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Lilly-SAT3. New frontiers in serotonin research

Chair: M Fava (USA)

Lilly-SAT3-1
TREATMENT APPROACHES TO POSTTRAUMATIC STRESS DISORDER

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Early reports of pharmacotherapy for PTSD were focused on acutely emergent syndromes during World War II. After a hiatus of 3 decades, investigators returned to the topic, and reported benefits for MAOI and TCA drugs, most particularly phenelzine, imipramine and amitriptyline. These studies were conducted in combat veterans who showed some responsiveness to these drugs. Later studies have concentrated on serotonergic drugs and, to a much lesser extent, anticonvulsants. Clear evidence exists for efficacy of fluoxetine and sertraline in civilians with PTSD, but both drugs proved to be ineffective in combat veteran populations with PTSD. Open-label trials also support the use of nefazodone, fluvoxamine and paroxetine. Platelet paroxetine binding may serve as a predictor of response to fluoxetine; carbamazepine, valproate and lamotrigine all may be useful in PTSD. This presentation will review evidence for and against the use of the above drugs.

Lilly-SAT3-2
ANGER ATTACKS IN DEPRESSED OUTPATIENTS AND THEIR RESPONSE TO FLUOXETINE

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A number of phenomenological studies have demonstrated the marked heterogeneity of unipolar depressive disorders. Hostility and anger are present relatively frequently among depressed patients. We have recently identified a subtype of depression characterized by the presence of irritability, hostility, and "anger attacks." These attacks are sudden spells of anger accompanied by symptoms of autonomic activation such a tachycardia, sweating, flushing, and tightness of the chest. They are experienced by depressed patients as uncharacteristic of them and inappropriate to the situations in which they occur. Approximately one third of depressed outpatients presents anger attacks. Patients with unipolar depression and anger attacks frequently experience significant anxiety and somatic symptoms, and are relatively more likely to meet criteria for avoidant, dependent, borderline, narcissistic, and antisocial personality disorders than depressed patients without these attacks. Anger attacks subside in 53–71% of depressed outpatients treated with antidepressants, and degree of improvement in depressive symptoms following antidepressant treatment is comparable across depressed patients with and without anger attacks. In addition, the rate of emergence of anger attacks after treatment with antidepressants (6–10%) appears to be lower than the rate with placebo (20%). Finally, antidepressants that affect serotonergic neurotransmission, seemingly more likely to be deranged in depression with anger attacks, may be particularly effective in this subtype of depression, but further studies are needed to support this hypothesis.

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Lilly-SAT3-3
TREATMENT OPTIONS FOR THE PHARMACOTHERAPY OF EATING DISORDERS

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Eating disorders such as anorexia nervosa (AN) and bulimia nervosa (BN) most commonly afflict adolescent and young women of middle and upper socioeconomic status. The prevalence of these disorders is increasing, particularly in industrialized societies. In both disorders, patients have a distorted sense of the shape of their body and a morbid fear of obesity. AN is manifested by marked weight loss, which may become life-threatening if untreated. BN is characterized by binge-eating and by induced vomiting and/or use of diuretics and laxatives while fasting or dieting rigorously.

Though limited in number, clinical trials in AN have yielded evidence that SSRIs are effective in preventing relapse after weight restoration. Additional studies are clearly warranted in this area.

Clinical trials in BN have shown that fluoxetine 60 mg/day is significantly more effective than placebo in lowering the frequency of binge-eating and vomiting episodes, with fluoxetine being the only SSRI with an indication for this disorder.

Psychotherapeutic approaches, specifically cognitive-behavioral therapy, play a central role in the treatment of eating disorders. However, clinical trials suggest that cognitive-behavior therapy combined with pharmacotherapy (fluoxetine) is more effective in treating these disorders than cognitive-behavior therapy alone.

Lilly-SAT3-4
DEPRESSION IN CHILDREN AND ADOLESCENTS

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Mood disorders are prevalent and serious disorders in children and adolescents. Using results from our research studies, information will be presented on 1) the symptoms of depression in children/adolescents; 2) degree of comorbidity; 3) an acute double-blind, placebo-controlled trial of fluoxetine; and 4) a one-year naturalistic follow-up.

Selective serotonin reuptake inhibitors (SSRIs) are well tolerated in children, and appear to have fewer side effects than tricyclics. We studied 96 children and adolescents with MDD in an 8 week trial of fluoxetine versus placebo. Of those randomized to fluoxetine, 56% were considered responders, compared to only 33% in the placebo group. In addition, depressive symptoms were significantly less in the fluoxetine group by 5 weeks of treatment.

Over the course of a one-year naturalistic follow-up period, 85% had recovered. While the majority of patients do recover, new episodes are common. Thirty-nine percent of subjects who recovered had a recurrence of depression during the one-year follow-up, with 55% of these occurring within 6 months. This finding is somewhat higher than the recurrence rates of MDD in adults.

In conclusion, early onset depression is similar to depression in adults. As with adults, SSRI's appear safe and effective in the treatment of children and adolescents with MDD. While the majority of patients do recovery, recurrence is common, and further research regarding maintenance treatment in children and

adolescents is needed to determine the most effective length of medication treatment.

Lilly-SAT3-5

SSRIs IN THE TREATMENT OF PMDD: AN UPDATE

M. Steiner. *Department of Psychiatry, McMaster University, St. Joseph's Hospital, Hamilton, Ontario, L8N 4A6, Canada*

The recent inclusion of research diagnostic criteria for premenstrual dysphoric disorder (PMDD) in the DSM-IV recognizes the fact that some women in their reproductive years have extremely distressing emotional and behavioral symptoms premenstrually. Through the use of these criteria, PMDD can be differentiated from premenstrual syndrome which has milder physical symptoms such as breast tenderness, bloating, headache and minor mood changes, as well as from premenstrual magnification which occurs when physical and/or psychological symptoms of a concurrent psychiatric and/or medical disorder are magnified during the premenstruum. Epidemiological surveys have estimated that as many as 75% of women with regular menstrual cycles experience some symptoms of premenstrual syndrome. PMDD, on the other hand, is much less common. It affects only 3 to 8% of women in this group, but it is much more severe and exerts a much greater psychological toll. These women report premenstrual symptoms that seriously interfere with their lifestyle and relationships. The etiology of PMDD is largely unknown but the current consensus seems to be that normal ovarian function (rather than hormone imbalance) is the cyclical trigger for PMDD-related biochemical events within the CNS and other target organs. The serotonergic system is in close reciprocal relationship with the gonadal hormones and has been identified as the most plausible target for interventions. Thus beyond the conservative treatment options such as lifestyle and stress management and the more extreme interventions that eliminate ovulation altogether the serotonin re-uptake inhibitors (SSRIs) are emerging as the most effective treatment options for this population. Results from several randomized placebo-controlled trials in women with PMDD, with predominantly psychological symptoms of irritability, tension, dysphoria and lability of mood, have clearly demonstrated that the SSRIs have excellent efficacy and minimal side effects. More recently several preliminary studies indicate that intermittent (premenstrually only) treatment with SSRIs is equally effective in these women and thus may offer an attractive treatment option for a disorder that is itself intermittent.

The Lundbeck International Psychiatric Institute

Lundbeck-IPI-SAT. Evidence-based medicine in depression

Chairs: H van Praag (NL), N Sartorius (CH)

Lundbeck-IPI-SAT-1

THE DEBILITATING BURDEN OF DEPRESSION

Norman Sartorius. *Hospitaux Universitaire de Genève, Département de Psychiatrie, 16-18 Bd. de St. Georges, 1205 Genève, Switzerland*

Depressive disorders are a major public health problem. They are frequent and severe in their consequences if left untreated.

Recent studies have demonstrated that people suffering from depressive disorders make up a significant proportion of all those seeking help from general and primary health care services. Depressive disorders are poorly recognized, and patients suffering from them often exposed to costly somatic examinations and treated for a variety of somatic diseases. Antidepressant treatment is provided to only half of those who were diagnosed as suffering from depression and the doses prescribed are often low.

It is highly probably that the prevalence of depressive disorders will increase in the years to come. The reasons for this include the ageing of the population, the increasing expectancy of life of people who suffer from chronic illness (who often have co-morbid depressive disorders) as well as the extended life expectancy of people suffering from depressive disorders.

There are also some indications that the incidence of depressive disorders is increasing. As a consequence it is of great importance to undertake measures likely to help in the control of depressive disorders. These include additional training for general practitioners and other health workers, the improvement of the undergraduate education about depressive disorders, and the education of the general public.

Lundbeck-IPI-SAT-2

EVIDENCE BASED MEDICINE IN DEPRESSION: THE DIFFERENCE BETWEEN THEORY AND PRACTICE

M. Linden. *Department of Psychiatry, Free University of Berlin, Germany*

There is a large literature on the epidemiology of care which shows many differences between treatment guidelines and routine treatment in depression. Examples are high rates of non-recognition, inappropriate diagnostic specificity, no treatment or application of inadequate drugs, insufficient daily doses of antidepressants, early treatment termination, or insufficient psychological interventions.

Additionally there are large differences between areas or medical specialties in the way how depressive disorders are treated.

The conclusions from such data are twofold: Firstly, physicians must be better trained and informed about available evidence about optimal treatment of depression. Secondly, reasons for this therapist-non-compliance with guidelines have to studied. Available data suggest, that many guidelines may not be valid for treatment problems in routine care or do not address crucial points in medical decision making.

Lundbeck-IPI-SAT-3

QUALITY IMPROVEMENT IN THE TREATMENT OF DEPRESSION THROUGH EDUCATION

Wolfgang Rutz. *Visby Hospital, Sweden*

In the years 1983–1984, the Swedish Committee for Prevention and Treatment of Depressions (PTD) offered an educational program to all general practitioners (GP:s) on the Swedish island of Gotland. The education has been shown to lead to a significant decrease in inpatient care, morbidity, mortality and costs caused by depressive illness on the island. Unspecific medication decreased and specific antidepressive medication increased.

A scrutinizing of all suicides on Gotland during the 1980:ies showed that the overall decrease in suicides due to the educational program mainly was caused by the decrease in suicides committed by female suicidants with recognized major depression and in contact with general practitioners. This was expected. However, the number of male suicides was almost uneffected by the educational program and the GP:s improved ability to diagnose and treat depressions.