Insomnia after bilateral stereotactic thalamotomy in man

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We think it interesting to report a case of insomnia, occurring in a Parkinsonian patient after bilateral stereotactic thalamotomy, as a clinical contribution to the physiopathology of variations of consciousness and regulation of the sleep-wakefulness rhythm.

Neurophysiological experimental findings in animals suggest that in addition to the activating or arousing mechanisms of the reticular formation, deactivating or hypnogenic mechanisms, also localized in the brain-stem, play a prominent part in the regulation of sleep-wakefulness alternation (Hess, 1944; Moruzzi, 1963; Rossi, 1964 and 1965). This hypothesis rests on the observation that an enduring sleep-like state, as well as a long-lasting insomnia, may be produced by brain-stem lesions, the sign of the effect being dependent exclusively on the site of the brain-stem damage (Batini, Magni, Palestini, Rossi, and Zanchetti, 1959a; Batini, Moruzzi, Palestini, Rossi, and Zanchetti, 1959b; Cordeau and Mancina, 1959, Candia, Favale, Giussani, and Rossi, 1962a; Candia, Minobe, and Rossi, 1962b; Jouvett, 1962, 1965a, b and c; Minobe, Candia, and Rossi, 1962).

In man there is much clinical, E.E.G., and anatomical evidence pointing to the existence of a passive mechanism for the reduction of consciousness; conversely, evidence supporting the theory of an active mechanism is scanty and not nearly so convincing. In fact, in neurosurgical and neurological experience, reduction of consciousness and vigilance levels (drowsiness, obtundation, hypersomnia, coma, and prolonged coma) as a consequence of more or less localized brain lesions, is frequently observed, while it is rare to find the opposite condition of insomnia. The latter or, more often, inversion of sleep rhythm, has been reported to follow diffuse rather than focal lesions (see the classical works of Von Economo, 1929 and 1930); these cases are of little interest to those who wish to determine a structural site for the neurophysiological mechanisms responsible for changes in the vigilance level.

CASE REPORT

This 58-year-old truck driver was in good health until the onset of his present illness. He began to exhibit symptoms of extrapyramidal Parkinsonism in 1958 (rigidity, tremor, and bradykinesia of the right hand). Within a year the same symptoms appeared in the right lower limb also. At the same time he complained of hypersalivation and nondescript pain in the right shoulder. These symptoms became slowly but progressively worse until 1960, when the patient was forced to give up his job. In the two years before admission to hospital the patient developed a progressive nocturnal insomnia: soon after retiring he would experience vague pains and a pulling sensation in all extremities, with some indefinite visceral disturbances that prevented sleep. Solitude, darkness, and silence seemed to aggravate the symptoms, so that the patient became increasingly anxious. His relatives confirmed that he was unable to sleep for several hours after going to bed, and that he got up very early in the morning in a groggy and irritable mood. Unless he took daytime naps, he would deteriorate over several days until a good night's sleep produced improvement.

On his first admission (8 January 1962) the patient appeared in good health; contributory physical findings were elicited only by neurological examination. He presented a marked right extrapyramidal syndrome with tremor, rigidity, and bradykinesia. He was entirely self-sufficient. During the pre-operative period we observed the sleep pattern reported above.

Routine laboratory tests as well as skull and chest radiographs contributed nothing. On 16 January left chemothalamectomy was done under local anaesthesia by Cooper's method. The pneumoencephalogram showed a fairly well-expanded ventricular system, with enlargement of the left ventricle. A lesion was made in the region of the nucleus ventralis lateralis (V.L.) by inflating a standard 7 mm. balloon (Fig. 1). With inflation, tremor and rigidity of the contralateral extremities were completely relieved. The following day the procedure was completed by injection of alcohol. The post-operative course was uneventful. At the time of discharge on 25 January the patient was well and his insomnia had disappeared.

The results of thalamectomy were consolidated in time; two months later he stated in a letter that he was 'com-

FIG. 1. Schematic representation of portions of ventricular system, with landmarks of the anterior and posterior commissure (AC and PC) and site of thalamic surgical lesions.

pletely well', able to use his right limbs normally, and free of insomnia. After about a year he began to complain of tremor, rigidity, and difficulty in moving the left extremities, with occasional tremors in the right limbs. Slowly but progressively the Parkinsonian symptoms in the left side increased, while the right side remained unimpaired. Sleep also remained normal.

On his second admission (8 April 1964) his general condition was good. Extraparallel Parkinsonian syndrome was present with tremor, rigidity, and marked akinesia of the left-side limbs; episodic mild tremor of the right extremities was also observed. He was entirely self-sufficient. No sleeping difficulty was noticed during clinical observation.

Laboratory tests still gave no information. On 13 April right cryothalamotomy was performed under local anaesthesia. The pneumoencephalogram showed no change since 1962. The area of the right V.L. was frozen (with the target more medial and more posterior than the contralateral lesion) and immediate resolution of left-side tremor and rigidity was thus produced (Fig. 1). After an uneventful first day, the patient could not go to sleep; he finally got out of bed and spent the rest of the night fretting in an armchair. The next morning he looked tired and presented a masked facies, though he was lucid and well orientated; active motility remained good. During the second post-operative day he was wide awake, and at night he was still fully alert, tense, and incapable of going to sleep; he asked for sleeping pills. During the next several hours he was given 300 mg. of phenobarbital orally and 100 mg. of perphenazine intramuscularly; nevertheless, he became increasingly anxious, restless, and agitated. He spent the whole night awake, although the environment was made as comfortable and restful as possible. The following day (third post-operative day), he was noticeably anxious and prostrated; he complained of

unbearable agitation and remained lucid and not at all somnolent. The third night was again sleepless. At 9 p.m. surface electrodes were placed on his head and on the periorbital region and a polygraphic recording was started. Unfortunately after 20 minutes this had to be discontinued because the patient was rebellious and tore off the electrodes, and behaved aggressively toward the physicians and nursing staff. Once he was again free to move he acted as on the previous night, complaining of vague pains, anxiety, and shaking nervousness. The E.E.G. tracings obtained in the first 20 minutes were diffusely desynchronized, with no reaction to opening and closing of the eyes (Fig. 2). The next day he was extremely tense, panicky, and intolerant of even the slightest noise and visual stimuli; his general condition had deteriorated and he could maintain the standing position only if assisted. On the fourth night generous doses of barbiturates and perphenazine were given. The patient relaxed but was still unable to fall asleep, though he was obviously exhausted. Only at about 10 a.m. the next morning did he fall into an apparently deep sleep of about three hours' duration, with short awakenings between. He awoke much relieved and remained relaxed enough to take several naps during the day, whenever conditions permitted. At night, however, he was again fully awake and sleepless, and spent the whole fifth night without sleeping. This insomnia, however, was offset by daytime drowsiness and morning naps on the sixth day. Once more, the patient was sleepless on the sixth night, but this time he was able to fall asleep at approximately 1 a.m.; this was his first instance of spontaneous nocturnal sleep since the operation, and was followed by shorter naps at dawn. During the ensuing morning he was in a happier mood, with less daytime drowsiness. On the seventh day it was possible to take an uninterrupted recording of the E.E.G., heart rate, and eyes movements during 14 consecutive hours, from

FIG. 2. E.E.G. recorded during the third sleepless night.

FIG. 3. Diagrammatic representation of sleep through a polygraphic recording (E.E.G., E.K.G., and E.M.) from 10 p.m. of the seventh post-operative night to 12 noon the following day. According to the simplified scheme proposed by Pisano, Rosadini, Rossi, and Zattoni (1964, 1966) and by the French authors (Tissot, 1965, and others) sleep was subdivided into four phases having the following electrographic characters: phase 1, disappearance of the alpha rhythm in the E.E.G. and appearance of low-voltage, irregular, though chiefly fast activity with some 4-6/sec. waves but no significant eye movements; phase 2, spindles and some 3-6/sec. waves in the E.E.G. but no eye movements; phase 3, very slow (1-3/sec.) waves of high amplitude in the E.E.G. and no eye movements; phase 4, E.E.G. similar to that recorded in phase 1, though often with peculiar bursts of saw-toothed waves at 3-4/sec. in the frontal leads; typical rapid movements of the eyes (Dement and Kleitman, 1957; Jouvet, Michel, and Mounir, 1960; Jouvet, 1965a, b, and c). 'W' = awake. Recording time = 840 min; total wakefulness time = 570 min. (67.8% of recording time); total sleep time = 270 min. (32.1%). Total time for each phase: phase 1 = 96 min. (35.5% of sleep time); phase 2 = 8 min. (2.9%); phase 3 = 166 min. (61.4%); phase 4 = 0.

10 p.m. to 12 noon on the following day. As shown in Fig. 3, the sleep rhythm in this case was abnormal with regard to phase sequence as well as in each single phase: phases 1 and 3 were markedly prolonged, phase 2 was poorly represented, and phase 4 was missing altogether. In the following days the patient's sleep-wakefulness rhythm gradually became more regular; however, he still required a fairly long time to fall asleep. Unfortunately, we were unable to secure further E.E.G. recordings because of the patient's refusal. On discharge, 27 days after surgery, tremor and rigidity of the left extremities were completely relieved; there was a slight residual bradykinesia, but functional recuperation of the left upper limb was satisfactory, and the state of anxiety had abated.

Follow-up examination on several occasions showed no recurrence of tremor and rigidity; conversely, a slowly progressing akinesia was noted. The patient reported that he was still having sleeping difficulties, approximately as before the first operation. He takes sedatives regularly.

DISCUSSION

From our experience of over 1,000 stereotactic thalamotomies, 500 of which were bilateral, we find that sleep disturbances are frequent in Parkinsonian patients: many of them complain of nocturnal reduction of sleep and induction insomnia or, less commonly, of daytime drowsiness. Generally thalamotomy modifies such disturbances: in the acute post-operative phase there may be many changes of consciousness, levels ranging from a state of extremely prolonged vigilance to hypersomnia and coma. Inversion of the sleep-wakefulness rhythm is also frequent during this phase, with a remarkable reduction in nocturnal sleep and prolonged daytime drowsiness. These disturbances usually abate rapidly and the patient returns to his normal level of consciousness with a regular sleep rhythm. Similar modifications, perhaps slightly more accentuated, occur after bilateral thalamotomy. Our experience, therefore, indicates that the thalamus (thalamic nuclei or crossing fibres?) is involved in the regulation of the sleep-wakefulness rhythm.

The case reported here is remarkable inasmuch as it is the only one in our own experience entailing total and prolonged loss of sleeping capacity.

Identification of the anatomical structures responsible for insomnia in this patient, and hence its pathological interpretation, is difficult on account of the well-known limitations inherent in human stereotaxis, particularly as regards precise anatomical recognition of target structures due to individual variability.

The lesion delivered in the left side by Cooper's chemothalamectomy in this case most probably involved the medio-ventral portion of the ventralis lateralis, most of the ventralis intermedius, and the

rostral portion of the ventralis posterior medially reaching the centro-medianus and arriving at the dorsal boundaries of the subthalamus. The second thalamic lesion delivered in the right side by a cryogenic system probably involved the ventralis lateralis (to a lesser extent), the ventralis intermedius, the centro-medianus, the rostral portion of the ventralis posterior, and the subthalamus, including the dento-rubro-thalamic bundle and Forel's H1 field.

With the limitation stated above, we believe that this case of unusual insomnia corroborates the hypothesis that the thalamus, especially the non-specific nuclei of the thalamus, is instrumental in the implementation of sleep-inducing mechanisms (Rossi, 1962).

SUMMARY

An unusual case of total and irreducible insomnia in a Parkinsonian patient after bilateral stereotactic thalamotomy is reported.

During 96 hours of total (night and day) insomnia the patient's behaviour differed from that of persons experimentally deprived of sleep by showing no capacity for sleeping; he was fully alert and well orientated. Subsequently the patient presented inversion of the sleep-wakefulness rhythm, which progressively became more regular. A polygraphic recording during the recovery stage showed abnormal sleep: phases 1 and 3 were markedly prolonged, phase 2 was poorly represented, and phase 4 was missing altogether. The stereotactic lesions, bilaterally delivered to the thalamus, involved, besides the ventralis lateralis, the ventralis intermedius, partially the ventralis posterior, and the centro-medianus, other nuclei of the so-called non-specific projection system.

This case may indicate that the thalamus, especially the non-specific thalamus, is involved in the determination of sleep induction.

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