p<0.1), while remitted CHR had dMMN amplitude (-5.11 ± 0.35μv, p=0.47) comparable to HC. There was no significant main effect of laterality or interaction of group × laterality.
In non-remitted CHR subjects, dMMN amplitude was significantly correlated with Glx level (r=-0.47, p<0.01) and with GABA level (r=-0.38, p<0.05) in the mPFC. However, the correlation of dMMN amplitude with Glx or GABA levels was not significant among either HC or remitted CHR.
Discussion: In line with previous studies, reduced dMMN amplitude distinguished between remitted and non-remitted CHR subjects, with remitted CHR not different from HCs. Our finding further supports the idea that reduced dMMN amplitude could be a candidate biomarker for predicting outcome in CHR. More importantly, we linked the reduced dMMN amplitude in non-remitted CHR to their Glx and GABA levels in mPFC, the region identified as one of dMMN sources (responsible for attention switching) thus supporting the idea that NMDA-mediated disruptions may play a key role in predicting psychosis and functional outcome.

F15. DIFFERENTIAL EXPRESSION PATTERNS OF EPIDERMAL GROWTH FACTOR (EGF) AND IMMUNE SYSTEM MARKERS IN DORSOLATERAL PREFRONTAL (BA46) AND ORBITOFRONTAL (BA11) CORTICES IN SCHIZOPHRENIA AND MOOD DISORDER

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Background: Environmental risk factors that operate at maternal, foetal and post-natal levels, causing immune activation are known risk factors for schizophrenia. How this risk is transduced is unknown but one plausible disease mechanism may be through immune activation perturbing central nervous system growth factor systems, such as the epidermal growth factor (EGF) system critical to neuronal differentiation, maturation and plasticity, altering neurodevelopment. These interactions between EGF and immune systems may involve specific critical brain regions and not others.
Methods: The expression of candidate genes from EGF and immune systems and related signalling pathways, including ligands, receptors and intermediary molecules, were examined in post-mortem dorsolateral prefrontal (DLPFC) (n=114 genes) and orbitofrontal cortical (OFC) (n=105 genes) tissues, from schizophrenia and mood disorder patients and healthy controls (n=68), using the Fluidigm Biomark qRT-PCR platform. Data were analysed by ANOVA or corresponding non-parametric test (Kruskal-Wallis) in GraphPad Prism 6/7 statistical software and p values were adjusted for multiple testing (Benjamini-Hochberg).
Results: In DLPFC, 68 genes were significantly differently expressed between diagnostic groups. In comparison to healthy controls, 60 genes were differentially expressed in schizophrenia and 14 in the mood disorder group. Collectively these differentially expressed genes belonged predominantly to ERBB signalling and associated MAPK, PI3K and MTOR pathways and with immune pathways involving toll like receptor (TLR), TNF, nuclear factor kappa B (NFB), JAK-STAT, and complement signalling. Although there was some overlap the expression profiles in schizophrenia and mood disorder differed considerably. There were genes (n=15) with significantly lowered expression in both patient groups compared to controls which belonged predominantly to immune pathways such as TNF and TLR. However, 36 genes were differentially expressed between schizophrenia and mood disorder, all of them having lower expression in schizophrenia, predominantly representing pathways PI3K/MTOR, MAPK, TLR and TNF signalling via NFKB. Gene expression in EGF system signalling via MAPK and PI3K pathways, and interleukin signalling via JAK-STAT were significantly lower in schizophrenia than in mood disorder and healthy controls. ErbB4 was the only gene significantly elevated in a patient group (mood disorder) compared to the controls.
In comparison to DLPFC, only five genes out of the 105 examined were differentially expressed between the diagnostic groups in OFC, which belonged to NFB, TLR, JAK-STAT and growth factor signalling pathways. In comparison to healthy controls all were differentially expressed in schizophrenia and three genes in the mood disorder group. The expression of most genes was decreased in the patient groups compared to control subjects in both brain regions.
Discussion: We conclude that there is a prominent regional difference in the expression of EGF and immune system markers, identifying the DLPFC as a region of high activity for the interaction between these two systems relative to the OFC. In this region, the differing profiles of gene expression between schizophrenia and mood disorder involved EGF signalling pathways including PI3K/MTOR and MAPK along with immune pathways such as TNF, TLR and JAK-STAT signalling, possibly reflecting variant pathological processes involving immune and EGF system signalling between these sets of disorders.

F16. GLUTAMATE AND GABA LEVELS IN ANTIPSYCHOTIC-NAÏVE SCHIZOPHRENIA PATIENTS ARE ASSOCIATED WITH TREATMENT OUTCOME AFTER 1.5 AND 6 MONTHS

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Background: Higher glutamate levels are found in the anterior cingulate cortex (ACC) of non-responder (NR) patients with schizophrenia in cross-sectional studies. However, it remains unclear if this reflects the pathophysiology of NR patients or the effect of antipsychotics and illness chronicity. Also, no previous study has assessed if levels of GABA in the ACC and glutamate in the thalamus are abnormal in NR patients from illness onset. To investigate this, we examined antipsychotic-naïve schizophrenia (SCZ) patients before and after treatment.
Methods: Longitudinal study of 38 initially antipsychotic naïve SCZ patients and 34 matched healthy controls (HC) assessed at baseline, after 1.5 months (NSCZ=29, NHC=33), and 6 months (NSCZ=26, NHC=28) of treatment. Patients were treated with aripiprazole for the first 1.5 months (open label). Hereafter, treatment could be modified. Responders (R) and non-responders (NR) were assessed using the Andreasen criteria. Glutamate spectra in the ACC and left thalamus were acquired with a PRESS sequence, and GABA spectra in the ACC with a MEGA-PRESS on a 3T MR scanner.
Results: First, the trajectory of glutamate/Cr and GABA/Cr levels were evaluated in SCZ patients and HC with a linear mixed model. In the left thalamus, a significant time*group interaction was observed (p=0.01) due to higher levels of glutamate/Cr in SCZ patients at baseline (p=0.03), but not after 1.5 and 6 months' treatment as compared with HC. In the ACC, a significant main effect of group was found for both glutamate/Cr (p=0.04) and GABA/Cr (p=0.003) due to lower levels in SCZ patients at all examinations, and the time*group interactions were non-significant.