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# MORPHOLOGY OF THE SUPERIOR TEMPORAL SULCUS IN PATIENTS WITH SCHIZOPHRENIA: A MARKER OF GENETIC OR ENVIRONMENTAL VULNERABILITY?

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with low/medium and high CT ratings. Likewise, interpersonal distance and comfort ratings of patients with and without delusions were compared.

**Results:** In our preliminary data ( $n = 27$ ), subjects with high CT ratings showed an increased need for interpersonal space compared to subjects with low/medium CT. Additionally, the high CT group showed reduced comfort ratings at varying fixed distances. Likewise, patients with delusions had an increased interpersonal space and reduced comfort at fixed distances. Moreover, interpersonal space was associated with the severity of childhood trauma, and in particular with emotional neglect. Finally, interpersonal distance was associated with the degree to which the delusional belief involves various areas of patients' lives ('extension' dimension of the DDE).

**Discussion:** Our preliminary data suggests that childhood maltreatment and dimensions of delusions are associated with increased safety behaviour in patients with schizophrenia. These findings are in line with previous studies, which found associations of interpersonal distance and childhood maltreatment in healthy controls as well as paranoia in patients with schizophrenia. Our findings are of particular interest, as increased safety behaviour may impact social functioning (i.e. lead to more social withdrawal) in patients with schizophrenia.

### M13. INCREASED SAFETY SEEKING IN PATIENTS WITH SCHIZOPHRENIA AND PARANOID THREAT

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**Background:** Schizophrenia is a disabling disorder with tremendous individual burden, reduced quality of life, leading to intense costs for society. Paranoia is a central feature of schizophrenia. In particular, paranoid experience is thought to be associated with aggressive behaviour, and poor social and functional outcome. Since paranoid threat is sometimes hard to detect in the clinical interview, a simple bedside test to identify patients suffering from paranoid experience was recently proposed: the interpersonal distance test.

**Methods:** For measuring interpersonal distance in patients with schizophrenia and age-, gender- and education-matched healthy controls, we performed a stop-distance paradigm. To accomplish the paradigm, we positioned experimenter and participant at opposite ends of the room with a distance of seven meters facing each other. The stop-distance paradigm contained four different conditions; two active conditions (i.e. participant is approaching experimenter) and two passive conditions (i.e. experimenter is approaching participant) both, with and without eye contact. Participants were instructed to stop or tell the experimenter to stop at a distance, at which they would start to feel less comfortable. Moreover, we assessed paranoid threat with the Bern Psychopathology Scale. We compared the interpersonal distance between patients with current experiences of paranoid threat, schizophrenic patients without paranoia and healthy controls.

**Results:** Patients with higher ratings in paranoid experience presented with higher interpersonal distance than patients without paranoid threat and matched healthy controls. This effect was most prominent in the passive conditions. Patients without paranoia did not differ from healthy controls in the interpersonal distance test.

**Discussion:** Interpersonal distance is a reliable indicator of current paranoid threat in patients with schizophrenia. In fact, interpersonal distance is not generally altered in schizophrenia. However, paranoid threat leads to impairments in interpersonal space regulation. This is of particular relevance as interpersonal distance might be predictive of social and functional outcome and aggressive behaviour in schizophrenia.

### M14. BDNF IS CORRELATE TO LOW EMOTION RECOGNITION IN UHR WOMEN: RESULTS FROM THE SSAPP POPULATIONAL UHR COHORT

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**Background:** Schizophrenia is a disorder with prevalence rates of 1% in the general population. Science turned its efforts towards researching prodromal states, named "Ultra-high Risk" (UHR), in the hopes of impeding conversion to psychosis. Cognitive impairments are recognized among core features of schizophrenia and it is noted that they are already present at early stages of psychosis, such as ultra-high risk for psychosis (UHR). Schizophrenia in women has a more favorable outcome than in men with the disease in part mediated by cognitive performance. Neurotrophins, such as brain-derived neurotrophic factor (BDNF), play crucial roles in the expression of synaptic plasticity underpinning cognitive function, particularly expression of learning and memory. Previous studies showed conflicting results regarding neurotrophin levels in patients with psychosis. We hypothesized that UHR individuals would also show altered BDNF and cognitive performance levels.

**Methods:** A sample of over 2500 individuals aged between 18 and 30 years old, from the city of São Paulo, Brazil, was drawn and screened with the Prodromal Questionnaire (PQ). 236 subjects with high scores (18+ points in the positive PQ subscale) were selected for psychiatric assessment with the SIPS (Structured Interview for Psychosis-Risk Syndromes), and 98 individuals were classified as UHR. Whole blood sample was collected and BDNF levels were analyzed with ELISA kits (Thermo-Fisher). Cognitive performance was measured by the emotion recognition task available via the UPenn Computerized neuropsychological testing (). Data was available for 93 UHR individuals (95%) and for 62 (46%) controls. IBM SPSS Statistics v23 for Mac was used to analyze data.

**Results:** BDNF levels and performance on emotion recognition task did not differ between control and UHR individuals. Differences were also not found if sample was analyzed according to sex. However, in UHR women (63% of UHR sample), worse performance was significantly associated with a higher BDNF level (Pearson correlation coefficient=-0.288,  $p=0.031$ ).

**Discussion:** In our study, we found a correlation of worse emotion recognition task and higher BDNF levels in UHR women. This might be due a compensatory mechanism in which patients more severely impaired at baseline show higher BDNF levels. Estrogen might play a role in this difference as it induces BDNF expression. Several studies with psychotic patients shows higher BDNF levels in affected individuals as well as one study with UHR individual show higher BDNF levels within this group, but none showed differences between sexes. One study showed that treatment with selective estrogen receptor raloxifene increased activation in the right hippocampus and left inferior frontal gyrus areas, which are involved in facial recognition. Overall, literature suggests that women outperform men regarding overall cognitive function, including emotion recognition. Our findings might be related to a before homeostasis state has been reached in which baseline measures for emotion recognition in UHR women could be worse than in men but along time ameliorated via estrogen-induced BDNF expression.

### M15. MORPHOLOGY OF THE SUPERIOR TEMPORAL SULCUS IN PATIENTS WITH SCHIZOPHRENIA: A MARKER OF GENETIC OR ENVIRONMENTAL VULNERABILITY?

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**Background:** Hallucinations are the most common and debilitating symptom in schizophrenia, affecting more than 70% of patients. The superior temporal sulcus (STS) is involved in the language process notably in the perception of the human voice and several studies show its implication in auditory verbal hallucinations (AVHs). Sulcal patterns in the white matter can reflect an early vulnerability, probably genetic since they set up at a very early stage and are stable over the life course. In contrast, the cortical thickness is dynamic and variable over the development and so can reflect the impact of environmental factors on the maturation of the brain. The aim of this study is therefore to determine whether AVHs are associated with morphological changes of the STS and in particular, whether these changes concern sulcal patterns or cortical thickness reflecting early (genetic) or late (environmental) vulnerability respectively.

**Methods:** Seventy-three schizophrenia patients (DSM-IV) with a proneness of AVH (53 AVH+) and without AVH (20 AVH-) and 100 healthy volunteers (HC) had a 3T MRI brain scan. Cortical reconstructions were generated using Freesurfer. Mean cortical thickness was measured over the entire brain in each participant. Number of sulcal pits, which represents the position with the maximum depth in the sulcus, was automatically counted on the white matter surface. Both measures were compared between groups and related to the Auditory Hallucination Rating Scale (AHRS).

**Results:** AVH+ patients compared to HC showed a significantly thinner cortical thickness in the left temporal and frontal regions and especially in the STS ( $p \leq 0.05$  FDR corrected). A negative correlation ( $r^2=0.25$ ) between the cortical thickness in the central part of the left STS and the AHRS score was found ( $p = 0.01$  uncorrected). A different distribution of the number of pits in the left STS is found in AVH+ patients compared to HC ( $p = 0.05$ ).

**Discussion:** The results suggest that AVH+ patients compared to HC have a lower cortical thickness in the left STS, but also have a specific white matter pattern of the left STS. These results support the hypothesis that a particular morphology of the STS related with auditory hallucinations might be due to both early (genetic) and late (environmental) factors.

## M16. PROFILING GLUTAMATE AND D-SERINE PATHWAYS IN TREATMENT RESISTANT EARLY PSYCHOSIS PATIENTS

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**Background:** Pharmacological, neurochemical and electrophysiological studies provide compelling evidence that N-methyl-D-aspartate-receptor (NMDAR) hypofunction is a pathologic feature of schizophrenia (SZ). GWAS studies highlighted risk genes such as Serine Racemase (SRR), which synthesizes D-Serine (D-Ser), the co-agonist of glycine site at NMDARs, and Serine Hydroxymethyltransferase (SHMT1) which synthesizes L-Serine (L-Ser), the substrate of SRR. Around 30% of patients do not respond to dopamine modulation and are considered to suffer from treatment resistant SZ (TRS). While the exact cause of TRS remains unclear, multiple lines of evidence suggest the involvement of a dysregulation of the Glutamate (Glu) neurotransmission. To test the hypothesis whether Glu system dysregulation mediated by NMDAR hypofunction is an underlying mechanism of TRS, we investigate the Glu and D-Ser pathways in TRS and treatment responder (RESP) early psychosis patients (EPP).

**Methods:** From a total of 621 EPP aged 18 to 35, included in the TIPP (early Intervention Program in Lausanne, Baumann & al., 2013), 225 EPP were classified as TRS (n=33) or RESP (n=192) according to the strict Treatment Response and Resistance in Psychosis (TRRIP) criteria (Howes & al., 2017), with compliance ascertained by antipsychotic plasma levels. A matched healthy control (HC) group (N=114) was also recruited (DIGS criteria). No patient was taking clozapine at baseline. Clinical data was collected over a 3-year period. At baseline, following systems were assessed: 1) D-Ser pathway: plasmatic D-Ser, L-Ser and Glycine by HPLC (Hashimoto & al., 2016), protein levels of SRR and SHMT1 by ELISA; 2) Glu pathway: Glu and glutamine in plasma (HPLC) and prefrontal cortex (magnetic resonance spectroscopy, Xin & al., 2016).

**Results:** D-Ser pathway: in TRS, SRR levels were decreased by 56% as compared to RESP. Interestingly, we observed a positive correlation between plasma levels of D-Ser (SRR metabolite) and L-Ser (SRR substrate) in the TRS ( $r = 0.58$ ;  $p = 0.0015$ ) but not in the RESP group, suggesting that SRR dysregulation might be a limiting factor in TRS patients. Moreover, in TRS patients, SHMT1 levels were decreased by 15% as compared to RESP, with a positive correlation between the substrate and metabolite of SHMT1, glycine and L-Ser ( $r = 0.48$ ;  $p = 0.011$ ). Dysregulation of SHMT1 might thus be a limiting factor in the TRS group. As compared to HC, L-Ser and D-Ser were significantly increased in patients ( $p < 0.001$  for L-Ser,  $p = 0.0001$  for D-Ser). However, no difference was observed in D-Ser, L-Ser and glycine in TRS as compared to RESP, although L-Ser tended to be higher in male TRS patients ( $p = 0.06$ ).

Glu pathway: comparing TRS with RESP patients, plasma Glu levels were increased in the TRS group ( $p < 0.0001$ ), whereas they were higher in both patient groups compared to HC ( $p < 0.0001$ ). Interestingly, plasma and brain Glu levels showed a negative correlation in EPP, mostly driven by RESP ( $r = -0.42$ ;  $p = 0.035$ ), a correlation which was absent in HC.

Global Assessment of Functioning (GAF): at baseline, TRS and RESP displayed the same range of GAF. After a 3-year follow-up, TRS patients had poorer functioning as compared to RESP group ( $p < 0.0001$ ).

**Discussion:** Taken together, our results suggest that the TRS group, in which the levels of SRR and SHMT1 were lower and Glu plasma levels were higher, display a different regulation of the synthesis, degradation and/or accumulation of D-Ser and Glu as compared to the RESP group. However, replication in larger groups is needed. Moreover, our findings highlighted a dysregulation of D-Ser and Glu pathways in TRS patients in their early phase of psychosis. On the clinical side, our results confirm the significantly poorer functioning outcome in TRS patients.

## M17. PREDICTION OF NEUROLEPTIC AND ANTIDEPRESSANT TREATMENT RESPONSES VIA FMRI OF THE EXTENDED REWARD SYSTEM

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**Background:** Neuroimaging techniques have been developed as important tools to assess brain dysfunctions that underlie mental disorders. In particular, modern functional magnetic resonance imaging (fMRI) holds the promise to provide neurofunctional biomarkers for improved differential diagnosis and optimized treatment of schizophrenic and affective disorders.

**Methods:** Neurofunctional connectivity MRI of the extended human reward system (Makris et al., 2008) was conducted in a large transnosological cohort of patients suffering from schizophrenia, bipolar disorder or major depressive disorder. Responses to neuroleptic treatments in patients with schizophrenic or bipolar disorder were determined retrospectively, while treatment responses to different antidepressants were directly assessed in a prospective naturalistic clinical study.

**Results:** Responders to neuroleptic treatment with aripiprazole showed significantly higher reward-related activation in a larger set of brain regions (including ventral striatum, hippocampus, amygdala, pregenual ACC