

We suppose, that the chronification of patient's psychotic state is followed by the decrease of MM level.

### Wed-P43

ZOTEPINE ENHANCES NORADRENALINE LEVELS IN RAT FRONTAL CORTEX MICRODIALYSATES: FURTHER SUPPORT FOR ANTIDEPRESSANT ACTIVITY

Ian C. Kilpatrick\*, Helen L. Rowley, Patricia L. Needham, David J. Heal. *CNS Biology, Knoll Pharmaceuticals Research and Development, Nottingham, NG1 1GF, UK*

Zotepine is an antipsychotic drug with a marked atypical profile that not only has efficacy for positive and negative schizophrenic symptoms but combines activity in animal models predictive of antidepressant activity (Needham *et al.*, 1997; *Biol. Psychiat.* 42, 175-176S) with antidepressant properties in patients (Fleischhacker *et al.*, 1989; *Psychopharmacol. Bull.* 25, 97-100). Since zotepine inhibits <sup>3</sup>H-noradrenaline (<sup>3</sup>H-NA) uptake by rat frontal cortex synaptosomes (Needham *et al.*, 1997), we studied the effects of zotepine and comparator antipsychotics on extracellular NA in the frontal cortex using *in vivo* microdialysis. In freely-moving male CD rats (250-350 g), basal levels of cortical NA were 31 ± 3 fmol/20 µl. Zotepine (0.5, 1.0 or 1.5 mg/kg, ip) evoked biphasic, dose-related rises in cortical NA with peaks at 60 min (+94% to +171% above basal values; *p* < 0.001 by ANOVA with *post hoc* Dunnett's *t*-test) and at 240 min (+142% to +212%; *p* < 0.001) post-zotepine. The increases in NA were sustained for up to 120 min beyond the initial peak. Clozapine (10 mg/kg, ip) increased NA levels by 72% (*p* < 0.05) but only for 20 min. Neither ziprasidone (3 mg/kg, ip) nor olanzapine (1 mg/kg, ip) had any action on cortical NA. The antidepressant, desipramine (a NA uptake inhibitor; 0.3 mg/kg, ip), elevated NA levels 5-fold (*p* < 0.001), an effect which declined over 240 min. Zotepine's elevation of cortical NA probably occurs via NA uptake inhibition. Clozapine's weaker action may derive from α<sub>2</sub>-adrenoceptor blockade. This action of zotepine may contribute to its antidepressant profile and its reported superiority *vs* clozapine in improving some cognitive deficits in schizophrenic patients (Meyer-Lindenberg *et al.*, 1997; *Pharmacopsychiatry* 30, 35-42).

### Wed-P44

COGNITIVE AND EMOTIONAL SIDE EFFECTS AND THE EFFICACY OF CLASSICAL AND ATYPICAL NEUROLEPTICS IN ACUTE SCHIZOPHRENIA

W. Lemmer\*, M.W. Agelink. *Klinik für Psychiatrie und Psychotherapie, Universitätsklinik, Ev. Krankenhaus Gelsenkirchen, Munkelstr. 27, 45879 Gelsenkirchen, Germany*

The importance of cognitive emotional side effects of neuroleptics is underestimated in general, but according to the statements of many patients, it is a reason for their noncompliance.

Within various double-blind studies on the efficacy and tolerance of classical and atypical neuroleptics in our hospital we applied a neuro-psychological test battery in order to record the influence of the substances on cognitive and emotional functions.

The results of these investigations were compared quasi-experimentally. The results showed that not only the serotonergic antagonistic atypical neuroleptics clozapine, olanzapine, risperidone and zotepine, but especially also the substituted benzamides remoxipride and amisulpride caused significantly less cognitive emotional side effects than the classical neuroleptics.

The described results also found their expression in the contentment with medication of the investigated patients.

The results shall be discussed in context with the problems of methodological measuring.

### Wed-P45

PSYCHOPHARMAKOLOGISCHE BEHANDLUNG UND PRÄVALENZ VON EPS BEI PATIENTEN MIT 15JÄHRIGEM VERLAUF EINER AFFEKTIVEN-, SCHIZOAFFEKTIVEN-, SCHIZOPHRENEN- BZW. WAHNHAFTEN PSYCHOSE

J. Wittman\*, R. Bottlender, A. Strauß, U. Wegner, H.-J. Möller. *Psychiatrische Klinik der LMU, 80336 Munich, Germany*

**Einleitung:** Das Vorkommen von extrapyramidal motorischen Nebenwirkungen (EPS) wird bei bis zu 90% der mit Neuroleptika (NL) behandelten Patienten beschrieben, das von irreversibel auftretenden Spätdyskinesien bei bis zu 40% der Fälle (Möller 1996). Im Rahmen der Münchener 15 - Jahres - Katamnesestudie werden bei Patienten mit der Diagnose einer affektiven-, schizoaffektiven-, schizophrenen- und einer (nicht schizophrenen) paranoiden Psychose zum Follow-up-Zeitpunkt die gegenwärtige psychopharmakologische Medikation und das Ausmaß unwillkürlicher Bewegungsstörungen nachuntersucht.

**Material und Methoden:** Bestimmung von EPS und Spätdyskinesien durch: Extrapyramidale Symptom-Skala (Simpson, Angus 1970) und AIMS (abnormal involuntary movement scale).

**Ergebnisse:** 35% der nachuntersuchten Patienten mit einer funktionellen Psychose erhalten 15 Jahre nach dem ersten stationär psychiatrischen Aufenthalt keinerlei psychopharmakologische Medikation. NL werden von 44% der Patienten eingenommen. 31% der nachuntersuchten Fälle zeigen EPS, ein Drittel davon weisen EPS auf, obgleich sie keine NL einnehmen. 30% der Patienten weisen tardive Dyskinesien auf, 2/3 davon nehmen NL ein. Ausmaß von EPS und Spätdyskinesien bei den betroffenen Patienten werden angegeben.

**Diskussion:** Bei Betrachtung der Patienten mit EPS zeigt sich, daß die Patienten ohne NL-Einnahme aber mit einer sonstigen psychopharmakologischen Behandlung Lithium erhalten, von welchem bekannt ist, daß es eine neuroleptikainduzierte EPS verstärken und auch selbst EP-Symptome verursachen kann. Die Patienten mit EPS und ohne jegliche psycho-pharmakologische Medikation sind im Durchschnitt um ca. 10 Jahre älter, als die Gruppe mit EPS und NL-Einnahme.

### Wed-P46

PHARMACOTHERAPY OF ANXIETY IN SCHIZOPHRENIA

M. Munjiza\*, D. Lapčević, N. Ljubomirović, M. Veličković. *Institute for Mental Health, Palmotićevo 37, 11000 Belgrade, FR Yugoslavia*

Nearly 75% of all persons are more or less anxious, which indicates that anxiety normally belongs to human being. At low grade it helps in quick reactions and in "planing" of adaptive activities. But, when anxiety last longer or appear more frequently with hard bearing intensity, we speak about pathological anxiety. In schizophrenia we are faced with syndromes of psychotic anxiety which is very often "intertwine" with other psychopathological features of schizophrenia.

In this research, 80 schizophrenics have been tested (57 male, 23 female) average age of 28-39 years (± 6.3) who were treated in Department for Psychosis of Day Hospital during 1996. The group was divided in two subgroups with 40 patients each who were treated with different pharmacotherapy. First, experimental