diffusivity (MD) was significantly increased in the hippocampal part of the cingulum in unmedicated patients (n=40) compared to healthy controls (n=41). Longitudinal analyses showed no changes in FA, MD, RD or white matter macrostructure in healthy controls over time, and no changes in patients after six weeks of treatment with risperidone.

**Discussion:** With state of the art data-processing methods we only found small areas of white matter integrity deficits in our predominantly medication-naive patients. This is consistent with prior reports of limited white matter alterations at disease onset that may progress with illness duration. Our data suggests that a short-term course of antipsychotic medication may not alter white matter microstructure, but studies with longer follow-up durations will be important to determine long term effects of antipsychotic medications.

**O6.7. COMMON NEUROANATOMICAL ABNORMALITIES IN FIRST EPISODE PSYCHOSIS ACROSS SEVERAL INDEPENDENT SAMPLES**

Sandra Vieira1, Cristina Scarppazza1, Benedetto Crespo-Facorro, Diana Tordesillas-Gutierrez, Victor Ortiz-Garcia de la Foz, Esther Setien-Suero, Floor Scheepers, Qiyou Gong, Tiago Reis Marques, Robin Murray, Anthony David, Paola Dazzan, Andrea Mechelli

1 Institute of Psychiatry, Psychology and Neurosciences, King’s College London; 2 Marqués de Valdecilla University Hospital, Instituto de Investigación Valdecilla, CIBERSAM; 3 University Medical Center Utrecht; 4 School of Public Administration, Sichuan University

**Background:** Structural abnormalities in first episode psychosis (FEP) tend to be subtle and widespread. Most studies investigating structural abnormalities in this clinical population have used small samples, and therefore may be under-powered. In addition, most studies have examined participants at a single research site, and therefore the results may be specific to the local sample investigated. Consequently, findings from existing studies have often been heterogeneous. This study aimed to overcome these issues by testing for neuroanatomical abnormalities in individuals with FEP relative to healthy controls that are expressed consistently across five independent datasets.

**Methods:** Structural Magnetic Resonance Imaging data were acquired from a total of 572 patients with FEP and 502 age and gender comparable healthy controls (HC) at five sites - London (UK), Utrecht (Netherlands), Chengdu (China) and two independent sites at Santander (Spain). Voxel-based morphometry (VBM) as implemented in Statistical Parametric Mapping software (SPM12) was used to investigate differences in gray matter volume (GMV) between the two groups. The statistical analysis was carried out using an analysis of variance (ANCOVA), with diagnostic group and scanning site as factors, and age and gender as covariates of no interest. Neuroanatomical alterations in patients with FEP relative to HC common to the five datasets were identified by comparing the total FEP group against the total HC group, and then using the inclusive masking option (at p=0.05 uncorrected) to identify those regions that survived the comparison between FEP and HC within each dataset. Individual clinical scores from each site were normalised and then used to test patients at a single research site, and therefore the results may be specific to the local sample investigated. Consequently, findings from existing studies have often been heterogeneous. This study aimed to overcome these issues by testing for neuroanatomical abnormalities in individuals with FEP relative to healthy controls that are expressed consistently across five independent datasets.

**Results:** Relative to HC, FEP showed a widespread pattern GMV reduction in fronto-temporal regions bilaterally, including the gyrus rectus, orbitofrontal, temporal, fusiform, precentral and lingual gyri, anterior cingulate and insula as well as in the parietal lobe in the precuneus gyrus. The largest GMV reduction was found in the left gyrus rectus which is part of the inferior frontal lobe. Negative correlations were found between this region and positive symptoms severity (r=-.2, p<.001) and duration of illness (r=-.1, p<.012), but not with negative symptoms (r=0.0, p=.991). Patients also showed GMV increases in the temporal gyrus bilaterally, left inferior frontal gyrus and right cerebellum relative to HC.

**Discussion:** This study identified a common pattern of fronto-temporal-parietal reductions in five independent FEP samples; in addition, some of these reductions were more pronounced in patients with more severe positive symptoms and longer duration of illness. This pattern of results suggests the presence of symptom- and stage-dependent neuroanatomical alternations in FEP that are expressed above and beyond site-related differences in recruitment criteria and scanning parameters.

**O6.8. GLUTAMATERGIC DYSFUNCTION AND TREATMENT RESPONSE IN MINIMALLY TREATED AND CHRONIC SCHIZOPHRENIA PATIENTS**

Elias Mouchlianitis1, Lucy Vareni1, Erica Barry1, Krishna Patel1, Katie Wong1, Lilla Porfy1, Sukhi Shergill1

1 Institute of Psychiatry, Psychology and Neuroscience, King’s College London

**Background:** Glutamatergic dysfunction as a result of NMDA receptor hypofunction has been implicated in antipsychotic treatment-resistant schizophrenia, however its nature in early stages and chronic stages of the disease is still unknown. Data on glutamate and treatment response are currently limited in two separate studies, one in first-episode patients (Egerton et al., 2012) and one in chronic patients (Mouchlianitis et al., 2016). Here we acquired proton magnetic resonance spectroscopy measures from a large sample of minimally treated first episode and chronic schizophrenia patients, and a group of matched healthy controls. Both first-episode and chronic schizophrenia groups were further stratified by treatment response. This allowed us to investigate glutamatergic dysfunction in both early and later stages of the disease in relation to treatment-response.

**Methods:** We acquired proton magnetic resonance spectroscopy (1H-MRS) at 3 Tesla from bilateral anterior cingulate cortex (ACC) from 170 participants. 137 participants with a diagnosis of schizophrenia (according to ICD-10 criteria) and 33 healthy controls matched for age, sex, and socioeconomic background consented to participate in this study. The patient sample included 95 minimally treated first-episode patients, with illness duration less than 36 months, of which 65 has shown good response and 26 have shown persistent psychotic symptoms; and a group of 42 chronically-ill patients with illness duration over 3 years. The chronic group was classified into 21 antipsychotic treatment-resistant patients and 21 antipsychotic treatment-responsive patients. 1H-MRS data were analyzed using a standard basis function within LC-Model. Our primary measure was glutamate to creatine ratio (Glu/Cre) and its correlation to N-Acetylaspartic acid to creatine ratio (NAA/Cre).

**Results:** The main new finding is that first-episode patients with persistent psychotic symptoms show significantly higher Glu/Cre and NAA/Cre correlation R(23)=0.76, P<0.001 compared to first-episode patients in remission R(65)=0.43, P<0.00, Fisher’s r-to-z, Z=1.97, P=0.05, effect size d=0.48. Compared to healthy controls (who did not show any Glu/Cre to and NAA/ Cr correlation R(3)=0.24, P=0.33) the FEP-resistant group showed a significant difference, Z=2.6, P<0.005, representing a large effect size of d=0.87 but not the FEP-responsive group, Z=0.97, P=0.17. Remarkably, when we examined first-episode patients with antipsychotic exposure of less than 6 months, we found an extremely high correlation in the non-responsive group R(5)=0.95, P=0.01, compared to the responsive group R(20)=0.44, P<0.05, which reflected a large effect size of d=0.99. Chronically-ill resistant patients showed a significant correlation R(21)=0.48, P<0.05 and responsive trend-level correlation R(21)=0.41, P=0.07, but neither group differed from healthy controls.

**Discussion:** Our study provides the first 1H-MRS evidence for acute metabolic perturbations in glutamatergic neurotransmission in minimally treated schizophrenia patients with persistent psychotic symptoms. These