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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.

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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 as 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.

(1) *Psychopharmacology Bulletin* 27: 275–279, 1991.

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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.

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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 recover, recurrence is common, and further research regarding maintenance treatment in children and