Thalamic inhibition by thalamic stimulation [1]

JOHN SCHLAG AND JAIME VILLABLANCA

UNIVERSITY OF CALIFORNIA, LOS ANGELES

Exploration of unit activity in the immediate vicinity of a thalamic stimulating electrode revealed that a considerable proportion of cells is silenced by an electrical stimulus. Therefore, the view that excitation is the effect of electrical stimulation of a brain structure like the thalamus may be a misleading over-simplification.

Electrical stimulation of the brain has become a routine procedure in psychophysiological experimentation. Although its ultimate usefulness as a tool is dependent on an understanding of what such stimulation does, no one seems to know exactly what takes place locally. It is implicitly assumed that highly synchronous volleys of discharges are triggered, as is the case when electric shocks are applied to peripheral nerves. Is this a correct and sufficient assumption?

Method

Cats were operated on under ether anesthesia and maintained in a stereotaxic apparatus under Flaxedil and local anesthesia. Pulses of 0.5 msec and 120-200 μA were administered through a concentric electrode (inside wire = 150μ) implanted in n. ventralis lateralis of the thalamus (VL), as verified by recording the response to stimulation of the contralateral brachium conjunctivum. The parameters of this stimulation were just sufficient to induce large positive-negative potentials on the VL cortical projection area, the motor cortex. Potassium citrate filled micropipettes (tip = 1-5μ, resistance = 2-10 megohms) were advanced in the direction of the point stimulated, and all units encountered were recorded. A special bridge was used to minimize the shock artifacts. The distance between each recorded cell and the stimulated point was evaluated on the basis of stereotaxic readings and measurements on histological sections.

Results

Thalamic units recorded were classified on the basis of those that responded to stimulation and those that did not. Among the first, there were two categories: (1) those that responded with 1-20 spike bursts, characterized by a stable latency and a consistent pattern of discharge; all such cells were silenced for 120 to 200 msec after the initial burst, and (2) those that were immediately silenced (i.e., having no initial burst). The silent periods, whether immediate or not, terminated in a long rebound-like burst of discharges. In 105 cells recorded within 0.6 to 4.0 mm of the stimulated point, 43% exhibited an initial burst, 18% were initially silenced, and 39% were considered non-responding.

When these modalities of response or no-response were considered with respect to the distance of each cell from the stimulated site, several findings appeared suggestive of a mechanism where a topographical factor played an essential role. First, non-responding cells could be found everywhere, even very close to the stimulating electrode (within 1 mm). Second, responsiveness was maximal, not close to the stimulating electrode, but between 2 and 2.5 mm from it. Third, the latency of initial discharges was between 1.5 and 18 msec, with the exception of one case where latency was less than 0.5 msec at a distance of 0.4 mm. This suggests a postsynaptic excitation for all but the single exception. These three points were verified in a second series of 73 thalamic units recorded in completely decorticate preparations. Fourth, most cells initially silenced were found between 2 and 3 mm from the stimulating electrode; none was closer than 1.9 mm. The probability that such a distribution could be obtained when the probability of initial silence is assumed to be the same for cells located at distances $d_1 < 2$mm and $2 \leq d_2 < 4$mm is p = 0.0039. The validity of this test rests on the accuracy of evaluations of distances, and these evaluations cannot be said to be error-free. However, there could be no doubt about the sequential position of cells encountered along a single track; analyses of responses along the tracks with the highest numbers of cells confirmed, for each individual track, that most immediately silenced units were situated in an intermediate area between a central zone where responsive cells showed initial bursts and a peripheral zone where the proportion of non-responsive cells became dominant.

A second pulse, identical to the first but administered 100 msec later, when most cells were silenced, induced initial bursts—not only in those cells which already responded in this fashion—but also in cells previously unresponsive or initially silenced. Within a radius of 4 mm, 58% of the units found responded with initial discharges to a second pulse (against 43% to the first pulse). This probably corresponds to the process of augmentation characterized by larger potentials more widely distributed on the cortex on repetition of the thalamic shocks at 10/sec.

Figure 1 summarizes our results; the distribution of thalamic units showing initial bursts (open circles) and of silenced units (filled circles) is represented at different times after the stimuli. These distributions were calculated exactly on the basis of our actual data. For convenience of presentation, the unit population was assumed to be homogeneous in all directions around the central stimulating electrode, although there is no argument to justify this assumption. Twenty percent of our cells were identified as
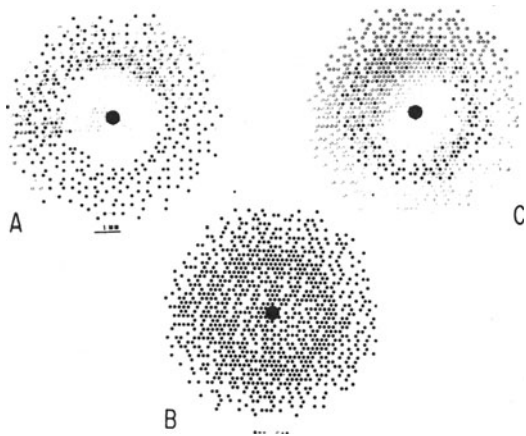
Fig. 1. Schematic representation of neuronal activity around a thalamic (VL) stimulating electrode (large central circle). Open circles: cells more active than during control. Filled circles: silenced cells. Non-responsive cells not represented. A: 10-25 msec after stimulus. B: 80 msec after same stimulus. C: 10-25 msec after a second stimulus applied 100 msec after the first one.

VL units by brachium stimulation and these cells did not differ from the others in their responsiveness to the VL stimulus. Comparable results were obtained by stimulating and recording in other thalamic regions (e.g., medial geniculate nucleus).

Discussion

Very rarely did thalamic units respond in less than 1 msec, even within a fraction of a mm of the stimulated point. The small probability of finding such cells suggests that the direct (non-synaptic) excitatory effect of an electrical stimulus applied to the thalamus (and having the parameters specified above) must be very limited. But many cells responded, probably through a synaptic mechanism and, of these, 18% were immediately silenced. This 18% is a gross figure coming from sampling along linear tracks. To evaluate the real proportions in an hypothetical spherical cell population, the successive samples taken at increasing distances from the stimulated point should grow as the square of these distances. For a sphere of 4 mm radius it has been estimated in this way that 22.5% of all cells (i.e., 42% of all responding) were immediately silenced and 53% of all cells (i.e., all responding) were silenced after 15-25 msec for 120-200 msec. Therefore, local depression of neuronal activity appeared as one of the major effects of electrical stimulation of the thalamus. This depression has to be taken into account in interpreting the consequences of such stimulation.

Quite generally, unit response studies lead to observations of the form: x% of excited, y% of inhibited, and z% of non-responding cells, regardless of the sites of stimulation and recording. Our data suggest that topographical analyses may be the key to understanding various modes of response in a cell population.