Variations in Motility Associated with Striatal Acetylcholine Levels

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Abstract

In the course of investigations of interstriatal relationships, studied with electrical stimulation, small unilateral lesions were placed into the dorsomedial reticular formation of rats at the superior collicular level. Following the placement of these lesions, the amplitudes of the summed and averaged interstriatal responses were greatly increased. A clinical correlate was reduction of the speed of locomotion, at times advancing to complete akinesia, catatonia, and frequently generalized clonus. The acetylcholine (Ach) level (as determined in five control animals) rose from the mean striatal level of $6.5 \mu\text{g/g}$ (± 1.02) by 100% to $13.3 \mu\text{g/g}$ (± 1.16) 6-8 h after the reticular lesion was placed. The Ach level was determined according to the method of Crossland after the animals were killed in liquid nitrogen. We then placed in a series of other rats large lesions into the amygdaloid complex, including the origin of the stria terminalis. Catalepsy did not occur when this procedure was followed by injury to the midbrain tegmentum. These rats showed spontaneous locomotion, and clonic seizures appeared only infrequently. In these animals, the mean amount of Ach in the striata was only slightly elevated to $7.1 \mu\text{g/g}$ (± 0.76). The elevation of Ach in the striate, produced in the previous set of experiments by lesions in the reticular formations, was prevented by the prior placement of amygdaloid lesions. In addition, the amygdaloid lesion prevented an increase of amplitude of the interstriatally evoked and recorded responses. Symmetrel (amantadine hydrochloride) is known to enhance dopamine turnover in the striata of untreated rats. It also increases spontaneous running speed during the initial dosages. Thereafter, repeated daily administration of large doses of Symmetrel was followed by decreased locomotion and eventually bradykinesia or akinesia with rigidity. In these rats, the striatal Ach level increased to $10.7 \mu\text{g/g}$ (± 0.92). Since the above mentioned experimental catatonia developed as a consequence of striatal excitation associated with Ach increase, we followed this line of experiments in another group of rats with subcutaneous injections of small amounts of bulbocapnine measuring $11.5 \mu\text{g/g}$ (± 0.91). This finding raised the possibility that the catatonia produced by bulbocapnine is the consequence of an elevation in the striatal levels of Ach and accompanying physiological events in the striatal system. The catatonia produced by the various manipulations described could be reversed by the injection of 80-100 mg L-dopa in solution, i.p. and sometimes locomotor activity was even greater than that observed in the control period.