FC06.02

FIRST RESULTS OF FLUVOXAMINE VERSUS LITHIUM AGGRESSIVITY PROTOCOL (FLAP)

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Objectives: To verify the efficacy of fluvoxamine versus lithium in reducing aggressive behavior in people with personality disorders.

Methods: Study partecipants were 50 physically health men (26) and women (24) randomly chosen within the inhabitants of Florence who were known to have aggressive behavior for a period longer than 1 years (total score on the Social Disfunction Aggressivity Scale (SDAS) greater than 14) and met DSM-IV criteria for personality disorders by administration of the SCID-II. They did not present axis I disorders, history of head trauma, previous ECT treatment, depressive symptoms (score lower than 18 at the Hamilton RS-D, lower than 14 at the Beck DI). The trial was a double-blind fixed-dose design comparing fluvoxamine (300 mg/day) and lithium (900 mg/day). During the first of 4-week single-blind placebo, before starting treatment, and after 30, 60, 90, 120, and 150 days of therapy, all patients had a global clinic assessment, and a specific one for aggressivity.

Results: Fluvoxamine resulted to be significatively more efficacious than placebo in reducing aggressive behavior and better than lithium for efficacy and safety though in a not statistically significative way.

FC06.03

ASSOCIATION OF SEROTONIN TRANSPORTER PROMOTER GENE VARIANTS WITH CLINICAL FEATURES OF MAJOR DEPRESSION

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We studied the association of the serotonin transporter promoter polymorphism (5-HTTLPR) with melancholia, psychotic symptoms and suicidality in 83 patients with major depression and 200 healthy controls in an exploratory logistic regression model under simultaneous adjustment of sex and age. In a second model we analyzed the contribution of distinct clinical features of melancholia according to DSM-IV (B-criteria of melancholia): distinct quality of depressed mood, diurnal variation, early morning awakening, psychomotor retardation, psychomotor agitation, anorexia and inappropriate guilt.

Testing model 1 with melancholia, suicidality and psychotic features as "independent" variables, only the global indicator of melancholia indicated a statistical relation to the 5-HTTLPR genotype (OR = 0.344; p = 0.038), in the singular score test for melancholia the statistical relation was even weaker (OR = 0.402; p = 0.057).

The Wald score test for the clinical features did not indicate a statistical relation to 5-HTTLPR genotype with the exception of psychomotor retardation (3.94, d.f. = 1, p = 0.047). Elimination of all disponible predictor variables resulted in a global model Chi-square of 9.032 (d.f. = 4, p = 0.06) with the singular score test for the indicator psychomotor retardation displaying a p-value of 0.022. All global model Chi-squares proved insignificant, mainly due to the high number of predictors.

This study indicates that melancholia – as a clinical subtype of depression – and psychomotor retardation – as clinical symptom – are interesting candidates for clinical features of major depression with possible associations with the 5-HTTLPR genotype and should be investigated in a confirmatory design.

FC06.04

SPECT IMAGING OF 5-HT_{2A} RECEPTORS DURING SSRI TREATMENT

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5-HT_{2A} receptors play an important role in e.g. the pathophysiology of mood disorders. The investigation of the influence of long term antidepressant treatment on these receptors has yielded controversial results, also in recent brain imaging studies. Using positron emission tomography (PET) and 18-F setoperone as a ligand, a decreased ligand binding after treatment with either desipramne or clomipramine was demonstrated. A study of frontal 5-HT_{2A} receptors, using the same ligang, during treatment with selective serotonin reuptake inhibitors (SSRIs) suggested, however, an upregualtion of these receptors.

In this study single photon emission computed tomography (SPECT) was used, with ^{123}I-R91150 as a ligand, to investigate 5-HT_{2A} receptors in depressed patients during treatment with SSRIs. Subjects were 7 drug naive major depressed patients, studied before and after 6 weeks of treatment.

Statistical analysis was performed on estimations of the specific ligand binding calculated as the ratio of the binding in a region of interest to the binding in the cerebellum. Solely frontal regions of interest were investigated.

The mean 17-item Hamilton Depression Rating Scale (HRSD) score (+/–SD) was 18.7 (+/–7.4) before, and 11.1 (+/–7.2) after treatment. Overall, no significant difference in binding was observed. However, considering the 4 responders to treatment (defined as presenting a reduction of at least 50% in HRSD score) an almost significant increase in binding was demonstrated (Wilcoxon signed ranks test, $p < 0.07$).

These preliminary results could indicate an up-regulation of 5-HT_{2A} receptors after succesfull antidepressant treatment with SSRIs.

FC06.05

MULTIPARAMETRIC BIOMONITORING OF AUTONOMIC FUNCTIONS IN PATIENTS TREATED WITH PSYCHOTROPIC DRUGS

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Most antidepressant drugs lead to enhanced synaptic availability of the neurotransmitters serotonine and/or norepinephrine. However, affecting also other transmitters, e.g. acetylcholine, antidepressants cause peripheral autonomic dysfunction (e.g. dry mouth, tachycardia or sudden cardiac death). Aim of our study was to objectify these autonomic dysfunction.

Therefore, we applied simultaneous recordings of ECG for assessment of heart rate variability (HRV), as well as skin blood flow and skin conductance level – indicating peripheral autonomic responses like inspiratory gasp response (IGR) and skin conductance response (SCR) – to patients under treatment with psychotropic drugs (amitriptyline, olanzapine, clozapine, fluoxetine, or hypericum extract; n = 20 each).

We found that heart rate variability was reduced in all patients treated with ami, ola, or clo but not under treatment with flu, or hyp. Exclusively in ami-, ola-, clo-treated patients 1) redilation of IGR was prolonged, indicating inhibition of norepinephrine re-uptake, and 2) in about 50% of these patients SCR was blocked completely, or reduced in the other 50% (due to anticholinergic effects).

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