

amine, methamphetamine, ephedrine, and phenmetrazine in that pulse rate was positively correlated with blood pressure; whereas, a negative correlation was seen with other drugs. The negative correlation between heart rate and blood pressure was probably a consequence of reflex inhibition of heart rate caused by hypertension. Methylphenidate has been shown to abolish reflex hypertension produced by carotid occlusion,¹⁶ and analysis has shown that the locus of this action is probably in the central nervous system.¹⁹ It is possible that methylphenidate also antagonizes centrally the baroreceptive reflex responsible for bradycardia.

The subjective effects of ephedrine were quite commensurate with its effects on mean blood pressure and did not support the commonly held position that its central effects are less marked than those of amphetamine. Ephedrine was disproportionately weaker than amphetamine in elevating diastolic blood pressure than in elevating systolic blood pressure. It is also noteworthy that ephedrine was the only drug that did not produce a significant degree of mydriasis and was the least effective agent in increasing body temperature.

Several drug effects that may reflect increased activity of central autonomic centers should be mentioned. Although the dose-response relationship for methylphenidate in increasing respiratory rate and rectal temperature and the dose response of methamphetamine in increasing body temperature were quite flat, both drugs induced significant increases of these variables. As previously mentioned, ephedrine did not cause mydriasis and was less effective than the other drugs in elevating body temperature. Interpretation of these disparities is difficult. If taken at face value, they would indicate that methamphetamine, ephedrine, and methylphenidate do differ from amphetamine and phenmetrazine, at least with regard to certain central actions. On the other hand, these discordant results stand by and large in contrast to an over-all concordance of

the potency estimates and may be attributable to sampling, despite the fact that these differences were statistically significant. These discordant results do deserve further investigation to determine if they are due to differences in selectivity of action, differences in intrinsic activity, or differences in modes of action of the drugs.

With regard to the subjective effects, the drugs were similar. Differences between potency estimates derived from the A, BG, and MBG scales should not be overly interpreted, since the items of all three scales assess affective states characterized by happiness, contentment, pleasantness, and feelings of proficiency. The predominant effect at low and intermediate dose levels was the production of feelings of relaxation, well-being, and contentment. Although these feelings were intensified by the largest doses, the largest doses also produced signs and symptoms of nervousness, as well as elevation of LSD scale scores. It is paradoxical that these drugs, which are classified as stimulants, produce symptoms and associated signs of contentment and relaxation; however, this is the most important aspect of their euphoriant actions.

In defining the abuse potentiality of a drug, a variety of factors are of importance including its ability to induce compulsive drug-seeking behavior, its organ and psychotoxicity, and its social toxicity.^{16, 17} As has been previously discussed, the five drugs studied produce similar types of subjective effects and peripheral effects, and because of these similarities it is probable that they have a similar mode of action in producing central changes that cause their abuse. Dependence of the amphetamine type is characterized by the production of compulsive drug use and by a toxic psychosis that is a consequence of intoxication.^{3, 6, 13} The abuse of amphetamine, methamphetamine, methylphenidate, and phenmetrazine is well recognized. Further, severe intoxication with methamphetamine,^{7, 11, 14} phenmetrazine,^{3, 2} and methylphenidate¹⁵ produces toxic psychoses that are in-