Mamillary-body lesions and visual recognition in monkeys

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Summary. Cynomolgus monkeys with complete bilateral destruction of the medial mamillary nucleus exhibited little, if any, deficit in object recognition, although they did show evidence of impairment in spatial memory. The pattern of effects thus resembled that found previously after either hippocampal ablations or transections of the fornix and suggests that, like such damage, mamillary-body damage alone is insufficient to produce the global amnesia attributed to it in clinical cases.

Key words: Monkey - Mamillary bodies - Amnesia - Korsakoff's syndrome

Introduction

Clinical evidence has accumulated throughout this century that the profound anterograde amnesia associated with diencephalic pathology is the consequence of damage to the mamillary bodies (Angerlergues 1969; Delay and Brion 1969; Brierley 1977). That conclusion has been challenged, however, by the proposal that medial thalamic necrosis may be necessary or even sufficient to induce the amnesic syndrome (Victor et al. 1971; McEntee et al. 1976). Unfortunately, the lack of well documented cases with both selective diencephalic lesions and precisely quantified memory loss has made it impossible to resolve the disagreement (Mair et al. 1979). In an attempt to determine experimentally the contribution of mamillary-body damage to amnesia of diencephalic origin, we have studied the effects of stereotaxic lesions of the mamillary bodies in monkeys trained to perform an object recognition task, delayed nonmatching-to-sample with trial-unique objects. This task was selected because it has proved sensitive to the effects of experimental lesions in other forebrain regions that have been implicated in the clinical amnesic syndrome (Aggleton and Mishkin 1983a, b; Bachevalier et al. 1984; Mishkin et al. 1982). The monkeys were tested also for their ability to learn spatial discrimination reversals. This task is highly sensitive to the effects of both hippocampal and fornical damage (Jones and Mishkin 1972; Mahut 1972) and hence could serve as an indicator of mamillary-body participation in a hippocampus-fornix-mamillary body circuit underlying spatial memory.

The lesions were directed at the medial mamillary nucleus, since only this part of the structure is consistently necrotic in patients with Korsakoff's syndrome (Victor et al. 1971; Mair et al. 1979), the most frequent cause of "diencephalic amnesia".

Materials and methods

Subjects

Six experimentally naive cynomolgus monkeys (Macaca fascicularis) weighing from 3.1-5.0 kg were used in this study. They were housed individually and maintained on a diet of Purina Monkey Chow and fruit. Water was available ad. lib.

Surgery

Operations were performed on the animals (MB1-MB6) after they had learned the principle of delayed nonmatching-to-sample. The animals were anesthetized with Ketamine (10 mg/kg) and Nembutal (35 mg/kg) and then placed in a stereotaxic apparatus. Surgery was carried out aseptically. Bone and dural flaps were opened above the dorsal tip of the central sulcus. The medial wall of the left hemisphere was retracted and, under microscopic control, part of the corpus callosum was transected sagittally to reveal the anterior part of the thalamic midline. The coordinates
for the lesions were based on the position of the rostral limit of the thalamus at the midline, as well as the positions of the sphenoid bone and posterior clinoid process as determined from X-ray films (Aggleton and Passingham 1981). An electrode (Radionics Model 1388z) connected to a radio-frequency-wave generator (Radionics Model RFG-4) was then lowered vertically, 0.4 mm lateral to the midline. Each lesion was produced by raising the temperature of the electrode tip to either 65°C (cases MB1-3) or 68°C (cases MB4-6) for a duration of either 15 s (MB1-2), 20 s (MB3), or 30 s (MB4-6). Two lesions, one centered 0.6 mm above the other, were placed in each hemisphere. The bone and dural flaps were then replaced and the overlying anatomical layers sutured. All animals were given Gentocin (5 mg/kg) as a precaution against infection.

**Histology**

At the completion of the experiments the animals were given a lethal dose of Nembutal and perfused intracardially with 10% formal saline. The brains were removed, blocked, embedded in celloidin, and cut at 25 μm in the coronal plane. Every fifth section was stained with thionine. The nomenclature for the mamillary bodies and the surrounding region is taken from the study by Veazey and Amaral (1982).

Four of the six animals (MB3-6) sustained complete bilateral destruction of the medial mamillary nucleus (Figs. 1 and 2). Animal MB1, on the other hand, had bilateral sparing of over 80% of the medial nucleus, and monkey MB2 showed a similar degree of sparing in one hemisphere (Fig. 1). In both cases, however, the remaining cells of the medial nucleus appeared more densely packed and less differentiated than normal. The lesions always invaded the lateral mamillary nucleus as well, although significant bilateral damage was found only in animals MB4, MB5, and MB6 (Figs. 2 and 3). Damage to the still more lateral paramamillary nucleus occurred in animals MB4 and MB5, but only unilaterally in both cases. The lesion in monkey MB4 extended caudally into the rostral part of the substantia nigra. Measurements of enlarged tracings of the sections indicated that the overall extent of damage in the region of the mamillary bodies could be ranked, from smallest to largest, as follows: MB1, MB2, MB3, MB5, MB4, and MB6.

Transsection of the callosum led in most cases to minor damage in the cingulate gyrus of the retracted hemisphere (MB1, MB2, MB5, and MB6); in addition, in the opposite hemisphere of animal MB6, there was more extensive ischemic damage to both the cingulate gyrus and the cingulum. Resultant retrograde thalamic degeneration marked by cell loss and gliosis was evident in nucleus anterior dorsalis ipsilateral to the limited cingulate damage in animals MB1, MB2, and MB5, and in all three anterior