There was no overall relationship between depressive symptomatology and serotonergic function across diagnoses. We conclude that a) depressive symptoms in major depression and organic depression are associated with reduced central 5-HT function, while those in schizophrenia are associated with increased 5-HT function; and b) depression may not have a common serotonergic neurobiological origin across diagnosis.

[1] Van Praag HM, Kahn RS, Asnis GM, et al (1987). Denosologization of biological psychiatry or the specificity of 5-HT disturbances in psychiatric disorders. J Affect Disord.; 13: 1–8.

LITHIUM AND SEROTONIN REUPTAKE INHIBITORS; THERAPEUTIC OR TOXIC?

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The aim of this presentation is to review all available data on the safety, tolerability and effectiveness of lithium in combination with serotonin specific reuptake inhibitors in the treatment of Major Depression.

All published reports, including case reports, uncontrolled series and controlled studies, regarding coadministration of lithium and SSRIs were identified for the purpose of the review. Reports made to CSM and to pharmaceutical manufacturers were also considered.

The data were not suitable for meta analysis. Although case reports suggest that toxicity may occur the data from systematic studies, although largely open and uncontrolled, indicate a benign adverse event profile with little risk of serious events. Based upon 90 evaluable cases, the most frequent adverse events appear to be tremor, nausea or vomiting and somnolence. Evidence for efficacy of the lithium add-on strategy rests upon one small placebo controlled study (n = 15). Data from the uncontrolled studies is not incompatible with this but must be interpreted cautiously.

The interpretation of the currently available data is, on balance, that i) lithium add on to SSRIs is an efficacious strategy for the treatment of refractory Major Depression, ii) the combination is associated with an increase in the number of adverse events but these are seldom severe or serious, iii) serious toxicity is an uncommon occurrence. There is sufficient data to justify a large placebo controlled study to evaluate efficacy and tolerability.

'SEROTONERGIC AUTORECEPTOR BLOCKADE IN THE REDUCTION OF ANTIDEPRESSANT LATENCY: A CONTROLLED TRIAL'

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Objective: To study augmentation of the antidepressant paroxetine with pindolol, a $5HT_{1A}$ autoreceptor blocker. Open studies suggest that, for SSRI antidepressants, the two-to three-week latency of antidepressant effect may be reduced if pindolol is taken simultaneously.

Method: Double blind, randomised, placebo controlled trial. All patients (n = 80; mean age 36 [range 19–65]; asthma, diabetes, cardio-pulmonary disease *excluded*) met criteria for major depression and received paroxetine (20 mg *o.d.*) plus, randomly, either pindolol (2.5 mg *t.d.s.*) or placebo. Assessment: days 4, 7, 10, 14, 21, 28, 42, using clinical measures, the Montgomery-Åsberg Depression Rating Scale [MADRS] and the Beck Depression Inventory. Patients are followed up for six months, allowing assessment of long term safety, tolerability and optimal dosage regimes, and subsequent service usage.

Results: Compared with day 0, 20% of *all subjects* showed a fall in MADRS score > 50% by day 4. By day 7, 30%, and on day 10, 40% of the patients scored > 50%, rising to 48% at day 14. On days 21, 28 and 42, 52%, 56% and 70% of patients registered a fall in MADRS score > 50%. Other measures showed comparable changes.

Conclusions: The markedly reduced latency of antidepressant effects has considerable implications for the future management of depression, and may have an impact on admission for and suicide rates. Larger multi-centre trials are warranted if the breaking of the blind has shown that these results are due to pindolol augmentation of paroxetine.

PROSPECTIVE STUDY OF THE EFFECTS OF INTERRUPTING ANTIDEPRESSANTS

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Antidepressant withdrawal symptoms, following discontinuation of antidepressants, include general somatic distress (flu-like syndromes, gastro-intestinal disturbances,), anxiety, sleep disturbances, movement disorder and manic reactions. Since most of the data come from case reports and retrospective study, it appeared to us of interest to assess, in a prospective manner, the effects of the withdrawal from tricyclic antidepressants and selective serotonin reuptake inhibitiors (SSRIs) in 16 patients answering to DSM-III-R criteria of major depressive episode.

All patients were hospitalized and a change of antidepressant treatment had been decided. Patients were assessed twice, just before the drug interruption and three days later. Clinical instruments were MADRS, Hamilton Anxiety Rating Scale, and the Scale for evaluation of benzodiazepine withdrawal symptoms which had been modified for the purpose of this study. We added two questions about gastro-intestinal symptoms often present in the case reports of antidepressant withdrawal.

87.5% of the patients presented symptoms following the withdrawal. Most frequent signs were anxiety (31%), irritability and jitteriness (25%), sleep disorders (19%), pain and contractions (20%), arousal and decrease in anergia (19%). Our results do not permit to establish a comparison between the rates of withdrawal syndrome induced by SSRIs and tricyclic antidepressants. They confirm the high frequency of withdrawal manifestations when antidepressant therapy is interrupted. Our results also stress the importance of the prevention of the withdrawal syndrome by a slow tapering of antidepressant dosage.

EVALUATION OF STRATEGIES IN THERAPY-RESISTANT DEPRESSION

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An evaluation of the first 73 patients who had attended our outpatient-clinic for therapy resistant depression revealed that only 41% (N = 30) fulfilled criteria for therapy resistant depression. 27 of these patients were followed up 3 months later and efficacy of therapy strategies were evaluated with HAMD and CGI.

6 patients were considered to be full responder (HAMD $\leq$ 6), 8 partial responder and 13 non responder.

There was no statistical significant difference between non responder and responder/partial responder before start of treatment strategies in age, sex, diagnosis, comorbidity on axis 1 or 2 (DSM-