proved effective first-line therapies for the rapid control of agitation associated with psychotic disorders. Although widely used, intramuscular benzodiazepines have been associated with excessive sedation, and typical antipsychotics, such as intramuscular haloperidol, have a high propensity for causing acute extrapyramidal symptoms. Distressing side effects may adversely impact on patient acceptance of, and adherence to, future antipsychotic therapy. Intramuscular atypical antipsychotics may provide superior alternative treatments owing to improved safety and tolerability versus typical agents. Clinical studies have demonstrated the safety and efficacy of intramuscular formulations of aripiprazole, olanzapine and ziprasidone for the treatment of agitation associated with schizophrenia, and these agents have been approved for use in the USA and some European countries. Although rapid control of agitation is the primary goal, the longer-term effects of antipsychotic therapy also require consideration. Patients initially treated with an intramuscular antipsychotic will typically transition to oral therapy for the long-term management of their disorder. Therefore, the long-term safety and tolerability of oral therapy is important. For example, treatment-associated sedation can adversely affect patient quality of life and social integration during longer-term treatment, whereas treatment with antipsychotics that are associated with significant risk of weight gain, glucose dysregulation and dyslipidaemia may have serious implications for long-term patient health. Transferring from an intramuscular to an oral antipsychotic may impose a risk of the emergence of adverse effects, breakthrough symptoms and loss of therapeutic advantage, particularly if transitioning between intramuscular and oral formulations of different antipsychotics; ideally, continuation with the same agent would minimise this risk.

SAT2 - Lunch Satellite symposium: SEROTONIN, NORADRENALINE, DUAL - WHAT IS STATE OF THE ART? *Sponsored by Lundbeck*

SAT2.01

Pharmacological treatment of anxiety disorders - is there a state of the art?

B. Bandelow. *Department of Psychiatry and Psychotherapy, University of Goettingen, Goettingen, Germany*

Selection of appropriate treatment for anxiety disorders is influenced by several considerations, including psychiatric comorbidity. Emerging data suggest that anxiety disorders have a chronic course and a high comorbidity with depression. Successful treatment can be facilitated by first establishing treatment goals, which include managing acute anxiety and following through to remission. Prevention of recurrence of anxiety disorders should be the ultimate objective.

Various treatment options exist for the treatment of anxiety disorders, including selective serotonin reuptake inhibitors (SSRIs), serotonin-noradrenaline reuptake inhibitors (SNRIs), tricyclic antidepressants, pregabalin, benzodiazepines, buspirone, and reversible and irreversible MAO inhibitors. Some SSRIs have been demonstrated efficacy in both acute and long-term trials. Regarding their risk-benefit ratio, they are established as first-line therapies. The combination of drug treatment with cognitive behaviour therapy (CBT) is also recommended.

The chronic nature of anxiety disorders, different treatment response among different anxiety disorders and the recognition of their frequent comorbidity with depression requires an informed and evidence based choice of the best pharmacological approach to the individual patient. The presentation will present the most recent data from randomised clinical trials of newer generation agents and put them into perspective, to help the physicians to appropriately diagnose anxiety disorders and achieve the goal of bringing patients to full remission.

SAT2.02

Requires severe depression a specific treatment?

S.H. Kennedy. *University Health Network, Toronto, ON, Canada*

Depression is a disabling disorder associated with considerable comorbidity, risk of suicide and social consequences. Although antidepressants are among the most prescribed therapeutic agents, recent reviews highlight the significant percentage of depressed patients who fail to achieve a response or remission.

Although epidemiological and clinical data do not support severe depression as a separate illness category, and there is no consensus on the definition of "severe depression" regarding diagnostic scales, evidence suggest that the severity of depressive symptomatology may be associated with a worse prognosis and an increased mortality. Furthermore is there a perception that specific subpopulations of depressed patients e.g. melancholic patients or treatment resistant patients suffer of more severe forms of depression. The treatment of severely depressed patients is thus of major concern in view of the debilitating course of the disease.

Some early studies suggested that tricyclic antidepressants (TCAs) like clomipramine were more effective that selective serotonin reuptake inhibitors (SSRIs) paroxetine or citalopram in "endogenously" depressed patients. Other reviews report comparable efficacy of TCAs and SSRIs in patients with severe or melancholic depression, with SSRIs being better tolerated.

Recent data suggesting a surprisingly better differentiation of escitalopram, the active enantiomer of racemic citalopram, regarding effeicacy in more severely depressed patients (MADRS $>$ 30 or $>$ 35) versus SSRIs such as paroxetine and citalopram as well as versus the SNRI venlafaxine argue for a differentiated treatment approach, based on severity of symptoms.

SAT2.03

OCD quo vadis? The Cape Town consensus statement

H.G.M. Westenberg. *Rudolf Magnus Institute of Neuroscience, Department of Psychiatry, University Medical Center Utrecht, Utrecht, The Netherlands*

The perception of Obsessive Compulsive Disorder (OCD), once seen as a rare refractory condition, has changed significantly over the past two decades. Neuroimaging and genetic findings have advanced the understanding of the neurobiology of OCD and new treatment options have improved the outlook for patients.

A consensus group at the International Anxiety Disorders Conference in Cape Town, South Africa in February 2006, felt it was timely and appropriate to revisit OCD, to identify key developments in the field of OCD and to examine how they might be translated into clinical practice.

The group reviewed the currently available data on symptomatology, diagnosis, assessment, psychobiology and treatment of OCD in order to provide an up-to-data summary of the literature and recommendations for the treating physician. Special attention was paid to the current controversies about the relationship of OCD to OCD

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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

N.A. Fineberg. *National OCD Specialist Service, Queen Elizabeth II Hospital, Welwyn Garden City, United Kingdom*

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

G.M. Goodwin. *University Department of Psychiatry, Warneford Hospital, Oxford, United Kingdom*

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

G. Racagni. *Center of Neuropharmacology, University of Milan, Milan, Italy*

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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