

patients. The severity of symptoms tended to change in individuals within the 10 years period, but remained stable in the sample as a whole.

#### P.2.053 Effects of risperidone and other antipsychotic agents on sleep quality

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It has been described that neuroleptics affect sleep structure of schizophrenic patients. In general, neuroleptics decrease sleep latency, increase sleep continuity, the total sleep time and the latency of sleep with rapid eyes movements (LREM)<sup>1</sup>. All this redound to a better sleep quality for these patients. Risperidone is a new antipsychotic agent that produces insomnia as side effect, so this special feature makes risperidone different from the other ones<sup>2</sup>. This study has been made in order to determinate if risperidone produces an effect on schizophrenics sleep quality in a bigger proportion than other antipsychotics. A naturalistic study have been made to control the sleep quality of 31 schizophrenic people, using as diagnostic tool the Spanish version of Pittsburgh Sleep Quality Index (PSQI). 13 people had risperidone, 12 other people had other oral antipsychotics, and 6 other had neuroleptics depot. The frequency having benzodiazepines by these three groups of patients was the same (no statistical differences, Chi-square test). There aren't any differences in the total score and the partial components of PSQI by these three groups (Kruskal-Wallis test). We conclude that risperidone has the same effects than other neuroleptics on sleep quality. Nevertheless, it would be necessary to make more researches in order to eliminate doubts with other psychotropic drugs and medicines in general.

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#### P.2.054 The use of risperidone for young patients: Clinical experience

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Since the apparition of Risperidone, our interest turns on the treatment of the first stages of psychotic disorders with young patients.

(Brief Reactive Psychotic Disorder 298.8 DSM-IV).

In the first place, we used the classic scheme already experienced for schizophrenic patients.

We noted that our young patients showed a major prostration state characterised by a reduced psychomotor function and other secondary effects specially in the sexual field.

In a second time, we reduced the posology at third of the classic scheme, the clinical state of our patients improved and the secondary effects, sexual effects included, diminished, without decreasing the anti-psychotic effects of Risperidone.

The purpose of this communication (poster) is to enlighten the use of Risperidone throughout our clinical practice for a better comfort of utilization for the pratician and a better quality of life for our patients.

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#### P.2.055 Acute phase proteins in major depressed and schizophrenic patients during acute episode of the illness

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There is now strong evidence that affective disorders and schizophrenia may be accompanied by abnormal immune reactivity (Ganguli 1994, Maes 1992, Sluzewska 1996).

Serum concentrations of four acute phase proteins (apps): C-reactive protein (CRP), haptoglobin (Hp), alpha-1-acid glycoprotein (AGP) and alpha-1-antichymotrypsin (ACT) as well as major microheterogeneity of AGP and ACT in 116 inpatients from Department of Adult Psychiatry. There were 81 patients with major depression (66 unipolar and 15 bipolar affective illness) and 35 patients with schizophrenia (20 paranoid type and 15 of residual type). Diagnoses were made according to DSM IV and ICD 10 criteria. Mean age of depressed patients was  $43 \pm 9$  years and of patients with schizophrenia was  $33 \pm 10$  years. All patients were studied during acute episode or exacerbation of the illness and were drug free for at least 7 days before blood sampling. We have also studied these parameters in 20 normal controls. All subjects in this study were medically healthy, they were free of chronic somatic illnesses and acute infections.

Concentrations of apps were measured by rocket immunoelectrophoresis and reactivity coefficient (RC) of their reactivity with concanavaline A (Con A) by crossed-affinity immunoelectrophoresis (CAIE) with free Con A as a ligand.

In depressed patients, concentrations of AGP, ACT, Hp and CRP were significantly elevated in comparison to healthy controls. In 35% of depressed patients, high values of reactivity coefficients of AGP and ACT which means type I of changes in glycosylation. The similar changes were observed in acute inflammatory states.

Patients with schizophrenia had increased concentrations of AGP and Hp. The concentrations of CRP and ACT in these patients were in the range of normal controls. In schizophrenic patients, low values of reactivity coefficients of AGP and ACT were found which means type II of glycosylation patterns with more Con A-unreactive variants. This type of changes in glycosylation was observed in chronic inflammatory states such as liver cirrhosis or rheumatoid arthritis as well as in pregnancy.

The results obtained point to significant changes in acute phase proteins in both major depressed and schizophrenic patients during acute episode of the illness. They also suggest possible differences in apps glycosylation patterns between these groups. None of schizophrenic patients presented type I of changes in glycosylation (characteristic for acute inflammatory states), observed in 35% of depressed patients. Schizophrenic patients showed type II changes of glycosylation similar to chronic inflammatory states.

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#### P.2.056 Effects of clozapine and haloperidol on hematopoiesis

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**Background:** Immunomodulatory effects of different antipsychotics are often discussed but there are hardly any investigations proving quantitative and qualitative immunologic alterations due to neuroleptic treatment. Influences on hematopoiesis are studied more intensively in terms of clozapine as for this atypical antipsychotic compound an increased incidence of severe agranulocytosis (1-2%) is reported. The risk for alterations in hematopoiesis caused by typical antipsychotics like haloperidol is much lower.

**Aim of the Study:** A comparison between clozapine and haloperidol in terms of influences on hematopoiesis and the cytokine system using a bioassay for hematopoietic progenitor cells.

**Methods:** We investigated the effects of clozapine and haloperidol on hematopoiesis as well as neopterin- and GM-CSF release in cell cultures. Microagarcultures of normal peripheral blood mononuclear cells (MNC) of 8 probands not receiving any kind of pharmacological treatment were incubated with increasing concentrations of clozapine respectively of haloperidol.

**Results:** As reported in a previous study (Barbara Sperner-Unterweger et al., 1993) we found no effects on erythropoiesis and megakariopoiesis due to clozapine incubation. A biologically relevant suppression of granulopoiesis (CFU-GM) could only be shown in cultures incubated with a clozapine dose above clinical use. Cytokine analysis presented a strictly dose-dependent suppression of GM-CSF and neopterin release in all cell cultures incubated with clozapine. Evaluation of cell cultures incubated with haloperidol, using clinical relevant doses, did not show any effect neither on erythropoiesis and megakariopoiesis nor on granulopoiesis.

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#### P.2.057 Release of serotonin in brain by neuroleptics: Effect of risperidone

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Previously we have shown that risperidone (RISP), an antipsychotic drug with high affinity for 5-hydroxytryptamine (5-HT)<sub>2A</sub> and dopamine (DA)<sub>2</sub> receptors as well as for  $\alpha_1$  and  $\alpha_2$  adrenoceptors, dose-dependently enhances 5-HT release in the rat frontal cortex (FC). To further analyze the influence of RISP on brain serotonergic neurotransmission, we compared its effects on both 5-HT cell firing and 5-HT release within the dorsal raphe nucleus (DRN), with those obtained with other antipsychotic drugs and selective receptor antagonists. Methods used were in vivo single cell recording and microdialysis in freely moving rats.

RISP (25–800  $\mu\text{g}/\text{kg}$ , i.v.) dose-dependently decreased 5-HT cell firing in the DRN, similarly to the antipsychotic drug clozapine (CLOZ; 0.25–4.0 mg/kg, i.v.) and amperozide (AMP; 0.5–8.0 mg/kg, i.v.) as well as the selective  $\alpha_1$  adrenoceptor antagonist prazosin (PRAZ; 50–400  $\mu\text{g}/\text{kg}$ , i.v.). In contrast, the selective  $\alpha_2$  adrenoceptor antagonist idazoxan (IDAZ; 10–80  $\mu\text{g}/\text{kg}$ , i.v.) increased the firing rate of 5-HT neurons in the DRN, whereas the DA-D<sub>2</sub> and 5-HT<sub>2A</sub> receptor antagonists raclopride (RAC; 25–200  $\mu\text{g}/\text{kg}$ , i.v.) and MDL 100,907 (MDL; 50–400  $\mu\text{g}/\text{kg}$ , i.v.), respectively, were without effect. Thus, the  $\alpha_1$  adrenoceptor antagonistic action of RISP may, at least partly, cause the decrease in DRN 5-HT cell firing. Interestingly, the inhibitory effect of RISP on DRN 5-HT cell firing was largely antagonized by blockade of inhibitory 5-HT<sub>1A</sub> autoreceptors by WAY 100,635 (5.0  $\mu\text{g}/\text{kg}$ , i.v.), indicating that RISP enhances 5-HT release in the DRN. Indeed, both systemic and local DRN administrations of RISP (0.2, 0.6 and 2.0 mg/kg, s.c. and 1.0–1000  $\mu\text{M}$ , respectively) were found to increase 5-HT release in the DRN. Thus, the reduction in 5-HT cell firing by RISP may also be related to enhanced 5-HT<sub>1A</sub> autoreceptor activation in the DRN. In principle, the observed acute actions of RISP on central 5-HT neuronal function are quite similar to those produced by 5-HT re-uptake inhibitors, namely increased output of 5-HT from nerve terminal areas and attenuation of single cell firing in the DRN. However, the effects of chronic RISP treatment on central 5-HT neuronal function remain to be clarified.

In short, our data provide both electrophysiological and biochemical evidence that RISP enhances 5-HT release not only in terminal areas, such as the FC, but also in the DRN. Several clinical trials have indicated that drugs which enhance availability of 5-HT in brain, i.e. selective 5-HT re-uptake inhibitors or  $\alpha_2$  adrenoceptor antagonists, in conjunction with treatment with neuroleptics is associated with significant amelioration of negative symptoms in schizophrenia. Consequently, the reported beneficial actions of RISP against negative symptoms in schizophrenia may,

at least partly, be related to a capacity to augment central serotonergic neurotransmission in some 5-HT mediated synapses. The augmenting action of RISP on central serotonergic neurotransmission may be of particular relevance for the treatment of schizophrenia when associated with depression and/or pronounced anxiety.

#### P.2.058 How pharmacotherapy affects factor analysis and internal consistency in schizophrenia

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A very critical issue in psychiatry is the need for the characterisation of psychopathological dimensions both from a qualitative and quantitative point of view: this approach could overcome the traditional perspective, which is mostly categorical, and could also constitute an operative definition of the target of our observations, which in our case is schizophrenia. This strategy, which was originally proposed by N. Andreasen, traces its own roots in the discipline of mathematical logic: a theory is "consistent" if no contradictions can be derived inside the theory itself.

In order to individuate and describe the different dimensions, it is necessary to analyse the inter-relations among the different symptoms. Internal consistency then is in itself a validating variable even from a psychometric point of view and it can be measured, from a practical standpoint, by means of an opportune statistical index, such as, for example, Cronbach's alpha. A high degree of internal consistency is a reliable sign of homogeneity of the examined issue, and is the result, as said, of the absence of contradictions among each of its constitutive elements.

Following this logic line, different authors have demonstrated that positive symptoms in schizophrenic disorders are an heterogeneous construct, while on the contrary, negative symptoms are homogeneous: in fact their evaluation is based on the observation of phenomena which are mostly objective. In these analyses the influence of pharmacological therapy has been scarcely or not at all taken into account.

In our study we present a factor analysis which corrects each symptom group according to the pharmacotherapy variables and individuates well characterised factors that strengthen existing literature data.

Our data also support the evidence that the increase of the number of factors, provided that their load score is high, can produce an increase of the internal consistency of a given set of symptoms.

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#### P.2.059 New perspectives in the treatment of schizophrenic patients

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Schizophrenia remains the most devastating and challenging disease of the major mental illnesses. Amisulpride (Ami) is a substituted benzamide considered as a new atypical antipsychotic agent. It displays a selective and high affinity for D<sub>2</sub> and D<sub>3</sub> cerebral dopaminergic receptors and binds more strongly to the receptors located in the limbic structures than to those of the striatum. Ami preferentially blocks presynaptic autoreceptors. This atypical pharmacological profile may explain the therapeutic efficacy of Ami on negative symptoms of schizophrenia at low doses and on positive symptoms at higher doses.

The clinical efficacy of Ami in the treatment of productive forms of schizophrenia has been established in several controlled studies carried out on acute phases of the disease. In all studies the efficacy was comparable to the reference compounds and tolerance and acceptability were in favor of Ami, together with low incidence of extrapyramidal