Rotational Behavior in Gerbils Following Unilateral Common Carotid Artery Ligation

M. Lavyne, M. Moskowitz, N. Zervas*, and R. Wurtman

The Department of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, Massachusetts, U.S.A., and
The Department of Neurosurgery, Beth Israel Hospital, Boston, Massachusetts, U.S.A.

Received September 2, 1974

With 1 Figure

Summary

Unilateral cerebral infarctions are produced in 30—50 % of all gerbils subjected to ipsilateral ligation of a common carotid artery. It has previously been shown that this infarction is associated with a major depletion of ipsilateral brain dopamine. The present studies characterize the spontaneous and drug-induced rotational behavior manifested by these animals and attempt to relate it to the functional activity of dopaminergic synapses. The tendency of animals to turn towards the side of the lesion 2—3 hours after surgery was found to correlate highly with the unilateral dopamine depletion observed after 24 hours. Two patterns of rotational responses were observed among animals showing symptoms that were treated with d-amphetamine or apomorphine; these could be correlated with mortality 24 hours after surgery.

Introduction

Unilateral ligation of a gerbil common carotid artery markedly reduces the dopamine (DA) content of the ipsilateral brain hemisphere among those animals that later develop cerebral infarction (Zervas et al., 1974). This vulnerability to infarction probably reflects the

* Harvard Medical School.
absence, in gerbils, of arteries connecting the carotid and basilar systems (Kahn, 1972). As early as 3 hours after ligation, dopamine content declines by 40–50% in the three parts of the neuraxis known to receive major dopaminergic projections (i.e., the neostriatum, the nucleus accumbens-olfactory tubercle, and the hypothalamus). This decline reflects the release of dopamine from anoxic-ischemic neurons, and not simply a decrease in its rate of synthesis (Lavyne et al.).

We have speculated that the release of large amounts of dopamine or other vasoactive compounds from infarcted brain might have pathophysiological consequences, perhaps even exacerbating the tissue injury resulting from a cerebrovascular accident (Wurtman et al., 1974). That dopamine might interact with surviving post-synaptic receptors is suggested by the tendency of the animals with clinical strokes to become hypothermic (unpublished observations) (a sign, in rats, of dopaminergic activation [Yehuda et al., 1972]) and to rotate around the short axis of their body towards the lesioned hemisphere (Kahn, 1972)—a phenomenon which, in rats, is also related to asymmetric dopamine release (Andén et al., 1966; Ungerstedt et al., 1970).

This study further characterizes the relationship between circling behavior and alterations in hemispheric dopamine content following common carotid ligation in the gerbil.

Materials and Methods

Preparation of Animals

Adult male and female Mongolian gerbils (Meriones unguiculatus) (Dennen Animal Industries, Wilmington, Massachusetts) weighing 60–80 g were caged in groups of 6–8 and housed in a room lit by Vita-Lite fluorescent bulbs (Duro-Test Corporation, North Bergen, New Jersey) between 9 a.m. and 9 p.m. daily. The temperature of the room was maintained at 20 °C. Animals had access to lab chow (24% protein) and water ad libitum.

Preparation of Tissues

Gerbils lightly anesthetized with diethyl ether underwent left common carotid artery ligation as described previously (Zervas et al., 1974). Thirty-five of the 110 gerbils undergoing surgery developed cerebral infarction, as evidenced by contralateral hemiparesis, contralateral ptosis, circling behavior towards the lesioned hemisphere, and neglect of sensory stimuli applied on the side contralateral to the lesion.

In the first experiment, rotational behavior was measured for 1 hour in lesioned gerbils with and without clinical signs, as well as in sham-operated and control animals, between 2–3 hours after surgery. The roto-