENTIAL PATTERN OF SOCIAL COGNITION IMPAIRMENT BETWEEN RURAL AND URBAN DWELLING PATIENTS OF SCHIZOPHRENIA AND ITS FUNCTIONAL CORRELATES

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narrative frame for encoding to investigate if unitization generalizes to a more relatable real-life context.

Methods: Twenty-two individuals with an RM deficit and a diagnosis of schizophrenia or related disorder were pseudo-randomized to either the unitization or control condition, from which 19 completed all TP tasks and 17 completed RTT. TP performance was measured at screening. TP and RTT task performances were measured pre-post learning unitization. During the RTT-unitized task, participants created their own unitizations, with assistance (50% of the task) and on their own. The control group received unitization training following study participation. The TP-unitized control group results were included in the analysis.

Results: TP task performance (percentage of correct trials) did not significantly differ between control (M = 49%, SD = 13%) and unitization groups (M= 60%, SD = 18%) at screening ($t(17) = -1.506$, $p = 0.15$). A 2-way mixed analysis of variance (ANOVA) did not reveal a group-task interaction for unitization and control group accuracy in the four TP versions ($F(3,51) = 2.38$, $p = 0.08$). A main effect of task ($F(3, 51) = 9.43$, $p > 0.001$) was decomposed using Tukey HSD pairwise post-hoc analyses and showed significantly higher TP task accuracy following unitization (M = 85%, SD = 19%) compared to the TP task at screening (M = 55%, SD = 16% $p > 0.001$), before unitization (M = 61%, SD = 19%, $p = 0.001$) and when prompting self-unitization (M = 68%, SD = 28%, $p = 0.04$). No other significant differences in task accuracies were revealed. Group accuracies in the RTT were compared using a 2-way mixed ANOVA, and yielded a significant interaction between group and task accuracy ($F(1,15) = 4.93$, $p = 0.042$). Simple main effect analysis showed that accuracy in the RTT post unitization training (M = 90%, SD = 9%) was higher than before training (M = 77%, SD = 14%, $p = 0.046$), but performance between the same versions of the RTT did not significantly differ in the control group (M1 = 73%, SD = 19%; M2 = 70%, SD = 23%; $p = 0.26$).

Discussion: TP performance improved when the unitization strategy was provided, but not when the self-generation of unitization was encouraged. Improved RTT performance was limited to the unitization group, suggesting that effects were unitization-specific rather than lead by practice. Logic follows that this strategy may be generalizable to more relatable, real-life contexts. Self-generation of unitization was effective in improving task performance when assistance was provided rather than merely encouraged, suggesting that patients may benefit from guidance generating their own unitizations rather than integrating this strategy on their own. These findings should be replicated in a larger sample, and strategies to provide effective self-generation of unitization should be explored. Moreover, the extent to which the RTT can detect differential relational memory impairment in individuals with schizophrenia when compared to healthy controls warrants further investigation.

S67. TREATMENT-RESISTANCE AFFECTS LONG-TERM COGNITIVE TRAJECTORIES IN SCHIZOPHRENIA: A LONGITUDINAL STUDY

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Background: Schizophrenia is a highly heterogeneous disorder, and despite extensive research progress approximately 30% of patients with schizophrenia show poor response to first-line antipsychotics, denoted as treatment-resistant schizophrenia (TRS). Meta-analytic evidence showed that clozapine is the most effective antipsychotic for TRS, although 40% of TRS patients do not respond even to clozapine (ultra-treatment-resistant schizophrenia -UTR). Recent studies indicated that TRS is neurobiologically and categorically distinct from treatment-responsive schizophrenia, being associated with elevated glutamate levels in the anterior cingulate cortex and unaltered striatal dopamine synthesis. Moreover, the striking majority of TRS patients do not respond to first-line antipsychotic therapy since disease onset and present more severe cognitive deficits since first episode of psychosis, further suggesting the presence of a distinct and more disrupted neurobiological substrate. It is widely known that cognitive impairment is a core feature of schizophrenia and determines a significant detrimental impact on long-term functional outcome, which represents the ultimate treatment goal. However, despite the central role of cognition in schizophrenia, to date no study has investigated longitudinal cognitive outcome among TRS patients.

Based on these evidences, the aim of this study is to evaluate longitudinal cognitive trajectories in a sample of clinically stabilized patients with schizophrenia, stratified according to antipsychotic response. We hypothesized that treatment-resistance is associated with a more severe long-term cognitive decline.

Methods: We enrolled 93 patients with schizophrenia (DSM-V), stratified as follows: 32 first-line responders (FLR), 42 TRS and 19 UTR. Cognition was longitudinally assessed at baseline and at least after 6 years of follow-up (mean: 9.3±2.8 years) using the Brief Assessment of Cognition in Schizophrenia (BACS). From BACS subscores we calculated for each patient a Cognitive Index, as a measure of overall cognitive functioning. In order to quantify global cognitive functioning changes during the course of illness, we estimated effect size score for Cognitive Index using Cohen's d. Finally, General linear Models (GLM) were performed with overall cognitive index effect size as dependent variable, treatment (FLR/TRS/UTR) as categorical variable and age, duration of illness and education as covariates.

Results: The first GLM (FLR vs TRS+UTR) showed a significant main effect of treatment ($F=7.34$, $p=0.01$), with worse cognitive outcome between resistant patients. Consistently, the second GLM (FLR/TRS/UTR) resulted significant as well ($F=17.90$, $p<0.001$), with UTR group showing worse cognitive trajectory (Fisher's post-hoc: $p<0.001$, UTR Cognitive Index effect size = -0.7).

Discussion: This is the first study to longitudinally evaluate cognitive trajectories of patients with schizophrenia according to their antipsychotic response. We showed that treatment resistance is associated with a more severe cognitive decline, with worse outcome among UTR patients. These data suggest that greater severity of treatment resistance in schizophrenia is associated with greater cognitive impairment, possibly due to the presence of a distinct and more disrupted neurobiological substrate that affects both cognition and antipsychotic response. These findings further highlight the necessity of early individuation and tailored pharmacological treatment for TRS patients, in order to improve long-term clinical, cognitive and functional outcome.

S68. DIFFERENTIAL PATTERN OF SOCIAL COGNITION IMPAIRMENT BETWEEN RURAL AND URBAN DWELLING PATIENTS OF SCHIZOPHRENIA AND ITS FUNCTIONAL CORRELATES

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Background: Cognitive deficits (both neuro & social Cognition) play a vital role in determining functional status in schizophrenia. It has been noted that functional outcomes are relatively better in Indian rural settings. This suggests that cognition might be better in rural patients. Considering the prevailing vast cultural differences there is paucity of research which delineates the differences in social cognition and its impact on the functional outcomes between rural and urban setups. Hence, we aim to explore differential impairment in social cognition in patients with schizophrenia residing in rural versus urban settings and their impact on real-world functioning.

Methods: 122 patients diagnosed with either schizophrenia or schizoaffective disorder from the rural taluk of Thirthahalli and Turuvekere were compared with 97 patients with similar diagnosis visiting a teaching hospital with urban residence. All the 219 patients met the standardized criteria for remission from positive and disorganized symptoms and were compared on culturally validated tests of SC—Social Cognition Rating Tool in Indian Setting (SOCRATIS) & Tool for Recognition of Emotions in Neuropsychiatric Disorders (TRENDS) to assess theory of mind, social perception and emotion recognition and NC—(attention/vigilance, speed of processing, visual and verbal learning, working memory and executive functions). Groningen Social Disabilities Schedule (GSDS) was used for the assessment of social dysfunction of the patients. Based on past factor analytical studies on these tests, social cognition dimensions were grouped into inferential social cognition which comprised of 1st order theory of mind & 2nd order theory of mind Index & socio-emotional cognition which included faux pas recognition, emotional recognition & social perception indices. These were compared using analysis of covariance after controlling for neurocognitive composite performance and other confounders Correlation between social-cognition and functioning among the two groups was assessed using Pearson correlation.
Results: Patients from rural population had significantly better inferential social cognition whereas patients form urban population had significantly better socio-emotional cognition. ANCOVA showed that even after controlling for effects of age, gender, duration of illness, family history, number of hospitalization & neuro-cognition composite scores the differences were significant. Social cognition composite score was significantly (negatively) correlated with functional disability. The socio-emotional cognition component had a stronger association (proportion of variance explained) with functioning in both rural & urban samples (r= -0.411, r= -0.403 respectively). Inferential Social cognition from both rural & urban samples (r= -0.212, r= -0.238) also has significant association with functioning but of lesser magnitude as compared to the former
Discussion: The two distinct components of social cognition - inferential and socio-emotional- were differentially impaired among rural & urban patients. With respect to its relationship with functioning, the socio-emotional cognition had a stronger association with functioning in both the groups. The reasons for the difference need to be explored by studying the socio-cultural characteristics of rural & urban dwelling patients which can moderate their expression of social cognition. These observations are critical in understanding how our micro- and macro-level environments can influence cognitive performance

S69. CLINICAL HIGH RISK STATE: STRATIFICATION BASED ON CLINICAL PROFILE AND REDOX STATUS

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Background: The Clinical High Risk state (CHR) concept was implemented to promote the early detection of young help-seeking patients with higher risk of psychotic transition. This category is based on specific clinical criteria (EPA, 2015) and require narrow frequency/duration ratings of subclinical positive psychotic symptoms to allow its definition. Prevalence of CHR "category" appears nevertheless rare in help-seeking young people and the rate of psychotic transition of CHR state is lower than predicted by early studies. Therefore, the binary outcome of transition to psychosis proposed by the "CHR model" actually fails to be an efficient marker to stratify, in neurobiological studies, people with different psychopathological trajectories, notably those who develop psychosis from those who do not. In order to rely on a vulnerability model for schizophrenic psychosis more sensitive to psychosocial functioning and negative dimension, we study prospectively with three years of follow-up a population of help-seekers addressed for clinical suspicion of prodromal state of psychosis.
We aimed here to identify subgroups of patients in a sample of subclinical psychotic states using psychological and cognitive outcomes as profiling criteria, focusing not only on transition but also on psychosocial functioning as main outcome.
Methods: A total of 32 help-seeking adolescents and young adults aged 14 to 35 were referred by health care providers for a specialized evaluation in case of suspicion of a prodromal psychotic state and/or detected by the French version of the Prodromal Questionnaire (PQ-16; cut-off 6/16). Their CHR status was assessed by the Structured Interview for Psychosis-Risk Syndromes (SIPS) and the Schizophrenia Proneness Instrument, Adult (SPI-A). Individuals included in the study presented either a CHR status, a subclinical CHR status or negative symptomatology. All subjects performed an additional neuropsychological battery and blood test for redox markers (Glutathione Peroxidase (GPx) and Glutathione Reductase (GR) activities) (Xin et al, 2016). Based on their clinical profile, we made a stratification of the patients using a Principal Component Analysis.
Results: Cognitive and psychological outcome stratification of all help-seekers revealed two subgroups (called group1 and group2) of patients with distinct profiles. Individuals in group1 (n=18) had greater levels of basic symptoms and general symptomatology. On the other hand, in group2 (n=14), individuals showed a weaker self-esteem and a lower rate of "living independently". Cognitive scores for speed processing, attention, verbal learning and social cognition were significantly lower in group2 compared to group1. In addition, these cognitive outcomes were negatively correlated with negative symptoms only in group2. Analysis of redox markers revealed a positive correlation between GPx and GR activities in group1, a correlation disrupted in group2.
Discussion: Stratification of a cohort of young help-seekers with suspicion of prodromal psychosis, regardless of their CHR status, allowed us to distinguish two subgroups with different clinical profiles: group1 with higher levels of basic symptoms and general symptomatology, and group2 with weaker self-esteem, less autonomy and poorer neurocognition. In addition, analysis of redox markers revealed a redox dysregulation in patients with poorer cognitive profile. Considering the impact of neurocognitive impairment on functioning, special focus to patients of group2 is needed, mostly in clinical practice. Moreover, they might benefit of supplementation with antioxidant compounds such as NAC, which may improve cognitive deficits (Conus et al, 2018).

S70. PROFILES OF SOCIAL COGNITION AND METACOGNITION IN FIRST-EPISODE PSYCHOSIS: A LATENT PROFILE ANALYSIS.

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