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Antagonism of (+)-amphetamine-induced hyperthermia in rats by pimozide

Whether hyperthermia induced by amphetamine in rats is due to a central or peripheral site of action is still unanswered. Hessa, Clay & Brodie (1969) stated that amphetamine-induced hyperthermia in rats is due to a peripheral site, whereas Hill & Horita (1970) attributed the hyperthermia in rabbits to a central site. The peripheral action was attributed to increased concentrations of plasma free fatty acid. However, we have demonstrated that increased plasma free fatty acid concentrations are not an integral part of hyperthermia observed after amphetamine administration in rats (Matsumoto & Shaw, 1971). We now present evidence for a central component of amphetamine-induced hyperthermia.

Male Wistar rats (Harlan Industries, Indianapolis, Indiana), approximately 175 g, were housed five per cage of 25 × 25 × 15 cm. After rectal temperatures were measured with a thermister probe (TRI-R), pimozide (10 mg/kg i.p, salt) was administered; 1 h later, (+)-amphetamine (5·52 mg/kg salt) was administered. Rectal temperatures were read at 30, 60, 120, 180 and 240 min after amphetamine,

Amphetamine increased body temperature from 36·8° by ~1° from 30 min to 2 h, and with a maximum at 1 h of 38·4°. At 3 h the temperature had fallen to 37·5° and was normal at 4 h and both saline and pimozide did not alter body temperature. However, pimozide effectively antagonized the hyperthermia due to amphetamine. According to Andén, Butcher & others (1970), pimozide antagonizes the action of dopamine in the cns. Moreover, Janssen, Niemegeers & others (1968) reported that pimozide is an effective antagonist of amphetamine's behavioral effects. Also, Costa & Groppetti (1971) reported that amphetamine increases the turnover of dopamine in the cns. Thus, the antagonism of amphetamine-induced hyperthermia by pimozide would be consistent with a central site of amphetamine's action and may involve a dopaminergic system.

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