correlated with the symptom severity. These findings underline the significance of subclinical symptoms, and may provide a possible explanation of its association with poor outcome.

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P.1.j.025 Abnormal cognitive salience but not WCST scores are associated with poor outcome in patients with schizophrenia

H. Bergaoui[1]*, A. Frajerman[2], M. De Hert[3], C. Tessier[1], P. Nuss[4] *[1]Saint-Antoine Hospital, Psychiatry, Paris, France; [2]University Pierre et Marie Curie, CHU Saint Antoine, Paris, France; [3]Catholic University Leuven, University Psychiatric Centre, Kortenberg, Belgium; [4]Saint-Antoine Hospital AP-HP, Psychiatry, Paris, France*

Purpose of study: Psychopathology and cognitive impairment are poor predictors of functional outcome in patients with schizophrenia. In contrast, recent data have demonstrated that dopamine-associated functions such as baseline motivational deficits and social cognition are more relevant to predict patient functionality. Social cognition is a complex entity that includes several information processes such as reasoning, attention and memory, all involved in social adjustment. These cognitive dimensions are known to be particularly impaired in schizophrenia patients. Among several components, it comprises cognitive salience, a measure of the aberrant dopamine signalling in brain. In the present study, functional outcome was correlated to (i) psychopathology, (ii) attention and frontal lobe executive function, and (iii) cognitive salience in a population of stabilised patients with schizophrenia (SCZ).

Method: Chronic medicated patients with schizophrenia (n = 35) have been examined and compared to a healthy control population (n = 34). Clinical characteristics, prefrontal functioning, and cognitive salience were assessed using PANSS (Positive and Negative Syndrome Scale), CGI (Clinical Global Impression), WCST (Wisconsin Card Sorting Test), SAT, and CPT-AX tests respectively. CPT-AX (Continuous Performance Test-AX version) and SAT (Salience Attribution Test) are two standardised and computerised tests to study cognitive salience. SAT: is a probabilistic reward learning game that employs cues that vary across task-relevant and task-irrelevant dimensions; it provides behavioural indices of adaptive and aberrant reward teaching. CPT-AX with salient stimuli doesn't use words but colour stimuli and assesses working memory by varying inter stimulus interval. Global Assessment of functioning (GAF) evaluated the overall functioning of patients.

Results: Compared to control subjects, 60% of SCZ patients showed a significant decrease in performance for WSCT (perseverative responses, perseverative and non-perseverative errors, and errors). SAT (Explicit Adaptive Salience) values were significantly different for 42% of subjects, while CPT-AX scores (Hit-score, False Alarm Rate, Response Time) were abnormal in only 27% of patients. Only the latter subgroup had abnormal scores in WSCT showing a possible participation of prefrontal involvement in this salience test.

Interestingly and in accordance with data of literature, abnormal responses to WCST did not predict low GAF score in our study. In contrast, subjects with low SAT scores and CPT-AX separately were significantly ($p < 0.05$) more frequent in the group of patients with low GAF scores. We also tested the hypothesis that the CPT-AX and SAT evaluate two different dimensions of salience. We reviewed patients with low scores on both SAT and CPT-AX. This subpopulation had indeed scores significantly ($p = 0.02$) lower in the GAF compared to patients without this combination.

Conclusion: Alteration of the cognitive salience tests CPT-AX and SAT is associated with functional outcome impairment in patients with schizophrenia. Preliminary data are indicating that these two tests can describe the activity of two separated neurobiological networks involved in cognitive salience.

P.1.j.026 Cognitive deficits caused by hippocampal disinhibition: attentional and memory deficits

S. McGarrity[1]*, K.C. Kevin[2], R. Mason[2], M.A. Pezze[1], T. Bast[1] *[1]Nottingham University, School of Psychology, Nottingham, United Kingdom; [2]Nottingham University, School of Biomedical Sciences, Nottingham, United Kingdom*

Background: Hippocampal disinhibition, i.e. reduced GABAergic inhibition, has emerged as a key pathophysiological feature of schizophrenia [1]. Disrupting processing both within the hippocampus and potentially also within hippocampal projection sites, hippocampal disinhibition may contribute to two main cognitive deficits in schizophrenia: deficits on hippocampus-dependent everyday memory tasks and, considering strong hippocampo-prefrontal projections, deficits in prefrontal-dependent attentional function [2]. If this hypothesis could be confirmed, this would highlight hippocampal disinhibition as a target for novel pharmacological treatment strategies to ameliorate cognitive deficits in schizophrenia, which are resistant to current treatments. To test this hypothesis, we combined hippocampal disinhibition, induced by acute local microinfusion of picrotoxin, with appropriate cognitive testing and with in vivo electrophyiological methods. Our disinhibition targeted temporal to intermediate hippocampus, which has been especially implicated in schizophrenia and has strong connectivity to prefrontal and subcortical sites [2]

Methods: In adult male Lister hooded rats, acute bilateral picrotoxin infusions (0, 75 ng or 150 ng in 0.5 ul per side, saline as vehicle) targeting the temporal to intermediate hippocampus were combined with behavioural testing or electrophysiological recordings. The 5-choice-serial-reaction-time (5CSRT) task, a rodent analogue of the human continuous performance task, was used to assess prefrontal-dependent attentional function. Rats were pretrained to criterion (80% accuracy, less than 20% omissions). They were then tested immediately following infusions. The watermaze delayed-matching-to-place (DMP) test, which resembles the everyday memory task of using newly learned place and route memory, was used to asses hippocampus-dependent performance based on rapid place learning; we used a novel version of the task which involves a measure of search preference and is particularly sensitive to disruption of hippocampal function [3]. Following pretraining on the task, picrotoxin was infused before a new learning trial, when rats had to learn a novel platform location, and search preference for the correct location was assessed after a retention delay of 20 min. We also assessed infusion effects on open-field locomotor activity. To characterise the neural effects of picrotoxin, we combined infusions with multi-unit and local field potential (LFP) recordings in the proximity of the infusion site, using a 1×8 electrode microarray.

Results: Picrotoxin infusions caused a temporary (about 30 min) increase of neuron firing rate in the temporal to intermediate hippocampus, consistent with disinhibition of hippocampal neurons. On the 5CSRT test, hippocampal disinhibition caused a highly selective attentional deficit, as indicated by reduced accuracy (with all other performance measures unaltered). On the DMP task, hippocampal disinhibition severely impaired memory performance, as indicated by a marked reduction of search preference. Finally, hippocampal picrotoxin infusion caused moderate dose-dependent locomotor hyperactivity in the open field, consistent with psychosis-related dopamine hyperfunction.

Conclusions: Hippocampal disinhibition caused attentional and memory deficits in rats, suggesting that hippocampal disinhibition in schizophrenia may causally contribute to two key cognitive deficits characterizing the disease. Hippocampal disinhibition may, thus, be a key target for novel pharmacological treatment strategies to ameliorate cognitive deficits. Our rat model may be useful in testing such strategies.

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P.1.j.027 Insight into illness and subjective quality-of-life assessment in chronic schizophrenia

C. Siu[1]*, O. Agid[2], M. Waye[3], C. Brambilla[4], G. Remington[2], P. Harvey[5] *[1]Data Power (DP) Inc, Quantitative Methodology, New Jersey, USA; [2]University of Toronto, Psychiatry, Toronto, Canada; [3]The Chinese University of Hong Kong, Biomedical Science, Shatin, Hong Kong; [4]National Research Council, Applied Mathematics and Information Technologies, Milan, Italy; [5]University of Miami, Psychiatry, Miami Florida, USA*

Background: Lack of insight into illness is a well-established phenomenon in schizophrenia. Poor insight has been associated with psychosocial dysfunction and increased re-hospitalization rates, as well as a barrier to accepting and staying in treatment [1]. Reduced insight has been reported for correlation with less rater-assessed functional performance, but better self-report quality-of-life in previous studies, including the CATIE schizophrenia trial [2]. We hypothesized that insight might have an impact on patient self-report assessments of quality-of-life or well-being, an important domain of treatment outcome. The objective of this study was to examine factors that might influence insight and self-assessment of quality-of-life using the large CATIE dataset.

Methods: This analysis utilized baseline data from the CATIE schizophrenia study [3]. Insight was assessed by the Insight and Treatment Attitudes Questionnaire (ITAQ) and PANSS item G12 'lack of judgment and insight'. Social and occupational functioning was assessed using the Heinrichs-Carpenter Quality of Life (HCQoL) scale, while self-report quality-of-life was assessed with the Lehman QoL Interview (LQOLI). We conducted a cross-sectional multivariate regression analysis to evaluate the potential factors.

Results: Consistent with previous reports (Mohamed et al., 2009), better insight into illness (higher ITAQ score) was associated with higher functioning (higher HCQoL total score, $p < 0.05$), greater neurocognitive composite ($p < 0.05$) and reasoning ($p < 0.05$) performance, but there was an inverse correlation to lower self-report quality of life (lower LQOLI, $p < 0.05$) and a higher level of depressive symptoms ($p < 0.05$) in patients with chronic schizophrenia. We found the inverse relationship between insight and self-report LQOLI was explained, in part, by levels of depressive symptoms ($p < 0.001$) and neurocognitive reasoning impairment ($p < 0.05$) (the factors combined explained 77% of total age-adjusted effect of insight on LQOLI). Overall cognitive performance was not significant after adjusting for depression effect ($p > 0.05$).

Among subjects with mild or no depressive symptoms on all 9 items of the Calgary Depression Scale ($N = 839$), self-report quality-of-life (LQOLI) was inversely related to both insight ($p < 0.05$) and cognitive reasoning performance ($p < 0.05$) after adjusting for age and symptom severity (CGI-S). Lower reasoning performance was found in patients who rated themselves pleased/delighted (LS Mean –0.21, standardized score), compared to higher mean reasoning score in the terrible/unhappy subgroup (LS mean 0.16) or in the mixed category (mostly satisfied, mixed or mostly dissatisfied) (LS mean –0.02). Associations of self-assessment LQOLI with neurocognitive composite score, and the other 4 domains (verbal memory, vigilance, processing speed, and working memory) were not significant (all p's > 0.30).

Conclusions: Our findings suggest that insight demonstrates significant associations with levels of depression and performance on neurocognitive reasoning, which in turn impacts self-assessment of quality-of-life. Greater insight into illness was associated with higher levels of depression and lower self-report quality-of-life, but better neurocognitive reasoning and less negative symptoms. Among subjects with mild or no depression, better self-report quality-of-life was associated with lower performance on neurocognitive reasoning and lower insight.

These observations have important clinical implications, and warrant further investigation.

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P.1.j.028 Dissecting reward processing in the brain: a human experimental model for biomarker discovery in major depressive disorder

C. McCabe[1]* *[1]The University of Oxford, Dept. of Psychiatry, Oxford Oxon, United Kingdom*

Purpose: Reward dysfunction in the human brain has been suggested as underlying anhedonia, the inability to experience motivation and pleasure during depressive episodes. Anhedonia is one of the two main diagnostic criteria for depression and has been suggested as a possible endophenotype as it seems to predate