not be confined to models of face-processing, but be extended to models of visual recognition in general.

AMISULPRIDE IN THE TREATMENT OF ACUTE EXACERBATIONS OF SUBCHRONIC OR CHRONIC SCHIZOPHRENIA: A DOSE RANGE FINDING STUDY

A.J. Puech [1], O. Fleurot [2], W. Rein [2], Amisulpride Study Group.
[1] *Dept of Pharmacology, Pitié-Salpêtrière, 75013 Paris;*
[2] *Synthélabo Recherche, 92 225 Bagneux, France*

Amisulpride (AMI) is an antipsychotic agent with highly selective affinity for dopamine D_2 and D_3 receptors, devoid of affinity for other neurotransmitters. In animal studies AMI preferentially binds to receptors in the limbic area. This profile suggests antipsychotic activity with a low risk of associated extrapyramidal symptoms. The short-term (4 weeks) efficacy and safety of AMI were evaluated in this study comparing four fixed doses of AMI (100, 400, 800 and 1200 mg/d) and 16 mg/d of haloperidol (H). All other AMI doses and H were compared with AMI 100 mg/d as potentially subtherapeutic dose. After a washout period of 3 to 7 days, patients fulfilling DSM III-R criteria for schizophrenia (paranoid, disorganized or undifferentiated type) could be included into the study. Efficacy was evaluated using the BPRS (main criterion), the PANSS Positive and Negative Subscales and the CGI. Safety evaluation included the UKU side effect scale, the Simpson-Angus (SAs) scale (parkinsonism), the Barnes Akathisia Scale (BAS) and the AIMS (tardive dyskinesia). A total of 319 patients (mean age 36 yrs, sd 11, mean duration of illness 10.1 yrs, sd 8.3) were included in the study. About half of the patients (46%) were pretreated with neuroleptics in the month before inclusion into the study. The mean BPRS total score (1 to 7 scoring) at inclusion was 61.2 (sd 11.4), the corresponding PANSS Positive and Negative scores were 25.9 (sd 6.0) and 27.3 (sd 8.1). 237 patients (74%) completed the study. The AMI 800 mg group had the lowest dropout rate for inefficacy (2/64 patients, $p < 0.05$ vs AMI 100 mg), whereas the H group had the highest dropout rate for safety reasons (10/64 patients, $p < 0.05$). The highest improvement (BPRS total score) was found in the AMI 400 and 800 mg groups (24.9 sd 18.4 and 26 sd 14.9, unadjusted $p < 0.05$). The corresponding response rates (CGI) were 66% and 78% respectively, ($p < 0.01$ for AMI 800). PANSS positive scores also improved significantly in the AMI 800 group (12 sd 6.9, $p < 0.05$). PANSS negative scores improved most in the AMI 400 and 800 groups (8.4 sd 7.9 and 9.6 sd 8.7) but this difference failed to reach significance. Extrapyramidal symptoms (parkinsonism) did not increase significantly in the AMI 400, 800 and 1200 mg groups compared with AMI 100, whereas increase was significantly higher in the H group ($p < 0.002$). Akathisia and tardive dyskinesia scores did not change significantly during treatment. Vital signs and biological tests showed no clinically relevant abnormalities in the different treatment groups. Overall, Amisulpride at daily doses of 400 and 800 mg proved to be highly effective on productive symptoms in acutely exacerbated schizophrenic patients with an additional effect on negative symptoms in these patients and significantly better extrapyramidal safety compared with haloperidol.

CLOZAPINE AND RISPERIDONE IN THE TREATMENT OF THERAPY-RESISTANT SCHIZOPHRENIA: A PRELIMINARY REPORT ON TWO ONGOING CLINICAL TRIALS

C. Konrad [2], C. Schormair [1], B. Eikelmann [1], K. Berger [2], P. Rottmann [1]. [1] *Westphalian Psychiatric Clinic Münster, Germany, Fr.-Wilhelm-Weberstr. 30, 48147 Münster;* [2] *Westphalian University Münster, Dep. Of Epidemiology, Münster, Germany*

Background: Clozapine proved to be effective in patients not responding to other neuroleptics. This effect has been known for years. More recently it has been shown that also Risperidone can effectively be used in these patients. We present preliminary results of two uncontrolled trials evaluating the effects of Clozapine and Risperidone on schizophrenic patients non-responding to other neuroleptic agents.

Methods: We performed two clinical trials in a parallel research design. 26 schizophrenic patients (ICD 10, mean age 46 y.) who had failed to respond to two or more different neuroleptics — each given for three weeks at least — were assigned by their individual psychiatrist to either Risperidone (n = 14) or Clozapine (n = 12). In both studies sociodemographic data were recorded, psychopathology and extrapyramidal symptoms were assessed by the same independent blind-observer in the washout period (week 0), after week 2 and after week 6 of treatment, using PANSS, BPRS, CGI, NOSIE and EPS rating scales. Statistic analysis was performed comparing rating scores between weeks 0, 2, and 6 using Students-t-test in each study separately.

Results: BPRS total score in the Clozapine Study decreased from 54.3 to 52 (−4.2%, week 2) to 50.1 (−7.7%, week 6). The corresponding score in the Risperidone Study was 52.9 (week 0), 47.9 (−9.5%, week 2) and 40.7 (−23.1%, week 6). PANSS total score in the Clozapine Study could be reduced from 84.1 to 80.3 (−4.5%, week 2) to 77 (−8.4%, week 6). Only the decrease in the positive syndrome scale was significant ($p = 0.01$). PANSS total score in the Risperidone Study was 81.2 (week 0), 72.4 (− 10.8%, week 2) and 61.0 (−24.9%, week 6). The decrease on positive syndrome scale (week 6), general psychopathology scale (week 6) and on total score of PANSS (week 2 and 6) was nearly significant ($p = 0.05$). Extrapyramidal symptom scores were remarkable low and decreased during treatment in both studies.

Conclusions: In this intermediate analysis we observed an effect of both drugs in the treatment of initially pharmaco-resistant schizophrenia which reached statistic significance in the so far small samples. However there was a difference in the magnitude of observed treatment effects favoring Risperidone. The observed differences may be due to the uncontrolled study design, unmeasured confounding risk factors, chance or a true difference between both drugs.

PSYCHOPATHOLOGY AND COGNITIVE (EXECUTIVE) DYSFUNCTION IN RELATION TO DURATION OF INITIALLY UNTREATED PSYCHOSIS IN SCHIZOPHRENIA

P.J. Scully, G. Coakley, A. Kinsella, H.A. Youssef, J.L. Waddington.
St. Davnet's Hospital, Monaghan, Rep. of Ireland; Royal College of Surgeons in Ireland, Dublin 2, Rep. of Ireland

While determinants of the course of schizophrenia are unclear, emerging evidence suggests that the longer psychosis proceeds unchecked before initiation of anti-psychotic therapy, the poorer may be long-term outcome. We have examined current psychopathology using the Positive and Negative Syndrome Scale (PANSS), general cognitive function using the Mini-Mental State Examination (MMSE) and executive/frontal function using the Executive Interview (EXIT) in 48 older patients with schizophrenia, many of whom were admitted in the pre-neuroleptic era. After controlling for age and for the duration and continuity of subsequent neuroleptic treatment, increasing duration of initially untreated psychosis was associated with greater severity of negative ($p < 0.005$) but not positive (NS) symptoms, and with lower scores on the MMSE ($p < 0.05$) but not with EXIT performance: duration of illness following initiation of treatment was not associated with psychopathology. Overall performance on the MMSE decreased prominently with age/duration of illness, while EXIT performance changed consid-