Electrophysiological topography of the human diencephalon

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Microelectrode recordings made in 64 human cases of movement disorder or intractable pain were used to study the relation of the site of electrical activity to the ventricular system. Standardizing the cases by dividing the AC-PC line in equal parts and using the same units to divide the areas above and below the intercommissural line and the distance of the electrodes to the midline revealed that the dispersion of the electrical activities in regard to AC-PC line was minimal and overlapping practically nonexistent. It is concluded that, at least for the areas explored, the size of each diencephalon nucleus is proportional to the size of other diencephalic nuclei, and its internal structure and relation to radiological landmarks are fairly constant.

KEY WORDS - diencephalon - electrical activity - microelectrode recording - ventricle

MICROELECTRODE extracellular recordings have been used in stereotaxic surgery to determine the borders of diencephalic structures. From these recordings various patterns of spontaneous and evoked electrical activity have been described. However, except for those sensory thalamic nuclei identified by evoked tactile responses and the difference in background activity between gray and white matter, there is no agreement on the type of electrical activity that characterizes diencephalic nuclei.

In recent publications a simple method of standardization of the size of the diencephalon was useful in analyzing, on anatomical grounds, the results of target localization and electrical stimulation in a large group of cases.

In the present report, we use the same method of standardization to analyze the results of microelectrode recordings from numerous diencephalic points in an attempt to identify the anatomical structures where each type of electrical activity was recorded.

Material and Methods

Frontal, parasagittal stereotaxic procedures were performed in 200 cases for the treatment of tremor, dystonia, or intractable pain. Of these, 64 cases were suitable for this study because they had adequate ventriculograms to demonstrate the anterior and posterior commissures and because the position of the microelectrodes in regard to the ventricular systems had been repeatedly checked with anterioposterior (AP) and lateral radiograms.

The instrumentation for microelectrode recording was the same in all cases and has been reported elsewhere. Unitary extracellular activity was obtained through a bipolar, 10 to 15 μ-tip size electrode and the sound and its visual images were recorded in a magnetic tape for storage and future analysis.
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Five to 15 different points were explored in each case. We then reconstructed on x-ray films the place where the recording had been obtained and so determined the relation of the electrode tip to the ventricular system. In the lateral radiograms the length of the AC-PC line was divided into 10 equal parts; a grid with squares the size of one such unit was superimposed on the space above and below the line. In the AP radiograms a grid of identical units was superimposed on the areas on each side of the midline. Thus, a

![Diagram](image)

Fig. 1. Standardization used for the lateral (A) and anteroposterior (B) radiograms was applied to the sagittal sections of the anatomical atlas by Schaltenbrand and Bailey (C and D). The shaded portion in the frontal projection indicated the anatomical area explored in our cases. VAC = vertical line to the anterior commissure; VPC = vertical line to the posterior commissure; AC = anterior commissure; PC = posterior commissure; ML = midline.
FIG. 2. A. Activity as the electrode tip passes from the acellular area into the thalamus (thalamic contact). B. Activity as the electrode leaves the densely cellular thalamic nucleus (Vci) to enter the sub-thalamus.

FIG. 3. a. Spontaneous rhythmic activity was recorded in many cases. This activity (upper record), although about the same frequency as the tremor, did not follow the electrical activity of the muscle (lower record). b. Proprioceptive cells: cell firing is rhythmic when the tremor involves the specific passive motion corresponding to that cell field. Notice that the cell fires immediately following the EMG burst. Trains of spikes 2 to 3 cps were recorded from the head of the caudate nucleus and globus pallidus internus, d,e,f. Recordings from different areas were characterized by spikes of different size (large spikes over 100 µV, medium size spikes from 50 to 100 µV, and low-voltage spikes below 50 µV). To each type of activity we gave a symbolic value to be used in the plotting of results as indicated at the left of each recording.
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Tridimensional framework was prepared on which all points recorded could be inserted and compared on a standard basis with other cases. The same method was used to divide the thalamic and subthalamic areas of anatomical sections taken from the atlas of Schaltenbrand and Bailey (Fig. 1). The results were plotted on master sheets giving symbolic values to each type of electrical activity.

Results

We were able to identify audio and visual background activity of the following types.

Contact and Exit Activity

The contact or exit from the thalamus or other structures surrounded by white matter (Fig. 2) are shown as the electrode tip passes from an acellular into a cellular area.

Spontaneous Rhythmic Cellular Activity

In cases of tremor this activity was about the same frequency as muscular contraction assessed by electromiograms (EMG) (4 to 5 cps). However, the rhythm existed independent of tremor since it was not modified either by voluntary arrest of the tremor (Fig. 3a) nor by applying passive movements to the joints. Moreover, the rhythm was recorded in cases such as intractable pain that had no tremor.

Rhythmic Cellular Activity from Tremor or Passive Movements

When evoked by the tremor, cellular activity had a rhythmic pattern that closely followed the muscular activity recorded by the EMG but in contrast to spontaneous rhythmic activity, the rhythm of the cellular firing disappeared when tremor was volun-

Fig. 4. Evoked potentials in response to light touch were explored with the electrode in a constant position in the upper two records. Arrows mark the approximated time at which a stimulus was applied. Touching the fingers elicited an evoked response barely seen on the background. Touching the lower lip evoked the maximal response; after advancing the electrode tip 1 mm we obtained a phase reversal (lower records).
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Trains of Spikes 2 to 3 cps

Trains or series of spikes 2 to 3 cps recorded from the head of the caudate nucleus and globus pallidus internus are shown in Fig. 3 c.

Areas of Spikes without Tendency to Rhythmicity

Areas of spikes without tendency to rhythmicity and no response to peripheral stimuli can be identified. The spike voltage varied from large spikes (over 100 μV), to medium (50 to 100 μV) and small spikes (less than 50 μV) (Fig. 3 d, e, and f, respectively).

Evoked Potentials to Light Touch and Pressure

The morphology of evoked potentials in response to light touch and pressure was similar to that described by Guiot and his group6,10 (Fig. 4).

Slow Waves

Slow waves were recorded both above and below the AC-PC line. Below the AC-PC line, the waves had a frequency of 12 cps and above the AC-PC line were 20 cps (Fig. 5).

Composite Results

The composite results are presented in Fig. 6. Points with the same electrical activity fell in well-circumscribed areas with practically no overlap. A superimposition of the results on anatomical sections is presented in Fig. 7. Since a brain with an AC-PC line of 20 mm was used for the elaboration of the atlas, each tenth of the line measures 2 mm and therefore each sagittal section (SI) taken at 9 mm from the midline (SI-9, 0 on the atlas) corresponds to 4.5/10 of our system of standardization.

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\frac{SI-9, 0}{20 \text{ mm}} = \frac{4.5}{10}.
\]

Fig. 5. Slow waves from 12 to 20 cps were frequently recorded and occasionally blocked by attention. This figure shows examples of such activity obtained in different places in the diencephalon. The letters represent the places where the activity was recorded according to our anatomical correlations. Abbreviations are as follows: THAL = thalamus; Vop = nucleus ventro oralis posterior; Dime = dorso intermedius externus; Sth = subthalamic nucleus; Ru = ruber nucleus.
Fig. 6. Activities after standardization of all cases in the three spatial dimensions (height, length, and width); there was practically no overlapping of activities. Cases are divided according to their distance from the midline (A = 5/10, B = 6/10, C = 7/10, D = 8/10). The symbols represent different types of electrical activity (see Fig. 3). Dash line = contact or exit from a nucleus; dark triangles = spontaneous rhythmic discharges; clear triangles = evoked rhythmic discharges; clear circles = 2 to 3 cps trains of spikes; (Λ) = large spikes; (Λ) = small spikes; shaded area = medium voltage spikes; crosses = evoked responses to deep pressure, and dark squares = slow waves. Finally, in two cases the simple introduction of the fine microelectrode shaft arrested tremor, and the places where this effect took place are indicated with dark circles. Drawings in the areas of evoked responses to light touch and movement represent the peripheral site from which those responses were obtained.
In Fig. 7, SI-9,0 has been superimposed to 5/10, SI-11,0 to 6/10, SI-13, 5 to 7/10, and SI-15,0 to 8/10. It was found that different electrical activities closely corresponded to different anatomical structures.

**Discussion**

**Role of Standardization**

Our results show that, using a method of standardization, it is possible to analyze anatomically the results of electrophysiological...
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studies performed in a large group of cases. Likewise the results have practical implications in that in spite of the well-known individual variations in the size of the human diencephalon, the nuclei of the basal ganglia are always in proportion to each other and in proportion to the size of the diencephalon and keep a fairly constant relationship with the ventricular system as visualized by x-ray film.

Fig. 7 (continued). dorso intermedius externus; Doa = dorso oralis; Lm = medial lemniscus; Ni = locus niger; Pm = pallidum mediale; PL = pallidum laterale; Pu = pulvinar; Sth = corpus subthalamicus; Th = thalamus; Vci = ventro caudalis; Vel = lateral ventricle; Vime = ventro intermedius externus; Voa = ventro oralis anterior; Vop = ventro oralis posterior; Zi = zona incerta; Zo = zentro lateralis oralis.

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We are aware of previous work on the subject of individual variations\textsuperscript{5,20,23,24,26,27} that has led several authors to contradictory conclusions. However, it is our impression that in their studies there was no standardization of sections taken from different brains, particularly for the distance of the section from the midline. From our results, one may expect that sagittal sections taken 10 mm lateral to the midline in a brain whose AC-PC line measures 20 mm would show a morphology arrangement of the basal ganglia corresponding to a sagittal section taken at 15 mm from a brain whose AC-PC line measures 30 mm. An attempt to confirm these observations anatomically has been frustrated due to distortion of anatomical material during fixation and cutting.

In practice the correction of the distance from the electrode to the midline according to the length of the AC-PC line has been found to be extremely important. Thus placement of the electrodes in the subthalamus for the arrest of tremor has been aimed at an area 8/10 behind the anterior commissure and 5/10 lateral to the midline. Whenever the placement was correct as checked in the radiograms, the tremor was arrested by the simple impact of the electrode’s tip.

Anatomical-Physiological Correlations

The results summarized in Fig. 7 coincide with the observations of Guiot, et al.,\textsuperscript{11} who demonstrated a striking difference between the background of microelectrode recordings obtained from white matter compared to those from gray matter. The same was true when the electrode passed from a nucleus formed by a compact net of neurons (nucleus dorsomedialis thalami, for example) into an area of sparse neurons (Lamella medialis thalami) or in the globus pallidus when the electrode left the pallidum laterale to enter the Lamina pallidi medialis and left this lamina to enter the pallidum mediale. That is, the background noise of the recording is a function of the cell population of the recorded area.

Moreover, when recording from the ventro oralis anterior and posterior (Voa and Vop) and dorso oralis (Doa) thalami, the background noise was high although spikes were seldom more than 75 μV (Fig. 3 a). This recording corresponds to a cell population formed by uniformly arranged medium and small cells. On the contrary, recordings from the nucleus ventro intermedius (Vim) were characterized by high voltage spikes (over 100 μV) clearly distinct on a low voltage background, corresponding to an anatomical structure formed by sparse large neurons.\textsuperscript{16,30} Therefore, it is possible that average spike voltage is related to neuron size in the explored area.

Different types of electrical activities characterize each nucleus of the ventral complex of the thalamus, and similar patterns may be recorded in afferent pathways that run through the subthalamus to the correspondent relay nuclei. Thus recordings made by this method may indicate that areas with the same electrical activity are anatomically related.

In the thalamus, similar spontaneous microelectrode recordings were obtained from the so-called “integrative nuclei” placed above the relay nuclei; such was the case of the Zentro lateralis oralis (Zo) and Dorso oralis externus (Doe) nuclei in regard to the Voa nuclei and Dorso intermedii in regard to Vop. Thus it may be hypothesized that these nuclei are probably functionally related.\textsuperscript{15,16}

Other pathways identified by this method were the medial lemniscus (Lm) in the subthalamus and ventro caudalis (Vc) in the thalamus. From those areas where one obtains light touch evoked responses in cells and fibers, no other peripheral stimuli (pressure or movement) were effective in evoking the potentials. The same was true for the places where passive movements produced cell firing in both thalamus and subthalamus. That is, in humans, like other species,\textsuperscript{21} thalamic neurons and lemniscal fibers are related to one and only one kind of peripheral stimulus.

The thalamic nuclei involved in proprioception seems to be the nucleus ventro intermedius (Vim) as referred to by Jasper, Bertrand, and coworkers.\textsuperscript{4,18} From the internal part of this nucleus (Vimi) where vestibular fibers end,\textsuperscript{25} we obtained rhythmic patterns when neck muscles were involved by tremor. This area seems, therefore, to be where neck muscle proprioception and vestibular responses are integrated.

Places where spontaneous rhythmic activ-
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ity was recorded corresponded to the sites where lesions are effective in the treatment of tremor. In the subthalamus these were the prelemniscal radiations and in the thalamus the areas of the ventro oralis anterior (VoA). Here we disagree with the concept that the area in which to treat the tremor is coincident with the thalamic zone of proprioception. We believe that in both the thalamus and subthalamus there are two different systems that eventually may give similar microelectrode recordings of rhythmic cell firing: one has relation to proprioception, forming part of the lemniscal fibers, ending in Vim from which they project to the postcentral gyrus; the other is spontaneous and extends caudally through the subthalamus to reach the mesencephalon. The fibers end in the VoA thalami as a relay nucleus and Zo and Doa as integrative nuclei and from there project to the precentral cortex.

In the precentral cortex they have connections with the pyramidal system. Interruption of this pathway at any level arrests tremor. The difference between subthalamus and thalamus is that in the subthalamus the fibers cover a small area and a minimal lesion is needed to interrupt the pathway whereas in the thalamus the area becomes larger and a lesion several times larger would be necessary to produce the same effect.

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