Beta wave activity in the electroencephalogram in cases of coma due to acute brain-stem lesions

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It is well known that the state of deep coma is usually associated with high-voltage slow waves in the electroencephalogram (E.E.G.). However, some exceptional cases have been reported which suggest an independence of the comatous state from slow waves in the E.E.G.

Loeb and Poggio (1953) reported a patient who fell abruptly into coma and died within 30 hours, showing slight abnormalities in an E.E.G. recorded six hours after the attack of coma, with 8-9 c/s alpha waves, 3-4 c/s theta waves bursts, low-voltage fast activity and positive spike discharges, even in the state of deep coma. At necropsy, massive haemorrhages of the middle part of the pons reaching to the lower part of the mid-brain were found. Loeb (1958) also observed similar electroencephalographic findings in a case in which massive haemorrhages ruptured into the ventricle invading the upper one-third of the pons. A patient was reported (Lundervold, Hauge, and Löken, 1956), who remained unconscious for one year and a half without any appreciable E.E.G. changes, following vertebral arteriography. In this patient, the area supplied by the posterior cerebral arteries had not been flushed by the contrast medium due to an obstruction of these arteries at their origin from the basilar artery. They were filled via the carotid system. At necropsy, the pontine region, including its reticular substance, was found to be severely damaged. In addition, there was bilateral atrophy of the posterior mesencephalon, including the pyramidal tract, the medial lemniscus, the cerebellum, and other structures supplied by the vertebral arterial system.

Kaada, Harkmark, and Stokke (1961) also reported a similar case. This patient died on the fourth day after the beginning of the disease, and showed bursts of 12 c/s alpha waves, 4-6 c/s theta waves, and low-voltage fast activity in the E.E.G. At necropsy, a fresh thrombus occluded the basilar artery from the vertebral to the posterior cerebral arteries, and damage to the pons and midbrain was found.

Chatrian, White, and Shaw (1964) found 8-10

c/s alpha waves and a considerable amount of 5-7 c/s theta activity, resembling the pattern associated with wakefulness, in an E.E.G. recorded on the sixth day in a case of traumatic unresponsive brain-stem infarction.

Marquardsen and Harvald (1964) reported two necropsied cases of basilar artery thrombosis, showing an almost normal E.E.G. in spite of the state of deep coma.

In this study, three patients were investigated, who died quickly after sudden deep coma, showing various neurological symptoms of brain-stem lesions, with unusual and possibly characteristic E.E.G. findings, such as very low-voltage fast activity. They suggest that slow waves do not depend on the depth of coma. At necropsy, occlusions and marked stenosis of the vertebral and basilar arteries were found.

CASE REPORTS

CASE 1 H.S. (Y.K. 2719), a 76-year-old woman, had had hypertension for seven years. In 1961, when she was admitted to the Yokufukai Geriatric Hospital, mitral insufficiency, electrocardiographic evidence of myocardial damage, and oedema of the lower extremities were found. The blood pressure subsequently varied between 230/140 and 180/85 mm.Hg, and oedema appeared intermittently in the face and extremities. In April 1964, she suddenly became deeply comatose after vomiting. The blood pressure dropped to 162/88 mm.Hg, and absence of pupillary response to light and of corneal reflexes was noted. There was no anisocoria or deviation of the eye-balls. Decerebrate rigidity, bilateral hyperactive tendon reflexes, and bilateral positive Babinski reflexes were present. Auricular fibrillation was noted on electrocardiography. There were no abnormalities of serum electrolytes or disturbances of liver function.

Cyanosis and respiratory distress increased and she expired four hours after the initial attack of coma. A secondary compression of the brain-stem due to massive midline haemorrhage or a primary brain-stem haemorrhage was suspected.

In the E.E.G. recorded 20 minutes after the onset of coma, neither alpha waves nor slow waves were recognized,

FIG. 1. The E.E.G. of case 1 (a 76-year-old woman), recorded 20 minutes after onset of deep coma. The record shows low-voltage very fast activity diffusely without any slow waves in all leads, in spite of deep coma. Reference leads (to ipsilateral ear): LF—left frontal, RF—right frontal, LMT—left midtemporal, RMT—right midtemporal, LP—left parietal, RP—right parietal, LO—left occipital, RO—right occipital.

FIG. 2. The E.E.G. of case 1, recorded five months before the onset of coma. The record shows 9 c/s alpha waves without any appreciable fast activity.

but very low voltage fast activity appeared diffusely in all leads (Fig. 1). Electroencephalograms in November 1962, 17 months before the attack, and in December 1963, five months before the attack, were normal, showing 9 c/s alpha waves without any appreciable fast activity or slow waves (Fig. 2).

At necropsy, chronic congestion of the lung and sclerotic changes of the mitral valves were found. There was marked cerebral arteriosclerosis and the vertebral and basilar arteries were occluded by fresh thrombi (Fig. 3).

In the brain tissue, old small haemorrhages were found in the left pallidum and in the white matter of the frontal lobe, and a relatively old small softening of the base of the pons was noted. Thus, no significant intracerebral pathology compatible with the attack was found.

CASE 2 Y.S. (Y.K. 2832), a 67-year-old woman, had a previous history of Basedow's disease and cholelithiasis. In 1957, hypertension of 220/104 mm.Hg was noted and since then, the blood pressure had continued to be above

FIG 3. The basilar artery of case 1. The artery has been occluded by fresh thrombus. Masson trichrome elastica staining. $\times 20$.

200/100 mm.Hg. In 1963, she suffered from cerebral haemorrhage causing left hemiplegia without sensory changes; increased deep tendon reflexes and positive Babinski reflex persisted on the left side. There was also a cardiac murmur, E.C.G. evidence of left ventricular hypertrophy, and marked hypercholesterolaemia ranging from 370 to 570 mg./100 ml. In May 1965 her consciousness became gradually disturbed and she fell into deep coma within two days. The blood pressure dropped to 162/84 mm.Hg. A slight fever and some rales in the chest were present.

Anisocoria, negative pupillary light responses, slight rigidity on the right side and slight deviation of the eye-balls to the right side were noted. The deep tendon reflexes were decreased or absent, without pathological reflexes.

The cerebrospinal fluid was clear, showing a pressure of 40 mm.H₂O. The cell count and protein content were within normal limits.

She died 30 hours after becoming comatose. A diagnosis of cerebral vascular insufficiency, possibly of the vertebrobasilar system, and bronchopneumonia was made.

The E.E.G. recorded five hours after the onset of coma showed 4-6 c/s theta waves with much low-voltage fast activity in all leads (Fig. 4). In the E.E.G. recorded nine hours after the onset of coma, diffuse slowing was prominent, with disappearance of fast activity (Fig. 5). In the E.E.G. of October 1963, 19 months before the attack, 8-9 c/s alpha waves with a few 7 c/s theta waves were observed without any appreciable fast activity (Fig. 6).

At necropsy, coronary sclerosis, myocardial infarc-

FIG. 4. The E.E.G. of case 2 (a 67-year-old woman), recorded five hours after the onset of coma. The record shows 4-6 c/s theta waves with low-voltage fast activity in all leads.

FIG. 5. The E.E.G. of case 2, recorded nine hours after the onset of coma. The record shows diffuse slowing with theta waves, denoting disappearance of fast activity recognized in Fig. 4.

FIG. 6. The E.E.G. of case 2, recorded 19 months before the attack. The record shows 8-9 c/s alpha waves with a few 7 c/s theta waves without any appreciable fast activity.

tion, pneumonia of minor degree, and severe sclerosis of the aorta were found. Sclerosis of the vertebral and basilar arteries was prominent and almost 90% of the lumen of these arteries was occluded (Fig. 7). Small old haemorrhages were noted in the internal capsule of the right side and the cerebellar cortex of the brain. A small fresh softening was recognized in the region of the substantia nigra and pes pedunculi on the right side of the midbrain (Fig. 8). A relatively old small softening was also found in the middle part of the pons.

CASE 3 Y.S. (Y.K. 2815), a 79-year-old man, had had ventricular extrasystole and cholelithiasis. The blood pressure was about 150/80 mm.Hg. Since January 1965 he had been in bed because of shortness of breath and palpitation. In February 1965 he fell into coma in the bathroom. Physical examination revealed cyanosis, respiratory disturbances, and lowering of the blood pressure to 118/62 mm.Hg. Myosis and absence of light reflexes were noted but no anisocoria was found. Both eye-balls deviated upward and rigidity of both upper

FIG. 7.

FIG. 7. The basilar artery of case 2 showing marked stenosis and arteriosclerosis. Masson trichrome elastica staining. $\times 20$.

FIG. 8.

FIG. 8. The midbrain of case 2. Fresh softenings are seen around the pes pedunculi and substantia nigra of the right side. Luxol fast blue staining.

extremities, bilateral hyperactive tendon reflexes, and bilateral positive Babinski reflexes were noted.

The cerebrospinal fluid was clear and showed a pressure of 180 mm.H₂O, normal cell count, and normal protein content.

He expired 28 hours after falling into coma. A diagnosis of cerebral vascular insufficiency, particularly of the vertebrobasilar system, was made. In the E.E.G. recorded nine hours after the onset of coma, low-voltage fast activity was mixed with intermittent 4-5 c/s theta

waves (Fig. 9). The E.E.G. recorded in December 1963, about 13 months before the attack, showed fairly well regulated 9 c/s alpha waves, with minimal 7 c/s theta waves only occasionally on the frontal regions. The one recorded in January 1965, just one month before the attack, showed similar findings (Fig. 10).

At necropsy, severe coronary sclerosis, myocardial infarction, marked pulmonary emphysema, and cholelithiasis were found, but neither appreciable cerebral arteriosclerosis nor significant intracerebral pathology

FIG. 9. The E.E.G. of case 3 (a 79-year-old man), recorded nine hours after the onset of deep coma, shows fast activity mixed with 4-5 c/s theta waves.

FIG. 10. The E.E.G. of case 3, recorded just one month before the onset of coma, showing fairly well-regulated 9 c/s alpha waves with minimal 7 c/s theta waves only occasionally in the frontal regions.

was noted. Acute heart failure was thought to be the cause of death. It was concluded that severe cerebral vascular insufficiency, in particular of the vertebro-basilar system, was produced by severe acute heart failure.

DISCUSSION

It is said that electroencephalographic changes are extremely slight or lacking in the vertebrobasilar syndrome (Cohn, Raines, Mulder, and Neumann, 1948; Strauss and Greenstein, 1948; Abbott and Bautista, 1949; Markovich, 1958; Paddison and Ferriss, 1961). Niedermeyer (1963) found normal E.E.G.s in 11 of 20 patients with vertebrobasilar insufficiency, while he observed normal E.E.G.s in only 26 of 89 cases of vascular insufficiency of the carotid and the middle cerebral arteries. Friedlander (1959) found slight electroencephalographic abnormalities in nine of 31 patients with cerebrovascular disorders of the brain-stem, and concluded that certain electroencephalographic abnormalities can be found without any characteristic locus or pattern. However, marked abnormalities in the E.E.G. strongly suggest the existence of some pathology in the brain-stem as well as vascular disorders.

Roger, Roger, and Gastaut (1954) classified E.E.G.s in vascular disorders of the brain-stem into two types. One is a type of diffuse neural hyperexcitability, namely, fast alpha, beta waves and spike discharges appearing at the Rolandic sulcus and the occipital regions. The other is a type with bursts of theta and delta waves and multiple spike discharges. The former is seen in the group with medullo-pontine syndromes, whereas the latter is observed mainly in

the group with pedunculo-subthalamic syndromes.

Meyer, Leiderman, and Denny-Brown (1956) drew attention to the appearance of bilateral slow waves in the regions supplied by the posterior cerebral artery during body tilt in cases of vertebrobasilar insufficiency. This has not been supported by Weiss and Froelich (1958).

Tucker (1958) found bilateral temporal slow waves and sharp waves in cases of vascular disorders of the brain-stem.

Birchfield, Wilson, and Heyman (1959) stated that the appearance of a normal E.E.G. suggests local softening of the brain-stem, but diffuse slow waves indicate extensive softening of the brain-stem. Paddison and Ferriss (1961) observed normal E.E.G.s in 14 (70%) of 20 patients with infarction of the vertebrobasilar system.

Potes, McDowell, and Wells (1961) stated that flat E.E.G.s existed in the acute stage of clinically diagnosed brain-stem infarction in eight of 42 patients; they disappeared with improvement of the clinical syndromes. Niedermeyer (1963) found low voltage E.E.G.s in 80% of patients with vertebrobasilar insufficiency, but in only 11.2% of patients with carotid artery insufficiency, and concluded that low voltage is fairly characteristic in cases with vertebrobasilar insufficiency.

Thus, there are considerable differences in the results of various workers and complete agreement has not been obtained as yet. One reason may be the difference in degree of vascular insufficiency. On the other hand, necropsied cases are very few and only clinical diagnosis was available in most

cases. Accordingly, differences in subjects selected and in the severity of the disorder are possible in various reports.

Furthermore, the description of the time lag between the E.E.G. recordings and the attack and of the state of consciousness at the time of E.E.G. recordings are obscure or lacking.

In addition, no description of E.E.G. findings before the attack (which may be indispensable for comparison) was found in any of the previous reports.

Thus it is not reasonable to compare the results of various investigators. However, summing up these reports, it may be said that the incidence of abnormal E.E.G.s in patients with brain-stem disorders is, in general, low and the degree of abnormality is also low. Low-voltage records can be seen relatively frequently, and in a few, fast activity could be found as well.

Cases confirmed at necropsy are reported by Loeb and Poggio (1953), Loeb (1958), Kaada, Harkmark, and Stokke (1961), and Strauss and Greenstein (1948) (case 4). Low-voltage fast activity is described in these reports, but no author gave much attention to it. Furthermore, as no electroencephalographic findings before the attack were described, it cannot necessarily be concluded that the observed low-voltage fast activity appeared in relation to the attack.

Apart from Niedermeyer (1963) who emphasized low-voltage E.E.G.s in cases of vertebrobasilar insufficiency, no report has yet appeared drawing attention to fast activity in disorders of the vertebrobasilar system.

Three patients in this report died within 30 hours of the initial onset of coma, with lethal vascular disorders of the brain-stem. In E.E.G.s recorded before the attack, no appreciable low-voltage fast activity had been observed. Accordingly, it can be said that fast activity noted in the state of deep coma might have appeared in relation to the attack.

In case 1, with the most sudden onset of coma and the quickest death (within four hours after the onset of coma), diffuse very low-voltage fast activity without any slow waves was noted in the E.E.G. recorded 20 minutes after the initial onset of coma. In case 2, on the other hand, in which the coma appeared gradually, low-voltage fast activity in the E.E.G. recorded five hours after the attack, disappeared in the one recorded nine hours after the attack, 21 hours before death. It showed diffuse slow activity.

This evidence may suggest that fast activity is apt to appear at the early stage of sudden and severe vascular insufficiency of the brain-stem.

Cate (1961) did experiments in cats, ligating the

vertebral artery at the level of the first cervical nerve, and observed a quick decrease in voltage which gradually returned to normal within several days after the operation.

It is well known that somnolence or coma can be produced easily by damage to the brain-stem (Lindsley, Schreiner, Knowles, and Magoun, 1950; French, 1952; French and Magoun 1952), in particular, to the ventral part of the diencephalon, and the rostral part of the midbrain.

Lindsley, Bowden, and Magoun (1949) and Moruzzi and Magoun (1949) reported that low-voltage fast activity appears following transection of the transitional parts between the pons and the midbrain or stimulation of the brain-stem.

Recently, Batini, Moruzzi, Palestini, Rossi, and Zanchetti (1958), Batini, Magni, Palestini, Rossi, and Zanchetti (1959), and Batini, Palestini, Rossi, and Zanchetti (1959) observed low-voltage fast activity and eye movement suggesting arousal in midpontine pretrigeminal cats in which the pons was transected immediately before the trigeminal nerve, and they concluded that such desynchronization may be due to the removal of a synchronizing or sleep-inducing mechanism in the lower part of the brain-stem, and that such mechanisms exist in the solitary nucleus and nucleus centralis reticularis in the medulla (Magnes, Moruzzi, and Pompeiano, 1961).

Acute disturbances of the brain-stem caused by sudden and severe vascular insufficiency can be assumed to have similar effects to transection or strong stimulation, and in this sense the above-mentioned results of animal experiments by various investigators may coincide with our clinical evidence, indicating the possible existence of an intimate relationship between acute brain-stem lesions and low-voltage fast activity, particularly with fast activity.

In these three cases, little intracerebral pathology compatible with the clinical attacks was found, probably due to too quick death, and no exact localization of the disturbance, which possibly produces low-voltage fast activity, was determined.

SUMMARY

Three exceptional cases were studied suggesting lack of dependence of slow waves in E.E.G.s from deep coma.

In these patients, the comatose state appeared suddenly, with the development of various neurological symptoms suggesting brain-stem lesions, such as myosis, upward deviation of the eye-balls, decerebrate rigidity, bilateral pathological reflexes, and marked respiratory distress. All the patients died within 30 hours of the onset of coma.

In E.E.G.s recorded at the early stages of the disease, marked low-voltage fast activity appeared diffusely in all leads in one case. In the other two, low-voltage fast activity was mixed with intermittent theta waves, even in the deep comatose states. In all cases, no appreciable low-voltage fast activity had been observed in E.E.G.s before the attack.

At necropsy, in two cases, cerebral arteriosclerosis was prominent, and marked stenosis of the vertebral and basilar arteries was present. In one of these, the basilar artery was occluded by a fresh thrombus, while in the other, a fresh softening was found in the midbrain. In the third case, neither cerebral arteriosclerosis nor significant intracerebral pathology was observed.

These electroencephalographic and clinico-pathological studies revealed the possible existence of an intimate relationship between acute severe brain-stem lesions and low-voltage fast activity, in particular fast waves, in the E.E.G.

This clinical evidence can be correlated with the results of animal experiments performed by Magoun, Batini, and others.

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