disorder 15%). Patients with arrhythmia were much more likely to accurately perceive their heartbeats than the other groups and the controls. Fear of bodily sensations was significantly higher in the sinus rhythm group and all three groups were significantly more worried about palpitations and about heart disease and illness than controls.

- The intervention was popular with patients who said that they found the explanation and advice helpful. Whilst for a number of patients in the control group outcome improved, significantly more treated patients had better outcomes in terms of frequency of palpitations, their distress and other reactions to them and in limitation of everyday life.

Conclusion: Psychiatric disorder and health anxiety were particularly common in the sinus rhythm group. All three groups described significant distress and limitation of everyday activities, often of long duration. A simple nurse-delivered intervention was effective.

S64-6

MIGRAINE AND PSYCHIATRIC DISORDERS. A POPULATION AND REGISTER BASED INVESTIGATION

L. Sørensen[1]*, M. Russell[2]. [1]*Department of Psychiatric Demography, Psychiatric Hospital in Aarhus, DK-8240 Risskov;* [2]*Department of Neurology, Glostrup Hospital, University of Copenhagen, Denmark*

The literature reports that migraine and depression are associated disorders. Such an association is interesting from an aetiological, psychodynamic, genetic epidemiological and health-care cost point of view.

We investigated the association of migraine and depression in a population-based sample of 484 migraineurs. The participants received a diagnosis by a physician according to the International Headache Society criteria and data on their psychiatric morbidity was drawn form the Danish Psychiatric Case Register. Drop-out analysis was performed. The data showed that migraineurs were not more prone to hospitalisation due to depression than people who never had migraine.

FC65. Biological psychiatry – basic research

Chairs: H D'Haenen (B), H Aschauer (A)

FC65-1

ACTION AS A DETERMINANT IN STIMULUS PROCESSING AS ASSESSED BY THE CONDITIONED TASTE AVERSION PARADIGM IN RATS

N. Fouquet*, G. Sandner. *INSERM U405, 67085 Strasbourg, France*

It has long been recognised that patients suffering from schizophrenia tend to have difficulties to take information from their environment in an "active" way. Surprisingly, this problem has received little attention. Thus, we have developed a rodent model allowing us to document the role of the action related to stimulus processing for its subsequent integration.

For this purpose, we used the conditioned taste aversion paradigm in rats. This paradigm consists in pairing the consumption of a flavoured solution -the target stimulus being the taste- with a gastric malaise induced by a systemic injection of lithium chloride. Taste processing is assessed by the ensuing null or weak consumption of the flavoured solution by the animal. This procedure can be achieved either "actively", -which requires from the rat the development of a self-generated activity to take the flavoured solution from a drinking tube-, or "passively", - which *does not* require such an activity, the flavoured solution being perfused intraorally-. The difference between these two procedures relies on the presence or not of an activity related to the consumption of the taste stimulus at the time of learning. We found an improved performance for the active condition, as opposed to the passive one. This suggests that the cognitive processing of the stimulus is modulated at least, by the presence of a related self-generated action.

We will present recent data from our laboratory aimed at documenting the psychological and pharmacological sensitivity of our model.

FC65-2

INDICATORS OF CHRONIC IMMUNE ACTIVATION IN SCHIZOPHRENIA

A. Sluzewska[1]*, E. Bosmans[2], J. Rybakowski[1], M. Sobieska[3]. [1]*Department of Adult Psychiatry, University of Medical Sciences, Poznan;* [3]*Department of Immunology, Poznan, Poland*
[2]*Eurogenetics, Tessenderlo, Belgium*

It has been hypothesized that schizophrenia may be accompanied by an acute phase response (apr).

Serum concentrations of interleukin-6 (IL-6), soluble interleukin-6 receptor (sIL-6R), soluble interleukin-2 receptor (sIL-2R), interleukin-1 receptor antagonist (IL-1RA) and Clara cell protein (CC 16) as well as concentration of acute phase proteins: C-reactive protein (CRP), α-1-acid glycoprotein (AGP), haptoglobin (Hp) and AGP microheterogeneity were measured in 35 schizophrenic patients during exacerbation of their symptoms and in 20 healthy controls subjects. Patients studied were hospitalized at the Department of Adult Psychiatry in Poznan. Diagnoses were made according to DSM-IV criteria. There were 20 schizophrenics of paranoid type and 15 of residual type. There were no patients suffering from the first schizophrenic epizode. All subjects were medically healthy. Measurements of cytokines were performed in Eurogenetics. Schizophrenic patients showed significantly higher serum concentrations of IL-6, sIL-6R, sIL-2R, IL-1RA, as well as AGP and Hp and significantly lower concentrations of CC 16 and lower values of glycosylation profiles of AGP than healthy controls.

The results obtained in this study confirm recent findings suggesting that schizophrenia is accompanied by immune activation of chronic type.

FC65-3

ARE THE STRUCTURAL BRAIN ABNORMALITIES IN SCHIZOPHRENIA MEDIATED BY PREGNANCY AND BIRTH COMPLICATIONS?

P. Fearon, P. O'Connell, P. Aquino, S. Frangou, L. Rifkin, R.M. Murray. *Department of Psychological Medicine, Institute of Psychiatry, De Crespigny Pk., Denmark Hill, London SE5 8AF, UK*

Background: A range of structural brain abnormalities have been reported in schizophrenia. Their origin is unclear but may be linked to the increased rate of pregnancy and birth complications (PBCs), particularly low birth weight, reported in schizophrenic patients. The purpose of the present study was to measure whole brain, cerebral grey matter, total ventricular and corpus callosum (CC)

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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

H. D'haenen[1] *, C. Baeken[1], P. Flamen[2], J. Mertens[3], D. Terriere[3], K. Chavatte[3], R. Boumon[3], A. Bossuyt[2]. [1]*Psychiatric;* [2]*Nuclear Medicine Department, Academic Hospital;* [3]*Cyclotron Unit, Free University of Brussels (V.U.B.), Belgium*

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 ^{123}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

J.P. Chabannes[1] *, D. Gérard[2], J.M. Chignon[3]. [1]*CHS Bassens, Chambery;* [2]*Laboratoires Synthélabo, Meudon;* [3]*Hopital général, Annecy, France*

Amisulpride is a, benzamide derivative atypical antipsychotic characterized by selective blockade of dopamine D_3 and D_2 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 schizophreniform 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_1 AND D_4-LIKE RECEPTORS IN UNTREATED SCHIZOPHRENIC PATIENTS AND HEALTHY CONTROLS

A. Klimke[1] *, C. Boy[2,3], M. Eickhoff[1], H. Herzog[3], M. Holschbach[4], H. Mühlensiepen[3], M. Weckesser[2,3], E. Rota-Kops[3], F. Sonnenberg[3], W. Gaebel[1], R. Markstein[5], G. Stöcklin[4], H.H. Coenen[4], H.W. Müller-Gärtner[2,3]. [1]*Dept. of Psychiatry, Bergische Landstrasse 2, W-40629 Duesseldorf;* [2]*Dept of Nuclear Medicine, University of Duesseldorf; Research Center Juelich;* [3]*Institute of Medicine;* [4]*Institute of Nuclear Chemistry, Germany*
[5]*Preclinical Research, Novartis AG, Basel, Switzerland*

This study uses the new radioligand ^{11}C-SDZ GLC 756 with especially high affinity for dopamine D_4 receptors (and additional affinity for D_1 receptors) in 9 untreated schizophrenic patients (5 never treated) and 3 human volunteers. The binding of ^{11}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_4 and D_1/D_5 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 bloked by treatment with olanzapine.

Our preliminary findings do not support the idea that dopamine D_4-like receptors are elevated in the striatum of acute schizophrenic patients. However, the role of extrastriatal thalamic dopamine receptors needs further investigation.