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EEG and sleep in aged hospitalized patients with senile dementia: 24-h recordings

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Summary. Polygraphic recordings of wake and sleep were performed on 10 partly bed-ridden, severely deteriorated patients with senile dementia. Compared with healthy elderly persons these subjects showed less SWS (slow wave sleep, characterized by high amplitude, slow EEG waves), less REM sleep (rapid eye movement sleep, usually accompanied by dream activity) and poorly organized stage 2 sleep (no sleep spindles, i.e. phasic EEG activity with a frequency of 12-14 Hz). Six of the 10 patients had no dominant alpha rhythm during wakefulness; this seemed to be related to their more deteriorated clinical state, to still less SWS and REM sleep and more time spent in stage 2. The basic NREM-REM cycle of sleep, i.e. the regular alternation between non-REM- and REM-periods, could still be distinguished, however, and showed similar average temporal characteristics as in healthy old and younger people. Similarly, although sleep was severely fragmented in most patients and many sleep episodes occurred during the day, the day-night alternation of wakefulness and sleep was maintained in the sample as a whole.

With advancing age, sleep is subjectively judged to be less deep and less refreshing, and interruptions are more frequent. Objectively there is less slow wave sleep (SWS), particularly stage 4, and less rapid eye movement (REM) sleep. The polygraphic trace shows a decreased overall amplitude and slower and less pronounced spindles, with long periods of theta activity[12,22]. A high percentage of sleep-related respiratory disturbances may contribute to the more interrupted nature of sleep[2]. Furthermore the alpha waves during wakefulness are found to be decreased in amplitude, slower in frequency and fewer in number. There is a progressive increase in slow wave activity thought to be associated with brain deterioration and intellectual impairment[13,14].

Senile dementia is a progressively deteriorating disorder which appears to be caused by one or both of two main diseases: a) vascular dementia (arteriosclerotic dementia, multiple infarct dementia), where there are multiple infarcts with subsequent softening of the brain; b) SDAT (senile dementia of the Alzheimer type) where on post mortem examination of the brain a larger than average quantity of neuritic (senile) plaques and neurofibrillary tangles are found. Brain atrophy can be seen using the computerized tomogram (CT) brain scan which aids diagnosis, but SDAT is reliably diagnosed only post mortem.

The few studies carried out so far with these types of patients[5,16,17] have shown that they have further decrements in SWS, REM sleep and total sleep time if compared with normal elderly, but these studies did not attempt to distinguish between different types of dementia with respect to the EEG patterns and sleep behavior.

The present study investigated aspects of the EEG of wake and sleep in relation to some clinical parameters.

Materials and methods

Ten partly bed-ridden patients from the Geriatric Clinic of the Kantonsspital, Basel, were studied after

Table 1. Clinical data of 10 SD patients

Patient No.	1	2	3	4	5	6	7	8	9	10
Age	76	90	79	82	76	74	80	90	85	70
Sex	f	f	f	m	f	m	m	m	m	m
Dementia type	mix	mix	SDAT	vasc.	mix	SDAT	SDAT	SDAT	mix	mix
Dementia rank	9	5	1	3	2	8	7	6	10	4
Health rank	3	6	5	2	4	9	7	8	10	1
Wake EEG	Deltaα	Deltaα	Deltaα	Deltaα	Deltaα	α	α	α	α	Deltaα
Hospitalized since	08/79	02/77	04/79*	04/75	10/77*	08/79	05/73	12/77	02/77	02/81*

Rank systems: 1 = worst condition; 10 = least ill; * = now deceased.

consent from their nearest relatives had been obtained. There were 4 females and 6 males in the age range 70-90 (mean age 80). All were free from centrally acting medication except for 1 who routinely received diazepam 2 mg/day. The subjects did not constitute a homogeneous group clinically or behaviorally; they ranged from anxious and active, verbal and sometimes coherent and capable of feeding themselves to inert and non-verbal (table 1).

Patients were restricted to their beds for a 24-h period which began at about 15.00 h. Electroencephalogram (EEG), eletrooculogram (EOG), electromyogram (EMG) from the chin and heart rate were recorded and the recordings were scored visually and manually as closely as possible into the stages of Rechtschaffen and Kales[18]. Day-time and night-time wake and sleep and the NREM-REM cycle (see Brezinova[1], Feinberg[4] and Spiegel[21]) were investigated.

Results

1. Description of the EEG and polygraphic sleep stages

Visual inspection of the recordings revealed 2 dominant rhythms in the EEG of both waking and sleeping: one that looked like alpha and the other that looked like delta.

a) Awake. Six patients had no dominant alpha rhythm. The EEG showed continuous 1-2 Hz high amplitude activity with a superimposed and intermingled low amplitude activity (fig. 1, upper part). While these tracings looked similar to those usually encountered in SWS, they were not the same since sometimes the patient was alert and moving with eyes open and often the muscle tone was high. Figure 3, upper part, shows stage 4 sleep from the same patient and the differences can be clearly seen. The lower part of figure 1 shows the EEG from one patient while awake

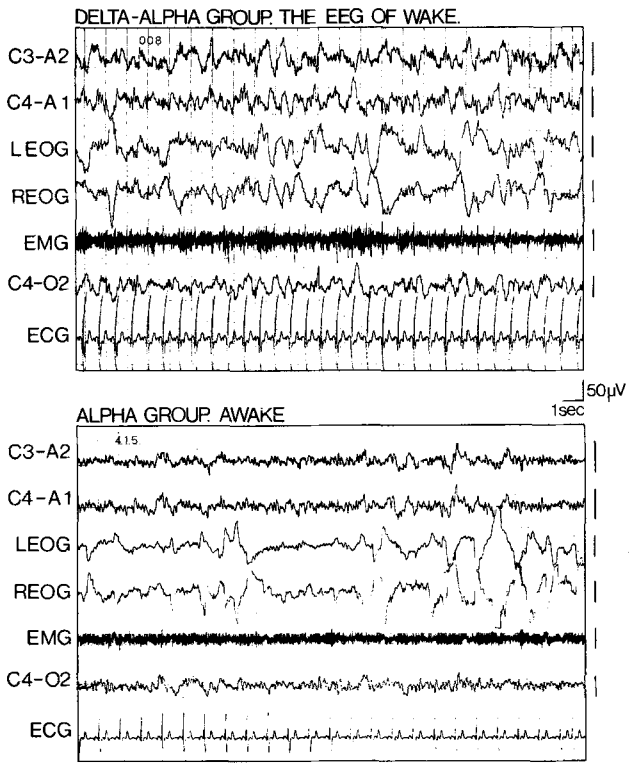

Figure 1. The polygraphic trace of wake of a patient in delta-alpha group (upper part) and alpha group (lower part). While the alpha subject shows a somewhat slow but otherwise unconspicuous EEG pattern, the delta-alpha subject displays large amounts of slow activity in all three EEG channels.

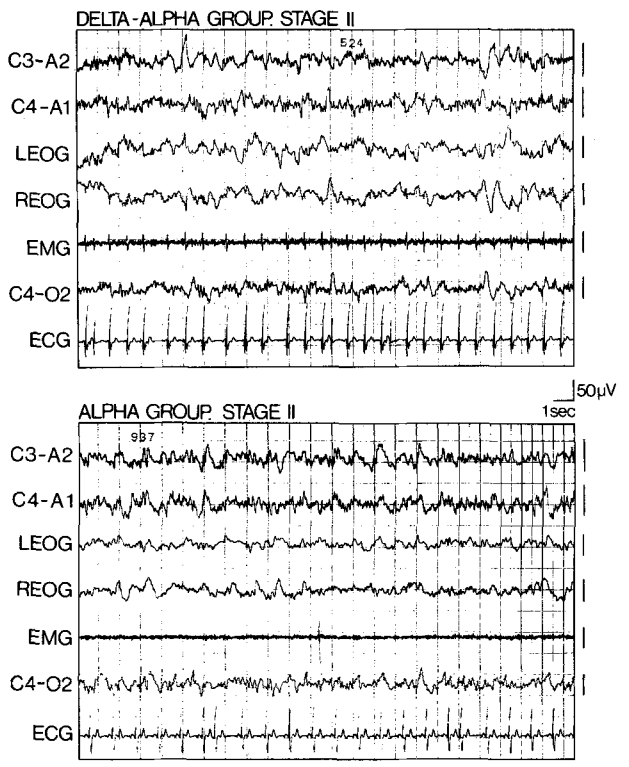

Figure 2. The polygraphic trace of stage 2 of a delta-alpha (upper part) and of an alpha (lower part) subject. No spindles are seen, but the gross differences between alpha and delta-alpha subjects present in wake patterns have disappeared.

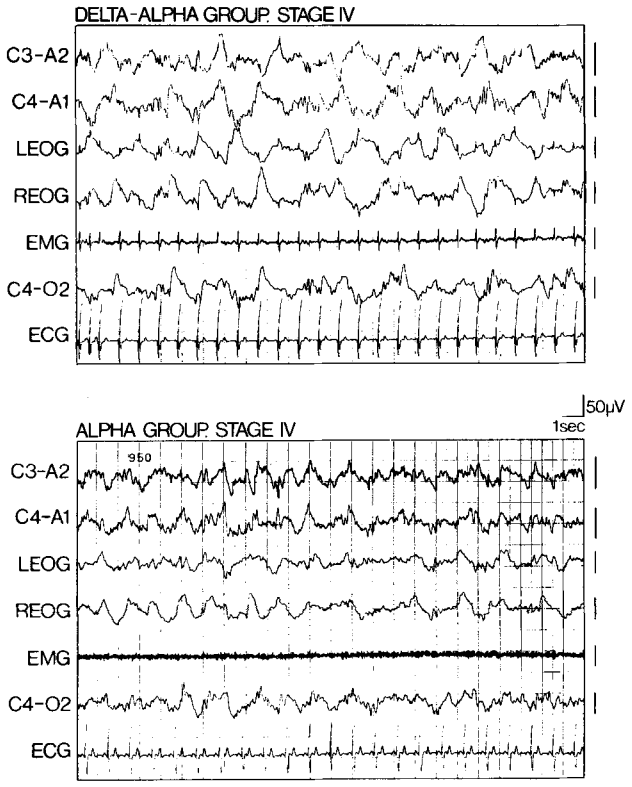

Figure 3. The polygraphic trace of stage 4 of a delta-alpha (upper part) and of an alpha (lower part) subject. From visual inspection (and from automatic analysis, to be reported separately) no gross differences are present.

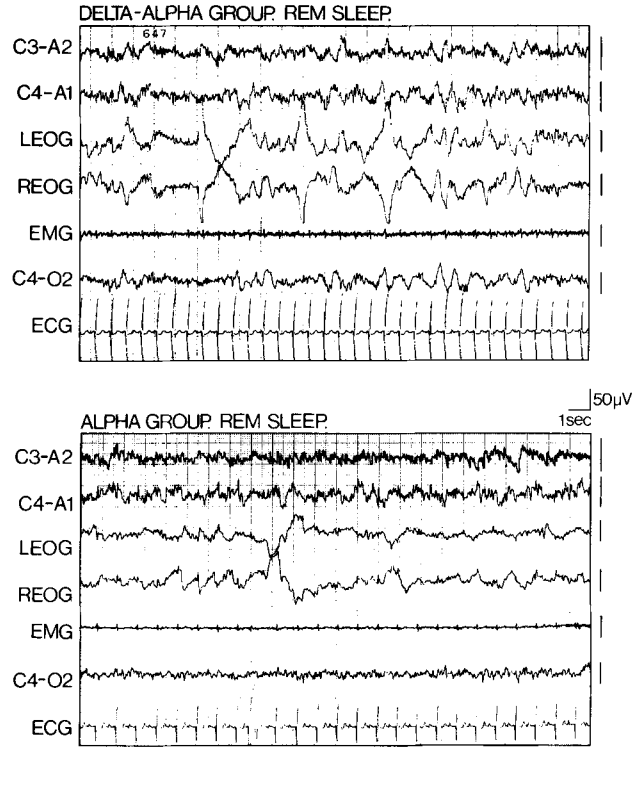

Figure 4. The polygraphic trace of REM sleep of a delta-alpha (upper part) and of an alpha (lower part) subject. REM sleep of all patients looked similar to that of normal subjects.

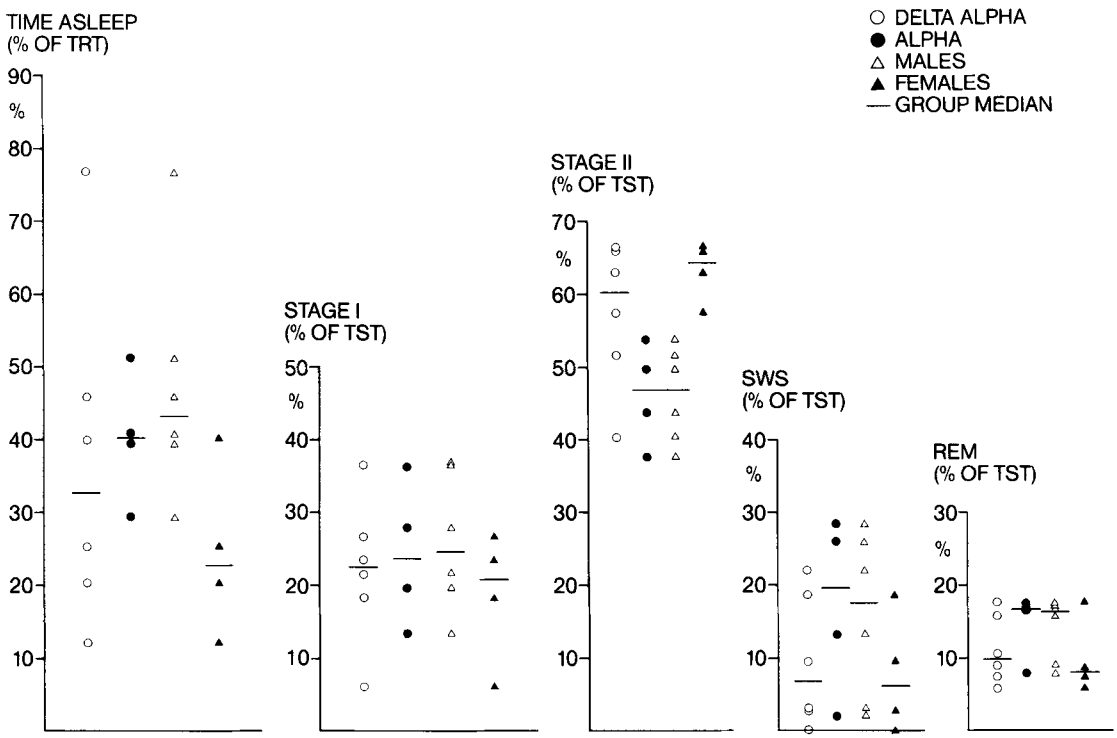

Figure 5. Awake and sleep stages (Percentages). Graphic comparison between delta-alpha and alpha subjects (circles) and between females and males (triangles). All 4 females were delta-alpha subjects and these had more stage 2, less SWS and less REM sleep. No formal statistics were applied due to the small number of subjects studied. TRT = total recording time; TST = total sleep time.

who did not have the slow activity. This record resembled a 'waking' EEG of a normal subject with almost continuous 8–9 Hz alpha rhythm. Age cannot account for this difference since the patient with the slow activity was 82 and the other 85. Both were male.

b) Stage 2. The usual distinguishing features of stage 2, i.e. spindles and K-complexes, were absent in all patients (fig. 2). This made it difficult to distinguish between waking, stage 1 and stage 2. Sleep was designated stage 2 when the patient showed no motor activity and was behaviorally asleep, and slow waves, though not enough for stage 3, were sometimes present and the characteristics of REM sleep were absent.

c) SWS. One patient had no SWS but the others showed SWS tracings similar to normal subjects, albeit the delta waves were slower and had a 'broken' appearance (fig. 3).

d) REM sleep. All patients had some REM sleep. Although there were fewer rapid eye movements and no saw-tooth waves, the records looked similar to those of normal subjects (fig. 4).

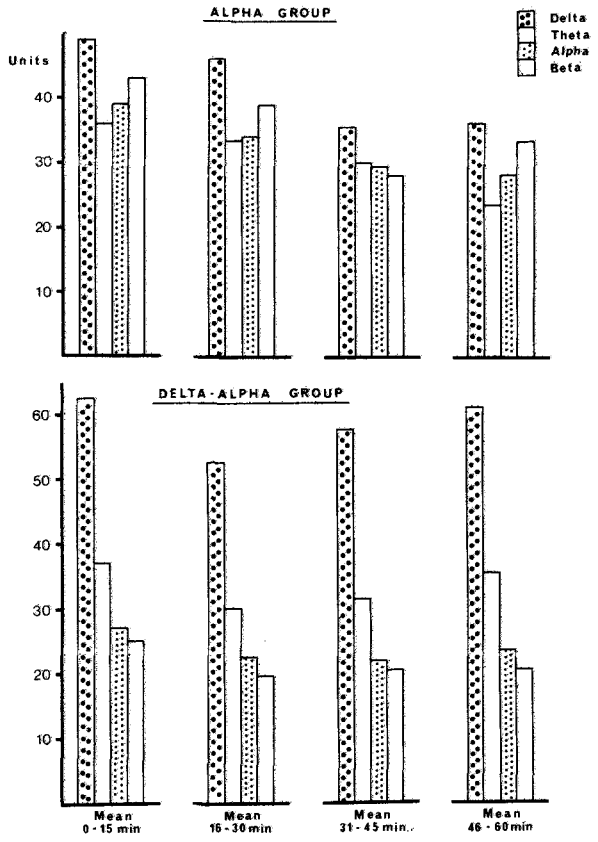

Figure 6. EEG analysis of 2 representative 'alpha'- and 'delta-alpha'-subjects. 1 h of wake EEG was analyzed off-line by means of an Ahrend von Gogh filter integrator; delta-alpha-subjects show a clear excess in delta activity. Units are the arbitrarily calibrated integrator output in mV^2 per min, averaged over 15 min (details of this will be published separately).

2. Time awake and in stages of sleep

The mean total recorded time was 22 h 38 min (table 2), and in spite of the continuous bed rest the median time spent asleep including stage 1 was about 9 h. On average, the males fared better than the females having more SWS and more REM sleep. Individual differences were considerable (fig. 5).

3. Delta-alpha and alpha groups

The 6 patients with pronounced slow activity were called the 'delta-alpha group' and the remaining 4, the 'alpha group'. The distinction was made following visual inspection of the EEG and later confirmed by using automatic quantitative EEG analysis (fig. 6). Despite the lack of great differences in total sleep time, the delta-alpha group had less SWS, less REM sleep and more time in stage 2 (fig. 5). This cannot be attributed to age, as the mean age of the delta-alpha group was lower than that of the alpha group.

4. Severity of illness

Patients were assigned (H.B.S., ignoring the polygraphic sleep data) a rank according to the severity of their illness (the lowest number signified the worst condition). There were 2 ranking systems which referred to: a) severity of dementia, b) condition of general health. The delta-alpha group had a lower mean rank than the alpha group. The female patients, all of whom were in the delta-alpha group, had a

Table 3. General health and dementia ranks

	Mean rank Dementia	General health
Females	4.3	4.5
Males	6.3	6.2
Deltaα ss	4.0	3.5
α Subjects	7.8	8.5

Lower values: worse condition.

Table 2. Sleep data of 10 SD patients

Patient No.	1	2	3	4	5	6	7	8	9	10
Total recorded time (min)	1363	1341	1349	1405	1314	1308	1314	1395	1408	1237
Total sleep time (min)	348	538	165	1082	267	387	537	554	724	570
Stage 1 (min)	64	144	39	236	17	77	151	203	98	209
Stage 2 (min)	231	339	109	438	154	193	203	298	317	294
Stage 3+4 (min)	33	15	0	240	50	61	153	11	188	7
REM (min)	20	40	18	171	47	68	92	43	122	52
Shifts to 0+1 from stage 2	46	113	26	131	11	39	18	168	54	117
Shifts to 0+1 from REM	4	7	5	47	4	5	30	11	21	17
Total shifts to 0+1	56	122	31	195	16	45	55	184	95	137

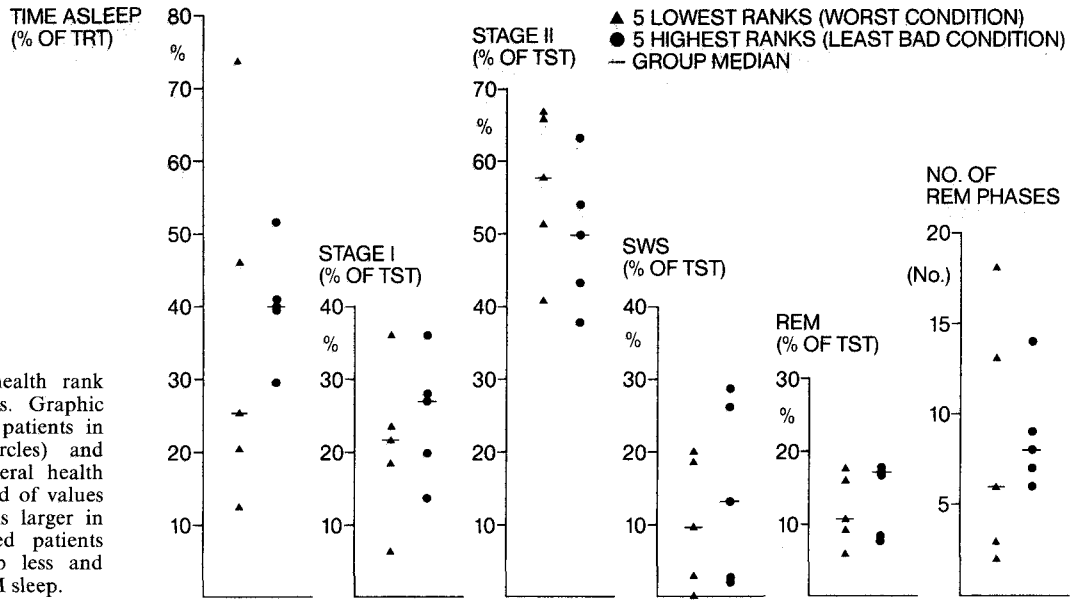

Figure 7. General health rank and sleep parameters. Graphic comparison between patients in relatively better (circles) and worse (triangles) general health conditions. The spread of values in most parameters is larger in the more deteriorated patients who tended to sleep less and spent less time in REM sleep.

lower mean rank than the males in both rank system (table 3).

The more severely ill patients tended to sleep less (fig. 7; exception: patient No. 4) and to spend less time in REM sleep. No difference in sleep parameters was apparent between more or less severely demented patients.

5. Dementia diagnosis

One patient (No. 4) was diagnosed as having purely vascular dementia, 4 were SDAT and there were 5 mixed cases. Table 4 shows that the vascular dementia patient slept much more than the others and had the most SWS and REM sleep. There were no striking differences between the SDAT and mixed cases, although the SDATs tended to sleep less, have more REM sleep and stage 1 and less stage 2. The 1 vascular dementia case plus 4 out of the 5 mixed cases had the wake delta-alpha pattern. 3 out of the 4 SDAT cases had the alpha pattern. The delta-alpha activity might then be associated with vascular dementia, either alone or mixed with SDAT.

6. The NREM-REM cycle

The NREM-REM cycle of healthy old people does not deviate greatly from the pattern seen in young adults[1,21]. The median values (fig. 8) show that the NREM-REM cycle, on average, is also maintained in the SD patients, although the spread of values is very high.

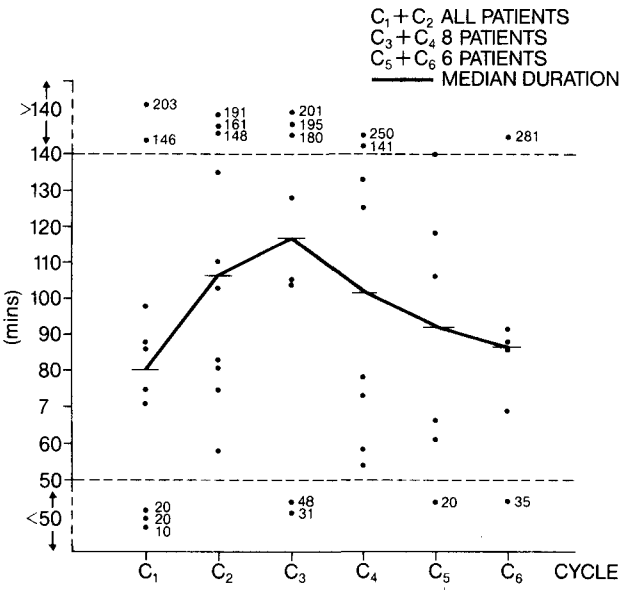

Figure 8. NREM-REM cycle duration of 10 SD patients. Despite the large spread of NREM-REM cycle durations with several very long and very short times, the median values still indicate average cycle times very similar to those of normal elderly and middle-aged subjects. Estimation of cycle duration as described[21]. C_1 etc means NREM-REM cycle No. 1 etc, as calculated from definite sleep onset.

Discussion and conclusions

1. Wake EEG. Slow wave activity in the wake EEG progressively increases with aging[12]. This is unrelated to the slow waves of sleep, since it reflects tissue injury whereas the latter represent the normal physiological state attained during sleep[16]. Also the wake slow activity is associated with greatly reduced cerebral metabolism and blood flow not seen in SWS[23].

Of the 4 patients who, while awake, did not have this slow activity, 3 were diagnosed SDAT and were also ranked as being the least severely ill. Slow activity appearing during waking which was not responsive to external stimulation might then reflect the presence of vascular dementia and would indicate that the brains of these individuals were very severely damaged. All

Table 4. Dementia diagnosis and sleep parameters

Dementia type	N	Asleep (% of TRT)	Stage 1 (% of TST)	Stage 2 (%)	SWS (%)	REM (%)	No. of REM phases	Shifts to 0+1 ./. TST
Vascular	1	77.0	21.7	40.4	22.1	15.8	18	0.18
SDAT	4	30.6	27.0	51.9	10.9	13.2	6.5	0.19
Mixed	5	36.1	20.3	56.5	11.9	10.9	8.4	0.16

patients were in a far too deteriorated condition to complete any test for mental function.

2. Sleep spindles. Sleep spindles are thought to play an active role for sleep maintainance[20]. They are not well formed in the elderly[7], and frequencies are lower than in young adults[8]. The changes in spindle activity in senescence are thought to be analogous to changes in the alpha activity during waking[4,5]; however, none of our SD patients showed spindles although 4 of them did have alpha activity.

Decreased or the absence of spindle activity has been observed also in mentally retarded children[19], and hyperkinetic children[11], with an increase in spindle activity when the patients improved with treatment. In Down's syndrome, patients were found to show fewer spindles, atypical K-complex, less, often poorly organized alpha rhythm[6], and sometimes no spindles at all[3]. Initial recordings after cerebrovascular accidents showed spindle activity to be very poor or absent, and if the spindle activity increased on subsequent recordings, then this was found to correlate with good recovery[9,10]. In 10 patients with senile dementia studied by Prinz et al.[15], spindles were absent in 2 and considerably reduced in the others.

The absence of spindles in stage 2 sleep of the adult person would thus appear to be linked with deteriorated mental functions and cerebrovascular malfunctions.

3. Sleep stages. The SD patients had impaired sleep compared with healthy old people, as demonstrated by the low percentages of SWS and REM sleep. This was in agreement with other studies. The delta-alpha patients tended to have less SWS and less REM sleep than the alpha patients, and the presence of the wake

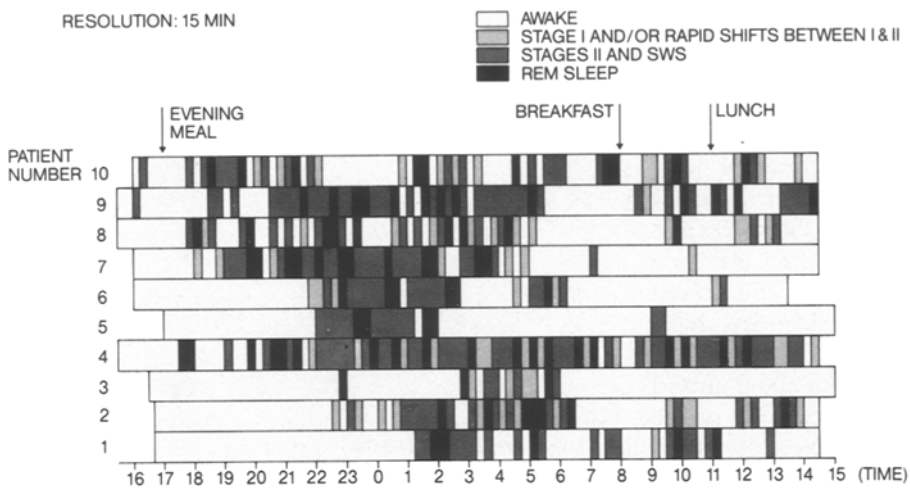

Figure 9. Distribution of sleep stages of 10 SD patients. Sleep was very fragmented in 7 of 10 subjects. Again, individual variations with regard to sleep duration and distribution within the time recorded were large. Resolution 15 min, means that, within 15-min intervals, the prevailing stage was determined and the interval then assigned to this dominating stage.

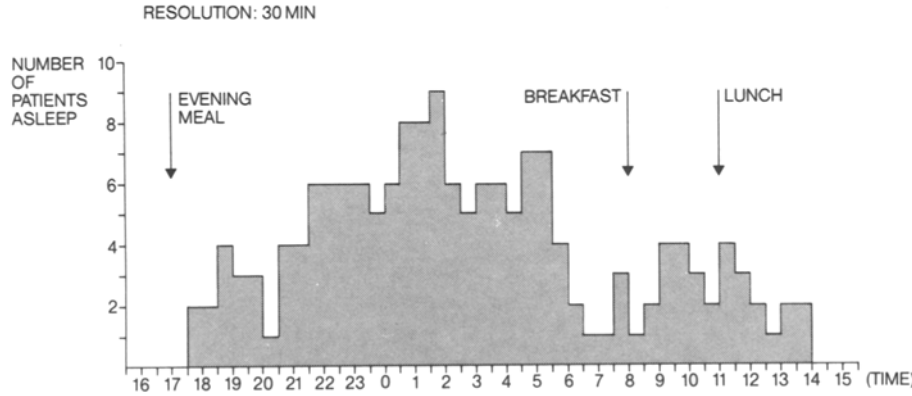

Figure 10. Distribution of sleep in 10 SD patients. For the sample as a whole, the day-night rhythm of wakefulness and sleep could still be determined. Meals had a brief arousing effect. Stages 2, SWS and REM were counted as 'sleep', and the procedure to assign 30-min intervals to wake and sleep was analogous to the one used for fig. 9.

slow EEG activity might indicate particularly severe deterioration of the brains of these individuals. Thus whatever damage has occurred to cause the appearance of these slow waves also seems to affect sleep quality.

4. Rhythmic aspects of sleep. In contrast to the great abnormalities in other sleep parameters, the NREM-REM cycles, on average and particularly in the males, did not show great deviation from the normal pattern. Although there was wide variation in individual NREM-REM cycle duration, this ultradian rhythm seems to be maintained in patients whose brain is no longer capable of producing synchronized alpha activity. Sleep, as might be expected, was severely fragmented in most patients (fig. 9), with numerous shorter and longer sleep episodes occurring during the day. However, the day-night cycle of wakefulness and sleep could still be recognized in the group of patients as a whole (fig. 10).

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Short Communications

Degraded monoterpenes from the opisthobranch mollusc *Melibe leonina*[1]

S.W. Ayer and R.J. Andersen[2]

Departments of Chemistry and Oceanography, University of British Columbia, Vancouver, B.C. V6T1W5 (Canada), July 20, 1982

Summary. 2,6-dimethyl-5-heptenal (**1**) and 2,6-dimethyl-5-heptonic acid (**2**) were isolated from skin extracts of the nudibranch *Melibe leonina*. The aldehyde **1** is responsible for the pleasant odour of the animals.

The dendronotid nudibranch *Melibe leonia* (Gould, 1852) has one of the most unusual feeding behaviors of any member of the phylum mollusca. Unlike other nudibranchs, *M. leonina* is not a predator of sessile bottom dwelling animals, rather, it feeds upon zooplankton by majestically sweeping the sea with its large oral hood[3].

Our chemical studies[4] on *M. leonina* were prompted by a report that the nudibranch's primary defense is an odifer-