serotonin-norepinephrine reuptake inhibitor, will examine venlafaxine's usefulness in a broad range of depressed patients and characterize features that distinguish venlafaxine from other antidepressants. Double-blind, parallel-group studies are planned to compare venlafaxine with other antidepressants including fluoxetine, paroxetine, sertraline, citalopram, and moclobemide. A series of studies is in progress to provide clinical confirmation for in vitro findings which suggest that venlafaxine has a low potential for producing drug interactions, because it does not significantly inhibit any of the major cytochrome P450 enzymes. Specific studies are in progress or planned to further elucidate venlafaxine's mechanism of action and onset of action. A once daily formulation of venlafaxine is under development to provide additional simplicity of dosage administration. Although depression will continue to be the major focus for venlafaxine clinical investigations, there is growing interest among researchers and clinicians in a variety of other clinical applications for antidepressants. Possible new applications include generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, social phobia, neuropathic pain syndromes, premenstrual dysphoric disorder, obesity, Alzheimer's disease, and attention deficit disorder.

A CLINICAL PERSPECTIVE ON THE THERAPEUTIC ROLE OF VENLAFAXINE, A SNRI, IN DEPRESSION

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Venlafaxine, a new serotonin-norepinephrine reuptake inhibitor (SNRI), has been evaluated over a range of doses in phase II and III clinical trials involving over 3,000 patients with major depressive disorder. Data from comparative studies with fluoxetine indicate that venlafaxine at the usual dose of 75 mg/day is comparable in efficacy and tolerability to selective serotonin reuptake inhibitors (SSRIs) in most patients with major depressive disorders. Among those patients who remained at the low dose level, ie, venlafaxine 75 mg/day or fluoxetine 20 mg/day, no significant differences in response were observed on the HAM-D total or factor scores or on the MADRS total. In contrast to many SSRIs, results from double-blind, randomized trials with venlafaxine provide evidence of a dose-response effect. This positive dose-response effect results in an improved clinical response with higher doses of venlafaxine in contrast to a relatively flat dose-response with SSRIs. In two randomized, comparative trials, venlafaxine at doses of $\geq$ 150 mg/day was superior to fluoxetine. Additional randomized, comparative trials of venlafaxine versus imipramine or fluvoxamine support the superior efficacy of higher venlafaxine doses. Thus, venlafaxine offers the potential for effectiveness comparable to SSRIs at its usual 75 mg/day dose with the option of improving the response with dosage escalation.

Janssen-Cilag/Organon Laboratories

ST4. New perspectives in the treatment of schizophrenia

Chairmen: E Johnstone, R Borison

Abstracts not received.

Smithkline, Beecham

ST5. Panic and depression: not all SSRI's are the same

Chairmen: J Ballanger, J Mendlewicz

Abstracts not received.

Pfizer Limited

ST6. The role of 5HT central synaptic transmission in the regulation of the extra pyramidal system

Chairman: T Dinan

DOPAMINE AND THE USE OF SSRIs FOR CONDITIONS OTHER THAN DEPRESSION

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Serotonin reuptake inhibitors (SSRIs) have been used as adjunctive agents in open and recently double blind studies of the treatment of patients with schizophrenia, showing improvements in negative symptoms over 6 months. Extrapyramidal symptoms (EPS) were not exacerbated. Serotonergic blockade is one mechanism advocated for the apparent efficacy of many atypical neuroleptics in the treatment of negative schizophrenic symptoms and also for the low rate of EPS. SSRIs undoubtedly cause EPS in some patients, perhaps linked to the modification both of dopamine and acetylcholine release. Recent PET studies show that SSRIs differ in their effects on striatal dopamine concentration and receptor binding. Both serotonin and dopamine have been implicated in the pathophysiology of OCD and use of combined neuroleptic and SSRI treatment has also been described in cases refractory to an SSRI alone with disorders related to OCD, such as Tourette's syndrome and tricotillomania. It has also been suggested that the anorectic effects of SSRIs are mediated by dopaminergic mechanisms. The dopamine reuptake blocker bupropion has been used to treat sexual dysfunction secondary fluoxetine, implicating dopamine in these side effects. Animal studies suggest a dopaminergic mechanisms for anhedonia, a core feature of major depression. Dopamine receptor blockade has been shown to reverse improvement seen with a range of antidepressants, including drugs selective for serotonin or noradrenaline, in animal models. This must be reconciled with the adjunctive effect of dopamine blockers added to antidepressants, including SSRIs, in psychotic depression.

SSRI'S AND MOVEMENT DISORDERS: IS SEROTONIN THE CULPRIT?

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Experimentally it has been shown that 5HT agonists or 5HT releasing agents in rodents produce the serotonin motor syndrome which

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