ROLE OF THE VESTIBULAR NUCLEI IN THE FORMATION OF THE MECHANISM OF SYNCHRONIZATION OF CORTICAL RHYTHMS

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In previous investigations it was shown that the hypersynchronization of the α-rhythm observed in patients with a lesion in the posterior cranial fossa is dependent on compression of certain areas of the medulla and pons by the tumor [2, 4, 5]. Pathological-anatomical investigations have shown that the vestibular and cochlear nuclei are situated in these areas. The study of the level of excitability of the vestibular nuclei and of hearing [3] in the presence or absence of synchronization in the cerebral cortex has led to the conclusion that the most important factor for the synchronization of the slow cortical vibrations is the cessation of the flow of vestibular afferent impulses. This influence on the cortex is evidently mediated through the reticular formation at that particular level, with which the vestibular nuclei are closely connected by numerous collaterals. Later, in chronic experiments on animals, peripheral vestibular deafferentation was performed [6], causing marked synchronization of the slow rhythms in the cortex. This fact confirmed my suggestion that cortical synchronization is largely dependent on a deficit of vestibular afferentation, and also that vesitbular afferentation plays an important role in desynchronization phenomena.

Moruzzi and co-workers [8] associated the existence of special structures synchronizing cortical activity, and also of structures whose importance to the maintenance of "waking" (desynchronization) is decisive and independent of the inflow of sensory impulses, with the caudal portion of the brain stem. These workers reached this conclusion from experiments in which the pons was divided. In their opinion, the EEG of the midpontine preparation differs from the EEG of the rostropontine preparation because of a special substance, found in the narrow band of the brain stem lying between these levels, whose activity is "autochthonous," i.e., independent of the inflow of sensory impulses as a result of the absence of sensory nuclei in this particular band.

On the basis of personal findings and of subsequent anatomical investigations on cats [10, 13-15], I suggested [6] that this area of the brain stem is also related to the vestibular system. In fact, it is at the level above and below which Moruzzi and co-workers transected the pons that the superior vestibular nuclei of Bekhterev lie (Fig. 1), giving rise to ascending tracts and closely connected with the reticular formation at this level by a mass of collaterals. Evidently the upper transection performed by these investigators (the rostropontine preparation) lay above the level of the nuclei. Under these circumstances the vestibular connections with the cerebral cortex, the oculomotor nuclei, and the eye muscles were interrupted. Consequently, the preparation was no longer capable of making coordinated, combined movements of the eyes and the cortex was deprived of its vestibular and its objective optic impulses, which evidently led to the development of cortical synchronization. The other transection (the midpontine preparation) passed below the nuclei or touched their caudal borders, and left all the ascending connections of these nuclei intact. The enabled the animal to coordinate its eye movements and to respond by a prolonged reaction of arousal and desynchronization to the extreme conditions of the experiment.

The object of the present investigation was to study the role of the vestibular nuclei in the mechanism of cortical synchronization and to verify the hypothesis that the difference between the EEG patterns of the rostro- and midpontine preparations is attributable, not to the activity of some special "autochthonous" substance, but to exclusion or preservation of the superior vestibular nuclei respectively.

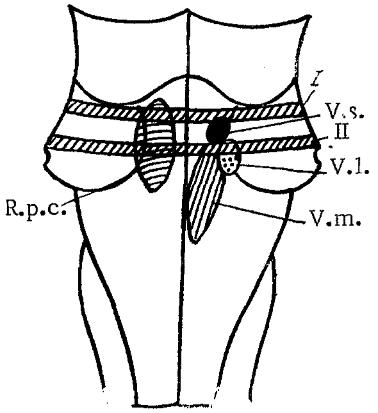

Fig. 1. Schematic comparison of level of transection of the brain stem performed by Batini, Moruzzi, Palestina, Rossi, and Zanchetti, and the location of the superior vestibular nuclei. V.s. —superior vestibular nucleus; V.m — medial; V.l. —lateral; R.p.c. —caudal reticular nucleus of the pons; I—upper transection (rostropontine preparation); II—lower transection (midpontine preparation).

EXPERIMENTAL METHOD

The investigations were conducted in chronic experimental conditions on seven unanesthetized cats with electrodes inserted into the superior vestibular nuclei in accordance with the atlas and stereotaxic technique of Szentagothai [14]. The cortical electrodes were inserted above the posterior and anterior portions of the lateral gyrus, and also above the posterior and middle portions of the suprasylvian gyrus (occipital, posterior parietal, and sensorimotor region). Monopolar recording of the EEG was always carried out after attainment of a resting state by the animal, starting from the first day after insertion of the electrode, and it continued for several days until the level of the resting electrical activity was stabilized. Next, after localized electrolytic destruction of the superior vestibular nuclei, the EEG was recorded for a further 2.5-3 weeks.

In all cases the results were compared with the localization of electrodes in the brain stem determined histologically in transverse sections of the brain stem of the cat, stained by Nissl's method.

EXPERIMENTAL RESULTS

In all the animals, local destruction of the superior vestibular nuclei led to considerable synchronization of the electrical activity of the cortex (Fig. 2). Bursts of spikes appeared, forming the background pattern of electrical activity. The amplitude of the spikes was greater than the initial, repeatedly-recurring maximal amplitude of the resting rhythms; in 4 animals 2-3 times, and in 3 animals 4-5 times greater. In cat No. 3, for example, the initial maximal amplitude of the potentials in the posterior lateral gyrus was 70 μV and on the 3rd day after coagulation it was 260 μV; in the posterior suprasylvian gyrus it was 75 μV and in the middle 60 μV, later becoming 270 and 260 μV respectively.

In cat No. 7 the initial maximal amplitude of the waves in the posterior lateral gyrus was 60 μV, increasing to 300 μV after coagulation; in the posterior suprasylvian gyrus it was 75 μV before coagulation and 270 μV after, while in the middle suprasylvian gyrus it was 90 μV before and 350-370 μV after coagulation. The synchronization was generalized in character and was recorded in both the posterior and the anterior parts of the cortex, but it was more marked in the parietal region (middle suprasylvian gyrus), less marked in the occipital region (posterolateral and suprasylvian gyrus), and least marked in the anterolateral gyrus (sensorimotor region). However, if the increase in the amplitude of the spikes was calculated as a percentage of the original values of the amplitudes, there was no great difference between the occipital and parietal regions. These changes were most obvious on the 3rd-5th day after coagulation, and at subsequent periods of observation the amplitude of the waves fell gradually and slowly.

The changes in the EEG after coagulation of the nuclei described above coincided in time with the changes in the animals' behavior. During the first 3-5 days after coagulation, they were mainly in a drowsy or sleeping state. To awaken the animal it was necessary to resort to stronger stimuli than required normally (knocking loudly several times on the cage in which the animal lay). The cat raised its head lethargically (at this time desynchronization was observed on the EEG), and then it again lay down and went to sleep (the EEG showed hypersynchronized spikes, changing with deeper sleep into a slow activity of the same high amplitude, and then into fast waves of low amplitude). Starting on the 6th day, the animals became more or less active, and a decrease in the maximal amplitude of the waves was recorded, while the spikes became less well defined.

After insertion of the electrodes into the nuclei, slight synchronization also was observed sometimes, although it was much less marked than after coagulation of the nuclei, with more rapid compensation and reestablishment of normal electrical activity.

Thus, the results obtained evidently confirm the hypothesis that the synchronizing mechanism in this particular portion of the caudal division of the brain stem is dependent on the exclusion of the superior vestibular nuclei of Bekhterev. The considerable synchronizing effect of the more caudal divisions of the brain stem, which was postulated

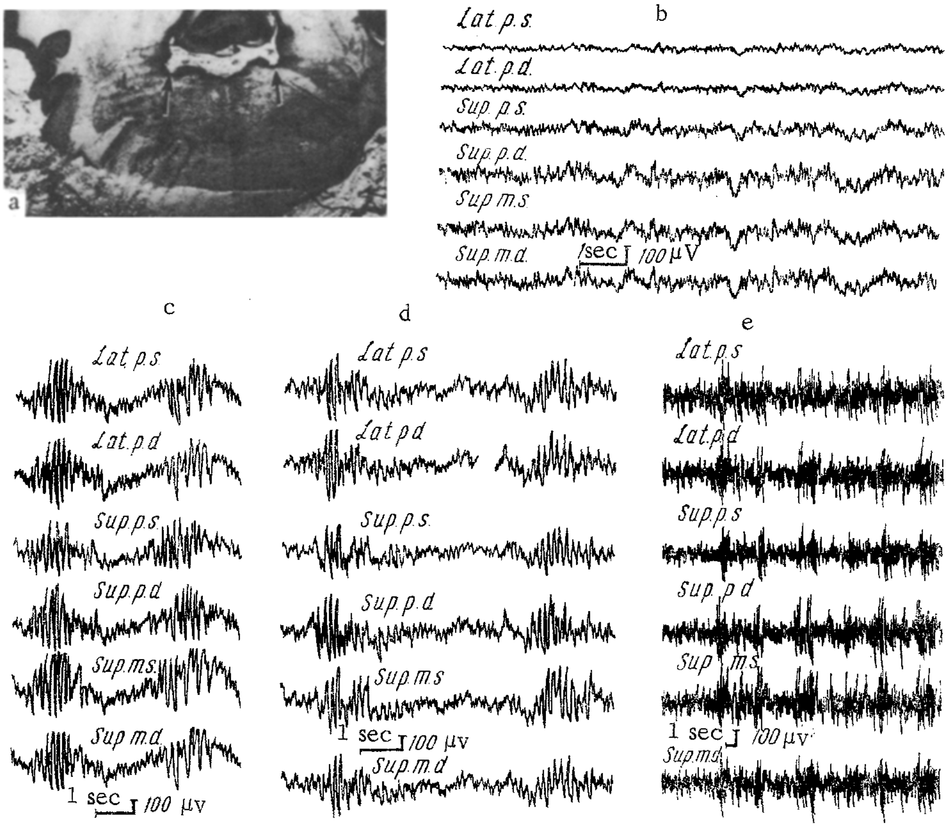

Fig. 2. Bilateral synchronization on the EEG as a result of bilateral exclusion of the superior vestibular nuclei. a) Histological preparation of the transverse section of the brain stem with the picture of bilateral destruction of the superior vestibular nuclei: the arrows point to the coagulated areas; b) EEG of the cat at rest before coagulation of the nuclei; c, d, e) EEG of the same cat at rest on the 2nd, 3rd, and 4th days after coagulation of the nuclei; Lat.p.) posterior lateral gyrus; Sup.p.) posterior suprasylvian gyrus; Sup.m.) middle; s) left hemisphere; d) right.

by Moruzzi and co-workers [8] and demonstrated by Cordeau and Mancia [11], on the cortex may evidently be explained on the basis of the observations described above and also of previous findings showing the importance of the peripheral vestibular deafferentation in determining synchronization of the cortical rhythms. Cordeau and Mancia observed the appearance of synchronized spindles in the contralateral hemisphere after hemisection of the brain stem, starting from the pretrigeminal level of the pons and continuing to the part of the pons situated 4-6 mm from its rostral border. It is in this segment of the brain stem that the medial vestibular nuclei lie. Since these nuclei also send fibers up into the cortex (but, unlike the fibers from Bekhterev's nucleus, they are crossed) the asymmetry observed by Cordeau and Mancia in their experiments may be explained [11]. Removal of the flow of impulses from one nucleus naturally evokes changes in the activity—synchronized spikes—in the contralateral hemisphere. This is confirmed by the results of my experiments in two animals in which the area of coagulation extended to cover not only the superior vestibular nucleus, but also the rostral part of the medial vestibular nucleus of Schwalbe (Fig. 3a, b, c).

As a result of coagulation, a generalized bilateral synchronization was observed. However, in the region of the middle suprasylvian gyri, against the background of generalized synchronization, a clear interhemisphere asymmetry was recorded in the form of marked predominance of the amplitude of the spikes in the contralateral hemisphere (Fig. 3e, f, g). A few days later the character of the asymmetry changed (Fig. 3h, i): against the background of a general fall of the amplitude of the waves, the difference between the amplitudes of the spikes in the two hemispheres was smaller, and, in addition, in the suprasylvian gyrus of the ipsilateral hemisphere the spikes began to appear earlier and were greater in amplitude than in the contralateral hemisphere. Injection of Nembutal in a dose of 20-25 mg/kg made the original asymmetry clearer and also showed up the displacement of the spikes into the ipsilateral hemisphere at the later periods.

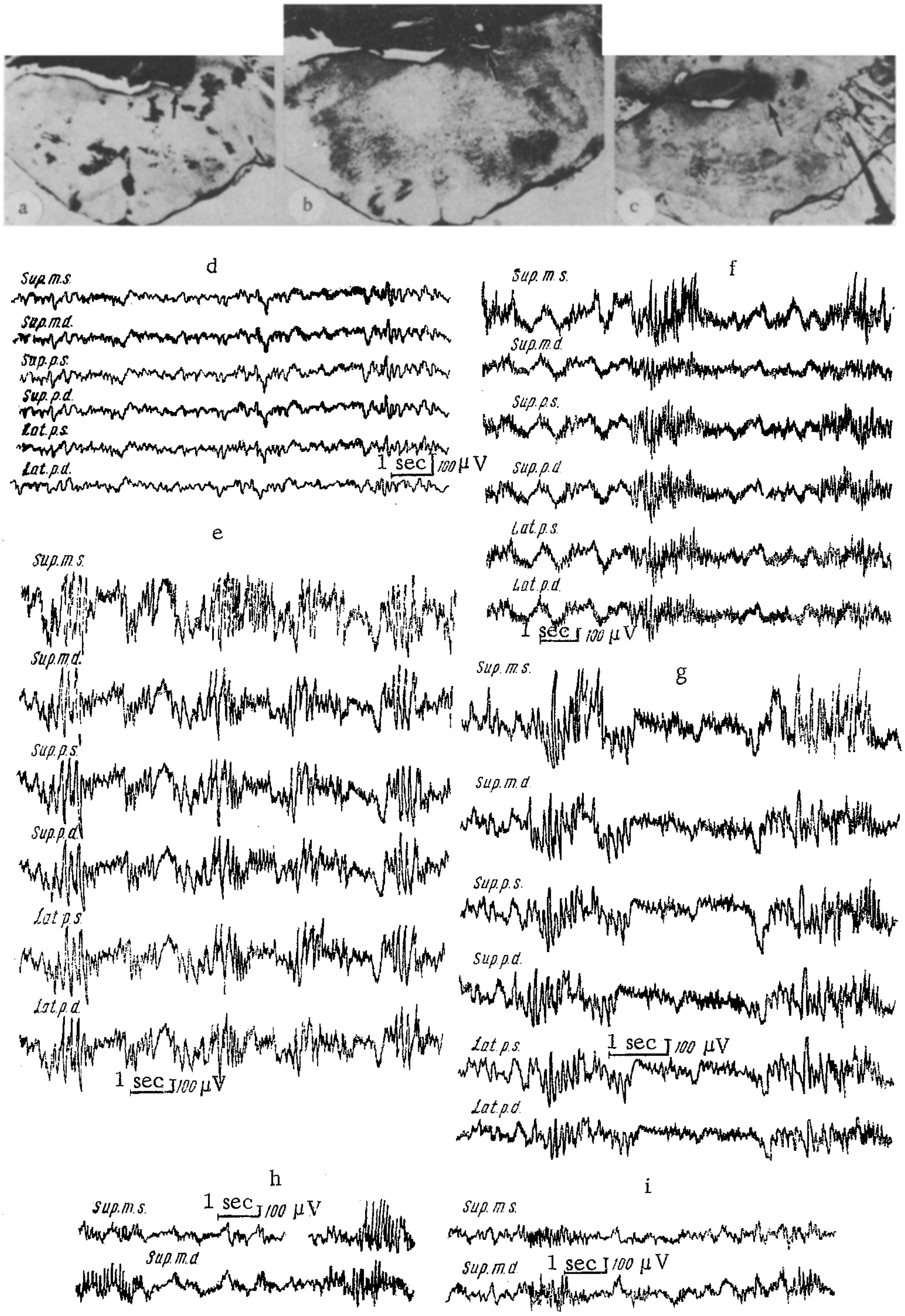

Fig. 3. Bilateral synchronization on the EEG with marked asymmetry in the medial suprasylvian gyrus following unilateral exclusion of the superior and part of the medial vestibular nuclei. a, b, c) Successive series of transverse sections of the brain stem with destruction of the superior vestibular nucleus and part of the medial vestibular nucleus on the right side; d) EEG of the cat at rest before coagulation; e,f,g) EEG of the same cat at rest on the 2nd, 3rd, and 4th days after coagulation; h) 10th; i) 11th day—shift of asymmetry: predominance of spikes in the suprasylvian gyrus of the ipsilateral hemisphere. Remainder of legend as in Fig. 2.

The shifting of the asymmetry was possibly determined by the more complete exclusion of the right, ipsilateral superior vestibular nucleus with its uncrossed connections, which was effective at the later periods, and by compensatory, activating influences from the left, intact superior vestibular nucleus, causing a decrease in the amplitude of the spikes in the hemisphere on the same side, but contralateral to the destroyed nucleus.

In the illustrations given by Cordeau and Mancia [11], interhemisphere asymmetry was well-marked in all leads, evidently because the bipolar recording, which was the only form used by these workers, always included the parietal region in which, from my own findings, the asymmetry predominantly appears. The bilateral, generalized character of the synchronization in the remaining leads recorded in the present experiments emphasizes the diffuseness of the changes in cortical activity, only possible in the event of participation by the reticular formation. At the same time, the fact that the spikes were more marked in the parietal region of one or other hemisphere, depending on the participation of the nucleus with the crossed or uncrossed ascending connections, apparently demonstrates that the cessation of the flow of specific impulses alone, without the participation of the reticular formation, may give rise to synchronization of cortical activity.

As a result of the findings described above, an addition can be made to the experimental results obtained by Batini and co-workers [8], who also identified a narrow band in the brain stem exerting a well-defined desynchronizing effect on the cortex, namely, that in this area decisive importance is attached to a still more limited region—the superior vestibular nuclei. In the more caudal portion of the brain stem, influences such as these are evidently largely associated with the medial vestibular nuclei. These nuclei and the impulses passing through them are probably the factor whose absence plays the principal role in triggering the mechanism of cortical synchronization, both directly and indirectly, through the intermediary of this particular level of the reticular formation. We cannot, therefore, accept the conclusions drawn by these authors, and also by Cordeau and Mancia, concerning the existence of special mechanisms of synchronization in the caudal brain stem and their view that the tonic activity of the reticular formation at this level is autochthonous. Evidently the predominent importance of the vestibular afferentation in the phenomenon of cortical synchronization may be attributed to the intimate connection between the vestibular nuclei and the reticular formation, which is unusual by comparison with the other analyzers, and also to their numerous connections with the other brain-stem nuclei. The existence of a "single reticulo-vestibular complex" may even be discussed [7]. It is, evidently, not by accident that the problem of whether the vestibular apparatus possesses cortical representation or not still remains unsolved, for in response to vestibular stimulation a simultaneous excitation of extensive regions of the cerebral cortex invariably develops, nor is it by accident that the vestibular stimulation used by several investigators [9, 12] proved to be "particularly effective" by comparison with trigeminal, optic, or auditory stimuli for producing a generalized electrographic arousal reaction.

These results indicating the considerable influence of the vestibular apparatus on the mechanisms of sleep and waking taking place in the cortex are in agreement, I consider, with the results obtained by A. V. Val'dman [1], who found that the reticulo-vestibular nuclear complex exerts a considerable descending influence on many autonomic functions (vascular tone, cardiac activity, and so on).

Bearing these facts in mind, it can be imagined that there is considerable scope for acting through the reticulo-vestibular apparatus on both the higher cortical functions and the peripheral autonomic functions. The chances of acting in this way are improved by the fact that the vestibular nuclei receive not only vestibular afferent fibers, but also fibers from the cerebellum, the spinal cord, the autonomic nuclei, the muscles of the eye, and the nuclei of the reticular formation, which is probably responsible for the considerable extent of the influences exerted by the vestibular nuclei. Consequently, the ways by which the external environment may influence the vestibulo-reticular complex of the brain stem, and through it the cortex and periphery, are not confined strictly to the labyrinths.

Not merely vestibular impulses, but also tactile, proprioceptive, and other impulses reaching the vestibular nuclei may help to determine the degree of excitability of this complex and the character of the ascending and descending influences.

SUMMARY

Proceeding from the author's earlier references to the great influence of the caudal portions of the brain stem and vestibular afferentation upon the cortical synchronization it is suggested that the portion of the bridge of Varolius with which Moruzzi and his collaborators associate the mechanism of synchronization possesses certain properties ascribed to it in view of the loaclization of Bechterew's superior vestibular nuclei within it. Chronic experiments on

nonanesthesized cats with local electrolytical destruction of the superior and medial vestibular nuclei and sharp cortical synchronization following the exclusion of nuclei have confirmed this suggestion. Apparently, the superior (and medial) vestibular nuclei are the stage whose absence plays a decisive role in the excitation of the mechanism of cortical synchronization both directly and through the reticular formation of the given level of the brain stem.

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