this was no longer significant. Scan-interval treatment days associated non-significantly with total brain decrease but significantly with cerebrospinal fluid increase even when adjusted with medication (beta = 0.41, $p = 0.04$). Alcohol use (g/day) associated surprisingly with less total brain decrease in women (unadjusted $r = -0.60$, $p = 0.001$), whereas no effect was seen in men.
*Conclusion:* Even after controlling for symptom severity, antipsychotic cumulative dose associated with total brain volume loss in our sample. Illness severity and substance use may also contribute to brain volume loss. In this population based sample factors associating to brain volume change can be characterized even after years of illness onset.
*Policy of full disclosure*: None.

**O-07-002**
**Familial and unique environmental influences on brain volumes in twins with schizophrenia**

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*Objective:* Reductions in whole brain and grey matter volumes are robust features of schizophrenia. The extent to which these pathological abnormalities are influenced by schizophrenia's genetic and environmental aetiological risk remains less well established.
*Methods:* We investigated the relationship between familial and environmental risk on brain volumes in monozygotic (MZ) and dizygotic (DZ) twin pairs varying in their concordance for schizophrenia, and in healthy control twins.
*Results:* Total brain, grey and white matter volumes were established from structural magnetic resonance images using an automated alogorithm in SPM8 from 86 twin pairs (n = 168), varying in their zygosity and concordance for schizophrenia. Hippocampal volumes were measured manually. We found that whole brain, grey, white and right hippocampal volumes were smaller in probands with schizophrenia compared to healthy controls, while well co-twins from DZ discordant pairs had smaller hippocampal volumes compared to the healthy controls. Well co-twins from MZ discordant pairs showed a trend towards lower white matter volume compared to the healthy controls. The patients with schizophrenia and their well co-twins from MZ discordant pairs did not differ from each other for any of the volumes measured. Lower birth weight and hypoxia were both associated with lower whole brain volumes, and lower white and grey matter volumes respectively. There were no significant effects in the patients of cumulative antipsychotic medication.
*Conclusion:* Our data suggest that total brain and grey matter volume reductions in schizophrenia are related primarily to unique environmental risk, that include perinatal complications. The evidence relating to the nature of white matter and local hippocampal volume reductions suggests an additional effect of genetic risk.
*Policy of full disclosure:* This work was supported by the Wellcome Trust and the EU.

**O-07-003**
**Greater reductions in grey matter volume in a cognitive-deficit subtype of schizophrenia**

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*Objective:* Considerable heterogeneity of brain disturbances in schizophrenia (SZ) highlights the need to determine brain-based phenotypes for further biological interrogation. Here we used voxel-based morphometry (VBM) to identify grey matter volume (GMV) differences among 'cognitive deficit' (CD) and 'cognitively spared' (CS) subtypes of SZ cases in the Australian Schizophrenia Research Bank (ASRB).
*Methods:* High-resolution T1-weighted scans for 263 SZ and 180 healthy controls (HC) were collected using 1.5T Siemens Avanto scanners at five Australian sites for the ASRB (Melbourne, Sydney, Brisbane, Perth and Newcastle). Previous Grade of Membership analyses (GOM) of SZ cases classified 156 CS participants and 106 CD participants with available scans. Using the VBM8 toolbox for SPM8, whole-brain differences in GMV were assessed, controlling for age, sex and scanner-site.
*Results:* The CD subtype showed substantial GMV reductions bilaterally in insula, inferior and medial frontal gyri, thalamus, temporal gyri, hippocampus and amygdala ($p < 0.0001$, FWE-corrected), relative to HC. Conversely, the CS showed a restricted pattern of GMV reduction encompassing smaller clusters within temporal lobe gyri, culmen, frontal gyri, and subcortically relative to HC. When the CD and CS groups were compared directly, no differences survived FWE-correction, however at a cluster corrected level (FWEc $p < 0.05$), the CD group showed significant reductions of the left insular cortex relative to CS. In the whole SZ group we found substantial GMV reductions bilaterally that reflected the breadth of regional alteration evident in both subgroups ($p < 0.0001$, FWE-corrected). Subsequent analyses of controls alone, grouped according to site, revealed no systematic effect of scanner-site on GMV ($p < 0.05$, FWE-corrected).
*Conclusion:* The extent of cognitive impairment was reflected in the magnitude of grey matter volume reduction (i.e., pronounced in CD). Insular cortex volume may represent a key region of pathology in emerging brain-based phenotypes that characterise SZ cases with severe cognitive deficits.
*Policy of full disclosure*: None.

**O-07-004**
**Supplementary motor area (SMA) volume correlates with psychotic symptoms associated with dysregulation of the motor system: a voxel-based morphometry (VBM) study**

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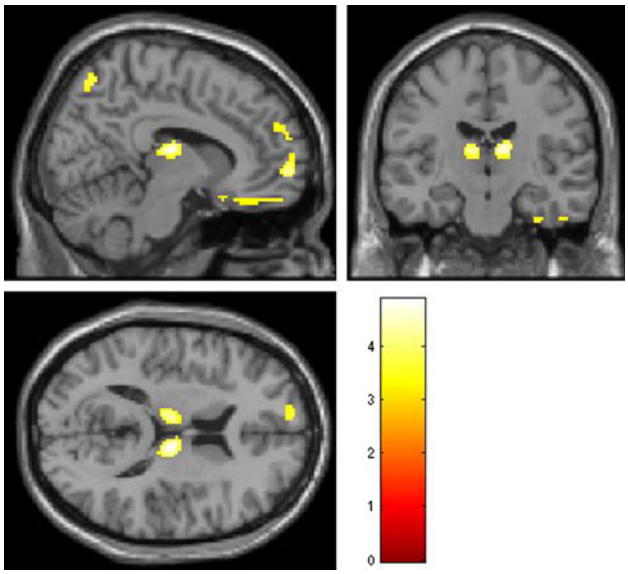
*Objective:* Investigations on grey matter in schizophrenia revealed substantial heterogeneity across studies. Differences in methodology and variance in symptom patterns may contribute to inconsistent findings. Recently, a psychopathology scale (Bern Psychopathology Scale, BPS) for the assessment of System-Specific Psychotic Symptoms has been proposed. The authors defined three symptom domains which were matched on three candidate brain circuitries, namely the language, the limbic and the motor system. The aim of the present study was to investigate whether a patient subgroup with severe motor dysregulation would show structural neuronal differences of the motor system.
*Methods:* 43 right-handed patients with schizophrenia and a control group of 34 healthy individuals underwent structural imaging at a 3T MRI scanner. Patients with schizophrenia were assessed with the BPS. Items of the BPS-subscale attribute to the motor system comprise symptoms such as spontaneous movements, spontaneous rest, velocity, and motor drive. A global score in the BPS assesses the severity of the motor symptoms, ranging from −3 to +3, while zero defines patients without motor symptoms. Whole brain voxel-based

morphometry was compared between patients with different symptoms of motor dysregulation. Central group comparisons were performed using one way ANOVA analysis.
*Results:* Patients with prevalent motor symptoms revealed decreased grey matter volume in the right SMA compared to patients without motor symptoms. No significant correlations were found between grey or white matter volume with number of episodes, duration of illness, and medical treatment.
*Conclusion:* Decreased grey matter volume in the SMA was associated with severe symptoms in the domain of motor dysregulation in schizophrenia patients. The SMA is an important region of the motor system, and was repeatedly found to be involved in motor sequencing. The present results support the hypothesis that specific clinical symptoms can be matched to brain systems, and allow identifying patient subgroups with structural abnormalities in the motor network.
*Policy of full disclosure*: None.

**Decreased GM density of the right SMA of patients with severe motor symptoms. For illustration purpose group map of volumes with lower concentration of GM was statistically thresholded at $p < 0.001$, uncorrected and displayed on the section of the standard:**




**O-07-005**
**Relevance of posterior parietal areas for auditory verbal hallucination in schizophrenia: a voxel-based grey and white matter morphometry study**

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*Objective:* Auditory Verbal Hallucinations (AVH) may result from abnormal local and interregional integration of brain signals in regions involved in language production and perception. To investigate the neuroanatomical underpinnings of such abnormal integration, we studied both grey matter (GM) and white matter (WM) volumetric correlates of AVH in schizophrenia patients.
*Methods:* Using a unified voxel based morphometry—DARTEL approach, we investigated correlates of AVH-severity in a sample of 51 schizophrenia patients (7 female, mean age 34), non-skewed for AVH-severity, and included 42 age and gender matched healthy participants to control for disease related factors. Results are report at $p < .05$, FWE corrected for the spatial extent of ap riori defined rois (superior temporal gyrus, posterior cingulate cortex, inferior frontal gyrus, corpus callosum).
*Results:* Patients showed lower relative GM volume of the left superior temporal gyrus and the bilateral parahippocampal gyrus than controls, which was unrelated to AVH-severity. In patients, WM of the adjacent inferior parietal lobule and GM of the posterior cingulate cortex showed a positive relation with AVH. Taking into account variations in delusion severity, general positive symptomatology and use of anti-psychotic medication did not change the results.
*Conclusion:* In a sample of schizophrenia patients, non-skewed for AVH severity, we found that lower volume of the left superior temporal gyrus was associated with a diagnosis of schizophrenia but unrelated to AVH–severity. AVH-severity, however, was associated with higher regional GM volume of the posterior cingulate cortex and higher WM (and subthreshold GM) volume of the left inferior parietal lobule, regions associated with voice hearing, sensory integration, body images, and concept of self. This suggests the left inferior parietal and posterior cingulate regions as important hubs in the pathophysiology underlying AVH.
*Policy of full disclosure*: None.

**O-07-006**
**Structural brain imaging correlates of At-Risk Mental State**

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*Objective:* At-Risk Mental State (ARMS) is characterised by a significant drop of global functioning over a period of 12 months and having a close biological relative with a psychotic disorder and/or experiencing attenuated or very brief episodes of psychotic symptoms. Young people meeting this profile have a profound risk of developing a severe mental illness such as schizophrenia. Since regional cortical grey matter reductions have been reported for prodromal, first-episode and chronic schizophrenia, we tested the hypothesis whether the defining clinical characteristics of ARMS are associated with reduced regional grey matter thickness.
*Methods:* Cortical grey matter thickness was measured in high-resolution MRI scans of 42 individuals meeting ARMS criteria of the Comprehensive Assessment of At-risk Mental State (CAARMS). Correlation maps of cortical grey matter thickness and summative scores of positive and negative CAARMS symptom ratings and function levels rated on the Global Assessment of Functioning (GAF), Socio-occupational Function Assessment (SOFA) and social/role functioning (GF), respectively, were generated with Freesurfer.
*Results:* High total CAARMS symptom rating scores correlated ($P < 0.05$ corrected) with reduced grey matter thickness in left and right superior frontal gyri, right anterior cingulate, and right lingual gyrus while negative symptom expression correlated with reduced grey matter in left and right superior occipital gyri. Low global, socio-occupational, and social/role function ratings correlated with reduced grey matter in frontal, prefrontal and occipital cortex in both hemispheres. Age, gender, handedness, history of substance abuse, and exposure to psychotropic medication were ruled out as potentially confounding factors.
*Conclusion:* Our findings provide evidence that reduced regional grey matter is associated with key ARMS criteria (i.e. low-grade psychotic symptom expression and functional impairment). Since grey matter reduction in these brain areas has also been found in schizophrenia, the corresponding regional grey matter reductions in ARMS may indicate increased risk of developing a psychotic illness.
*Policy of full disclosure*: None.