P.1.044 Calcium homeostasis in lithium-treated patients with bipolar depression

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We investigated platelet thrombin-induced intracellular calcium mobilization and cAMP, ^{14}C-serotonin uptake, plasma amino acids, cortisol and prolactin and platelet 5-HT_2-receptor mediated secretion of adenosine triphosphate (ATP) in 13 lithium-treated female patients in clinical remission from bipolar depression (MADRS < 10). The control group consisted of 13 healthy volunteers without heridity for affective disorders, matched for age, gender and season. Mean age was 44 ± 8 years. Mean plasma lithium concentration in the patient group was 0.56 ± 0.16 mmol/L. The plasma electrolytes Na^+, K^+ and Ca^{++} were within normal ranges in both groups. However, patients had significantly higher values of intracellular Ca^{++} than controls (1.271 ± 0.056 and 1.215 ± 0.045 mmol/L respectively, $p < 0.01$). There was also a positive correlation between intracellular Ca^{++} and plasma Ca^{++} in the patient group ($r = 0.83$, $p = 0.0004$) and in the control group ($r = 0.76$, $p = 0.0024$). K_m and V_{max} for platelet serotonin uptake were similar in both groups. Data from cAMP, cortisol, prolactin and plasma amino acids analysis are in preparation and will be included to the results later. Earlier studies by Kallner and Pettersson have revealed a subgroup of lithium treated patients with enhanced levels of ionized calcium. The present study will widen our knowledge about calcium homeostasis and monoaminergic and neurohormonal modulation in long-term lithium treatment.

P.1.045 Open parallel 8-week study of sertraline versus imipramine in depressed outpatients without melancholia

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Objective: To compare the efficacy and tolerability of sertraline and imipramine in the treatment of depressed outpatients without melancholia.

Method: After a washout period of at least five half-lives of any previous psychotropic medication, 239 outpatients from 12 Spanish centres with major depression without melancholia and with or without dysthymia were randomized to 8 weeks of open treatment with sertraline or imipramine in a 1:1 ratio. The initial daily dosage was sertraline 50 mg/day or imipramine 75 mg/day with increases in steps of 50 mg/day permitted at 2-week intervals to a maximum of sertraline 200 mg/day or imipramine 225 mg/day. All patients receiving at least one dose of medication and one follow-up efficacy evaluation were included in the intent-to-treat analysis. Patients receiving at least 4 weeks of treatment were included in the efficacy evaluable analysis. Patients were assessed on the Clinical Global Impression (CGI) Scales, the Hamilton Depression Rating Scale (HAM-D), the Hamilton Anxiety Scale (HAMA), and the Battelle Quality of Life Scale (BQLB).

Results: 88.0% of sertraline- and 89.9% of imipramine-treated patients were CGI-Improvement responders (much or very much improved) at endpoint, with 57.5% of sertraline- and 46.8% of imipramine-treated patients achieving a CGI-I score of 1, or very much improved. Absolute mean HAM-D scores were reduced by 16.6 (65.7%) in the sertraline group and 15.7 (64.1%) in the imipramine group. HAMA scores were reduced 14.2 (62.3%) and 12.2 (55.1%) in the sertraline and imipramine groups, respectively. A total of 47 (51.1%) sertraline patients and 35 (44.3%) imipramine patients were evaluated as having a CGI-Severity score of 1 (ie, "normal") at endpoint. A total of 93 (82.3%) sertraline- and 78 (64.4%) of imipramine-treated patients completed 8 weeks of treatment; 10.3% of the sertraline group and 24.4% of the imipramine group discontinued for adverse events.

Conclusion: This study demonstrates that sertraline and imipramine are both effective treatments for depressed outpatients without melancholia but that sertraline is better tolerated.

P.1.046 Augmentation treatment by combination of high and low frequency rTMS in depression: bilateral versus left hemispherical stimulation

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The antidepressive potency of repetitive transcranial magnetic stimulation (rTMS) apparently depends on different variables such as the stimulation placement(s) [i.e. left or right dorsolateral prefrontal cortex (DLPC)], and on different frequencies. Thus, stimulation at ≤1 Hz (low frequency) over the right DLPC inhibits ispilateral neuronal activity and seemingly activates the controlateral area. An inverse mechanism may be assumed for a stimulation at ≥1 Hz (high frequency) over the left DLPC. In contrast, ipsilateral stimulation at alternating low and high frequencies might synchronize neuronal excitation and inhibition over the stimulation side. The aim of this naturalistic, prospective, controlled study was to investigate the augmentation properties of rTMS, combinig bilateral low and high frquencies' stimulation as compared to the alternating use of both frequencies over the left DLPC solely in the identical sessions. We recruited 24 severely depressed medicated patients (18 psychotic, 13 unipolar, 6 bipolar, 5 dsytymic ICD-10). They were subdivided into two groups (n = 12) comparable in age (48.2 years ± 16.1/44.8 ± 14.8) sex (9 females/8), handedness (right 10/12), duration of illness (10.3 years ± 10.8/7.9 ± 8.7) and episode (5.3 months ± 2.9/4.9 ± 4.0) and numbers of episodes (6.1 ± 3.7/5.7 ± 4.9). rTMS was delivered with a Cadwell stimulator on 5 consecutive days, 1 session/d with a figure-8 water-cooled coil. For group 1 we used a stimulus intensity of 110% of the motor threshold of ADM (MT), a frequency of 10 Hz, 10 trains, train duration 10 sec each with an intertrain interval of 60 sec over the left DLPC; over the right DLPC 110% of MT, 1 Hz, 1 train at 300 sec for a total dose of 6500 stimuli was applied. In group 2 only the left DLPC was stimulated at 110% of MT, 10 Hz, 10 sec lasting train (100 stimuli) alternated with 110% of MT, 1 Hz, 30 sec train (30 stimuli) with an interval of 6 sec for 10 times/session, resulting in a total dose of 6.500 stimuli in 5 days. No significant statistical differences (χ^2 categorical comparison) were noted in clinical response as measured by CGI. 6 patients (50%) of group 1 and 8 (66.7%) of group 2 had a good clinical outcome; 4 of each group (33.3%) showed no change and 2 (16.7%) of group 1 deterioreted. However, the comorbidities in terms of personality disorders and history of alcohol dependency revealed an opposite effect on clinical outcome in the two groups; 5 (83.3%) of the 6 patients in group 1 diagnosed as suffering from these comorbidities were difined as non responders, whereas 6 (66.7%) of 9 patients with comorbidities of group 2 were qualified as responders (χ^2 of $p < 0.05$). In both groups no serious side effects were registered, but it is noteworthy that 5 patients in group 2 reported a pleasent drowsiness during the stimulation sessions. These preliminary findings suggest that varying the frequencies and the stimulation placements rTMS might provide a selective treatment approach in depressives associated with the comorbidities described.

References

[1] Post, R.M., Kimbrell, T.Al, Frye, M., George, M.S., McCann, U., Little, J., Dunn, R., Li, H., and Weiss, S.R.B. (1997). Implication of kindling and quenching for the possible frequency dependence of rTMS. CNS Spectrum, 2, 54–60.

[2] Weiner, R., Krystal, A. (1993). EEG monitoring of ECT seizures. In: The Clinical Science of Electroconvulsive Therapy. Coffey CE (ed), Washington, D.C., American Psychiatric Press, Inc., 93–109