

volumes in non-psychotic adults born weighing less than 1500 g (very low birthweight (VLBW)) and to establish possible similarities to those volume abnormalities observed in schizophrenia.

**Methods:** We compared volume measurements of the whole brain, cerebral grey matter, cerebral ventricles, whole corpus callosum and the anterior, middle and posterior sections of the corpus callosum obtained using stereological methods from brain MRI scans of low birth weight subjects ( $n = 33$ ; age range 18–28) and their normal birth weight adult siblings ( $n = 18$ ).

**Results:** Mean total ventricular volume in VLBW subjects was significantly larger than that in their normal birthweight siblings (15.78 mls vs 10.79 mls;  $p = 0.02$ ). The volume of the total CC and the posterior section of the CC was smaller in low birth weight subjects ( $p = 0.03$  and  $p = 0.002$  respectively). No significant differences were seen between groups for total cerebral volume (1073.76 mls vs 1119.79 mls;  $p = 0.27$ ) or total cerebral grey matter (703.52 mls vs 737.68 mls;  $p = 0.15$ ).

**Conclusions:** Non psychotic VLBW subjects have brain abnormalities comparable to those seen in schizophrenic patients. This suggests the possibility that structural brain abnormalities in schizophrenia may be mediated at least in part by the effects of PBCs. These results point to a significant environmental effect contributing to the abnormalities observed in schizophrenia.

#### FC65-4

#### HARM AVOIDANCE AND 5-HT2A RECEPTORS: A BRAIN IMAGING STUDY

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In the Biosocial personality model which has been proposed by R. Cloninger, the dimension of harm avoidance has been linked to a hypothetical brain behavioural inhibition system, with serotonin as its major neuromodulator.

In a recent study in depressed patients, a significant negative correlation between a measure of harm avoidance and serotonin 5-HT2A receptors, measured in blood platelets, has been demonstrated.

In this study single photon emission computerized tomography (SPECT) was used to investigate the relationship between 5-HT2A receptors in the brain of healthy volunteers and harm avoidance.

The Temperament and Character Inventory (TCI) was administered to 26 normal volunteers. SPECT imaging was performed with a 3 headed gamma camera and <sup>123</sup>I-5-I-R91150 as a ligand for the 5-HT2A receptors. Scores on the TCI varied between 0 and 31 (mean 13.6, s.d. 8.4).

No correlation between TCI scores and 5-HT2A ligand binding could be demonstrated.

#### FC65-5

#### AMISULPRIDE IN ACUTELY ILL SCHIZOPHRENIC PATIENTS: EFFICACY, SAFETY AND RELATED SOCIAL ADAPTATION

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Amisulpride is a benzamide derivative atypical antipsychotic characterized by selective blockade of dopamine D<sub>3</sub> and D<sub>2</sub> receptors, limbic selectivity and preferential blockade of dopamine autoreceptors at low doses.

In order to determine its safety and efficacy in a large sample of patients under naturalistic conditions of use, a multicenter open trial of amisulpride was conducted.

A total of 445 patients with DSM-III-R criteria of schizophrenia, paranoid type, or schizopreniform disorder (293 men and 152 women, mean age 32.2 years), were included in the study. The patients received amisulpride with flexible dosage between 600 and 1200 mg/d during a 3-month period (mean dose: 792 mg/d ± 318) with a follow up of six months. During the 3-month follow-up period, 124 patients (27.9%) dropped out the trial.

Intent-to-treat analysis showed a significant improvement of the Brief Psychiatric Rating Scale (BARS) scores (D0: 67.6/DEnd: 40.2;  $p < 10^{-4}$ ), of positive scores of the Positive And Negative Symptoms Scale (PANSS) (D0: 27.7/DEnd: 15.0;  $p < 10^{-4}$ ), and of negative PANSS scores (D0: 28.6/DEnd: 18.3;  $p < 10^{-4}$ ) between D0 and D90. A scale of social adaptation (EAPS) showed an improvement of social adaptation during the study (D0: 4.89/DEnd: 6.93;  $p < 10^{-4}$ ). Follow-up assessment at D180 showed a sustained response on BARS, PANSS and EAPS scores.

Amisulpride was well tolerated in this study, with 21% of patients reporting adverse events. Extra pyramidal symptoms, as measured with Simpson-Angus scale, remain low during the study (D0/DEnd  $p: 0.30$ ). In conclusion, under treatment with amisulpride an improvement in patient's ability to social adaptation was observed.

#### FC65-6

#### DOPAMINE D<sub>1</sub> AND D<sub>4</sub>-LIKE RECEPTORS IN UNTREATED SCHIZOPHRENIC PATIENTS AND HEALTHY CONTROLS

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This study uses the new radioligand <sup>11</sup>C-SDZ GLC 756 with especially high affinity for dopamine D<sub>4</sub> receptors (and additional affinity for D<sub>1</sub> receptors) in 9 untreated schizophrenic patients (5 never treated) and 3 human volunteers. The binding of <sup>11</sup>C-SDZ GLC 756 in striatum, cortex and thalamus was evaluated in vivo using repeated studies with positron emission computed tomography (PET) before and after pharmacological blockade with the atypical neuroleptic olanzapine.

In 3 healthy volunteers without pharmacological pretreatment, the regional uptake of SDZ GLC 756 was highest in the basal ganglia, followed by thalamus and several cortical regions. This distribution corresponds well to the autoradiographic distribution of D<sub>4</sub> and D<sub>1</sub>/D<sub>5</sub> dopamine receptors. In 9 unmedicated acute schizophrenic patients a preliminary analysis demonstrated no significant difference of the binding of SDZ GLC 756 (calculated as region-of-interest to cerebellum-ratio) in striatum and cortex, but a trend to an increased binding of the ligand in the thalamus, which could be specifically blocked by treatment with olanzapine.

Our preliminary findings do not support the idea that dopamine D<sub>4</sub>-like receptors are elevated in the striatum of acute schizophrenic patients. However, the role of extrastratal thalamic dopamine receptors needs further investigation.