P.2.022 Efficacy of a psychoeducational program for weight gain control in patients taking olanzapine

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Weight gain has been associated with olanzapine and, to varying degrees, with many other neuroleptic medications. It has been reported that gender, age, appetite, outcome of the treatment and Body Mass Index (BMI) at baseline are predictive variables of the subsequent weight increase during neuroleptic therapy.

Little is known about behavioural, dietary, and pharmacological interventions in relation to weight management in psychiatric patients so that it may be possible that "lifestyle change" programs could be helpful in managing body weight increase associated with antipsychotic treatment.

The aim of this study is to observe the efficacy of a psychoeducational programme in managing the increased weight in patients being treated with olanzapine.

Thirty-one outpatients treated with olanzapine monotherapy, who showed an increase of BMI >7% from the beginning of the treatment, have been included in the study. Patients were randomised in a 1:1 ratio into 2 treatment groups: olanzapine + psychoeducational programme (group 1) or olanzapine alone (group 2). After 12 weeks, both groups of patients were included in an additional 12 weeks of psychoeducational programme. The mean differences from baseline to endpoint in total body weight and BMI were taken as primary outcome measures for the psychoeducational programme with paired samples t-test. Nineteen patients (6 in group 1, 13 in group 2) completed the study and 12 patients dropped out (3 because of the worsening of psychiatric illness, 3 because of drug non-acceptance, 5 because of difficulties of adopting the psychoeducational programme, 1 because of patient decision). Significantly more patients with a higher initial BMI completed the study; females and patients over 40 showed a non-statistically significant tendency to complete the study. The patients who completed the study showed a mean decrease of body weight = 3.5 kg and of BMI = 1.3 at the end of the trial ($p < 0.001$). During the first 12 weeks of therapy, in the patients of group 2, who did not follow the psychoeducational programme, body weight and BMI were practically unchanged (body weight: −0.3 kg; BMI: −0.2) ($p = 0.68$ and 0.74 respectively). The same patients receiving 12 weeks of psychoeducational treatment, in the following period of the study, showed a mean decrease of body weight = 2.2 kg ($p = 0.019$) and of BMI = 1.1 ($p = 0.022$). Patients over 40 showed an average weight decrease of 5.0 kg while patients below 40 reduced their weight by 2.5 kg; this difference was statistically significant ($p < 0.001$). Overall quality of life tended to improve during the psychoeducational program. No significant changes in any of the laboratory values nor akathisia were observed in any patient.

According to the initial results of this still ongoing study, we have observed a marked improvement in weight control when patients were enrolled in this psychoeducational programme.

Anxiety disorders and anxiolytics

P.3.001 Discriminative stimulus effects of mexidol in rats

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Benzodiazepine anxiolytics like other established agonists of $GABA_A$-benzodiazepine receptor chloride channel complex produce high stimulus control [1]. There are poor data about discriminative effects of anxiolytic agents with nootropic properties. Mexidol (2-ethyl-6-methyl-3-hydroxypyridine succinate) possesses anxiolytic, nootropic and neuroprotective properties which have been revealed both in experiment and in clinic practice. It was shown that anticonflict effects of nootropic anxiolytic mexidol are clearly inhibited by the selective benzodiazepine antagonist flumazenil [3]. The present experiment has been performed to determine the discriminative stimulus properties of mexidol in male albino outbred rats.

The animals were trained to discriminate mexidol (50–100 mg/kg, i.p., 40 min before training) and saline in a two-lever liquid discriminative procedure. During the initial phase of operant FR10 training, mexidol at 50 mg/kg for 24 sessions failed to act as a discriminative stimulus. However, when the dose was increased to 100 mg/kg mexidol was discriminated from saline in 10% of trained rats. These animals responded with accuracy of more than 80% for the initial lever selection. This effect was close to that in rats that had acquired discrimination of the benzodiazepine derivatives (phenazepam or gidazepam) from vehicle [3]. In the same way, under FR1 operant schedule only 10% of rats trained successfully to discriminate mexidol (100 mg/kg) from non-drug state.

Thus, the results suggest the lack of stimulus properties of mexidol in 90% of tested animals and high stimulus control in 10% of rats to be acquired in both FR1 and FR10 schedules. Interceptive cues of mexidol are estimated as moderately discriminable.

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P.3.002 Discriminative stimulus effects of cycloprolyl-glycine

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Data about stimulus properties of medicines with anxiolytic and nootropic properties are rather scanty. The present study assessed the discriminative stimulus effects of endogenous neuropeptide cycloprolyl-glycine (cPG) [1], which has been shown to be a metabolite of proline-glycine containing dipeptide with cognitive enhancement and anxiolytics properties – noopept (ethyl ester of N-phenyl-L-prolylglycine, GVS-111). cPG was studied in a two lever liquid reinforced operant discrimination procedure in albino male outbred rats. Animals were trained to discriminate the cPG from the equivalent volume of the vehicle under operant schedules FR1 and FR10. cPG was injected 15 min before training procedure in the dose of 0.1 mg/kg, i.p. Under schedule FR1 cPG discrimination was established after initial 15 training sessions in 33% of the rats. Stimulus controls were more than 80% for both cPG- and vehicle stimuli in these animals. 67% of animals tested failed to demonstrate any discriminative operant behaviour. After 30 sessions under FR1 operant schedule rats were exposed to discriminative training procedure under FR10 schedule. During the following 40 trials rats did not demonstrate discriminative behaviour: response accuracy was at 20–70% of correct lever choices. The data obtained suggest that stimulus control by cPG is weak compared to that of well-known anxiolytics (benzodiazepines, buspirone) [2,3]. Moderate discriminability of cPG allows to suggest a poor potential of development of drug dependence for CPG.

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P.3.003 The effect of Selank on the seasonal depressed animal behaviour

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Background: It has been found that hibernating animals demonstrate a wide range of behavioural activity from profound depression in autumn to the complex behavioural patterns in summer. That is why hibernators are a unique natural model for studying the mechanisms of pharmacological correction of seasonal depressive-like states of the CNS. Recently, it has been shown that the degree of behavioural changes in hibernators by similar pharmacological agents increasing the level of serotonin in the brain depends on the phase of the annual cycle the animals are in. The present study was undertaken to analyze more precisely the seasonal variation in the effect of the original agent of peptide nature Selank on the behaviour of hibernators. Selank was produced by modifying the endogenous immunomodulator tetrapeptide taftsin. Comprehensive pharmacological studies of Selank, carried out in Zakusov State Institute of Pharmacology, Russian Academy of Medical Sciences, revealed its anxiolytic activity.

Methods: Experiments were carry out on Jakutian ground squirrels (n=28) in different seasons: summer