Medial Forebrain Bundle Projections to the Nucleus of the Diagonal Band of Broca

The septal component of the nucleus of the diagonal band of Broca (nDBB) is a stream of fibres and cells situated in the midportions of the septal region[1]. The nDBB has been postulated by PETSCHE et al.[2,3] to be the pacemaker for the hippocampal theta rhythm. Nevertheless, reticular formation stimulation can induce the theta rhythm[2-4].

The reticular formation communicates with the nDBB via the medial forebrain bundle (MFB), which is a complex pathway of fibres and cells[5-7]. To understand how the nDBB organizes hippocampal activity requires, then, some understanding of the influence of MFB projections on cells in the nDBB. The present study is an investigation into the nature of MFB input to the nDBB.

Cats, anaesthetized with either sodium pentobarbital (35–45 mg/kg) or a thiamylal sodium (20–30 mg/kg)-chloralose (40–40 mg/kg) combination, were acutely prepared in a standard fashion. The dorsal aspects of the septum were exposed by removal of the overlying cerebral cortex and corpus callosum. Bipolar stimulating electrodes with an interpole distance of 0.5 mm (100–150 Kohm) were stereotaxically placed in the pathway of the medial forebrain bundle (MFB) at AP levels ranging from +13 to +15 (Topographischer Hirnatlas der Katze für experimentalphysiologische Untersuchungen by F. REINOSO-SUAREZ, 1961), and visually placed upon the ipsilateral fimbria (IFim). Microelectrodes were used to record field potentials, extra- and intracellular unitary potentials in the vertical limb of the nDBB following MFB stimulation. More details of the experimental procedure are available elsewhere[8,9].

The Figure A shows field responses recorded in the nDBB subsequent to MFB stimulation. The field responses, typically, were made up of a small early negativity (downward arrow) followed by a larger negativity (e.g., N at 5000 μ), and finally a shallow positivity (e.g., P at 5000 μ). The early negativity behaves like a compound fibre volley when studied by paired-stimulus testing

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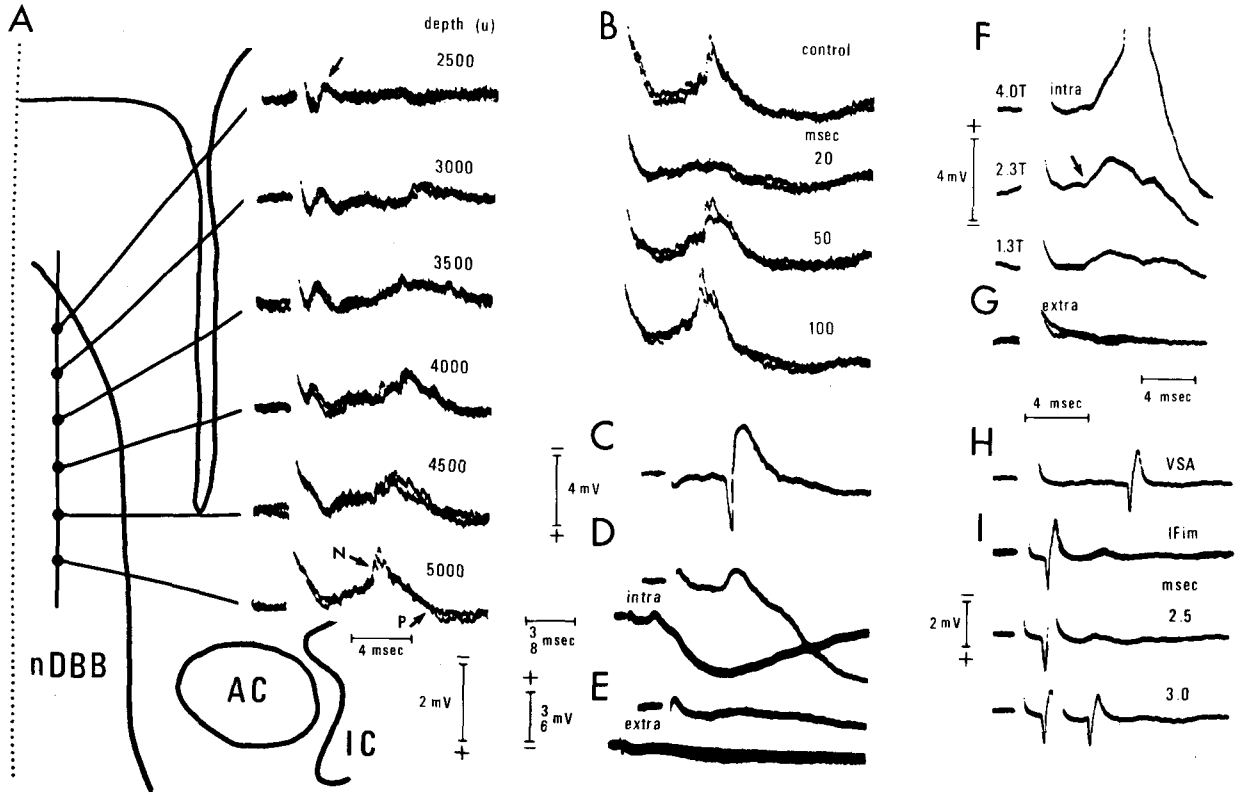

A) Schematic locating position of probe in the NDBB and profile of field responses to MFB stimulation. Abbreviations: nDBB, nucleus of the diagonal band of Broca; AC, anterior commissure; IC, internal capsule. B) Test field responses from paired-stimulus testing (PST) series at 5000 μ. The control and responses from 20 msec, 50 msec, and 100 msec interstimulus intervals (ISI) are shown. C) Extracellular unitary response to MFB stimulation. D) Depolarizing-hyperpolarizing sequence after penetration of cell which gave discharge in C; shown at 2 gains and sweep speeds. E) Extracellular control for D. F) Intracellular responses to MFB stimulation with changes in stimulus intensity. Responses are shown for 4.0 T, 2.3 T, and 1.3 T. G) Extracellular control for F at 4.0 T. H) Cell giving unitary discharge to MFB stimulation. I) Same cell as in H responding to IFim stimulation. The control and PST sequences for 2.5 msec and 3.0 msec ISIs are shown.

(PST) showing refractory periods of 1.0–1.8 msec. Its short latency is also indicative of its fibre-like nature. Moreover, no somatic unitary responses were recorded which were associated with the early component. This component most likely reflects the activity of the relatively coarse fibres of Zuckerkandl's bundle[10].

In this probe the negativity (N) associated with the synaptic activation of nDBB neurons appears at a depth of 3000 μ. Here, the latency to peak is 7.5 msec. As the probe descends the negativity steadily increases in amplitude and decreases in peak latency. At 5000 μ, the peak negativity has decreased to 5.5 msec. The relative stability of the peak latency with changes in stimulus intensity (not shown) and relative stability of the peak latency when recovering from paired-stimulus testing (PST) (see Figure B) is an indication of the monosynaptic nature of the N negativity. The conduction distance, for this instance, was estimated to be approximately 6 mm. A calculated conduction velocity for MFB fibres of 0.9–1.2 m/sec supports the notion that such field responses probably represent the monosynaptic excitation of cells.

The typical behavior of the field response with PST is illustrated in Figure B. Record specimens of test responses from 20 msec, 50 msec, and 100 msec interstimulus intervals (ISI) are presented. There is no substantial recovery in the 20 msec ISI, but the response is almost completely recovered in the 50 msec ISI. At 100 msec, there is actually a slight facilitation of the test response.

Extracellular unitary discharges appear out of the negative envelope (Figure C) of the field response. After penetration of the cell whose discharge was shown in Figure C, and after deterioration of the spike potential, a depolarizing-hyperpolarizing potential sequence remains. The intracellular recording shown in Figure D is shown at two different gains and with two different sweep speeds. The EPSP nature of the depolarizing potential is shown in Figure F.

The behavior of such depolarizing potentials was then examined by systematically changing the stimulus intensity (Figure F). With a stimulus intensity a 4.0 T (4 × threshold), a spike is issued. As the stimulus intensity is reduced the spike disappears and the depolarizing potentials decrease in amplitude. However, there is no significant increase in the latency to onset (the arrow indicates the onset at 2.3 T). The wave form, graded nature, and lack of latency shift for these depolarizing potentials indicate that they represent monosynaptic EPSPs.

Some of the cells which were orthrodromically activated by MFB input could be antidromically activated by IFim stimulation. An example is shown in Figure H and I. Figure I shows a unitary discharge recorded from the same cell, with a latency of 2 msec following IFim stimulation. The antidromic nature of this unit is evidenced by recovery in a 3.0 msec ISI.

The data presented here indicate that at least some of the projections coursing via the MFB are excitatory with respect to their target cells in the nDBB. This is in agreement with other electrophysiological studies[11,12] where MFB stimulation leads to the appearance of extracellular unitary activity in the nDBB.

Summary. The electrophysiological characteristics of the medical forebrain bundle (MFB) projections to the nucleus of the diagonal band of Broca (nDBB) were studied in acutely prepared cats. MFB stimulation evoked field potentials which consisted of a large negative wave followed by a shallow positivity. Extracellular unitary discharges appeared out of the negativity. In addition, intracellularly recorded EPSPs showed no significant shift in the latency to onset with changes in stimulus intensity. These observations indicate that at least some of the MFB projections to the nDBB are excitatory with respect to their target cells.

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Blood Pressure Regulation in Spontaneously Hypertensive Rats[1]

Spontaneously hypertensive rats (SHR) from a Wistar strain[2], exhibit a sustained increase in vascular resistance, at least when they are 18 weeks or older[3]. Studies on SHR, as well as on human essential hypertension, suggest that an increased media thickness, partly encroaching upon the vascular lumen of resistance vessels, forms the main background of the increased flow resistance[4,5].

Increased vascular reactivity in SHR is also reported and attributed to an increased ionic permeability regulating smooth muscle tension[6–8]. In spite of the high blood pressure, efficient baroreflex regulation occurs. We described some histological aspects of intimal and medial vascular hypertrophy in the carotid arteries and aortic arch of our SHR colony[9].

The present study provides morphometric data on the medial vascular hypertrophy, which will diminish the transmission of the pressure pulse signal to the baroreceptors, located between the media and the adventitia[10].

Material and methods. Male SHR were compared to normotensive Wistar rats (NWR) of our own permanent laboratory colony established in 1956. The animals were transiently anaesthetized with ether and the femoral artery was catheterized under local anaesthesia with lidocaine. 1 h after recovery from the ether anaesthesia, heart rate, systolic and diastolic blood pressures were recorded. Thereafter, the rats were anaesthetized with Hypnorm® (haloanisone, 10 mg/kg and fentanyl, 0,1 mg/kg s.c.). Under free venous outflow, the arterial circulation was fixed retrogradely in situ with 2% glutaraldehyde in 0.1 *M* cacodylate buffer at a sustained perfusion pressure of 120 or 200 mm Hg. The internal carotid artery was taken at 2 mm from its origin and the aortic arch at 1 cm from the heart. The samples were postfixed, embedded, stained and transversely cut as previously described[9].

The perimeters of the inner and outer side of the media were measured with a curvimeter (precision = 1 mm) on