P01.127

EVENT RELATED POTENTIALS (CNV AND P300) IN CHRONIC OPIATE USERS: PRELIMINARY RESULTS

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a) Background: IV administration of flesinoxan (highly potent and selective 5HT1A full agonist) induces a significant and dose-dependant increase in ACTH, cortisol, prolactin (PRL), growth hormone (GH) and total neurophysins and a decrease in body temperature. There is no effect of age and gender on hormonal and temperature responses to intravenous flesinoxan. Effects of age and gender on neurophysins and temperature responses to flesinoxan was studied.

b) Design: Sample: 39 healthy volunteers (22 M, 17 F) - mean age 35.5 ± 10.7 years. Total neurophysins, vasopressin and temperature were assayed at 0, +15, 30, 60, 90 and 120 min after the injection of flesinoxan 1 mg/70 kg. We performed an ANOVA for the area tinder the curve relative (AUCr) values of temperature, total neurophysins, vasopressin and oxytocin responses, with age as a covariate.

c) Results: There was no significant difference between male and female neither for the AUCr values of temperature responses (−32.4 ± 22.1 vs −34.6 ± 29.3 °C min.) nor for total neurophysins (48.0 ± 133.9 vs 75.4 ± 148.2 pg min/l), vasopressin (18.3 ± 35.8 vs 19.0 ± 37.5 pg min/l) and oxytocin (29.8 ± 116.7 vs 56.5 ± 118.8 pg min/l) responses. Furthermore, there were no significant correlations between age and temperature (r = 0.06) or total neurophysins (r = 0.06), vasopressin (r = 0.008), and oxytocin (r = 0.07) responses neither among male nor female.

d) Conclusion: The sensitivity of 5HT1A receptors mediating neurophysins and temperature responses is neither age nor gender-related.

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REDUCED DOPAMINERGIC ACTIVITY IN DEPRESSED SUICIDES

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a) Background: Several data are available about the implication of the dopaminergic system in the control of inward-directed aggression. Previously, we suggested an involvement of D2-dopaminergic function in the expression of suicidal behavior by demonstrating a smaller growth hormone (GH) response to apomorphine, a dopaminergic agonist, in depressed patients with a history of suicide attempts in comparison to nonattempters. In the present study, the purpose was to analyze GH responses to apomorphine in depressive patients who later died by suicide.

b) Design: Sample: 8 male depressive inpatients who died by suicide within one year after hospitalisation, compared to 18 male major depressed inpatients who never attempted suicide. The two groups did not differ in mean age, weight or Hamilton Depression scores. Blood samples were collected at −20, 0, +20, 40, 60 and 120 min after injection of 0.5 mg apomorphine.

c) Results: Mean GH peak responses to apomorphine differed significantly between suicide completers and controls: for GH peak, 7.6 +/− 4.1 ng/ml vs 18.9 +/− 14.2 ng/ml, U = 30, Z = −2.33, p = 0.02.

d) Conclusion: Our results tend to confirm the role of dopamine in the biology of suicide in depression. However, this study should be controlled on a larger sample.

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THREE SYNDROMES OF SCHIZOPHRENIA – RESULTS OF AN EFA - CFA - CROSSVALIDATION APPROACH

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Background: Factor analyses of schizophrenic symptoms typically come to different solutions, although a model with three dimensions has been obtained with some consistency. We compared different factor structures of schizophrenic phenomenology in an unselected, hospital based patient sample.

Methods: Psychopathological symptoms were originally evaluated with the AMDP-system and afterwards grouped according to the SANS/SAPS-subscales. The sample included 1053 inpatients with schizophrenia. Exploratory and confirmatory factor analyses were conducted to test the hypothesis of one-, two-, three- and four-factor models.

Results: Results support a three-factor model, where dimensions can be termed as 'positive', 'negative' and 'disorganized' dimension, in line with previous reports. Factor loadings were not entirely pure in a sense, that two symptom subscales from the 'negative' factor also loaded on the 'disorganized' factor.

Conclusions: Despite mounting evidence, that schizophrenia symptomatology is not adequately represented by one or two dimensions, most studies continue to use such a simplified model. Forthcoming research should instead be based on three dimensions for the assessment of schizophrenia on a syndromal level beyond the nosological level, to reduce sample heterogeneity. However, further refinement of syndrome definition seems necessary, to obtain 'pure' dimensions.

P01.130

ALTERATIONS OF GAIT IN HEALTHY CONTROLS COMPARED TO DEPRESSED PATIENTS TREATED WITH TCA AND SSRI

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Objective: Parameters of human gait are important components of motor functioning controlled on the spinal level and by central motor programs. Gait patterns are altered in depression and may be associated with cerebral pathophysiology of the disease. In addition, tricyclic antidepressants (TCA), but not selective serotonin reuptake inhibitors (SSRI), may affect psychomotor dysfunction. Therefore, kinematic analysis of gait patterns was performed in patients with major depression treated with TCA and SSRI and in healthy controls.

Method: Spatial and temporal gait parameters including velocity, stride length, stance phase, and cadence, were measured in patients with major depressive disorder (MDD) (DSM-IV) (n = 18) treated with TCA and SSRI and in matched healthy controls. Depressive symptoms were documented by HAMD, Widlöcher Depressive Retardation Scale (WDRS), SHAPS-D and others.

Results: Spatial parameters including stride length (MDD: 146.42 ± 25.31 cm, CTRL: 159.65 ± 16.84 cm) and step length/leg length (MDD: 0.75 ± 0.06 cm, CTRL: 0.83 ± 0.10 cm) were decreased in patients. Temporal parameters including double limb support (MDD: 167.06 ± 30.54 ms, CTRL: 140.51 ± 20.60 ms) were increased and velocity (MDD 1.21 ± 0.13 m/s, CTRL: 1.48 ± 0.18 m/s) was decreased in patients, without significant differences in cadence (steps/min). Gait parameters in patients treated with SSRI were less altered than in the TCA group. Cadence correlated

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with velocity (r_s = 0.78, $p < 0.01$) in depressed patients, but not in controls

Conclusions: Quantitative measures revealed impaired gait performance in depression and may indicate dysfunction of basal ganglia. Psychomotor functioning was less affected by antidepressant treatment with SSRI than with TCA. These preliminary results warrant further longitudinal and experimental studies. Kinematic analysis of gait performance represents a practicable method to quantify psychomotor alterations and basal ganglia functions in depression and other psychiatric disorders.

P01.131

TREATMENT OF DEPRESSION IN PARKINSON'S DISEASE WITH REBOXETINE

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Objective: Depression occurs frequently in Parkinson's disease and appears to be associated with greater frontal lobe dysfunctions including motivational systems and dopaminergic and noradrenergic mechanisms than in non-depressed Parkinson patients. Reboxetine, a novel norepinephrine reuptake inhibitor, is effective in major depression with specific effects on negative self perception and lack of motivation towards action with little effects on psychomotor and cognitive functioning. Therefore, efficiency of reboxetine was investigated in Parkinson patients with depression.

Methods: Patients with Parkinson's disease and depression were included if prior treatment with antidepressants was ineffective or accompanied by intolerable side effects (anticholinergic, motor signs). Depressive symptoms were documented over 4 weeks by clinical ratings (HAMD, SDS, SHAPSD) and motor symptoms by UPDRS (motor scale, social functioning).

Results: Patients were 67 ± 3.5 years old and were treated with levodopa (375.8 ± 38.7 mg/d) on stable dosages. There was a significant improvement in symptoms including mood, drive, anhedonia, negative self-perception and appetite. Zolpidem was prescribed for initial problems with sleep and stopped later. Transient sweating and feelings of slight agitation disappeared after three weeks. There were no significant side effects concerning gastrointestinal functions or motor performance, no changes in blood count, EKG, or EEG.

Discussion: Prospective studies of reboxetine in Parkinson's patients with depression are warranted on the basis of our findings, assumed effects of reboxetine on motivation toward action and social functioning and noradrenergic mechanisms involving motivational systems in depressed Parkinson's patients. In the meantime, there are good theoretical and clinical reasons including pharmacological specificity of effects and low incidence of side effects to administer reboxetine for treatment of depression in Parkinson's disease in clinical practice.

P01.132

SAFETY DURING LONG-TERM EXPOSURE TO SEROQUEL® (QUETIAPINE)

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Background: The long-term safety of quetiapine (Seroquel®) has been evaluated in the open-label extension (OLE) phases of clinical trials, with patients being treated for up to 3 years.

Methods: Patients completing the randomised treatment phase of their respective trial were eligible for entry in the OLE phase. Open-label treatment with quetiapine consisted of an initial dose-titration period, during which the dose was increased according to the patient's clinical condition. Thereafter, quetiapine dosing was flexible, up to a maximum of 800 mg/day.

Results: 455 patients with schizophrenia or schizoaffective disorder received quetiapine; mean age: 39 years (range: 18–89); mean time from first diagnosis: 10.9 years (range: 0–42). Mean daily doses during the 3-year OLE treatment averaged between 450–500 mg. Mean duration of exposure to quetiapine: 47.2 weeks (range 0–246 weeks). At 1 year, 160 patients (35%) were receiving quetiapine treatment, most of whom continued to receive treatment for two additional years. The total number of patient-years exposure to quetiapine was 413.1 years. Approximately 25% of the trial population were receiving anticholinergic medication at trial entry; after 1 years' quetiapine treatment this value had decreased by two-thirds. The adverse event profile during OLE was similar to that observed during the trials, and no new safety concerns were raised.

Conclusion: In adult patients who received long-term open-label quetiapine treatment, this antipsychotic continued to be well tolerated, with a continuation rate at 12 months similar to those observed in long-term studies with other atypical antipsychotics.

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P01.133

EFFICACY OF 'SEROQUEL' (QUETIAPINE) COMPARED WITH HALOPERIDOL AND PLACEBO IN THE SHORT-TERM TREATMENT OF ACUTE SCHIZOPHRENIA

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Background: The efficacy of quetiapine ('Seroquel') in relieving the positive and negative symptoms of schizophrenia has been demonstrated in a number of controlled and open-label extension studies.

Objectives: To compare the efficacy of quetiapine with existing treatment options, a meta-analysis was performed on data from four studies in which quetiapine was compared with haloperidol and placebo in the short-term treatment of acute schizophrenia.

Methods: Within each trial, the proportion of patients who experienced a clinically relevant response to treatment (≥40% reduction in the Brief Psychiatric Rating Scale (0–6) score from baseline to endpoint) was calculated for each treatment. The homogeneity of treatment effects was assessed across studies. The combined odds ratio (OR) and associated 95% confidence interval were calculated, with an OR > 1 indicating superiority of quetiapine over haloperidol or placebo.

Results: The response rates in the individual trials ranged from 26–43% for quetiapine, 19–47% for haloperidol, and 6–26% for placebo. There was no indication of heterogeneity of treatment effect between trials ($p = 0.183$). The combined OR for quetiapine vs placebo was 2.31 (95% CI 1.50, 3.56; $p < 0.001$), and for quetiapine vs haloperidol was 1.32 (95% CI 1.04, 1.68; $p = 0.020$).

Conclusions: In the short-term treatment of acute schizophrenia, quetiapine is significantly superior to haloperidol and placebo in terms of clinically relevant response rates. This would suggest that quetiapine is a first-choice antipsychotic.

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