SHORT REPORT

Sleep abnormalities in traumatic apallic syndrome

Franco Giubilei, Rita Formisano, Marina Fiorini, Agnese Vitale, Jessica Faroni, Danilo Toni, Valter Santilli

Abstract

Sleep patterns in 10 patients with traumatic apallic syndrome were studied, together with 10 healthy controls matched for sex and age. All patients underwent neurological examination, brain CT, and polysomnographic recording within six months (mean 99 (SD 45) range 47–180 days) from the onset of symptoms. Clinical follow up was performed six months after enrolment in the study. Sleep patterns were recorded in nine out of 10 patients. In the tenth patient there was no rhythm resembling physiological sleep. This patient was the only one who remained in a persistent vegetative state and died before the six month follow up. The severity of neurological deficit at follow up was significantly related to the duration of coma. There was no significant difference between patients and controls with respect to sleep architecture. The time spent awake after sleep onset was longer in patients than controls. Our data highlight the presence of sleep fragmentation in traumatic apallic syndrome, which might be due to changes in brain structures responsible for sleep maintenance. The absence of sleep-wake cycles might indicate a poor outcome.

(*J Neurol Neurosurg Psychiatry* 1995;58:484–486)

Keywords: brain injury; apallic syndrome; sleep

Department of Neurological Sciences, University la Sapienza, Rome, Italy
F Giubilei
M Fiorini
A Vitale
J Faroni
D Toni

Rehabilitation Center Clinica Santa Lucia IRCCS, Rome, Italy
R Formisano
V Santilli

Correspondence to:
Dr Franco Giubilei, Dept Scienze Neurologiche, V le Dell'Università, 30, 00185 Roma, Italy.

Received 22 June 1994
and in final revised form 28 November 1994
Accepted 2 December 1994

The apallic syndrome is a severe clinical condition that may develop during the recovering phase from deep coma as a consequence of traumatic or non-traumatic acute brain damage.[1–3] According to Gerstenbrand,[1] traumatic apallic syndrome may have three stages: (*a*) the initial complex of symptoms, characterised by the appearance of both mesencephalic and bulbar acute syndromes[4]; (*b*) the true apallic syndrome, in which the patient becomes awake without being aware[5]; (*c*) the possible remission of apallic syndrome, with the gradual reintegration of damaged functions. The last stage differentiates traumatic apallic syndrome from persistent vegetative state, a condition that should be diagnosed only after several months of impairment of consciousness, when clinical recovery is likely to be excluded.[6 7] Therefore, as our patients were evaluated during the first months after their brain injury, we decided to use the term traumatic apallic syndrome instead of persistent vegetative state. Traumatic apallic syndrome is a chronic decerebrate state caused by either a lesion or a functional block of corticosubcortical, diencephalic, or brainstem structures.[8] Although brainstem cell populations are thought to play a crucial part in sleep regulation, no data are available on sleep architecture in traumatic apallic syndrome. On the other hand, previous studies showed the prognostic value of EEG sleep patterns in post-traumatic comatose patients, as well as the reliability of standard EEG findings as a prognostic index in patients with traumatic apallic syndrome.[9 10] The aim of our study was to determine the sleep morphology and its clinical correlations in patients with true traumatic apallic syndrome or during its remission.

Materials and methods

We studied sleep patterns in 10 patients (seven men and three women, mean age 28 (SD 12) range 15–55 years) with traumatic apallic syndrome, admitted to hospital at the rehabilitation centre, Clinica Santa Lucia, IRCCS of Rome. All patients had been in intensive care, because of their status of coma, due to severe brain injury. Duration of coma was considered as the total period of unconsciousness from coma onset until the first convincing sign of contact with the environment (optic fixation following eye movements, emotional responses, answer to simple orders, beginning of verbal contact). On admission (mean 99 (SD 45), range 47–180 days from head injury) all patients underwent brain CT (table 1), polysomnographic recording, and neurological functional evaluation (by RF), graded according to the Barthel index and Glasgow outcome scale.[11 12] The same tests were repeated after six months by the same neurologist. Table 1 shows the neurological status on admission and at six month follow up.

Patients with a history of previous neurological disease or with severe pulmonary, hepatic, or renal complications were excluded. Patients were given standard

Table 1 Clinical and brain CT data of 10 patients with head injury

Patient	*Age/sex (y)*	*Coma duration (days)*	*Barthel index (1)*	*Barthel index (2)*	*GOS (1)*	*GOS (2)*	*Brain CT*
1	20/M	30	60	100	SD	GR	No densitometric lesions
2	20/M	120	30	45	PVS	SD	Corticosubcortical atrophy
3	15/M	120	35	70	SD	MD	R frontal hygroma; L frontal hypodensity
4	36/F	60	30	75	PVS	MD	Hydrocephalus
5	28/M	30	30	45	PVS	SD	R temporoparietal hypodensity
6	27/M	120	35	35	SD	SD	R frontal hygroma; R capsular hypodensity
7	24/F	60	20	70	PVS	MD	Corticosubcortical atrophy
8	28/M	120	20	70	PVS	MD	R frontal hygroma
9	55/F	30	35	80	SD	GR	R frontotemporal hypodensity
10	57/M	150	15	Dead	PVS	Dead	L temporo-occipital hypodensity

GOS = Glasgow outcome scale; PVS = persistent vegetative state; SD = severe disability; MD = moderate disability; GR = good recovery; (1) = at admission; (2) = at six months follow up; R = right; L = left.
Barthel index score from 15 (maximum functional deficit) to 100 (no functional deficit).

treatments as required, when possible avoiding drugs known to modify sleep patterns. Five patients took carbamazepine because of their seizures. The polysomnographic investigations were performed with a mobile recording system (Oxford Medilog 9000) that allowed continuous registration on eight channels. The 12-hour recording started at 7.00 pm. Four electroencephalographic (F3-C3; P1-O1; F4-C4; P4-O2) and two electro-oculographic derivations were installed by chloride silver cup electrodes. The ECG and EMG of submental muscles were also recorded simultaneously. The evaluation of sleep recordings was done manually from the Oxford screen, according to the international criteria of Rechtschaffen and Kales, with 32 second epochs.[13]

The following variables were evaluated to describe sleep patterns: (*a*) total sleep time—that is, recording time minus time spent awake, in minutes; (*b*) NREM sleep, in minutes; (*c*) REM sleep, in minutes; (*d*) percentage of each sleep stage in relation to total sleep time; (*e*) REM:NREM ratio; (*f*) REM latency—that is, the time from sleep onset to the first epoch of REM sleep; (*g*) number of REM phases; (*h*) number of awakenings; (*i*) number of awakenings from mid-REM; (*j*) time spent awake after sleep onset, in minutes. With the same environmental conditions, we studied sleep patterns in 10 healthy controls, matched for sex and age (seven men and three women, mean age 29 (12), range 16–52 years).

The results were evaluated by Student's unpaired *t* test, χ^2 test, and Spearman correlation coefficient.

Results

Table 2 gives mean values of the sleep variables of patients with traumatic apallic syndrome and controls. Typical polysomnographic sleep patterns at night were recorded in nine out of 10 patients. In the other patient we did not see any rhythm resembling those of the physiological sleep pattern. This patient was the only one who remained in a persistent vegetative state and who died before the six month follow up.

There was no significant difference between patients and controls with respect to sleep architecture. The time spent awake after sleep onset was longer in patients, however, than in controls (table 2). This is also emphasised by the number of awakenings (9·89 (SD 6·33) in patients and 4·1 (SD 1·97) in controls; $p < 0·01$, Student's *t* test) and by their duration (table 2).

Although the percentage of REM sleep time was the same in patients and controls (table 2), we found a significant increase in the short REM period (less than 10 minutes) in the patient group. Twelve of the 35 (34·3%) REM periods recorded in patients lasted less than 10 minutes, whereas the short REM periods were five out of 42 (11·9%) in the control group ($p < 0·05$, χ^2 test). Furthermore, patients with traumatic apallic syndrome showed a mean of 2·56 (SD 2·19) awakenings from mid-REM sleep per night *v* a mean of 0·9 (SD 1·2) awakenings for the controls ($p < 0·05$, Student's *t* test).

At six month follow up, the severity of neurological deficit, evaluated by the Barthel index, was significantly related to the duration of coma (table 1; $p < 0·03$, Spearman correlation). There was no correlation of sleep patterns with clinical outcome, evaluated by Glasgow outcome scale and Barthel index, or with the neurological deficit on admission.

Discussion

Our data show that patients with traumatic apallic syndrome have an increase in time

Table 2 Quantitative sleep variables of nine patients with brain injury and 10 control subjects

	Patients (n = 9) Mean (SD)	*Controls (n = 10) Mean (SD)*
TST (min)	349 (124)	382 (67)
NREM (min)	284 (112)	305 (62)
REM (min)	65 (23)	78 (16)
REM (% of TST)	18·68 (5·58)	20·34 (4·34)
Stage 1 (% of TST)	6·39 (4·86)	7·59 (2·18)
Stage 2 (% of TST)	53·58 (9·01)	54·88 (5·19)
Stage 3–4 (% of TST)	21·30 (8·7)	17·20 (5·19)
REM: NREM ratio	0·23 (0·08)	0·25 (0·07)
REM latency (min)	79 (40)	71 (25)
No REM phases	3·89 (1·17)	4·20 (0·92)
No of awakenings	9·89 (6·33)	4·10 (1·97)**
No of awakenings >2 min	7·33 (4·92)	2·70 (2·16)**
No of awakenings <2 min	2·56 (2·65)	1·40 (0·84)
No of awakenings from mid REM	2·56 (2·19)	0·90 (1·20)*
WASO (min)	77 (76)	25 (18)*

In one patient no sleep pattern was found.
TST = total sleep time; WASO = time spent awake after sleep onset.
*p <0·05; **p <0·01, controls *v* patients, Students *t* test.

spent awake after sleep onset, because of a higher number of awakenings in both REM and NREM sleep. It could be argued that this fragmentation of night sleep depends on the hospital environment. A similar environment did not influence the sleep pattern of our controls, however, even though recording was carried out on the first night. A potential problem in our method is the lack of records of breathing during sleep, so sleep apnoeas could have contributed to the sleep disturbance in our patients. We did not find any breathing disorder during sleep, however, when patients were observed directly during the recordings. Furthermore, a feature of the patients' nocturnal awakenings was their long duration. Because we did not monitor naps, it is possible that frequent or prolonged daytime naps contributed to nocturnal sleep disturbance.

On the other hand, although the specific mechanisms that are responsible for sleep maintenance are not understood, the pons, midbrain, and basal forebrain are probably involved and morphological changes in these brain regions could cause sleep fragmentation. This is supported by previous studies showing a sleep fragmentation in patients with progressive supranuclear palsy.[14 15] Pathological examination in this disease showed degenerative changes in several brainstem structures presumed to be involved in sleep regulation, such as the locus ceruleus, periaqueductal grey matter, and pontine tegmentum.[16] Therefore, despite the limitations of our study, the sleep fragmentation in our patients might have been determined by either a lesion in or a functional block of corticosubcortical, diencephalic, or brainstem structures, which are usually involved in traumatic apallic syndrome.[5]

Previous reports suggest that the absence of cyclic EEG sleep patterns in post-traumatic comatose patients is an unfavourable prognostic sign.[9 17] Rumpl *et al* found that in patients with traumatic head injuries who developed secondary brainstem dysfunctions, an unfavourable prognosis was indicated by the disappearance of sleep or sleep like activities.[18] This would apply in our patient without EEG sleep patterns who died before the six month follow up. This absence of patterns suggests damage to the diencephalic or mesencephalic system which, unfortunately, we cannot confirm in our patient as he did not undergo MRI.[19 20]

In conclusion, these results indicate that in traumatic apallic syndrome there are no specific sleep patterns and there is a sleep fragmentation that might be due to changes in brain structures responsible for sleep maintenance. The absence of sleep-wake cycles during the first period of traumatic apallic syndrome might be a prognostic index of poor outcome. A larger study, combined with MRI, is required.

We thank Professor Cesare Fieschi for his comments on the manuscript. The study was supported by a grant from the Rehabilitation Center "Clinica Santa Lucia" IRCCS of Rome.

1 Gerstenbrand F. *Das traumatische apallische syndrom*: New York: Springer-Verlag, 1967.
2 Higashi K, Hatana M, Abiko S, Ihara K, Katayama S, Wakuta Y, Okamura T, Yamashita T. Five-year follow up study of patients with persistent vegetative state. *J Neurol Neurosurg Psychiatry* 1981;**44**:552–4.
3 Levy DE, Knill-Jones RP, Plum F. The vegetative state and its prognosis following non traumatic coma. *Ann NY Acad Sci* 1978;**315**:293–306.
4 Plum F, Posner JB. *The diagnosis of stupor and coma.* 3rd ed. Philadelphia: Davis 1980:373.
5 Jennet B, Plum F. Persistent vegetative state after brain damage. *Lancet* 1972;i:734–7.
6 Bricolo A, Turazzi S, Feriotti G. Prolonged post-traumatic unconsciousness. *J Neurosurg* 1980;**52**:625–34.
7 Sazbon L, Grosswasser Z. Prolonged coma, vegetative state, post-comatose unawareness: semantics or better understanding? *Brain Inj* 1991;**5**:1.
8 Pagni CA. The prognosis of head injuries in patients in state of coma with decerebral posture. Analysis of 471 cases. *J Neurosurg Sci* 1973;**17**:289–95.
9 Lessard CS, Sances A jr, Larson SJ. Period analysis of EEG signals during sleep and post-traumatic coma. *Aerospace Medicine* 1974;**45**:664–8.
10 Strnad V, Strnadovà V. Long-term follow-up EEG studies in patients with traumatic apallic syndrome. *Eur Neurol* 1987;**26**:84–9.
11 Mahoney F, Barthel DW. Functional evaluation: the Barthel Index. *Maryland State Medical Journal* 1965;**14**: 61–5.
12 Jennet B, Bond M. Assessment of outcome after severe brain damage: a practical scale. *Lancet* 1975;i:480–4.
13 Rechtschaffen A, Kales A. *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. US Public Health Service.* Washington: Government Printing Office, 1968:204.
14 Gross RA, Spehlmann R, Daniels JC. Sleep disturbances in progressive supranuclear palsy. *Electroencephalogr Clin Neurophysiol* 1978;**45**:16–25.
15 Aldrich MS, Foster NL, White RF, Bluemlein L, Prokopowicz G. Sleep abnormalities in progressive supranuclear palsy. *Ann Neurol* 1989;**25**:577–81.
16 Steele JC, Richardson JC, Olszewski J. Progressive supranuclear palsy. *Arch Neurol* 1964;**10**:333–59.
17 Bricolo A, Turazzi S, Faccioli F. Combined clinical and EEG examinations for assessment of severity of acute head injuries. *Acta Neurochir Suppl (Wien)* 1979;**28**: 35–9.
18 Rumpl E, Lorenzi E, Hackl JM, Gerstenbrand F, Hengl W. The EEG at different stages of acute secondary traumatic midbrain and bulbar brain syndromes. *Electroencephalogr Clin Neurophysiol* 1979;**46**:487–97.
19 Naquet R, Vigouroux RP, Choux Baurand C, Chamant JH. Etude electroencephalographique des traumatismes craniens recents dans un service de reanimation. *Rev Neurol* 1967;**117**:512–3.
20 Bricolo A, Gentilomo A, Rosadini G, Rossi GF. Akinetic mutism following cranio-cerebral trauma. Physiopathological considerations based on sleep studies. *Acta Neurochir (Wien)* 1968;**18**:67–77.