of the endogenous opioids would be useful in elucidating the mechanisms involved in the pathophysiology of sleep-related abnormal movements.

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FLUOXETINE IN THE TREATMENT OF CATAPLEXY

To the Editors:

Cataplexy, sudden brief paralysis of voluntary movement and loss of muscle tone following any momentary decrease in alertness, occurs in both humans and dogs, almost always in association with narcolepsy (1). Cataplexy, although a disorder of wakefulness, is thought to be mediated via the same pathways that determine muscle atonia during sleep. It has been known for a long time that tricyclic drugs, imipramine, desmethylimipramine and, in particular, clomipramine, prevent cataplexy in both humans and animals; although the exact neurotransmitter mechanisms involved are unknown and long-term treatment in man often results in considerable weight increase, anticholinergic effects, and delayed ejaculation (2). Recently it has been shown that fluoxetine (3-*p*-trifluoromethylphenoxy-*N*-methyl-3-phenylpropylamine), a specific inhibitor of serotonin uptake, will reduce cataplexy in dogs (3,4). We have investigated the action of this drug in humans with cataplexy.

Twelve patients with narcolepsy-cataplexy, 6 men, were investigated. Five patients had hypnagogic hallucinations and nine had sleep paralysis. The mean age of onset of cataplexy was 32 years (range 7–49 years), and of narcolepsy 28 years (range 7–45 years). All subjects were established on dexamphetamine 5–60 mg daily or other stimulant drugs for narcolepsy, and on clomipramine 25–150 mg (mean 52 mg) daily for cataplexy. Clomipramine was directly replaced by fluoxetine 60 mg daily (9:00 a.m.) in all subjects. Central stimulant drugs were continued in unchanged dosages. This resulted in a severe rebound of cataplexy in one patient, who was withdrawn from the study. Over the following 4 weeks, four of 11 subjects considered that cataplexy was less frequent while taking fluoxetine 60 mg daily than when previously taking clomipramine 25–150 mg daily; five subjects considered both treatments equally effective; and two subjects considered that cataplexy was more frequent on fluoxetine than clomipramine. The mean number of attacks of cataplexy each day as recorded by self-rating scales before any treatment was 2.1 attacks; on fluoxetine 0.5 attacks; and on clomipramine 0.6 attacks (difference between treatments not significant, $p > 0.1$, Student's t test). Fluoxetine was associated with mild nausea and indigestion in one subject, and with dry mouth in four, but did not cause anorexia. There was no change in blood pressure, pulse rate, weight, urine analysis, full blood count, ESR, liver function tests, urea, and electrolytes during the 4 weeks of study. After 4 weeks of treatment with fluoxetine, plasma mean fluoxetine concentration 4 h after oral 60 mg dosage was 329 ± 70 ng ml^{-1} (mean ± 1 SEM), and norfluoxetine 286 ± 147 ng ml^{-1}. Plasma fluoxetine concentrations were not related to the number of attacks of cataplexy or the severity of side effects.

As in dogs, fluoxetine appears to be effective in humans with cataplexy, and has about the same potency on a mg/kg basis as clomipramine. Fluoxetine may have some advantages over clomipramine in the treatment of cataplexy, since it is almost totally devoid of anticholinergic activity and, at least in dogs, has an anorectic rather than appetite-stimulant effect. The major effect of fluoxetine in synaptosome preparations is to inhibit 5-hydroxytryptamine (5-HT) re-uptake, and the anticataplectic action may be related to this pharmacological effect since descending reticulo-spinal systems which are probably activated during cataplexy, and which also mediate sleep atonia, have a 5-HT input.

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