spectrum disorders, and the subtyping of OCD. An important issue was also of whether OCD should be considered as a distinct disorder, separate from the anxiety disorders. Based on the available evidence, it was proposed to remove OCD from the anxiety disorders and place it within a separate category of OCDs. To do justice to the complex and heterogeneous presentation of OCDs it was also proposed to utilize a combination of categorical and dimensional approaches in the diagnostic process. The consensus was that this would enable not only the tailoring of treatment, but would also be helpful to studies on the neurobiology and endophenotyping of OCD.

Key issues in the neurobiology OCD, including the role of serotonin and dopamine, the cortico-striatal circuits and genetic factors, were addressed with respect to their relationship to special populations, such as treatment resistant patients, tic disorders and "schizo-obsessive' patients, and the response to various treatments.

SAT2.04

Escitalopram - a new option in OCD treatment

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Substantial evidence from controlled studies demonstrate efficacy for clomipramine and SSRIs in the acute treatment of OCD across the lifespan. There have been fewer studies of long-term treatment and it remains less conclusively understood as to how well treatments that have been shown to be effective in short-term studies maintain their efficacy over the longer term, though placebo-referenced trials suggest efficacy for clomipramine, fluoxetine and sertraline up to twelve months. Most relapse prevention studies in acute responders revealed a significant advantage for remaining on active treatment (paroxetine, sertraline and fluoxetine at higher doses). For some of these studies methodological problems impaired their ability to discriminate active from placebo treatment on the chosen relapse criterion.

In a double-blind dose-finding study, 458 OCD patients were randomized to escitalopram (fixed at 10mg or 20mg), or 40mg paroxetine or placebo. At week 12 - the primary efficacy endpoint - 20 mg escitalopram showed a significant improvement in the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) compared to placebo ($p<0.005$). At week 24, escitalopram 10mg ($p<0.05$) and 20mg ($p<0.005$) showed significantly greater improvements in Y-BOCS total scores than placebo - as did paroxetine 40 mg ($p<0.005$). In a relapse prevention study, 320 patients (ITT) who had responded following 16 weeks of open treatment with escitalopram, were randomized to placebo or escitalopram for a further 24 weeks of double-blind treatment. The primary analysis (time to relapse) showed a significant advantage for escitalopram (Log-rank test $p<0.001$), and the risk of relapsing was 2.7 times higher for placebo compared to escitalopram. These results suggest that escitalopram is effective for acute and long-term treatment and relapse-prevention in OCD.

SAT3 - Satellite symposium: RESETTING THE INTERNAL CLOCK IN DEPRESSION: A NEW THERAPEUTIC APPROACH

Sponsored by Servier

SAT3.01

Effective management of depressed mood with agomelatine, a melatonergic antidepressant

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Agomelatine is a new antidepressant with an unique pharmacological profile. It is a potent agonist of melatonin receptors (MT1 and MT2) and also an antagonist at 5-HT2C receptors Agomelatine's acute efficacy in treating MDD was seen in three placebo-controlled studies, including a dose-ranging study with paroxetine as active comparator.

The meta-analysis of these trials showed a significant difference between agomelatine and placebo in the main efficacy analysis, the HAMD score (= 2.86 0.56; $P<0.001$) and in the CGI scale (=0.47 0.10; $P<0.001$).

Furthermore, evidence of agomelatine's efficacy in severe depression was illustrated by the meta-analysis of the patient subgroup with a baseline HAMD 25. Analysis of pooled data demonstrated an increase in the magnitude of the agomelatine-placebo difference with increasing severity at baseline.

The antidepressant efficacy of agomelatine was also evaluated in direct comparison to venlafaxine in 2 trials. Agomelatine showed at least comparable efficacy to venlafaxine in depressed patients after 6 and 12 weeks of treatment.

Agomelatine did not show the typical side effects found with selective serotonin reuptake inhibitors (SSRIs) (ie, gastrointestinal disorders, weight gain, serotonergic syndrome, and insomnia).

Moreover, agomelatine was shown to lack discontinuation symptoms compared with placebo in a study showing significant discontinuation symptoms with paroxetine.

In conclusion, the experience with agomelatine across a wide range of clinical trials suggests that agomelatine offers an important alternative for the treatment of depression, combining efficacy, even in the most severely depressed patients, with a favourable side-effect profile.

SAT3.02

A new pharmacological step: The melatonergic approach

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A breakthrough has recently been made in antidepressant research with the development of agomelatine. Agomelatine has a distinct pharmacological profile compared with all other classes of clinically available antidepressants.

Agomelatine is a high-affinity agonist at both the melatonergic MT1 and MT2 receptor types, and, in addition, blocks 5-HT2C receptors. Agomelatine did not significantly bind to any other site studied. In accordance with this profile, agomelatine resynchronized circadian rhythms and elicited a dose-dependent elevation in extracellular levels of noradrenaline and dopamine in the frontal cortex of freely moving rats while exerting no effect upon serotonin levels. The antidepressant actions of agomelatine have been described in several validated animal models: learned helplessness, forced swim, chronic mild stress, mice with impaired glucocorticoid receptors, isolated aggressive mice, and the marble burying test, with antidepressant-like effects being shown in all behavioral paradigms examined. Based on these results, the nocturnal sleep pattern of psychosocially stressed male tree shrews (a valid animal model for depression) was investigated: agomelatine resynchronized disrupted circadian rhythms and antagonized the effect of stress on the total amount of rapid eye

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