ABSTRACT

The elucidation of the neurochemical basis of movement disorders is currently one of the most challenging and important preclinical research endeavours (Gabay, 1981). The last decade has seen an explosive development of our knowledge about central dopamine neurones and their role in behaviour. The great interest in dopamine mechanisms and their relation to behaviour stems not only from clinical findings indicating an important role for dopamine in diseases such as schizophrenia and parkinsonism but also from the availability of a number of excellent experimental tools enabling control over dopamine neurotransmission (Ungerstedt, 1979).

In a recent review, Cools (1977) discussed a number of evidences which suggests that in man there seems to exist an unmistakable correlation between central dopaminergic activity and psychomotor diseases such as Huntington's chorea, Parkinson's disease, tardive dyskinesia and some psychotic disorders. In the case of the Hyperkinetic Child Syndrome (Attention Deficit Disorder), even though the underlying neurochemical mechanisms are unknown, previous experimental evidence (Fog et al., 1967) and earlier work in this

laboratory (Wray and Egbe, 1975; Wray, 1976; Wray and Egbe, 1976; Egbe and Wray, 1977) suggested an underlying striatal dopaminergic/cholinergic activation.

However, in spite of an increasing number of studies (Marshall, Richardson and Teitelbaum, 1974; Ljungberg and Ungerstedt, 1976; Hornykiewicz, 1973a; Teuber, 1976; Denny-Brown and Yanagisawa, 1976; Rolls et al., 1979) designed to investigate the role of the neostriatum in various psychiatric, psychomotor and neurologic disorders, the paleostriatum (globus pallidus) which is the principal outflow of the basal ganglia (Niimi et al., 1970; Johnson and Rosvold, 1971; Carpenter, 1976; Nauta and Domesick, 1979; Nauta, 1979b) and quite likely modifies dopaminergic activity in the neostriatum and thus controls activity, has been subject to only superficial examination (Pycock and Horton, 1976; Costall and Naylor 1979).

In light of the above, the present study was designed to investigate more closely the possible relationship between the globus pallidus (Paleostriatum), spontaneous motor activity and drug-induced stereotyped behaviour, with an aim to better understand the biologic bases of certain neurologic disorders and the mechanism of psychotic phenomena in man.

Stereotaxic surgery was preformed on two groups of

male Sprague-Dawley rats (mean body weight, 350±50g). In one group bilateral pallidal ablation was produced by a heat lesion generator at 50° C for 60sec. the other group was sham operated and functioned as controls. All drugs, except reserpine (given i.m.) were given intraperitonially, at a volume of 1.0 ml/kg body weight. The behaviours examined were locomotor activity (LA) measured in a photocell activity cage, spontaneous motor activity (SMA) by a jiggle platform and stereotypy (ST) by a standardized behavioural rating scale. Each rat was isolated at least 10min. prior to the 60-min. test period.

The experimental plan was a partial repeated design which involved the examination of selected doses of d-amphetamine, apomorphine, haloperidol and reserpine on both sham and lesioned animals.

Under non-drug condition (saline 1.0ml/kg) the activity of lesioned animals as revealed by their SMA, LA and ST scores was significantly lower than that of their sham controls. Under subsequent drug studies however, except for reserpine (0.5mg/kg, i.m.) in which the SMA and LA of lesioned animals were significantly lower than that of their sham controls, lesioned animals could not be significantly distinguished from their sham controls. Of interest was the bimodal effect of apomorphine on motor activity as measured

in the photocell cage and on the jiggle platform. The level of pallidal lesion reported in this study did not significantly affect this effect of apomorphine.

The results of the present study tend to support the suggestion of Iansek (1980), that pallidal discharge is normally a prerequisite for the performance of spontaneous motor activity and that pallidal neuronal firing may provide a background excitability to motor regions involved in the maintenance and elaboration of natural motor activity. With regards the dyskinesias of neurologic disorders and the hyperactivity of the hyperkinetic syndrome, it would appear that a partial, selective pallidectomy may alleviate these symptoms without significantly affecting vital neurologic and psychologic components of normal behaviour.

Finally, there were some evidence which would suggest that stereotypy in relation to the globus pallidus may be presented as a behavioural model for determining the efficacy of psychostimulants in the treatment of hyperkinetic children.