that his preoccupation was without foundation. He thereafter continued with testing and identified other changes such as time compression and alterations of body image, which came in "waves" for about 5 hr. Because the patient was comfortable, in good contact with staff, and willing to continue, no attempts were made to terminate these symptoms.

With 2 other subjects, hallucinogenic effects were more pronounced. One man with considerable LSD experience became mute some 45 min after taking fenfluramine, and for the next half-hour communicated by making animal-like noises and gestures. Upon recovering his voice, he explained that he had been on a "beautiful trip," which began with his noticing that the shadows cast by the venetian blinds reminded him of a reptilian underbelly. Subjectively, he was very quickly transformed into a large and fearsome dinosaur, searching, during what seemed like a period of years, for his dinosaur wife and child—an experience that culminated in an ecstacy of reunion and closeness with his family group. The subject later explained that he was at all times aware that his experiences were drug-induced and unreal, but his decision to remain mute was to prolong the state as long as possible. The thematic content of his hallucinogenic state was connected by the subject to a troubled domestic relationship.

A second subject also experienced derealization, rapid, and polar alterations of mood, visual hallucinations, distortions of perspective, changes in body image, vivid sexual hallucinations and ideas, and transient paranoia. In contrast to the episodes described above, this subject evaluated his experience as mostly unpleasant, except for the sexual hallucinations. He and the above subject experienced infrequent, short-lived episodes of unreality for 3 days postdrug.

Discussion

Previous studies from the Addiction Research Center have shown the relationship between amphetamine structure and amphetamine activity in man or, more specifically, the pharmacologic profiles obtained by modifications of the isopropylamine side chain (methamphetamine, phenmetrazine, methylphenidate, ephedrine, diethylpropion, benzphetamine). These structural configurations were observed to have a profound effect on weight potencies but pharmacologic profiles were essentially unchanged. In other words, for a given effect on appetite, all drugs produced equal degrees of euphoria and vasopressor change despite differences in physical potency ranging from 1:1 to 1:20.[13, 18]

It was significant to learn whether a different type of structural modification (ring substitution), as exemplified by fenfluramine, would give qualitative alterations in pharmacologic responses and not merely qualitative differences in overall potencies. Our study indicates that the most conspicuous similarity between the effects of amphetamine and fenfluramine is an anorexigenic effect, fenfluramine being about ¼ as potent as amphetamine—an estimate in keeping with other efficacy studies in man[23] and inhibition of food intake by oral fenfluramine in the dog.[1] In rat assays, fenfluramine is relatively more potent,[2] perhaps because this animal can parahydroxylate the reference drug, amphetamine, more rapidly. This is a minor pathway in man. There is also good evidence that fenfluramine and amphetamine-induced anorexia may involve different pharmacologic mechanisms.[9, 14, 21]

In most other respects, the effects of fenfluramine were quite different. Fenfluramine, unlike amphetamine, caused substantial and generally dose-related subjective expressions of lethargy, sedation, dysphoria, and unpleasant somatic symptomatology. While fenfluramine was to some degree euphorogenic, as evidenced by elevated Amphetamine and Subjects' Liking Scale scores, this response could be differentiated from amphetamine by the transitory MBG response, subjects' drug identifications, and clinical manifestations. The physiologic profiles were also different. Fenfluramine was a weak vasopressor and a potent mydriatic, whereas amphetamine caused substantial increases in blood pressure and mild pyrexia, but effects on pupils had a rather long latency. Only amphetamine induced significant postural differences in blood pressure. These data indicate that fenfluramine is not amphetamine-