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First-Night Effect in Normal Subjects and Psychiatric Inpatients

*Michel Toussaint, *Rémy Luthringer, *Nicolas Schaltenbrand, *Gabriella Carelli, *Eric Lainey, *Anne Jacqmin, †Alain Muzet and *Jean-Paul Macher

**Foundation for Applied Neuroscience Research in Psychiatry, Centre Hospitalier, Rouffach, France; and*
†Laboratoire de Physiologie et de Psychologie Environnementales, CNRS, Strasbourg, France

Summary: The goal of the present study was to evaluate the first-night effect in psychiatric inpatients using large subject samples ($n > 30$) in order to obtain a good statistical evaluation. Thirty-two normal subjects and 94 psychiatric inpatients (38 depressives and 56 insomniacs) were studied for three consecutive nights in the hospital sleep laboratory. Our results showed clearly that there was a first-night effect in normal subjects, similar to that reported in previously published data, characterized by a longer rapid eye movement (REM) sleep latency ($p < 0.05$), increased wakefulness ($p < 0.01$) and total sleep time ($p < 0.02$) and a decreased sleep efficiency ($p < 0.01$). REM sleep latency and stage REM in the first third of the night were still altered in the second night. Both clinical groups had a less marked first-night effect than normal subjects, showing alterations only observed in REM sleep ($p < 0.01$) (decreased REM sleep, longer REM sleep latency, increased REM sleep gravity center). However, the first-night effect was more pronounced in insomniacs than in depressed patients. No statistical differences between the second and third nights' recordings were found in sleep parameters. It is suggested that first-night data should not be simply discarded but could be used in subsequent analyses. **Key Words:** First-night effect—Depression—Insomnia—Sleep—Polysomnography.

The first-night effect is a well-known phenomenon in sleep recordings, especially when carried out in sleep laboratories. That is why it has become a common practice to exclude the first night of sleep from the analysis. So far, most of the studies have been performed in normal subjects (1–4). The first-night effect is mainly characterized by longer stage 2 and rapid eye movement (REM) sleep latencies, lower sleep efficiency and percentage of REM sleep. Second, the major factors held responsible for this effect are the unfamiliar surroundings of a sleep laboratory and the adaptation of the subjects to the application of several instruments to their body. Some studies tried to corroborate the first-night effect in eliminating these factors using ambulatory recordings of sleep electroencephalography (EEG) in the subject's home (5–7) or in using only wrist-worn activity monitors (8). Others tried to improve the sleep laboratory recording comfort, offering conditions described as resembling a "good hotel" and the staff being "friendly and open" (9,10). Each of these studies tended to prove that the first-night effect was lessened once the improvements had been made. The age factor was also considered as a variable (7,11,12), evidencing a greater first-night effect in older subjects. Finally, other studies tried to use the first-night effect as a model of transient insomnia in pharmacological investigations (13) or stress and anxiety situations (14).

Concerning psychiatric patients, however, it is often impossible to do ambulatory recordings at home, and laboratory recordings are mostly used in general sleep practice. Up to now very few studies have been realized on psychiatric inpatients (15–17), and further investigations should be made to assess the various factors involved in different diagnostic categories as compared with normal subjects. Results obtained in various diagnostic groups of psychiatric inpatients have shown no difference in sleep parameters between the first and the second night (16), but this study was carried out on small patient subgroups ($n < 12$). It was suggested that the pathological nature of the sleep pattern itself limits the adaptation to the experimental situation.

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Address correspondence and reprint requests to Michel Toussaint, Ph.D., Foundation for Applied Neuroscience Research in Psychiatry (FORENAP), Centre Hospitalier—Secteur 8, 68250 Rouffach, France.

For this reason and because all-night sleep EEG studies have yielded significant findings in the study of affective disorders, and particularly depression and insomnia (18), we therefore decided to better evaluate the first-night effect in inpatients with depression and insomnia using large subject samples ($n > 30$) for purposes of statistical validity.

We studied 32 normal subjects and 94 psychiatric inpatients (38 depressives and 56 insomniacs) from our sleep clinical database and herewith report a comparison of sleep for the first three consecutive nights in each group of subjects.

METHODS

To best examine and measure the first-night effect on psychiatric inpatients, we first studied it in normal subjects in order to evaluate and compare our sleep laboratory environment to that from reports of first-night effects already published. Concerning healthy volunteers, the data used for our study were part of different pharmacological sleep studies in placebo condition (single-blind design) performed in the laboratory on paid volunteers.

We next evaluated the first-night effect on two psychiatric inpatient groups that were predominant in our database: depressed and insomniac patients.

Subjects

Three groups of subjects, 32 healthy volunteers (18 males, 14 females) ranging from 18 to 49 years of age (mean age 26.3 ± 7.3), 38 depressed patients (16 males, 22 females) ranging from 18 to 57 years of age (mean age 39 ± 9.2) and 56 insomniac patients (25 males, 31 females) ranging from 17 to 57 years of age (mean age 42.9 ± 9.6), were studied.

All healthy volunteers had regular sleep–wake habits and underwent laboratory tests, drug screening for psychotropic substances and a psychological examination before final inclusion in the study. Moreover they were requested not to ingest alcohol or drugs during 1 month prior to the study and were not allowed to take any drug during the entire duration of the study. Furthermore they signed informed consent forms prior to entering the study, which was performed in accordance with the rules and regulations for the conduct of clinical trials stated by the World Medical Assembly of Helsinki, Tokyo, Venice and Hong-Kong and by the French law.

All patients underwent laboratory tests and a 5-week period free of any drug or other substances known to affect sleep structure or central nervous system function. They underwent both a standard clinical interview and a structured interview: Schedule for Affective Disorder and Schizophrenia—Lifetime Version (19). They were diagnosed by consensus of two psychiatrists, including a sleep expert and a psychologist.

Depressed patients were diagnosed as suffering from a major depressive episode according to DSM-III-R criteria, with or without melancholia but without mood-incongruent psychotic features (20). The criteria for inclusion were the following: depressed mood as the central feature of the complaint; accompaniment of the depressed mood by "vital" complaints, e.g. retardation, agitation, loss of weight, diurnal variation and sleep complaints; no precipitating life events adequately explaining the depression; a minimum total score of 17 on the Hamilton depression scale (21). Presence of significant medical problems (e.g. recent myocardial infarction) or high suicide risk led to exclusion of the patient.

Insomniacs were diagnosed on the basis of a medical history, a full clinical examination and clinical laboratory determination and were selected according to the following criteria: they met DSM-III-R criteria for primary insomnia (20); they reported complaints of insomnia (sleep maintenance and sleep onset troubles) in the absence of any hypnotic; they had no history of alcoholism, toxicomania, psychiatric illness, mental retardation, dementia or abnormal sleep habits; they showed no medical conditions that could lead to the complaint of insomnia; there was no evidence of sleep apnea, nocturnal myoclonus, restless legs or narcolepsy in baseline sleep recordings.

In order to prevent daytime sleep and to have a homogeneous diurnal activity for all subjects, patients had to stay out of their bedrooms during the whole day and participated in different activities organized by the nursing staff. Healthy volunteers were requested to stay in the hospital during the entire duration of the study and placed under the control of the nursing staff.

Recordings and sleep stage classification

Subjects who came to the sleep laboratory for the very first time were recorded polysomnographically on the first three consecutive nights. Each subject reported to the laboratory about 1 hour before bedtime and slept in an individual sound-attenuated and comfortably furnished bedroom. Patients were studied at their habitual sleep times but nevertheless within the 10:00 to 12:00 p.m. time range. Healthy volunteers were studied on an entrained routine (10:00 p.m.).

Sleep stages were scored visually every 30-second epoch, directly from a computer screen having the same visualization features as a classical polygraph (22), according to Rechtschaffen and Kales (23) criteria. Recordings were based on two EEG derivations (C3 or C4 vs. A2 or A1 and Cz-O1 or O2), one chin electro-

myographic (EMG) derivation and one electro-oculographic (EOG) derivation (left vs. right outer eye canthus). Movement time epochs were not scored separately but were included in wake stage. Inter-expert variability, estimated in the laboratory, indicated an average agreement rate of 87.5% (24).

All-night summary variables were derived from the visual scoring of recordings using standard criteria. Sleep latency (SL) was measured from lights-off to the first occurrence of a stage 2 or REM sleep epoch. REM sleep latency (REM SL) was measured from sleep onset to the first epoch of stage REM. In addition, we used another REM SL parameter called REM SL 2, better adapted to depressed patients' recordings. In this case sleep onset was measured from lights-off to the first 10 minutes of continuous stage 2 sleep not interrupted by >2 minutes of wake or stage 1 sleep. REM sleep gravity center is defined as the mean position (gravity center) of REM sleep across the night, in minutes, calculated from the total recording period

$$\left(\sum_{i=1,n} t_i/\text{stage}_i = \text{REM}\right) \Big/ \text{total minutes of REM},$$

where i = page number in the recording; n = total number of pages; t_i = time of occurrence of page i only if stage of page i is REM. Sleep stage periods were also calculated in each third of the night, giving a more dynamic overview of the sleep process.

Statistics

Statistical analysis was carried out in two parts. First, to assess possible differences among the three nights across all subjects within each group, we used a one-way analysis of variance (ANOVA) for repeated measures, with each sleep parameter alternatively as factor and time of sleep studies (night 1 vs. night 2 vs. night 3) as the repeated measures. Second, to evaluate the presence of a first-night effect, we used statistical two-tailed paired Student t tests to assess the significance of differences of polygraphic sleep parameters between nights 1 and 2 and between nights 2 and 3. The test between nights 2 and 3 was intended to determine if the significant effect obtained between nights 1 and 2 was to be considered as a first-night effect or rather as a more extended adaptation process. Because multiple comparisons were carried out, a correction method was applied (25) to achieve statistical significance-adjusted levels.

A significance threshold was set at $p = 0.05$ for all analyses, and results were expressed as mean ± standard deviation. In order to verify the normality of the data distribution, a graphical display and a test of symmetry were performed.

RESULTS

Healthy subjects

Table 1 lists the data and significant differences observed in normal subjects between nights 1 and 2 and between nights 2 and 3 on the various sleep parameters. All parameters showing significant differences ($p < 0.05$) between consecutive nights are included.

On the first night, compared to the second night, total sleep time was shorter (415.9 vs. 441.7 minutes; $p < 0.02$), sleep efficiency was lower (85.8% vs. 91.1%; $p < 0.01$), wakefulness was increased (68 vs. 43.2 minutes at $p < 0.01$ and 17.4% of the total sleep time vs. 10.1% at $p < 0.01$), and REM SL 2 was delayed (97.9 vs. 82 minutes; $p < 0.05$).

Stage 2 and REM sleep durations and percentages were decreased during the first and second nights, but these differences were not significant even at 0.05 level because of the large standard deviation of the samples. As shown by the slow wave sleep (SWS) results presented in Table 1, no significant differences were found either in stage 3 or stage 4 sleep duration and percentage.

When comparing nights 2 and 3, two parameters were still significantly modified, showing a residual first-night effect: REM sleep in the first third of the sleep period was decreased (15.3 vs. 23.1 minutes; $p < 0.01$), and REM SL 2 was delayed (82 vs. 70.9 minutes; $p < 0.05$).

Patients

Results of sleep parameters and significant differences ($p < 0.05$) among nights 1, 2 and 3 in depressed patients and in insomniac patients are presented in Table 2 and Table 3, respectively. Indeed, there was a steadiness in nearly all sleep parameters when comparing night 1 to night 2. Sleep continuity and sleep architecture parameters were not significantly modified for depressed patients. In insomniacs, only REM sleep duration and percentage were significantly ($p < 0.01$) reduced during night 1 (86.9 minutes; 22.6%) compared to night 2 (97.3 minutes; 24.8%).

For both clinical groups, only derived REM sleep parameters were significantly modified due to the first-night effect, but it was less marked in depressed patients than in insomniacs. Time in REM sleep in the first third of the sleep period was significantly ($p < 0.01$) decreased in night 1 of the insomniac group (13.9 vs. 19.7 minutes). A decrease was also evidenced in the depressed group but it was not significant (18.4 vs. 22.2 minutes). Both REM sleep latencies were significantly ($p < 0.01$) longer owing to a first-night effect in both clinical groups, but this effect was more pronounced

TABLE 1. *Effects of first night on sleep parameters in healthy volunteers*

	Controls (n = 32)							
	Night 1		Night 2		Night 3		Night 1 vs. Night 2	Night 2 vs. Night 3
Sleep parameters	Mean	SD	Mean	SD	Mean	SD	p	p
Total sleep time (minutes)	415.9	55.0	441.7	55.0	455.0	56.3	<0.02	ns
Sleep efficiency (%)	85.8	7.3	91.1	4.3	89.1	4.9	<0.01	ns
Sleep onset latency (minutes)	19.1	14.1	15.0	11.9	18.1	16.1	ns	ns
Wake (minutes)	68.0	35.0	43.2	21.8	55.0	22.6	<0.01	ns
Wake after sleep onset (minutes)	52.7	34.0	32.3	18.9	40.5	15.9	<0.01	ns
Stage 2 (minutes)	221.4	45.0	238.4	52.4	233.1	38.1	ns	ns
SWS (minutes)	92.5	29.2	90.5	22.1	98.3	30.4	ns	ns
REM (minutes)	89.1	26.2	99.8	28.5	110.2	29.4	ns	ns
Wake (%)	17.4	11.6	10.1	5.7	12.6	6.7	<0.01	ns
Stage 2 (%)	53.3	9.1	53.7	8.3	51.4	6.6	ns	ns
SWS (%)	22.3	7.0	20.7	5.5	21.7	6.5	ns	ns
REM (%)	21.3	5.1	22.5	5.2	24.0	4.8	ns	ns
Non REM/REM	4.0	1.3	3.7	1.1	3.3	0.9	ns	ns
SWS—first third (minutes)	57.8	22.8	61.7	18.7	64.1	18.4	ns	ns
SWS—second third (minutes)	24.0	18.0	21.0	10.3	25.7	19.8	ns	ns
SWS—third third (minutes)	10.8	11.0	7.9	9.7	8.5	10.6	ns	ns
REM—first third (minutes)	13.5	8.1	15.3	10.7	23.1	11.3	ns	<0.01
REM—second third (minutes)	33.8	9.4	36.5	12.8	37.8	12.2	ns	ns
REM—third third (minutes)	41.8	16.9	48.1	16.9	49.2	15.5	ns	ns
REM SL (minutes)	85.4	46.8	77.4	35.7	71.5	28.7	ns	ns
REM SL 2 (minutes)	97.9	56.5	82.0	39.9	70.9	29.4	<0.05	<0.05
REM gravity center (minutes)	299.1	46.3	299.7	40.4	304.9	41.3	ns	ns
Mean cycle (minutes)	110.2	25.1	105.4	23.0	102.8	14.6	ns	ns

ns, not significant ($p > 0.05$).

TABLE 2. *Effects of first night on sleep parameters in depressed inpatients*

	Depressives (n = 38)							
	Night 1		Night 2		Night 3		Night 1 vs. Night 2	Night 2 vs. Night 3
Sleep parameters	Mean	SD	Mean	SD	Mean	SD	p	p
Total sleep time (minutes)	381.7	85.4	380.3	87.5	392.4	63.9	ns	ns
Sleep efficiency (%)	73.6	13.6	76.3	13.6	76.9	11.6	ns	ns
Sleep onset latency (minutes)	46.2	44.7	33.9	30.8	33.1	29.6	ns	ns
Wake (minutes)	135.8	70.7	115.6	62.0	121.0	67.5	ns	ns
Wake after sleep onset (minutes)	93.8	48.7	86.7	57.2	92.7	60.6	ns	ns
Stage 2 (minutes)	206.2	65.6	197.1	67.9	204.6	58.3	ns	ns
SWS (minutes)	63.8	31.1	60.7	33.8	66.7	34.6	ns	ns
REM (minutes)	86.9	39.3	97.3	40.3	98.0	35.1	ns	ns
Wake (%)	42.9	42.3	37.9	43.3	33.3	22.5	ns	ns
Stage 2 (%)	53.7	11.9	50.9	11.2	52.1	11.8	ns	ns
SWS (%)	16.4	6.9	16.2	9.4	17.2	8.5	ns	ns
REM (%)	22.6	8.5	24.8	7.9	24.7	7.6	ns	ns
Non REM/REM	4.3	2.7	3.3	1.3	3.5	1.7	<0.01	ns
SWS—first third (minutes)	39.5	22.7	39.3	22.6	42.9	26.8	ns	ns
SWS—second third (minutes)	17.1	16.2	15.0	14.6	16.4	16.9	ns	ns
SWS—third third (minutes)	7.1	11.1	6.4	9.0	7.3	9.1	ns	ns
REM—first third (minutes)	18.4	13.2	22.2	15.8	24.4	15.1	ns	ns
REM—second third (minutes)	33.5	20.4	34.5	17.2	34.8	20.4	ns	ns
REM—third third (minutes)	35.1	19.6	40.6	24.7	38.9	20.0	ns	ns
REM SL (minutes)	83.0	58.7	60.8	42.6	77.6	49.2	<0.01	ns
REM SL 2 (minutes)	99.4	77.9	65.1	44.5	77.4	53.2	<0.01	ns
REM gravity center (minutes)	310.7	51.6	290.3	59.0	295.8	61.6	ns	ns
Mean cycle (minutes)	126.4	52.9	106.3	29.8	112.2	21.3	<0.01	ns

TABLE 3. *Effects of first night on sleep parameters in insomniac inpatients*

	Insomniacs (n = 56)							
	Night 1		Night 2		Night 3		Night 1 vs. Night 2	Night 2 vs. Night 3
Sleep parameters	Mean	(SD)	Mean	SD	Mean	SD	p	p
Total sleep time (minutes)	375.3	74.8	394.9	84.3	397.5	66.4	ns	ns
Sleep efficiency (%)	73.2	13.3	76.9	14.5	79.5	12.2	ns	ns
Sleep onset latency (minutes)	31.3	30.7	28.3	28.5	26.1	41.4	ns	ns
Wake (minutes)	138.3	72.8	118.1	75.6	102.4	60.9	ns	ns
Wake after sleep onset (minutes)	110.8	56.4	94.0	72.2	80.1	51.1	ns	ns
Stage 2 (minutes)	215.6	52.6	218.6	55.8	219.3	45.4	ns	ns
SWS (minutes)	60.7	31.0	59.9	38.2	68.0	37.0	ns	ns
REM (minutes)	77.9	34.2	91.9	29.6	91.8	30.4	<0.01	ns
Wake (%)	42.7	35.9	40.6	63.9	30.0	29.3	ns	ns
Stage 2 (%)	57.5	8.7	55.7	7.9	55.4	7.7	ns	ns
SWS (%)	16.1	7.6	14.8	8.3	16.8	8.7	ns	ns
REM (%)	20.3	7.3	22.9	6.1	22.9	6.3	<0.01	ns
Non REM/REM	4.8	2.7	3.5	1.2	3.8	1.6	<0.01	ns
SWS—first third (minutes)	36.1	23.4	39.6	25.4	43.7	24.5	ns	ns
SWS—second third (minutes)	16.2	14.5	14.7	17.4	17.1	16.8	ns	ns
SWS—third third (minutes)	8.3	10.4	5.5	8.0	7.2	11.0	ns	ns
REM—first third (minutes)	13.9	14.7	19.7	13.8	21.9	15.5	<0.01	ns
REM—second third (minutes)	27.8	16.1	33.2	16.6	35.1	14.6	ns	ns
REM—third third (minutes)	36.2	16.4	39.0	15.7	34.8	15.3	ns	ns
REM SL (minutes)	116.4	68.5	81.9	61.7	77.4	47.1	<0.01	ns
REM SL 2 (minutes)	127.6	79.4	74.7	46.1	80.6	47.6	<0.01	ns
REM gravity center (minutes)	319.9	54.2	298.4	60.9	286.0	45.5	<0.01	ns
Mean cycle (minutes)	134.1	64.2	114.9	31.6	112.6	33.8	ns	ns

in insomniacs (116.4 vs. 81.9 minutes in insomniacs and 83 vs. 60.8 minutes in depressed patients for the REM SL). In the depressed patients a mild REM rebound was observed between nights 2 and 3, mainly in the REM SL (60.8 vs. 77.6 minutes) and the REM SL 2 (65.1 vs. 77.4 minutes). But this effect was not significant, and night 3 REM parameters were in the normal range for these patients. The REM sleep gravity center was significantly ($p < 0.01$) delayed in the first night in insomniacs (319.9 vs. 298.4 minutes).

No significant differences were found when comparing night 2 with night 3 in either of the two groups of patients.

DISCUSSION

Our data from healthy volunteers agree with previously published normative data (2,4,11). Furthermore, our results confirm the presence of a first-night effect in laboratory recording of sleep, characterized by a longer REM SL, an increased wakefulness and decreased total sleep time and sleep efficiency. In both nights 1 and 2 the first REM sleep period was delayed, and the distribution of REM sleep across the night was altered, i.e. with a smaller portion occurring in the first third as compared to night 3. One may argue that the second night might not adequately reflect a habitual sleep pattern, but rather a sleep pattern following partial sleep deprivation caused by the first night recording. Therefore, the habituation process takes >1 night concerning the REM sleep distribution across the night, as already demonstrated by Schmidt and Kaelbling (4). Our results in REM sleep concur with REM sleep deprivation findings (26) that demonstrated that it takes at least 2 nights to recover after REM sleep deprivation, and thus the stage REM restoration is a slow phenomenon. Like Webb and Campbell (11), we did not find either a significant decrease in the amount of both stage REM and stage 2 or significant modifications in stage-shifts. These findings validate the usual procedure of eliminating the first night of recording as representations of subjects' basic sleep structures. In addition, the present study demonstrates that our clinical sleep laboratory conditions were quite similar to those of others.

The first-night effect is the result of the general influence of a traditional laboratory compared to the more familiar home environment and the adaptation of a person to the application of electrodes. Our results, in combination with other studies, concur with the conclusions of Coble et al. (9) and Browman and Cartwright (10) that sleep environment is a critical factor in the process of adaptation in normal subjects. A familiar setting (comfortable hotel-type laboratory and cordial staff) as already reported (9,10) is sufficient to reduce but not fully eliminate the first-night effect of sleep in normal adults. Findings related to healthy el-

derly (age 50–98 years) using the activity monitor as a method to evaluate sleep have shown no first-night effect (8), but such studies were not replicated on healthy young subjects or patients with sleep disorders.

The results from our psychiatric inpatient groups are similar to those of the control subjects but with less significant changes from night 1 to night 2. Furthermore, the only meaningful differences were observed between night 1 and night 2, but there were none between night 2 and night 3. However, our results reveal a considerable between-patient variability of all sleep measures in both clinical groups compared to normal subjects. In addition, these findings demonstrate that clinical patients have a time-limited adaptation process to the sleep laboratory compared to control subjects. This lack of adaptation may be the evidence of a lessened adaptability to stress-provoking situations (16).

Concerning the depressed patient group, our results show an obvious first-night effect observed on REM sleep parameters that was not reported in previously published studies (15,16). This can be explained by a greater variability in sleep parameters observed in these studies, probably due to the small sample size and the nonspecific clinical constitution of the diagnostic groups involved. Sleep continuity and sleep architecture parameters remained fairly constant throughout the three consecutive nights. The increase of the REM SL parameter during the first night might have broader implications in the diagnostic evaluation of depressed patients when based on a single night.

In the insomniac patient group we can observe a more pronounced first-night effect than in the depressed group. REM sleep duration and percentage were decreased because of the first-night effect. The distribution of stage REM across the night was modified and delayed. This was characterized by a later REM sleep gravity center, a decreased REM sleep duration in the first third of the night and an increased REM SL. These findings on REM sleep were also observed by Coates et al. (5) on an insomniac group (n = 12) recorded at home. Therefore, unlike in normal subjects, the first-night effect on insomniac patients cannot be eliminated through ambulatory recordings at home. A similar behavior was found in patients with insomnia based on generalized anxiety disorder (27).

It seems therefore obvious that first-night data should not be discarded simply because of current practice, but they could be used in subsequent analyses. Like Wauquier et al. (7), we think that the first night effect is more than a mere laboratory artifact, and rather represents "the constitutional age-related functional adaptability of the CNS" (p. 10). Finally, our data confirm that lessened sleep adaptation in psychiatric patients may be a manifestation of the disorder. For this reason further studies should be conducted in different psychiatric disorder subgroups.

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