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A comparison of fenfluramine and amphetamine in man

dl-Fenfluramine hydrochloride (60, 120, 240 mg), d-amphetamine sulfate (20, 40 mg), and placebo were compared in 8 postaddict volunteers, each dose given orally in random sequence at weekly intervals using a double-blind crossover design. Fenfluramine had little effect on blood pressure and temperature, but caused a marked dilation of pupils, whereas amphetamine was a potent vasopressor and a weak mydriatic. While fenfluramine produced euphoria in some subjects, its overall effects were unpleasant, sedative, and qualitatively different from amphetamine. Three subjects given 240 mg of fenfluramine experienced brief but vivid hallucinogenic episodes characterized by olfactory, visual, and somatic hallucinations, abrupt polar changes in mood, time distortion, fleeting paranoia, and sexual ideation. These observations indicate that fenfluramine is a hallucinogenic agent with a pharmacologic profile in man that is not amphetamine-like.

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Human subjects given the anorexigenic drug, fenfluramine (N-ethyl-m-trifluoromethyl phenylisopropylamine, Pondimin), often report a sense of unpleasant lethargy from the drug rather than a euphoric "high,"[8] and concomitant electroencephalographic patterns can be more characteristic of sedative agents than drugs of the amphetamine class.[3-5] Moreover, with animal paradigms of human drug-seeking behavior, fenfluramine is not reinforcing[22] and relatively devoid of amphetamine-like sympathomimetic properties.[2]

From these and other studies, one might conclude that fenfluramine is unique and not likely to lead to amphetamine-like psychotoxicity or abuse—an estimate corroborated by the very few reports of fenfluramine abuse in Europe where the drug has been available clinically for some years.[7, 20] On the other hand, Levin has reported descriptions of 60 young men from South Africa (where the drug could be obtained without prescription) who self-administered fenfluramine in doses of 80 to 400 mg on one or more occasions to obtain a euphoric effect.[15, 16] The constellation of symptoms remembered by these men included hallucinogenic, sedative, and amphetamine-like effects. Of possible concern are still other reports of dysphoria and sleep disturbance after chronic fenfluramine use and abrupt withdrawal,[12, 19] a like sequence also following amphetamine.

There is therefore the possibility that fenfluramine may have reinforcing properties (amphetamine-like or otherwise) not previously identified in controlled clinical studies. To explore this issue, the subjective and physio-

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