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The usefulness of sleep and sleep deprivation as activating methods in electroencephalographic recording

Contribution to a long-standing discussion

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Sedated sleep and sleep deprivation are commonly used methods to increase the diagnostic yield of the electroencephalogram (EEG), especially in the evaluation of people with epilepsy, but the rate of activation achieved by them is controversial, as is the issue of whether it is sleep itself, or sleep deprivation which is responsible for their alleged efficacy. We retrospectively studied the EEGs of epileptic patients, examined in our laboratory, who, after having undergone an inconclusive initial routine recording, had then been examined with a second recording. This was after either: (1) sleep deprivation with evidence of drowsiness in the recordings, (2) sleep deprivation without drowsiness (indicative of the effect which sleep deprivation per se has in eliciting abnormal patterns), or (3) drug-induced sedation. The activation rates found were (1) 22.5%, (2) 24% (22.6% for sleep deprivation collectively, regardless of the presence or not of subsequent drowsiness) and (3) 27% respectively. Only the sleep deprivation rate was statistically different from the 9.6% increased rate of abnormal patterns elicited by the simple repeating of a second routine recording, while the rate of drug-induced sleep was not. Although, sleep deprivation appeared to be more effective as an activating method of EEG compared with sedated sleep, no conclusions could be drawn about which stage of sleep, wakefulness or drowsiness, is primarily responsible for the method's efficacy.

Key words: abnormal EEG; sleep; sleep deprivation; drug-induced sleep; activating methods.

INTRODUCTION

When a routine EEG fails to reveal epileptic activity, especially in patients with a strong clinical evidence of epilepsy, a number of activation methods, such as recording after sleep deprivation or drug-induced sleep, may increase the diagnostic yield of the EEG[1–7]. Despite their long-standing use there is still controversy regarding these methods. Some authors have proposed that sleep deprivation per se, with its stressful effect on the patient, is the true activator[6, 8, 9]. Others have attributed the increase in epileptic discharges that occur during sleep to sleep itself[10], regardless of whether this sleep occurs as a spontaneous nap[11], is induced after sedation[12–14], or ensues after 24-hour sleep deprivation[15–17]. Others have emphasized the increased probability of epileptic discharges emerging with repeated recordings[12, 18, 19]. As a consequence, a clear distinction between the effects of sleep deprivation, drug-induced sleep and simply repeated routine recordings can be difficult to make.

In order to compare the relative efficacy of activation methods of the EEG, such as recording after sleep deprivation and drug-induced sleep, we have conducted a retrospective study of the EEG records of the patients examined in the EEG laboratory of Athens Medical School's Department of Neurology, in the Eginition Hospital, from 1984 to 1998.

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MATERIALS AND METHODS

From approximately 10 000 EEGs of patients (both outpatients and inpatients) examined in the Eginition Hospital during the years 1984–1998, we retrospectively selected the EEGs of patients who, after having undergone a routine EEG, had subsequently been examined with either: (1) a second routine EEG, (2) an EEG after 24-hour sleep deprivation or (3) an EEG during drug-induced sleep. EEGs of 721 patients (394 male, 327 female, aged 17–75 years, mean 46 SD 14) were chosen, studied and allocated to four major groups—1, 2A, 2B, 3—according to the activation procedure employed, as shown below.

Each major group was then divided into two subgroups according to the medical condition of the patients. One consisted of patients with definite (in well-established cases) or clinically suspected (in new cases presenting to our hospital for evaluation) epileptic seizures (clinically defined epilepsy (CDE)), whilst a second subgroup consisted of patients suffering from other disorders such as headaches, syncope, polyneuropathy, myopathy, multiple sclerosis, ALS, psychiatric disorders etc (other disorders (ODS)).

In group 1, 143 patients, 87 male, 56 female (52 in subgroup CDE and 91 in subgroup ODS) had two routine recordings of which the initial one had been normal.

In the general group 2, 538 patients underwent a routine EEG followed by an EEG after sleep deprivation. Of these, 491(group 2A), 263 male, 228 female (195 and 296 in subgroups CDE and ODS respectively) had both wakefulness and drowsiness periods during the recording after sleep deprivation which were evident both clinically and on the EEG, whereas 47(group 2B), 25 male, 22 female (23 and 24 in CDE and ODS respectively) proved to be fully alert during the same recording, again both clinically and on EEG analysis.

In group 3, 40 patients, 19 male, 21 female, (22 and 18 in subgroups CDE and ODS respectively) had a routine EEG followed by an EEG during drug-induced sleep.

Routine EEGs, EEGs following sleep deprivation and EEGs during drug-induced sleep were made with three EEG recorders, a 12-channel ALVAR Reega 2000, a 16-channel OTE Biomedica , and a 16-channel ELEMA-SCHONANDER. A routine EEG recording was at least 45 minutes long and an EEG following sleep deprivation or during drug-induced sleep 60 minutes long. If patients were receiving medication in particular, the treatment remained unchanged between recordings. Twenty-one electrodes were placed according to the 10–20 system. In the 16-channel machines a monopolar and two dipolar montages (one longitudinal, one transverse) were recorded on paper. In the 12-channel machine two longitudinal, three transverse and two monopolar montages were used. Three minutes hyperventilation and photic stimulation were standard methods for all recordings[20].

Two separate specialists examined the EEGs. In the event of different conclusions, the opinion of a third, more experienced neurophysiologist, was sought.

Interictal epileptic activity was defined as spikes or sharp waves clearly distinguished from the background activity, spike and wave or polyspike and waves[18]. Benign epileptiform transients of sleep, 6 s/wave, 14 and 6/s positive spikes, and wicket spikes were considered as normal variants.

Statistical analysis. In order to detect statistically significant differences between two proportions of two independent samples, the two-tailed proportion test was employed to perform a two-sample null-hypothesis test.

Table 1: Activation rate.

Method	CDE (patients with epilepsy)	ODS (patients with other disorders)
Sleep deprivation (general group 2)	45/199 (22.6%)	37/308 (12%)
Sleep deprivation with drowsiness (group 2A)	40/178 (22.5%)	36/285 (12.6%)
Sleep deprivation without drowsiness (group 2B)	5/21 (24%)	1/23 (4.3%)
Drug-induced sleep (group 3)	5/18 (27.7%)	2/18 (11%)
Repeated routine (group 1)	5/52 (9.6%)	2/91 (2.2%)

The hypothesis tests were computed using the normal approximations with a correction for continuity. Where the total sample size was less than 40, Fisher's exact test was used instead. All tests were considered significant at the 0.05 level.

RESULTS

Our study revealed the following results, listed by group.

(1) Repeated routine recordings (group 1) revealed epileptic activity in 9.6% (5/52) of the epilepsy group (1 CDE) and 2.2% (2/91) of the group of patients with other disorders (1 ODS).

(2A) Among the 491 patients who underwent a routine and after sleep-deprivation recording and

who had periods of wakefulness and drowsiness during the recording after sleep deprivation, specific epileptic patterns were detected in 28, 17 in group 2A CDE and in 11 other patients (of group 2A ODS) during the initial routine EEG. The remainder (who had inconclusive initial recordings) were 178 in CDE and 285 in ODS. In their sleep-deprived recordings 22.5% (40/178) CDE and 12.6% (36/285) of the group ODA others had activated patterns.

Of the 40 activated EEGs in the CDE group, the specific epileptic activity appeared only in the wakefulness portion of the recording in five, only during the sleep stages in 20, and in both the wakefulness and the sleep portions of the EEG in 15.

(2B) Among the group of the 47 patients who, during the same activation method, failed to reveal clinical or EEG signs of drowsiness in the second recording, two CDE patients and one patient of the ODS subgroup had epileptic patterns in the initial EEG, while 21 CDE patients and 23 of the ODS subgroup had normal or non-specific initial recordings. During the second recording, 24% (5/21) of the CDE group and 4.3% (1/23) of the other group had specific epileptiform activity.

(3) Thirty six of the 40 patients with drug-induced sleep EEGs had normal or non-specific initial recordings (18 CDE, 18 others), while four, who were all CDE, did not. The activation rate in the second recording was 27% (5/18) in the CDE group versus 11% (2/18) in the other group respectively.

Our statistical analysis gave the following results:

(1) General group 2 CDE vs. group 1 CDE
45/199 vs. 5/52: 0.0376 (corrected *P* value).

(2) Group 3 CDE vs. group 1 CDE
5/18 vs. 5/52: 0.13 (corrected *P* value).

In addition, the rates of groups 2A and 2B were:

(a) Group 2A CDE vs. group 2B CDE
40/178 vs. 5/21: 0.89 (corrected *P* value).

(b) Group 2A CDE vs. group 1 CDE
40/178 vs. 5/52: 0.06 (corrected *P* value).

(c) Group 2B CDE vs. group 1 CDE
5/21 vs. 5/52: 0.22 (corrected *P* value).

(d) Group 2A CDE vs. group 3 CDE
40/178 vs. 5/18: 0.82 (corrected *P* value).

(e) Group 2B CDE vs. group 3 CDE
5/21 vs. 5/18: 0.93 (corrected *P* value).

DISCUSSION

There is controversy regarding the actual efficacy of some long-standing activating procedures which are commonly used in current practice to increase the diagnostic yield of an EEG recording. Particularly in patients presented with new onset seizures, which are clinically suspicious for epilepsy and have normal initial EEGs, a recording after sleep deprivation or a drug-induced sleep's recording can be employed. However, the rates of activation achieved, as reported in the literature, vary considerably.

In addition, there are several opinions regarding the mechanism by which sleep deprivation activates epileptiform discharges. It may be:

(1) the effect of the lack of one night's sleep, per se, (Naitoh and Dement[21], Spadetta[8], Deisenheimer and Klingler[6], Rodin[22]);

(2) the effect of the sleepiness or sleep that usually, but not invariably, ensues the next morning (Janz[23], Jovanovic[24], Gastaut[25], Niedermeyer and Holler[26]);

(3) the increased probability of abnormal findings with repeating recordings (Veldhuizen[12], Salinsky[18], Pratt[19]).

It has been proposed that sleep deprivation is more effective in children than in adults, in tonic–clonic myoclonic or partial seizures than in absence seizures and the sleep portion of the recording reveals abnormal findings more often than the waking portion (Scollo-Lavizzari *et al.*[27], Veldhuizen[12], Klingler[28], Degen and Degen[29], Naitoh and Dement[21]).

In people with epilepsy, serial EEGs are expected to increase the probability of disclosure of specific epileptic patterns, which could be revealed in 50% of patients in the first recording, in 17.44% in the second recording, among those with a normal or non-specific initial one, and in as much as 92% in the fourth recording, as reported by Salinsky in a sample of people with definite epilepsy[18]. We found a 9.6% increased yield in the repeated recording, far less than that of Salinsky's 17.44%. The difference could be explained by the small size of our sample and by the fact that our population comprised both people with definite epilepsy and people with new onset seizures being evaluated for probable epilepsy.

As far as sleep deprivation is concerned, its activation rate reported in the literature varies widely (from

7% by Broeker *et al.*[15] to 83% by Spadetta[8]). However, our result (22.6%) for the epilepsy group is comparable with the more recent reports of 25% from Klinger *et al.*[30] in patients with epilepsy, 23% from Logethetis *et al.*[31] in patients with definite and possible epilepsy and 25% from Bubien *et al.*[32]. Degen *et al.*[33] have published an increased activation rate up to 33.6% in the waking portion and up to 53.2% in the sleep portion of the recording.

The distribution of the appearance of epileptic activity reported in the literature is more or less similar to our results. Fountain[34] specified that, in 15 activated recordings of epileptic patients, there were six patients with activation only during sleep, one patient with activation only during wakefulness, and eight patients with activation during both portions of the recording. El-Ad[35] found that in 76 patients with activated recordings, 40% of them had activation only during sleep, 9% only during wakefulness and 51% during both portions of the recording.

Degen and Degen[29] did not find any difference between sleep deprivation and drug-induced sleep (in patients with atypical absences), but Rowan[36] estimates that the respective activation rate is 44% for sleep deprivation and 14% for drug-induced sleep, Aguglia *et al.*[37] estimates this rate to be 60% and 75% respectively (in a sample of patients with definite epilepsy), while Drake[11] compared sleep-deprived recordings to recordings during naturally occurring naps in people with epilepsy and he found rates of 66% vs. 54%.

According to our results, sleep deprivation proved to be more effective than drug-induced sleep, as its activation rate was statistically different from the repeated routine recording rate, while drug-induced sleep was not. It is noteworthy, that the group of patients who underwent sleep deprivation, but managed to remain awake and alert the following morning, had a similar activation rate to sleep-deprived patients who had drowsiness during their recording. Neither of these rates, though, had a difference, compared with the repeated routine recording rate, that reached statistical significance. So, no definite conclusions can be drawn about the relative contribution of lack of sleep and sleep itself to the efficacy of sleep deprivation as an activating method of EEG. Applying the same procedure to a larger numbers of patients might elucidate the question better.

It seems that both the lack of a night's sleep and sleep itself have an effect on eliciting epileptic activity, although it is not clear which is more effective. It may depend in any given patient on what type of seizures are experienced or whether seizures occur primarily when the patient is awake or asleep. Such factors will determine what method is used. On the other hand, sleep deprivation seems to be more effective than drug-induced sleep and the relative lack of use of the latter method in recent years is justified.

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