

like and probably would not substitute in amphetamine-like patterns of abuse.

In support of Levin's studies,^{15, 16} fenfluramine was observed to have hallucinogenic activity in 3 of 5 subjects who experienced syndromes characterized by visual hallucinations, sensory distortion, fleeting paranoia, derealization, depersonalized awareness, somatic symptomatology, labile mood, a modest increase in pulse rate and blood pressure, mydriasis, and hyperactive tendon reflexes—the last not measured systematically. This configuration resembles that produced by a number of hallucinogens, including LSD and certain ring-substituted amphetamines. This similarity, plus the cases cited by Levin, suggests that LSD-like, rather than an amphetamine-like, abuse potential should be considered. This issue aside, hallucinogenic and dysphoric symptoms may well limit the therapeutic utility of fenfluramine as an anorexiant.

While 3 subjects experienced hallucinogenic phenomena (without sedation), 5 others were moderately sedated following the largest dose of fenfluramine and denied psychotomimetic symptoms. No reasons can be given for these differences. Preliminary data suggest that the hallucinatory response may result from a rapid absorption of oral fenfluramine or its conversion to norfenfluramine.

The similarity between the effects of fenfluramine and endogenous emotional depression, both characterized by symptoms of dysphoria, hypochondriasis, insomnia, emotional lability, and anorexia, is of interest, suggesting that ring-substituted phenethylamines may be used as tools to investigate these functional states.

The authors thank Mr. Robert Eads for his technical assistance.

References

1. Alphin, R. S., and Ward, J. W.: Anorexigenic effects of fenfluramine hydrochloride in rats, guinea pigs, and dogs. *Toxicol. Appl. Pharmacol.* **14**:182-191, 1969.
2. Cox, R. H., and Maickel, R. P.: Comparison of anorexigenic and behavioral potency of some phenethylamines. *J. Pharmacol. Exp. Ther.* **181**:1-9, 1972.
3. Fink, M., Shapiro, D. M., and Lül, T. M.: EEG profiles of fenfluramine, amobarbital and dextroamphetamine in normal volunteers. *Psychopharmacologia* **22**:369-383, 1971.
4. Firth, H., Lewis, S. A., Ogunremi, O. O., and Oswald, I.: The effect of acute administration of (*meta* trifluoro methyl-phenyl)-1-(benzoyl oxy) ethyl amino-2-propane (780 SE) and fenfluramine on human sleep. *Br. J. Pharmacol.* **39**:462-453, 1970.
5. Foxwell, M. H., Funderburk, W. H., and Ward, J. W.: Studies on the site of action of a new anorectic agent, fenfluramine. *J. Pharmacol. Exp. Ther.* **165**:60-70, 1969.
6. Fraser, H. F., Van Horn, G. D., Martin, W. R., Wolbach, A. B., and Isbell, H.: Methods for evaluating addiction liability. (A) "Attitude" of opiate addicts toward opiate-like drugs; (B) A short-term "direct" addiction test. *J. Pharmacol. Exp. Ther.* **133**:371-387, 1961.
7. Gaultier, M., Efthymiou, M. L., and Cottreau, C.: Intoxications aiguës par les anorexigènes récents (amphétamines exclues). *Eur. J. Toxicol.* **1**:55-73, 1968.
8. Gotestam, K. G., and Gunne, L. M.: Subjective effects of two anorexigenic agents fenfluramine and AN448 in amphetamine-dependent subjects. *Br. J. Addict.* **67**:39-44, 1972.
9. Groppetti, A., Zambotti, F., Biazzi, A., and Mantegazza, P.: Amphetamine and cocaine on amine turnover. In Usdin, E., and Snyder, S. A., editors: *Frontiers in catecholamine research*, New York, 1973, Pergamon Press, pp. 917-925.
10. Haertzen, C. A.: Development of scales based on patterns of drug effects, using the Addiction Research Center Inventory (ARCI). *Psychol. Rep.* **18**:163-194, 1966.
11. Haertzen, C. A.: Subjective effects of narcotic antagonists cyclazocine and nalorphine on the Addiction Research Center Inventory (ARCI). *Psychopharmacologia* **18**:366-377, 1970.
12. Harding, T.: Fenfluramine dependence. *Br. Med. J.* **3**:305, 1971.
13. Jasinski, D. R., Nutt, J. G., and Griffith, J. D.: Effects of diethylpropion and *d*-amphetamine after subcutaneous and oral administration. *CLIN. PHARMACOL. THER.* **16**:645-652, 1974.
14. Jespersen, S., and Scheel-Kröger, J.: Evidence for a difference in mechanism of action between fenfluramine- and amphetamine-induced anorexia. *J. Pharm. Pharmacol.* **25**:49-54, 1973.
15. Levin, A.: Abuse of fenfluramine. *Br. Med. J.* **2**:49, 1973.
16. Levin, A.: The non-medical misuse of fenfluramine by drug-dependent young South Africans. *Postgrad. Med. J.* **51** (Suppl. 1): 183-185, 1975.
17. Martin, W. R.: Assessment of the abuse potential of amphetamines and LSD-like hallucinogens in man and its relationship to basic