Striatal influences on paravermal cerebellar activity*

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Summary. Units were recorded extracellularly in paravermal cortex (lobule VI) of the cerebellum of chloralose anesthetized cats. Electrical stimulation of the striatum evoked excitation followed by inhibition in these neurons. In addition, the somatosensory properties of these cells were also affected by the striatum. A conditioning-test paradigm (C-T) was used in which conditioning stimulation was applied to the striatum. Test responses were evoked in cerebellar neurons by facial stimulation. As a function of the C-T interval, striatal stimulation could either enhance or suppress the test facial responses. In another procedure, a moveable electrode was used to map the thresholds for affecting the cerebellum from different points in the striatum. The lowest mean threshold was in the putamen followed respectively by the internal capsule and caudate nucleus. Control experiments suggested that striatal effects on the cerebellum were due neither to extra-striatal current spread nor antidromic activation of corticostriatal fibers. These data were discussed with regard to models of striatal motor functioning that indicate a role in postural control and sensory gating.

Key words: Striatum – Vermis – Postural control – Sensory gating

Introduction

Functional interrelationships between the cerebellum and basal ganglia (BG) are taken as common currency in neurological practice. Indeed, in discussing this state of affairs, Snider et al. (1976) were prompted to state that these interactions “... are so widely recognized in the clinical and basic science fields that additional comments appear superfluous.” Until recently, it was suspected that converging BG and cerebellar outputs terminating in the ventral thalamus were the substrate for these interactions (e.g. Frigyesi 1975). However, current anatomical work has shown that cerebellar and BG efferents terminate in different areas of the thalamus that, in turn, project to separate areas of cortex (Kievit and Kuypers 1977; Schell and Strick 1983). Some have suggested that the BG might have a relatively direct effect on the cerebellum (Coxe and Snider 1956; Fox and Williams 1968; Gresty and Paul 1969; Gresty and Paul 1976). Short latency field potentials were evoked in the inferior olive (Sedgwick and Williams 1967) and cerebellar cortex (Coxe and Snider 1956; Fox and Williams 1968; Gresty and Paul 1969) by caudate stimulation. However, these data are difficult to interpret for two reasons. First, field potentials do not reveal the nature of neuronal participation in the observed response. Second, technical problems in the use of electrical stimulation of the striatum were not recognized (Laursen 1963; Lidsky et al. 1980). Specifically, the striatum is traversed by numerous fiber bundles and, in addition, is adjacent to the internal capsule. Therefore, an assessment must be made of the contribution of fiber activation and extra-nuclear current spread to effects evoked by striatal stimulation. Furthermore, numerous cortical output fibers terminate in the striatum so that responses from stimulating this nucleus can also be due to antidromic activation of the cortex.

The present experiment was intended to investigate BG influences on the cerebellum. Because both the BG and also the paravermal cortex have been implicated in postural control (Ito 1984; Martin 1967), the latter was chosen as the site of neurophysiological recording. Electrical stimulation was delivered to the striatum (caudate nucleus and putamen) to allow comparisons with work from other

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laboratories. An effort was made to determine the extent to which observed effects were due to activation of fiber systems in or adjacent to the striatum rather than the striatum itself.

**Methods**

Experiments were performed in thirteen adult cats that were anesthetized with alpha chloralose (70 mg/kg, i.v.). The cisterna magna was punctured to minimize brain pulsation and the trachea was cannulated. At the completion of all surgery, animals were artificially respirated, a pneumothorax was created and gallamine triethiodide (Flaxedil) injected intravenously. Neuromuscular block was allowed to dissipate at regular intervals to enable assessment of anesthetic level. It should be noted that the high dosage level of chloralose that was used resulted in deep anesthesia that lasted at least 15 h. Chloralose was re-administered periodically to maintain deep anesthesia.

Side by side bipolar stimulating electrodes made of stainless steel insect pins (0-0-0), insulated except at the tip (0.5 mm), were implanted in the head of the caudate and in the putamen. Stimulation pulse durations varied from 0.01 to 0.5 ms. Two to three pulse trains, with 10 ms interpulse intervals, were used for all brain stimulation. Repetitive stimulation of this type has been shown to be optimal for activating striatal output (e.g., Levine et al. 1974). Response latencies were derived with respect to the first pulse. Two stainless steel wires were inserted subcutaneously in the perioral vibrissa field to activate trigeminal sensory afferents. Stimulation currents were adjusted to a level right below that necessary to evoke a cutaneous twitch (before infusion of Flaxedil) in the area immediately surrounding the skin electrodes.

The skull was removed over the cerebellar vermis and thalamic nucleus ventralis lateralis. Saline agar was poured into the bone faults to minimize pulsation. Extracellular single units were recorded with glass micropipettes filled with 1.6 M potassium citrate. Paravermal cortex of lobule VI was chosen because of its responsivity to somatosensory stimulation (Ito 1984). All data were stored on FM tape and subsequently analyzed with a small laboratory computer.

After isolation of a unit, a baseline period of "spontaneous" activity was recorded. Statistically significant (Schneider and Lidsky 1981), increases or decreases in firing rate that were time-locked to striatal stimulation were categorized as "excitation" and "inhibition" respectively; no inferences of underlying synaptic mechanisms were intended. In addition, striatal stimulation was used as the conditioning stimulus in a conditioning-test (C-T) paradigm. A determination was made of the effects of a prior conditioning stimulus upon test responses evoked by somatosensory stimulation. The time course of effects was measured by varying the interval between conditioning and test stimuli (C-T interval).

The depths of all units were recorded with respect to the cortical surface. At the completion of the experiment, the pipettes were broken off in the recording track and left in situ while the animal was perfused with formol saline. Subsequently, the brains were sectioned (50 μ thick) and stained with cresyl violet for later histological analysis.

**Stimulation controls**

Although current spread must be assessed when any area of the brain is electrically stimulated, the need is particularly pressing with the regard to the striatum. Both the caudate nucleus and also the putamen lie immediately adjacent to the internal capsule. Therefore, when striatal stimulation produces any effect, it must be determined if these results are due to activation of striatal tissue per se or from extra-nuclear current spread to the internal capsule. Moreover, the caudate nucleus and the putamen receive a massive projection from the cortex and are also traversed by numerous corticofugal fibers of passage. Thus, electrical stimulation of these nuclei could conceivably produce its effects via antidromic activation of the cortex. Because of these potential problems, several control procedures were used.

**Threshold mapping.** A moveable bipolar stimulating electrode was passed through the striatum and electrical stimulation was applied at 1 mm intervals to map the thresholds for affecting cerebellar paravermal activity. To do this, the effectiveness of striatal stimulation was assessed in terms of its use as a conditioning stimulus in a C-T paradigm. Test responses were paravermal field potentials evoked by facial stimulation (cf. Fig. 2 inset). If striatal effects were due to current spread to the internal capsule, then thresholds would decrease as a function of proximity to that area. In addition, thresholds within the capsule should be lower than in the striatum.

At the completion of each experiment, small marking lesions (0.5 mA, 5 s) were made. To avoid effects on subsequent passes, these lesions were made below and above BG structures.

**Strength-duration curves.** Chronaxie, proportional to the time constant of the population of neural elements that are affected by electrical stimulation (see "Discussion"), can be calculated from strength-duration curves. By use of this procedure, the chronaxie of the cells giving rise to effects on the cerebellum can be deduced. This value was then compared to that of striatal cells per se and capsular as well as corticofugal fibers with the following rationale. The configuration of the strength-duration curve reflects the membrane time constant and differs for neural soma as compared to fibers (Ranck 1975). Thus, determination of chronaxies helps to discriminate between stimulation effects due to activation of the striatum versus the associated axonal systems.

The thresholds were determined for evoking an effect on cerebellar unit activity with successively longer stimulus pulses (starting with 0.01 ms) delivered to the striatum. These values were then plotted (see Fig. 4); rebase and chronaxie were derived from these curves. The mean chronaxie, from several replications of this procedure (see "Results"), was taken as representative of the population of neural elements that affected the cerebellum when stimulation was applied to the striatum.

For purposes of comparison, the chronaxie of striatal neurons was independently calculated as follows. The striatum has a strong synaptic influence on thalamic cells in nucleus ventralis anterior (Nauta and Mehler 1966). Strength-duration curves calculated for activation of the ventral thalamus by striatal stimulation would therefore yield a reasonable estimate of the true chronaxie of striatal neurons. Thus, the thresholds were determined, with pulses of increasing duration, for evoking thalamic single unit and field potential responses with striatal stimulation. To estimate the chronaxie of the fibers passing through or synapsing in the striatum, strength-duration curves were constructed for antidromic activation of the cortex from stimulation in the striatum in two cats. Intensities were increased until responses were recorded that had latencies compatible with activation of a spectrum of fiber diameters ranging from heavily myelinated to more lightly myelinated. In addition, strength-duration data were compiled for effects on the vermis from capsular stimulation.

**Lesions around stimulation electrodes.** To assess the role of current spread to structures adjacent to the striatum, the following