significant consideration in studies of the COMT gene, likely involving the catechol-estrogens which are substrates of COMT. As expected there was no significant results with control SNP rs165599, indicating that findings were due to the influence of SNPs rs4680 and rs4818 on COMT activity.

S177. IMPACT OF NOS1AP AND ITS INTERACTION PARTNERS AT THE GLUTAMATERGIC SYNAPSE ON WORKING MEMORY NETWORKS - AN FMRI IMAGING GENETICS STUDY

Eva Raspor*[1], Peter K. Hahn[1], Tom Lancaster[2], David E. J. Linden[3], Florian Freudenberg[1], Andreas Reif[1], Robert A. Bittner[1]
[1]University Hospital Frankfurt, Goethe University; [2]Cardiff University School of Medicine; [3]School for Mental Health and Neuroscience, Maastricht University

Background: N-methyl-D-aspartate receptor (NMDAR) hypofunction is an important pathophysiological mechanism in schizophrenia. At the postsynapse the NMDAR interacts with the post-synaptic density (PSD). Neuronal nitric oxide synthase 1 (NOS1) binds to the PSD scaffolding proteins PSD-93 and PSD-95, enabling NMDAR-mediated release of nitric oxide via NOS1. NOS1AP (adaptor of NOS1) is capable of disrupting the interactions between NOS1, PSD-93, and PSD95. Therefore, NOS1AP is closely involved in both glutamatergic and nitrinergic neurotransmission. NOS1AP has been implicated as a risk gene for schizophrenia and cognitive dysfunction. Its increased expression has been observed in dorsolateral prefrontal post-mortem brain tissue of patients with schizophrenia, and NOS1AP SNPs have been associated with established schizophrenia endophenotypes. These findings suggest that the influence of NOS1AP variants should be observable in neural systems implicated in schizophrenia. In the present study, we investigate the impact of NOS1AP and its interaction partners at the glutamatergic synapse on the cortical working memory (WM) networks using fMRI and a gene set analysis approach.
Methods: 97 right-handed individuals with no personal or family history of psychiatric disorders underwent fMRI in a 3T Siemens Trio scanner during the performance of a visuospatial change detection WM task. Data analysis in Brain Voyager QX 2.8 included standard data preprocessing. Additionally, a multiscale curvature driven cortex based alignment procedure was used to minimize macro-anatomical variability between subjects. Subsequently, data were analyzed using a random-effects multi-subject general linear model. We investigated 19 regions of interest (ROIs) within the core fronto-parietal WM network. We studied all phases of our WM paradigm (encoding, maintenance, retrieval), which were modeled by a total of 5 regressors (encoding, delays 1–3, retrieval). Genetic data was quality controlled and imputed using the RICOPILI pipeline. Gene-set analyses of the 19 ROIs were performed using MAGMA. Two gene sets were selected: 1) NOS1AP/NOS1; 2) NOS1AP/glutamatergic synapse. We applied a Bonferroni correction for the total of 19 ROIs and 5 regressors (95 tests) to both analyses.
Results: Both gene set analyses revealed multiple associations between brain activation in core fronto-parietal WM areas. For the NOS1/NOS1AP set, most associations were observed during the late maintenance phase (Delay 3) of our WM paradigm. One association was significant Bonferroni correction: a cluster in the left intraparietal sulcus during the late maintenance phase (Delay 3; β=2.2459, SD=0.0239, SE=0.6451, p=0,00025). For NOS1AP / glutamatergic synapse interaction partners, two associations were significant after Bonferroni correction: a cluster in the right IPS during the early maintenance phase (Delay 1; β=0.8525, SD=0.0257, SE=0.2127, p=0.0000308) and a cluster in a different part of the right IPS during the late maintenance phase (Delay 3; β=0.7186, SD=0.0216, SE=0.2119, p=0,000348).
Discussion: In our gene set analyses we observed multiple associations between brain activation during WM and NOS1AP and its interaction partners, which were most pronounced during the late maintenance phase of our WM task in bilateral areas within the IPS. Both the more constrained NOS1AP / NOS1 gene set and the NOS1AP / glutamatergic synapse gene set showed similar association patterns. Our results implicate the NOS1AP interactome and the glutamatergic system in information processing and brain function in a cognitive domain strongly impaired in schizophrenia. They also indicate that altered activation of parietal WM areas during the maintenance phase is most strongly affected.

S178. SHOULD SCHIZOAFFECTIVE DISORDER DEPRESSED-TYPE BE DISTINCT FROM SCHIZOPHRENIA? ANALYSIS OF GENETIC LIABILITY AND LIFETIME CLINICAL CHARACTERISTICS.

Charlotte Dennison*[1], Sophie Legge[1], Leon Hubbard[1], Amy Lynham[1], Peter Holmans[1], Alastair Cardno[2], Michael J. Owen[1], Michael O'Donovan[1], James Walters[1]
[1]Cardiff University; [2]Division of Psychological and Social Medicine, Leeds Institute of Health Sciences, Faculty of Medicine and Health, University of Leeds

Background: Schizoaffective disorder depressed type (SAD) has been considered a distinct diagnostic entity since 1987, yet it is rarely recognised in clinical and research settings as it is considered analogous to schizophrenia with comorbid depression. However, these assumptions are often based on anecdotal evidence, as little research has attempted to examine differences between the two disorders. We aimed to establish the validity of SAD as a diagnosis, by investigating phenotypic and genotypic differences between schizophrenia and SAD.
Methods: Participants were from the Cardiff Cognition study and included if they met ICD-10 criteria for schizophrenia (n=713) or SAD (n=151). Diagnosis was determined via consensus assessment by trained researchers using lifetime symptom data from the SCAN interview alongside patient medical records. Polygenic risk scores were derived for schizophrenia and major depressive disorder using PRSice. Logistic regressions were used to measure the association between diagnosis and lifetime clinical characteristics across five categories: demographics, premorbid functioning, illness progression, psychosis, and depression. Sex and age at interview were included as covariates. Logistic regressions were used to measure the association between diagnosis and polygenic risk scores for schizophrenia and depression at a threshold of p<.05, covarying for sex and principal components.
Results: Compared to schizophrenia, SAD was significantly associated with female sex (OR= 3.19, 95% CI= 2.23 - 4.59, p=5.0x10-9), lower global assessment score in worst episode of depression (OR= 0.47, 95% CI= 0.37 – 0.59, p=5.0x10-9), higher global assessment score in worst episode of psychosis (OR= 1.44, 95% CI= 1.20 – 1.72, p= 6.8x10-4), a greater likelihood of an admission for depression (OR= 2.24, 95% CI= 1.48 – 3.40, p= 1.2x10-3), greater alcohol abuse or dependence (OR= 2.12, 95% CI= 1.41 – 3.20, p= 2.3x10-3), longer duration of depression (OR= 1.46, 95% CI= 1.19 - 1.84, p= 3.5x10-3), experiencing childhood abuse (OR= 2.07, 95% CI = 1.35 – 3.17, p= 3.9x10-3), a reduced likelihood of an involuntary admission for psychosis (OR= 0.40, 95% CI= 0.22 – 0.75, p= 0.01), depression onset occurring prior to psychosis onset (OR= 2.40, 95% CI= 1.37 – 4.43, p= 0.01), having a higher number of children (OR= 1.34, 95% CI= 1.08 – 1.67, p= 0.03), and better cognitive functioning (OR= 1.20, 95% CI= 1.04 – 1.40, p= 0.05).
Depression polygenic risk score was higher in participants with SAD (OR= 1.33, 95% CI= 1.06 – 1.66, R2= 0.015, p= 0.01); schizophrenia polygenic risk score was not associated with diagnosis (OR= 0.94, 95% CI= 0.75 – 1.17, R2= 0.001, p= 0.58). Secondary analyses were conducted to