relatives share genes with their affected family member, but do not share the disease process, abnormalities present in relatives are likely associated with the genes for schizophrenia.

**Results:** Evidence was found for disease-specific, genetic risk and compensatory brain mechanisms associated with schizophrenia that were complementary between the results from brain morphology, structural connectivity, and brain functioning.

**Discussion:** Isolating the biological and genetic basis of these deficits could ultimately aid in developing novel psychosocial and pharmacological treatments to facilitate improved day-to-day functioning in schizophrenia.

**S12. THE ‘AUTOANTIBODYOME’ IN PSYCHOSIS: A PILOT STUDY AND BLUEPRINT FOR BIOMARKER DISCOVERY**

Thomas Pollak*,1, Cassandra DeMarshall2, Abhirup Sarkar2, Timothy Nicholson,1 Philip McGuire1, James Stone1, Anthony David1, Robin Murray1, Robert Nagele1

1Institute of Psychiatry, Psychology & Neuroscience, King’s College London; 2Rowan University School of Osteopathic Medicine

**Background:** Recent studies seeking to describe the prevalence and significance of autoantibodies in psychotic disorders can be characterized as ‘top-down’ in theoretical approach; that is, autoantibodies to specific (usually CNS) antigens are sought based on a) the known function of the antigen (e.g. NMDAR) and its putative role in psychosis or b) the clinical observation that these autoantibodies can cause psychosis as part of a more complex neuropsychiatric presentation (e.g. autoimmune encephalitis). No candidate autoantibodies with a clear diagnostic or prognostic role have been definitively established.

We sought to take an alternative, ‘bottom-up’ approach to the significance of autoantibodies in psychosis that remains agnostic to the potential significance of any one antigen. Every individual harbours autoantibodies directed against many thousands of self-antigens and the vast majority are not disease-causing. Indeed production of autoantibodies may represent a normal, non-pathological process that is ongoing in that individual and can thus serve as a ‘readout’ of the disease state in question.

**Methods:** Sera from 20 patients with a first episode of psychosis (FEP) (males: n=16; mean age: 29.35 s.d.: 7.07) from the Genetics and Psychosis (GAP) study and 20 matched controls were analysed, using Invitrogen’s ProtA/Array v5.1 Human Protein Microarrays, for the presence of IgG to 9486 unique human protein antigens which had been expressed as GST fusion proteins in insect cells, purified and spotted onto slides. Following application of a fluorescent secondary IgG, reactivity patterns were automatically read using a fluorescence scanner. Samples were split into testing and training sets, and the top 50 most differentially expressed and differentially depleted antibodies were then chosen as biomarkers.

**Results:** The top 50 expressed biomarkers from the training set correctly identified 100% of psychosis subjects from the testing set, and 80% of healthy controls (OOB estimate of error rate 10%). When training and testing sets were swapped, biomarker overlap was 46% and 90% of psychosis subjects and 90% of controls were correctly identified (OOB estimate of error rate 10%). The top 50 depleted biomarkers from the training set correctly identified 90% of psychosis subjects from the testing set, and 90% of healthy controls (OOB estimate of error rate 10%). When training and testing sets were swapped, depletion biomarker overlap was 2% and 70% of psychosis subjects and 40% of controls were correctly identified (OOB estimate of error rate 45%).

**Discussion:** The autoantibodyome in FEP differs from that of healthy individuals. In this novel pilot study, a panel of 50 differentially expressed autoantibodies allowed confident discrimination between patients and controls, potentially paving the way for development of antibody-based diagnostics for psychosis using a simple blood test and fewer autoantibodies. Depletion biomarkers, thought to represent antibodies selectively depleted from the blood due to target binding in tissues, had less replicability and utility than expression biomarkers, which may offer insights into the active role of the adaptive immune system in psychosis. Further work will attempt to validate this approach in larger samples, using psychiatric disease controls. This autoantibodyomic approach may also show promise for the identification of predictive and prognostic biomarkers in psychotic disorders.

**S13. DO PATIENTS WITH RECENT-ONSET DEPRESSION DIFFER CLINICALLY AND NEUROBIOLOGICALLY FROM DEPRESSED PATIENTS WITH A CLINICAL HIGH-RISK STATE FOR PSYCHOSIS?**

Rachel Upthegrove1, Renate Reniers1, Pawan Mallikarjun1, Eva Meisenzahl1, Katharine Chisholm1, Stefan Borgwardt3, Stephan Ruhrmann1, Raimo Salokangas2, Paolo Brambilla1, Stephen Wood1, Nikolaos Koutsouleris2, Paris Alexandros Laloussis4,1

1University of Birmingham; 2Ludwig Maximilians University; 3University of Basel; 4University Hospital, University of Cologne; 5University of Turku; 6University of Milan; 7Orygen, the National Centre of Excellence in Youth Mental Health

**Background:** Major depressive disorder (MDD) is one of the most common mental disorders, with a lifetime prevalence of 14.6%. The impact of depression is considerable; poor social and economic functioning and significant life limitations [1]. Depression is also the most common co-morbidity seen with other mental disorders. The prevalence of depressive disorder in schizophrenia has been reported to be around 40% [2]. When examining very early phases of illness, in groups identified as at clinical high risk (CHR) for psychosis, high rates of ‘co-morbid’ axis one diagnoses are reported, with over 50% reaching criteria for a depressive disorder. Those people with schizophrenia send depression are significantly more likely to relapse, to be a safety concern (be arrested, victimized or suicidal), have greater substance-related problems and poorer recovery [2]. In addition, depression has been linked to increased risk of transition from CHR to FEP, suggesting that in this group depression also indicates a poorer outcome [3]. Currently, the diagnosis of depression is based on the phenomenological evaluation of symptoms and behavior. However, there remains significant debate around the heterogeneity of depressive symptoms and their function as prognostic indicators [4]. Neuroimaging holds “diagnostic potential” for depression [5]. However, studies show that brain alterations are often small and reliability is difficult, and there has been no neuroimaging investigation of depression as a co-morbid diagnosis. We aim to further understand the symptom profile of depression in emerging mental disorders, including in the clinical high risk group (CHR) and recent onset psychosis (ROP) as compared to those with recent onset depression (ROD). This has important implications for the accurate identification of a potentially malleable target for treatment, and indeed development of novel therapeutic options. We also aim to explore the ability of brain imaging (structural MRI) to add accuracy to the classification prediction models.

**Methods:** Data from the PRONIA study, an EUFP7 funded 8 center study recruiting ROAD, CHR and ROP participants will be presented. Analysis will include demographic information and BDI-II (Beck Depression Inventory), CAARMS (Comprehensive Assessment of the At Risk Mental State), SANS (Scale for the assessment of negative symptoms) total score PANSS (Positive and Negative Symptom Score) and SPI-A together with structural MRI imaging. We will report descriptive detail from the PRONIA discovery sample (n=716), machine learning classification with Neurominer® and VBM analysis of sMRI scans across groups.

**Results:** Data from BDI-II symptom endorsement suggests a ‘classical depression phenotype’ corresponding to Beck’s ‘cognitive triad’; ‘life is pointless, future hopeless, self as worthless’ may separate depression in ROD from ROP, with other symptoms potentially able to separate ROP...
GABAergic and glutamatergic systems play an important role in the neurobiology of schizophrenia, and changes in their markers are reported in both postmortem human brain and in animal models. Recent studies have demonstrated that abnormalities in DNA methylation may underlie the alterations in various indicators of GABAergic and glutamatergic functions in schizophrenia. As our group previously found decreased NR2 protein plasma levels and downregulation of parvalbumin (PV ALB) mRNA in first episode of psychosis (FEP) patients, we hypothesised that changes in DNA methylation may be responsible for these indicators of glutamatergic and GABAergic deficits in FEP patients.

Background: GABAergic and glutamatergic systems play an important role in the neurobiology of schizophrenia, and changes in their markers are reported in both postmortem human brain and in animal models. Recent studies have demonstrated that abnormalities in DNA methylation may underlie the alterations in various indicators of GABAergic and glutamatergic functions in schizophrenia. As our group previously found decreased NR2 protein plasma levels and downregulation of parvalbumin (PV ALB) mRNA in first episode of psychosis (FEP) patients, we hypothesised that changes in DNA methylation may be responsible for these indicators of glutamatergic and GABAergic deficits in FEP patients.

Methods: Blood samples were collected from patients in FEP (n = 35) after their first contact with the mental health assistance, siblings (n = 21) and population-based controls (n = 35). Bisulfite conversion and pyrosequencing were used to determine methylation levels in 4 CpG sites in promoter sequence of PV ALB and 5 CpG sites at GRIN2B (gene which encodes NR2).

Results: We found hypermethylation at a CpG site within the PV ALB promoter sequence in patients and their siblings compared to population-based controls (p < 0.001) while overall hypomethylation was found in the 5 CpGs analysed within GRIN2B promoter sequence (p < 0.01).

Discussion: Our PV ALB findings are consistent with our previous studies using ROD. In classification, a 65% sensitivity and specificity are found. Data will also be presented on the CHR group and their alignment, together with VBM analysis for structural MRI examining correlates with highly weighted classifying symptoms in and across all three groups.

Discussion: When given early in the course of illness, interventions have the greatest potential impact, and characterization and accurate diagnosis of depression in emerging mental disorders is an important goal. This study suggests it may be possible to accurately identify depression in different diagnostic categories, including major depressive disorder, psychosis and clinical high risk, and that neuroimaging holds potential to add to diagnostic accuracy in complex co-morbid disorders.

S14. DNA METHYLATION CHANGES IN GABAERGIC AND GLUTAMATERGIC MARKERS IN EARLY SCHIZOPHRENIA

Helene Fachim1, Camila Loureiro1, Fabiana Corsi-Zueli2, Paulo Rossi Menezes2, Paulo Louzada Jr2, Caroline Dalton1, Cristina Marta Del-Ben2, Gavin Reynolds2
1Sheffield Hallam University; 2University of Sao Paulo

Background: GABAergic and glutamatergic systems play an important role in the neurobiology of schizophrenia, and changes in their markers are reported in both postmortem human brain and in animal models. Recent studies have demonstrated that abnormalities in DNA methylation may underlie the alterations in various indicators of GABAergic and glutamatergic functions in schizophrenia. As our group previously found decreased NR2 protein plasma levels and downregulation of parvalbumin (PV ALB) mRNA in first episode of psychosis (FEP) patients, we hypothesised that changes in DNA methylation may be responsible for these indicators of glutamatergic and GABAergic deficits in FEP patients.

Methods: Blood samples were collected from patients in FEP (n = 35) after their first contact with the mental health assistance, siblings (n = 21) and population-based controls (n = 35). Bisulfite conversion and pyrosequencing were used to determine methylation levels in 4 CpG sites in promoter sequence of PV ALB and 5 CpG sites at GRIN2B (gene which encodes NR2).

Results: We found hypermethylation at a CpG site within the PV ALB promoter sequence in patients and their siblings compared to population-based controls (p < 0.001) while overall hypomethylation was found in the 5 CpGs analysed within GRIN2B promoter sequence (p < 0.01).

Discussion: Our PV ALB findings are consistent with our previous studies using ROD. In classification, a 65% sensitivity and specificity are found. Data will also be presented on the CHR group and their alignment, together with VBM analysis for structural MRI examining correlates with highly weighted classifying symptoms in and across all three groups.

Discussion: When given early in the course of illness, interventions have the greatest potential impact, and characterization and accurate diagnosis of depression in emerging mental disorders is an important goal. This study suggests it may be possible to accurately identify depression in different diagnostic categories, including major depressive disorder, psychosis and clinical high risk, and that neuroimaging holds potential to add to diagnostic accuracy in complex co-morbid disorders.

S14. DNA METHYLATION CHANGES IN GABAERGIC AND GLUTAMATERGIC MARKERS IN EARLY SCHIZOPHRENIA

Helene Fachim1, Camila Loureiro1, Fabiana Corsi-Zueli2, Paulo Rossi Menezes2, Paulo Louzada Jr2, Caroline Dalton1, Cristina Marta Del-Ben2, Gavin Reynolds2
1Sheffield Hallam University; 2University of Sao Paulo

Background: GABAergic and glutamatergic systems play an important role in the neurobiology of schizophrenia, and changes in their markers are reported in both postmortem human brain and in animal models. Recent studies have demonstrated that abnormalities in DNA methylation may underlie the alterations in various indicators of GABAergic and glutamatergic functions in schizophrenia. As our group previously found decreased NR2 protein plasma levels and downregulation of parvalbumin (PV ALB) mRNA in first episode of psychosis (FEP) patients, we hypothesised that changes in DNA methylation may be responsible for these indicators of glutamatergic and GABAergic deficits in FEP patients.

Methods: Blood samples were collected from patients in FEP (n = 35) after their first contact with the mental health assistance, siblings (n = 21) and population-based controls (n = 35). Bisulfite conversion and pyrosequencing were used to determine methylation levels in 4 CpG sites in promoter sequence of PV ALB and 5 CpG sites at GRIN2B (gene which encodes NR2).

Results: We found hypermethylation at a CpG site within the PV ALB promoter sequence in patients and their siblings compared to population-based controls (p < 0.001) while overall hypomethylation was found in the 5 CpGs analysed within GRIN2B promoter sequence (p < 0.01).

Discussion: Our PV ALB findings are consistent with our previous studies using ROD. In classification, a 65% sensitivity and specificity are found. Data will also be presented on the CHR group and their alignment, together with VBM analysis for structural MRI examining correlates with highly weighted classifying symptoms in and across all three groups.

Discussion: When given early in the course of illness, interventions have the greatest potential impact, and characterization and accurate diagnosis of depression in emerging mental disorders is an important goal. This study suggests it may be possible to accurately identify depression in different diagnostic categories, including major depressive disorder, psychosis and clinical high risk, and that neuroimaging holds potential to add to diagnostic accuracy in complex co-morbid disorders.

S14. DNA METHYLATION CHANGES IN GABAERGIC AND GLUTAMATERGIC MARKERS IN EARLY SCHIZOPHRENIA

Helene Fachim1, Camila Loureiro1, Fabiana Corsi-Zueli2, Paulo Rossi Menezes2, Paulo Louzada Jr2, Caroline Dalton1, Cristina Marta Del-Ben2, Gavin Reynolds2
1Sheffield Hallam University; 2University of Sao Paulo

Background: GABAergic and glutamatergic systems play an important role in the neurobiology of schizophrenia, and changes in their markers are reported in both postmortem human brain and in animal models. Recent studies have demonstrated that abnormalities in DNA methylation may underlie the alterations in various indicators of GABAergic and glutamatergic functions in schizophrenia. As our group previously found decreased NR2 protein plasma levels and downregulation of parvalbumin (PV ALB) mRNA in first episode of psychosis (FEP) patients, we hypothesised that changes in DNA methylation may be responsible for these indicators of glutamatergic and GABAergic deficits in FEP patients.

Methods: Blood samples were collected from patients in FEP (n = 35) after their first contact with the mental health assistance, siblings (n = 21) and population-based controls (n = 35). Bisulfite conversion and pyrosequencing were used to determine methylation levels in 4 CpG sites in promoter sequence of PV ALB and 5 CpG sites at GRIN2B (gene which encodes NR2).

Results: We found hypermethylation at a CpG site within the PV ALB promoter sequence in patients and their siblings compared to population-based controls (p < 0.001) while overall hypomethylation was found in the 5 CpGs analysed within GRIN2B promoter sequence (p < 0.01).

Discussion: Our PV ALB findings are consistent with our previous studies using ROD. In classification, a 65% sensitivity and specificity are found. Data will also be presented on the CHR group and their alignment, together with VBM analysis for structural MRI examining correlates with highly weighted classifying symptoms in and across all three groups.

Discussion: When given early in the course of illness, interventions have the greatest potential impact, and characterization and accurate diagnosis of depression in emerging mental disorders is an important goal. This study suggests it may be possible to accurately identify depression in different diagnostic categories, including major depressive disorder, psychosis and clinical high risk, and that neuroimaging holds potential to add to diagnostic accuracy in complex co-morbid disorders.