Neurophysiological assessment of alpha pattern coma

J A OBESO, MI IRAGUI, JF MARTI-MASSO, E MARAVI, JM TEIJEIRA,
N CARRERA, AND J TEIJEIRA

From the division of Neurology, Residencia Sanitaria, San Sebastian, and the Department of Clinical Neurophysiology and division of Neurology, Residencia Sanitaria, Pamplona, Spain

SUMMARY Somatosensory evoked potentials, blink reflexes, and H wave reflexes, were recorded on several days from three patients with alpha pattern coma. Coma was secondary to cardiac arrest in two cases and to brainstem infarction in one. Results are compatible with damage to the brainstem reticular formation with sparing of thalamo-cortical circuits as the main physiopathological characteristic of alpha pattern coma. This condition should not be regarded as a discrete entity when establishing the prognosis of patients in coma, since they only differ from other patients in coma from the point view of the EEG record.

Comatose patients whose electroencephalographic activity is predominantly of alpha frequency have been the subject of several reports over the last few years. Early publications correlated brainstem lesions, particularly in the pons, with the appearance of this type of EEG tracing,^{1–4} and only recently have there been reports of alpha pattern coma in patients after cardiopulmonary arrest.^{5–7} The general opinion is that alpha pattern coma has an extremely bad prognosis, but recent evidence indicates that the chance of survival is no lower in comatose patients with EEG rhythm of alpha frequency than in those in coma associated with slow EEG waves.⁸

Whether the alpha pattern represents a pathological rhythm or retained normal activity has not been elucidated. In the present paper we describe a detailed electrophysiological study of three patients with alpha pattern coma, and the neuropathological data from one of them.

Case reports

CASE 1

A 72 year old woman was admitted to hospital because she was dysarthric and complained of unsteady gait. By the time she reached hospital she was in coma and her pupils were myotic but reactive to light. Horizontal oculocephalic move-

ments were normally present, but vertical movements could not be elicited. Corneal reflexes were present bilaterally. Her extremities were diffusely rigid, and plantar responses were extensor. Five days later the patient showed spontaneous decerebrate motor posture on both sides of her body. Oculocephalic and oculovestibular reflexes were no longer present; breathing was spontaneous. On the thirteenth day in hospital her temperature rose to 41°C, with a respiratory infection. Breathing became irregular and mechanical respiration was needed. Three days later she died. The brain necropsy revealed thrombosis of the basilar artery with infarction involving the entire rostral two-thirds of the basis pontis bilaterally, with scattered ischaemic lesions in the tegmentum (fig 1). The infarct also involved both sides of the cerebellum.

CASE 2

A 55 year old man had a sustained period of cardiac arrest during a traffic accident, after which he remained unconscious. On admission, pupils were in mid position and reactive to light. His extremities were diffusely rigid, and a right extensor plantar response was noted. Corneal reflexes were depressed but present on both sides. Oculocephalic movements were normal; breathing was regular. Two days later, a right lobar pneumonia became an important hazard, and the patient died four days after the cardiac arrest. Data from necropsy could not be obtained.

Address for reprint requests: Dr JA Obeso, Augusto Linares 4, Torrelavega, Santander, Spain.

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Fig. 1 Myelin sheath stain of a transverse section through the rostral part of the pons in case 1. Extensive infarction of the basis pontis is observed, with scattered lesions appearing on the tegmentum.

CASE 3

This 48 year old man suffered a cardiac infarction and secondary cardiac arrest while coming to the hospital. On admission he was in coma, pupils were myotic, oculocephalic and corneal reflexes were normal bilaterally, and lower limbs were slightly hypotonic but tendon jerk reflexes could be elicited easily. An extensor plantar response was noted on the right. Breathing was normal. The ECG showed signs of acute anterior myocardial infarction. On the following days the pupils were clearly reactive to light, but no other sign of recovery was observed. Eight days after admission, he had a new and irreversible cardiac arrest. Necropsy was not performed.

Neurophysiological procedure

The EEG was recorded with an eight channel portable apparatus. Spin electrodes of 7 mm

diameter were used for recording of both the EEG and somatosensory evoked potentials (SEPs). They were placed according to the 10-20 system.⁹ All patients were stimulated by hand claps, light flashes, and pinching of the extremities. Electroencephalograms were recorded every two or three days, thus case 1 had eight tracings at daily intervals. Case 2 had only three recordings, and case 3 had five EEGs. Somatosensory evoked potentials were elicited by median nerve stimulation at the wrist, using a stimulus amplitude of 10% above the motor threshold for the opponens pollicis muscle. The stimulation rate was 0.5 per second. The active electrode was placed 20 mm behind C3 and C4, while the reference electrode was on the midfrontal region (F_z). One set of tests consisted of 256 responses, repeated two or three times. Analysis time was 200 ms, and the amplifiers had a flat frequency response from 2 to 1000 Hz and a high frequency

roll-off at 24 dB/octave above 1500 Hz. Latencies were measured from the stimulus to each peak, and the amplitude was defined as the height of successive positive-negative peaks. Somatosensory evoked potentials were recorded at least three times on different days. The blink reflex was obtained by supraorbital nerve stimulation over the supraorbital foramen, and the muscular responses were recorded from the orbicularis oculi muscle on both sides simultaneously. $H_{\max}$ and $M_{\max}$ waves were recorded over both soleus muscles after stimulation at the popliteal fossa as recommended by Hugon.¹⁰ Each potential represents the average of 10 responses.

Results

ELECTROENCEPHALOGRAPHY

The dominant EEG activity was within the alpha frequency at the first recording in the three patients. However none had reactivity to external stimulation, and alpha waves were diffused over frontal regions. Cases 1 and 3 deteriorated rather slowly and their EEG became progressively abnormal on the days after admission. The evolution of case 2 was very fast, and his EEG changed from alpha frequency to being isoelectric.

SOMATOSENSORY EVOKED POTENTIALS

Mean values for SEP parameters over both hemispheres are shown in table 1. The SEPs of case 1 were nearly normal on the first day, becoming progressively simplified in later recordings, along with EEG deterioration (figs 2, 3, and 4). High amplitude of N3 and N4 waves on the first days, and later attenuation of these waves were the most constant findings. A monophasic positive wave (fig 4) was eventually the only recordable response. No SEP could be evoked in any case with an isoelectric EEG tracing.

Table 1 Somatosensory evoked potentials: mean values and H/M amplitude coefficient in three patients with alpha coma

		N1	SEPs* N2	N3	H/M* %
Case 1	Amplitude (μ V)	5.0	4.5	14**	68**
	Latency (ms)	21	33	72	
Case 2	Amplitude (μ V)	4.6	4.8	Absent	59**
	Latency (ms)	20.5	31		
Case 3	Amplitude (μ V)	5.3	4.9	Absent	62**
	Latency (ms)	22.8	32		

*Average of both sides.

**More than 2.38 standard deviations from normal.

BLINK REFLEX

The R1 blink responses were normal bilaterally in the three cases, but R2 responses were delayed on both sides in cases 2 and 3, while the late response was absent bilaterally in case 1 (table 2).

Table 2 Mean latencies of R1 and R2 components of the blink reflex in three patients with alpha coma (46 responses considering both sides together)

Case	R1 (ms)	Difference between sides (ms)	Direct R2 (ms)	Consensual R2 (ms)	Difference between sides (ms)
1	10.3	0.38	Absent	Absent	
2	10.7	0.41	46.2*	48.8*	2.12
3	11.5	0.82	48.9*	52.4*	2.08

*More than 2.38 standard deviations from normal.

H REFLEX

The H/M amplitude ratio was pathologically increased in all three patients (table 1), with case 1 showing the most remarkable increment.

Discussion

It seems well established¹⁻⁶ that the neuronal population responsible for generating a wakeful type of alpha pattern lies rostral to the ponto-mesencephalic junction. Experimental data suggest that generation of alpha rhythm depends on thalamocortical circuits,¹¹ while EEG desynchronisation is not possible when the nucleus reticularis pontis oralis has been destroyed.¹²

In our three patients, SEPs had an evolution similar to those recorded from patients in coma without alpha pattern.¹³⁻¹⁴ Most reports on evoked potentials during coma agree in showing relatively normal short latency potentials and abnormal or absent long latency waves at the early stages of coma.¹³⁻¹⁶ High amplitude of SEP late waves are seen in patients with brainstem lesions,¹⁷⁻¹⁸ which seems related to damage of the brainstem reticular formation.¹⁹⁻²⁰ On the other hand high H/M ratios occur after removal of supraspinal inhibition by a lesion of the reticulospinal pathways,²¹ *et al* and the late blink reflex response (R2) is absent when the pontomedullary reticular formation is sectioned.²²

For these reasons we think that alpha pattern coma occurs from damage of the brainstem reticular formation with sufficient sparing of the diencephalic and cortical neurones to generate an alpha rhythm. Our three patients with alpha coma did not differ from a neurophysiological point of view from other patients in coma, and cortical responses may be present in patients with

Fig 2 EEG and SEPs of case 1 two days after admission. Alpha rhythm and SEPs of normal latencies and high amplitude of N3 wave were recorded.

Fig 3 The same record on case 1 on the sixth hospital day. The EEG is slower and SEPs have lost their late waves.

Fig 4 Marked EEG slowing along with a simple positive wave in both SEPs at the final stage of life in case 1.

alpha coma when the afferent pathways are spared, as in case 1 (fig 1). The failure of the EEG to desynchronise in most reported cases may be related to a lesion of the nucleus reticularis pontis oralis, but further neuropathological data from patients with alpha coma of metabolic origin are needed to establish such a correlation. Alpha coma does not invariably portend a poor prognosis, and indeed the chance of survival or residual disability is the same as in other individuals in coma.⁸ Thus alpha coma should

be only considered as a dissociation between consciousness and the EEG, because both phenomena are partially independent. Detailed neurophysiological studies along with clinical data may be useful in the evolution of patients with alpha pattern coma, overcoming the absolute limitation of EEG recording.

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