ELECTROPHYSIOLOGICAL EVIDENCE OF THE CONNECTIONS BETWEEN THE GLOBUS PALLIDUS AND OTHER DIVISIONS OF THE CENTRAL NERVOUS SYSTEM IN MAN

REPORT 2. CONNECTIONS BETWEEN THE GLOBUS PALLIDUS AND THE SPINAL CENTERS AND AUTONOMIC FORMATIONS OF THE BRAIN STEM

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In our first communication [1] we described the electrophysiological manifestations of functional connections between the globus pallidus and the cerebral cortex. In the present report we shall examine the descending effects of the globus pallidus on the motor centers of the spinal cord and the autonomic centers of the brain stem.

The fact that the principal signs of Parkinsonism are tremor and rigidity of the muscles of the limbs and face suggested long ago that a lesion of the basal ganglia may affect the motor centers of the spinal cord, causing them to become hyperactive and hypertonic. By recording the EMG on an ink-writing electroencephalograph it is possible to tell only that tremor is present or absent and to detect changes in its intensity and frequency. By simultaneously recording the EMG, the EEG, and the electropallidogram, using the technique described in our first communication, we were able to examine certain aspects of the effect of the structures of the globus pallidus on the effectors.

The usually good clinical results of operations to exclude the globus pallidus (diminution or disappearance of tremor and rigidity) coincided with a diminution or disappearance of the theta-waves in the cortex of the opposite hemisphere. This effect was observed when a needle was inserted once or repeatedly into the globus pallidus, and it disappeared when the needle was withdrawn. It also developed and persisted for a long period when the globus pallidus was inactivated with alcohol. In patient Kh., for instance, the theta-waves were more marked in the right hemisphere (Fig. 1). This corresponded with the clinical picture of a lesion principally of the basal ganglia on the right side. Introduction of the needle into the right globus pallidus (artefact on the upper curve) led to the immediate disappearance both of the theta rhythm on the right and of the tremor and rigidity of the left upper limb. It is interesting that the theta-waves in the left hemisphere (less marked on the original curve) also diminished slightly on the introduction of the needle, which corresponded to a temporary reduction, although not disappearance, of the tremor of the right upper limb. These observations also confirmed the connection between the globus pallidus and the basal ganglia of the opposite side.

However, these changes in the theta-waves in the cortex and in the tremor of the limbs did not always follow a parallel course. Sometimes, when the electrodes remained stationary, coagulation of the globus pallidus led to complete disappearance of the theta-waves in the cortex of the ipselateral hemisphere, yet theta-waves continued to be recorded in the globus pallidus. Meanwhile the tremor persisted in the contralateral upper limb, and disappeared only after injection of alcohol into the globus pallidus. In this connection it is interesting to note that in some patients with the Parkinsonism syndrome and with marked tremor the EEG was close to normal, but in recordings from the globus pallidus groups of theta-waves appeared periodically. The presence of a theta-rhythm in the globus pallidus and tremor were thus more closely interdependent than tremor and the presence of a theta-rhythm in the cortex. It seems that the theta-rhythm arises secondarily in the cortex as a result of definite corticopetal connections.

Relationships such as these, indicating that the tremor is associated more closely with rhythms of subcortical origin, were also apparent during generalization of the theta-waves, as was sometimes observed during operations on the globus pallidus. In these cases the sequence of the spread of the theta-rhythm into the various structures of the brain

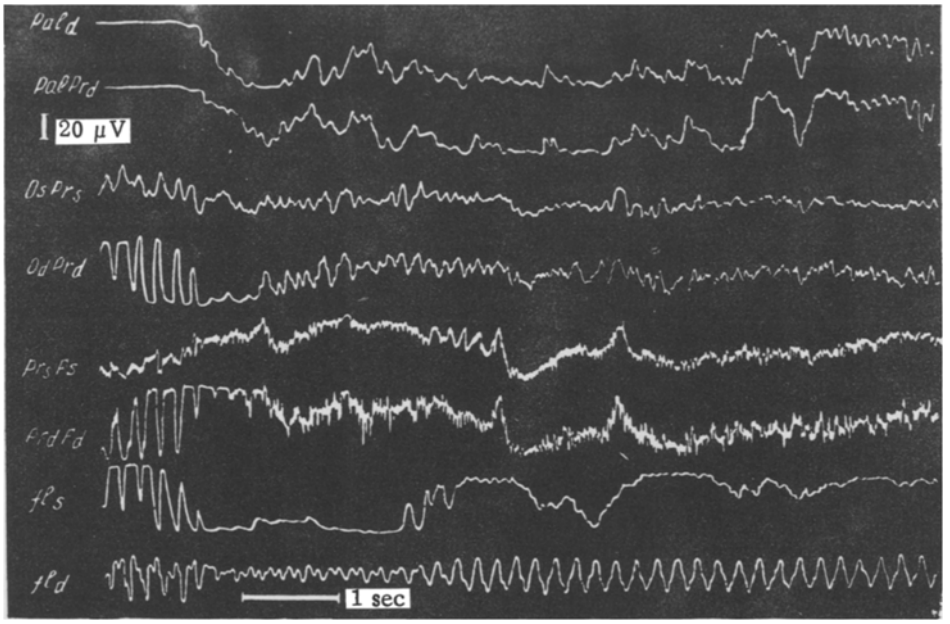

Fig. 1. Effect of introduction of a needle electrode into the right globus pallidus on the EEG, the electropallidogram, and the EMG in man: disappearance of the theta-rhythm in the cortex and of the tremor in the left upper limb. Pald) Unipolar lead from the right globus pallidus; Pald Prd) bipolar leads between the globus pallidus and premotor area on the right side; OP) occipito-premotor leads; PrF) premotor-frontal leads; Fl) EMG of the muscle flexor digitorum sublimis.

was seen especially clearly. In one case, for instance, it was recorded initially in the globus pallidus (right-sided pallidectomy), and it then became generalized, spreading firstly into the cortex of the ipsilateral hemisphere. After a short interval the theta-rhythm was found in the cortex of the oposite hemisphere, although it was much weaker there: lower in amplitude, less regular, and recorded together with other rhythms. The state of the electrical activity in the period of generalization in this patient is illustrated in Fig. 2. Besides in the leads connected with the globus pallidus (the upper two curves) the theta-rhythm was also considerably predominant in the right hemisphere, especially in its anterior divisions (right premotor-frontal leads). It was weakest in the left hemisphere, in both posterior and anterior divisions.

The spinal motor centers of the limbs were evidently involved in this process of generalization. For instance, the tremor which ceased after pallidectomy in the contralateral upper limb reappeared during generalization of the theta-waves, and in the same rhythm. Furthermore, in the other limb, contralateral to the intact globus pallidus, the frequency of the initial tremor was 10-12/sec. After generalization of the theta-rhythm the frequency of the tremor fell to 4-6/sec and became synchronous with the pallidary theta-rhythm. In the cortex of the contralateral hemisphere to this limb the theta-rhythm was less marked than in the hemisphere on the same side as the operation of the globus pallidus.

These facts demonstrate that the descending influences from the globus pallidus become apparent more rapidly than those in the ascending direction towards the cerebral cortex. In the same way, the complete disappearance of the theta-rhythm from the cortex after coagulation of the globus pallidus and the persistence of the tremor, accompanied by recording of an obvious theta-rhythm in the globus pallidus, confirms that descending influences from the basal ganglia are predominant over ascending influences.

This does not mean that we envisage a direct connection between the theta-rhythm and the origin of the tremor, on the one hand, and a lesion of the globus pallidus on the other. Jung [6, 7] considers that the central zone responsible for the tremor lies in the intraneuronal bulbospinal system. Experience of the performance of stereotactic operations in man has shown that tremor is diminished if the thalamus and globus pallidus are injured. Some facilitating effect of these cerebral structures on the lower mechanisms of tremor must evidently be assumed [7]. The globus pallidus is a link (possibly an important one) in the system, the component parts of which show pathological impulsation. Impulses from the globus pallidus are directed along the efferent pathways to the thalamus, to the hypothalamic and mesen-

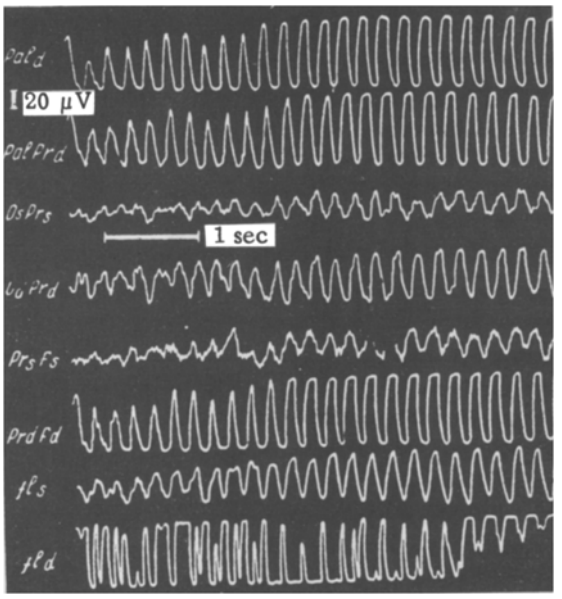

Fig. 2. Spread of the process of generalization of the theta-rhythm. Legend as in Fig. 1.

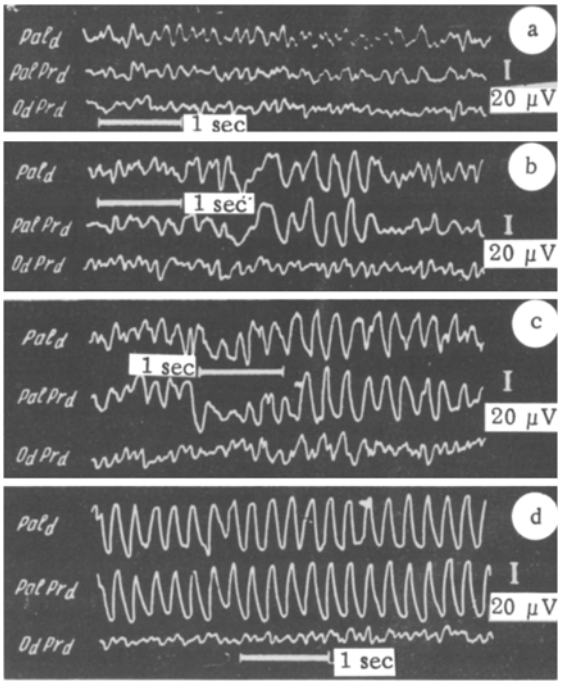

Fig. 3. Appearance and spread of the theta-rhythm in the globus pallidus simultaneously with marked autonomic reactions in a patient. a) Initial EEG and electro-pallidogram; b) appearance of clearer theta-waves of greater amplitude; c) predominance of theta-waves in leads connected with globus pallidus; d) registration of a hypersynchronized theta-rhythm in leads connected with the globus pallidus only. Remainder of legend as in Fig. 1.

cephalic nuclei, and to the reticular substance, and are subsequently transmitted to the spinal motor centers by systems arising in the formations of the brain stem. However, there are no direct efferent fibers from the globus pallidus to the spinal cord [7, 8, 9]. As a component part of the affected system, the globus pallidus is a constant source of impulses acting on the reticular formation of the brain stem. According to Granit and Kaada [4, 5], stimulation of the reticular formation affects the γ-efferent system of the anterior horns of the spinal cord, causing hyperactivity, which may lead to rigidity and spasticity. Hyperactivity of the γ-system, by exciting the α-motor neurons of the anterior horns, facilitates the departure of impulses to the effectors, causing a tremor which takes over, by some means or other, the rhythm of the globus pallidus and, probably, of other subcortical formations. Blocking the globus pallidus, even when the source of pathological impulses is not the globus pallidus itself, is effective because of interruption of the pathways along which these impulses flow.

The syndrome of Parkinsonism includes a disturbance of autonomic functions. Clinically and experimentally, in lesions of the basal ganglia the manifestations of this disturbance correspond to the anatomically and physiologically established connections between these ganglia and the nuclei of the hypothalamus and other formations of the brain stem. Our patients also showed disorders of autonomic functions. Autonomic reactions were especially marked when the needle was inserted into the globus pallidus. Changes, sometimes considerable, were frequently observed in the activity of the cardiovascular and respiratory systems. At times the autonomic changes were so severe that inhibition developed, and in rare cases consciousness was lost for a short time. In the EEG, these severe autonomic changes corresponded to the appearance of generalized groups of theta-waves. Sometimes they appeared and spread gradually (Fig. 3). Evolution of the theta-rhythm led to its becoming the only one in the leads connected to the globus pallidus. It could not be recorded, however, in the cortex of either hemisphere, coinciding with loss of consciousness by the patient. In other cases generalization of the theta-rhythm took place paroxysmally in the form of high-amplitude groups, cortical and pallidary, synchronous in all leads. In the hemisphere opposite to the globus pallidus on which the operation was performed, however, the theta-rhythm appeared later and its amplitude was lower, and other types of waves were superimposed on it. From the generalization of the theta-rhythm in the pallidary and cortical leads and its coincidence in time with the considerable changes in the autonomic functions, and also from the presence of direct connections between the globus pallidus and the nuclei of the hypothalamus, it appears that these autonomic reactions result from the influence of the globus pallidus primarily on the hypothalamus. So far as intensive generalization is concerned, when the hypersynchronized theta-rhythm

covered all regions from which recordings were made to the exclusion of other types of waves, as a rule this picture corresponded to a state of stupor or unconsciousness. Generalization of the theta- and delta-rhythms during loss of consciousness has been reported by several writers [2, 3].

We thus discovered certain electrophysiological features of the connections between the globus pallidus and the remaining divisions of the central nervous system. There are apparently two types of connection with the cortex: direct, with the ipsilateral hemisphere, and through the thalamic structures,with the anterior divisions of the cortex of both cerebral hemispheres. The considerable changes in the autonomic functions during manipulation of the globus pallidus demonstrate that the latter is connected with the hypothalamic and other autonomic nuclei. The globus pallidus also exerts its influence on the effectors of the limbs in two ways: by connections between the globus pallidus and the motor centers of the spinal cord and by its effect on these centers through the reticular formation.

SUMMARY

Introduction of a needle-electrode into the pallidum during hemipalidectomy usually arrested the theta-rhythm recording from the cortex of the ipsilateral hemispheres, in parallel with a temporary reduction or disappearance of the tremor on the contralateral upper extremity. These data point to a more rapid appearance of descending pallidum influences (on the motor spinal cord centers) than of the ascending ones (on the cortex of large hemispheres). Introduction of the needle also caused disturbances of the vegetative functions (respiratory, cardiovascular, and others). In cases of significant vegetative functional disturbances there was generalized high-amplitude theta-rhythm recorded on the electroencephalograms and electropallidograms.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
