

**Physiologic, subjective, and behavioral effects of
amphetamine, methamphetamine, ephedrine,
phenmetrazine, and methylphenidate in man**

Five centrally acting sympathomimetic amines, d-amphetamine, d-methamphetamine, ephedrine, phenmetrazine, and methylphenidate, were studied in man. All of these agents increased blood pressure and respiratory rate, produced similar types of subjective changes, and increased the excretion of epinephrine. With regard to these parameters, there was a high concordance between estimates of their relative potencies. The concordance between the potency estimates for the different parameters suggests, but does not prove, that these five agents share a common mode of central action. Further, if the peripheral modes of action as elucidated by animal studies are true for man, this study suggests that it is unlikely that their central actions in man are a consequence of the release of norepinephrine in the brain.

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Several central nervous system stimulants, including d-amphetamine, d-methamphetamine, methylphenidate, and phenmetrazine, have been increasingly abused and their abuse seems to share many features in common. Patients taking these drugs to obtain feelings of well-being and euphoria frequently escalate the dose to the extent that a toxic psychosis is produced. On the basis of animal experi-

ments, these drugs have several known modes of action including release of catecholamines, blockade of uptake of catecholamines, inhibition of monoamine oxidase, a serotonergic action, and cocaine-like effects. Our experiments were conducted in man comparing the effects of d-amphetamine, d-methamphetamine, phenmetrazine, methylphenidate, and ephedrine (Fig. 1) on several physiologic, behavioral, and neurochemical measures to delineate their mode or modes of action in producing subjective effects. Closely related to this end was the goal of validating meth-

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