

A B S T R A C T

The spontaneous motor activity of rats has been used extensively in psychopharmacology as an index of drug effects on the central nervous system. Not very many studies however have investigated the developmental variations in spontaneous motor activity occurring during ontogenesis in the rat. Several reports indicate changes in the biochemistry, physiology and morphology of central neurotransmitter systems as well as other neural systems in the postnatal period, suggesting that there might be related changes in the behaviour of developing animals and in their responsivity to drugs affecting the central nervous system. Levels of spontaneous motor activity were therefore measured at specific stages during development and the effects of drugs affecting particular neurochemical substrates observed.

Spontaneous motor activity was measured in circular photocell activity cages and in a Y-maze at 14-, 21-, 28-, 40- and 60 days of age. In the photocell activity cages, activity was measured for one hour following drug or saline administration, while in the Y-maze the standard observation time of three minutes was employed. No habituation period to the photocell activity cages was allowed and this activity cage measured largely locomotor activity. The drugs used in this study were amphetamine, atropine, eserine, p-chlorophenylalanine and L-Tryptophan, and all drugs were administered intraperitoneally.

Rats at 14 days of age had the lowest levels of spontaneous locomotor activity. This was followed by a steady increase in activity with age up to 40 days, after which time there was a decline in the level of spontaneous activity. The initial increase in levels of spontaneous activity can be related to certain postnatal maturational changes in the brain and skeletal musculature as well as to increases in neurochemical activity in the central nervous system. The decline in spontaneous motor activity after 40 days may be due to a later maturation of certain inhibitory centers in the brain.

Rats were sensitive to the locomotor stimulant effects of amphetamine at the youngest age measured i.e. 14 days. The locomotor stimulation produced by amphetamine was greater at 21 days of age than at 14 and 28 days of age when spontaneous activity was measured in the Y-maze. Rats at 40 days of age were unresponsive to all doses of amphetamine used (2.0, 4.0 and 10.0 mg/kg) in the Y-maze. The increase in the responsivity to amphetamine between 14 and 21 days of age may be related to the increasing levels of catecholamines in the brain during this period. The lack of effect of amphetamine at 40 days of age may be related to the high baseline levels of spontaneous motor activity observed at this age or to the maturation of certain inhibitory systems in the brain tending to suppress behavioural arousal.

L-Tryptophan (250 mg/kg) had no significant effect on spontaneous motor activity in 14 day old rats as in adult rats. P-chlorophenylalanine however caused a significant increase in spontaneous motor activity in 40 day old rats, but had no significant effect on 14 day old rats. These results suggest that serotonergic mechanisms mediating spontaneous behaviour mature later than catecholaminergic ones.

Atropine in higher doses (10 mg/kg) had a biphasic effect on spontaneous motor activity in rats over 21 days of age, activity being depressed in the initial period after drug administration, followed by significant increases in behavioural arousal after 30 minutes. In 14 day old rats, atropine (10 mg/kg) either had no effect (photocell activity cages) or depressed levels of spontaneous motor activity (Y-maze). 21 days of age seemed to represent a transitory period in development in that atropine initially depressed spontaneous motor activity (when measured in the photocell activity cage) but had no significant effect after 30 minutes.

Eserine (0.05 mg/kg) had no significant effect on spontaneous motor activity at 14 and 40 days of age, but significantly increased motor activity at 21 and 28 days of age.

The changing patterns of response to atropine and eserine during development may be related to a sequential maturation of

caudal-rostral brain systems mediating the effects of these drugs. The early depressant effect of a high dose of atropine may be due to an inhibitory action on cholinergic elements in the earlier maturing brainstem reticular formation and/or to blockage of cholinergic transmission peripherally. The significant increases in behavioural excitation which appear later in development may be attributed to an action of the drug on the later maturing cholinergic limbic-neocortical complexes.

In conclusion therefore, the findings of this study demonstrate a definite developmental trend of spontaneous motor activity in rats, as well as a differential pattern of responsiveness to drugs affecting central neurotransmitters. Catecholaminergic mechanisms modulating spontaneous motor activity mature earlier than serotonergic and cholinergic ones. The results can be interpreted in terms of demonstrated neurochemical changes occurring during developmental, and in terms of a caudal-rostral sequence of brain maturation.

The findings have implications for certain developmental disorders such as Minimal Brain Dysfunction (MBD) hyperkinesis, where it is felt that a delay in the development of certain forebrain inhibitory systems may be responsible for the observed behavioural deviations.