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The Central Nervous System Stimulant Effects of Dextro-Amphetamine Sulfate.

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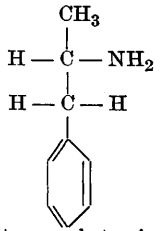
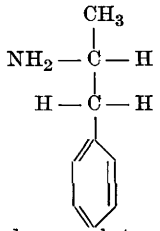
Amphetamine (Benzedrine) contains in its structure one carbon atom which is asymmetric and it has been resolved by suitable means into 2 optically active forms:



dextro-amphetamine



levo-amphetamine

A study of the comparative physiological actions of these isomers in experimental animals and in 3 normal persons, by Alles,[1] showed that the peripheral actions of these isomers are closely the same and similar to those of the racemic compound. However, the central actions of these compounds were found to differ considerably, the dextro isomer being more active than the racemic compound and from 2 to 4 times more active than the levo isomer. Trevan[2] has reported the analeptic effect against paraldehyde anesthesia of mice to be greater for the dextro isomer than for the levo isomer.

These observations made it of interest to determine whether dextro-amphetamine (dextro-Benzedrine) would prove to be more efficient clinically than either the racemic compound or its levo isomer. The clinical conditions chosen for study were those which have been found to be benefited principally by the central nervous system stimulant effects of the racemic compound (Benzedrine). The method of study in narcolepsy was similar to that of Prinzmetal and Bloomberg,[3] and in post-encephalitic Parkinson's disease like that of Solomon, Mitchell and Prinzmetal.[4] Four cases of narcolepsy were each under observation for several months, until at least 2 sets of

1 Alles, G. A., *Univ. Calif. Publ. Pharmacol.*, 1939, **1**, 129.

2 Trevan, J. W., *Proc. Roy. Soc. Med.*, 1939, **32**, 391.

3 Prinzmetal, M., and Bloomberg, W., *J. A. M. A.*, 1935, **105**, 2051.

4 Solomon, P., Mitchell, R. S., and Prinzmetal, M., *J. A. M. A.*, 1937, **108**, 1765.

observations of the effective dosage of the optically active isomers and of the racemic compound were completed. Two cases of post-encephalitic Parkinson's disease have also been under observation for several months, and while it is more difficult to quantitatively evaluate therapy in this disease than in narcolepsy, the relative effectiveness of the isomers is clearly apparent. One case of postural hypotension has also been studied with the isomeric compounds. In all cases studied the method was to determine a minimal effective dosage of each compound that produced comparable degrees of effect.

Dextro-amphetamine was found to be much more active than the levo isomer in all the cases studied. The ratio of their relative activities varied from 2 to 4. It was likewise found that the dextro isomer was more active than the racemic compound, which in turn was more active than the levo isomer. Theoretically, if the levo : dextro ratio is as 1 : 4 for their activities, the corresponding racemic : dextro ratio should be as 5 : 8. Our observations indicated that the activity of the dextro isomer was indeed from about 1.5 to 2 times that of the racemic compound.

Some supplementary observations† have been carried out on 10 normal individuals with regard to the comparative effects of the dextro and the racemic compounds on alertness and mood. These observations naturally have a low degree of precision and depend upon subjective impressions, but the dextro isomer was very clearly the more active.

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Electroencephalographic Studies in Relatives of Epileptics.*

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In studying heredity in nervous and mental diseases it has proved useful to study not only the incidence of identical clinical entities in other members of the family but also to observe the occurrence of other personality or physical trends, which appear to be related in some way to the disease under study. Such characteristics may be

† These observations by Dr. Harvey Lewis.

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