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Sleep in a sitting position: effect of triazolam on sleep stages and EEG power spectra

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Abstract. The effect of triazolam (0.25 mg) and placebo was investigated in healthy, male subjects who slept in a sitting position. After the intake of placebo, sleep efficiency, rapid eye movement (REM) sleep and subjective sleep quality were lower than in the preceding sleep episode in bed, while stage 1 and REM sleep latency were higher. Triazolam did not prevent this impairment of sleep. However, in comparison with the placebo condition, the percentage of slow wave sleep was higher in the first third of the night, and in the morning sleep was rated as more quite. EEG power density in nonREM sleep was reduced in the frequency range of 1.25–10.0 Hz and enhanced in the range of sleep spindles (12.25–13.0 Hz). These changes were still present in the last third of the night. In REM sleep, triazolam reduced spectral activity in some frequency bins between 4.25 and 10.0 Hz. The sitting position itself affected the nonREM sleep spectra, since the placebo level in the 2.25–21.0-Hz range exceeded the baseline level. We conclude that a 0.25 mg dose of triazolam does not effectively counteract a posture-induced sleep disturbance, but induces changes in the EEG spectra which are typical for benzodiazepine receptor agonists.

Key words: Sleep disturbance – Hypnotics – Spectral analysis – Benzodiazepine – Sleep quality – Sleep posture

In humans the transition from wakefulness to sleep is typically associated with a change from the upright to the supine posture. The recumbent posture is not a prerequisite for sleep to occur. Sleep can be initiated and maintained while sitting in a chair. Although the reclining seat of a chair provides some comfort, the subjective sleep quality is usually not equivalent to sleep in a recumbent position. Polysomnographic recordings of day time sleep while sitting in a chair in a well-lit room have been obtained in sleep-deprived subjects (Balkin et al. 1989). It was shown that, despite the sleep deprivation, sleep efficiency in the 6-h sleep episode was only 71.5% and only 35 min of slow-wave sleep (SWS; stages 3 + 4) were obtained. In that study no sleep data were obtained while subjects were in bed. In a comparable sleep deprivation study (Dijk et al. 1991) in which the recovery sleep in the morning was recorded from subjects in bed, a sleep efficiency of approximately 92% and 127 min of SWS (sleep episode 458 min) were obtained. This comparison indicates that objective sleep parameters are severely affected when sleep occurs in a sitting position under non-sleep-conducive conditions.

Objective sleep parameters can be improved by benzodiazepine and non-benzodiazepine hypnotics in healthy subjects without sleep complaints when sleep is experimentally disturbed. Thus, the increase in nocturnal sleep latency after a nap in the late afternoon can be counteracted by temazepam (Dijk et al. 1989). Likewise, midazolam and zopiclone have been shown to normalize sleep latency in a phase-advanced sleep schedule (Trachsel et al. 1990). Balkin et al. (1989) reported that administration of triazolam (0.125, 0.25 or 0.5 mg) significantly increased SWS, when subjects were sleeping in a chair. This latter finding is surprising because under baseline conditions triazolam (0.5 mg) has been shown to reduce EEG power density in the frequency range of 0.75–10.0 Hz (Borbély et al. 1985). This reduction of EEG power density has also been observed for other benzodiazepine receptor agonists belonging to the class of the benzodiazepines (Dijk et al. 1989), cyclopyrrolones (Trachsel et al. 1990), and imidazopyridines (Brunner et al. 1991).

In the present study we investigated to what extent triazolam (0.25 mg) could counteract the sleep disturbing effect of a sitting sleep position. In addition to visual scoring of the EEG, the sleep EEG was analyzed by spectral analysis, and subjective sleep quality was assessed by the self ratings in the morning.

Materials and methods

Subjects. The study was carried out in eight healthy male subjects (mean age 24.1 years; range 23–26) who did not report any sleep

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disturbances. They were recruited among university students and were paid for participating in the study. Their sleep habits and the absence of sleep disorders were established on the basis of questionnaires. Informed consent was obtained before the experiment.

Protocol. The subjects were requested to refrain from alcohol and excessive caffeine consumption, and from daytime naps during the entire experiment. Moreover, they were requested to maintain their habitual bedtime on the night preceding the adaptation night. The bedtimes at home were checked by a wrist-worn activity monitor. Sleep was recorded in the sound-attenuated bedrooms of the sleep laboratory during two blocks of 4 consecutive nights. Each block consisted of an adaptation night and a baseline night (BL-TR, BL-PL), both recorded in bed. In the third night the subjects slept sitting in a chair after taking the drug (Sit-TR) or placebo (Sit-PL); the 4th night was recorded in bed under the same conditions as the first 2 nights (Post-TR, Post-PL). The initial nights of the blocks were 1 week apart. The subjects went to bed at 23.00 hours, and arose at 07.00 hours. A double-blind, balanced crossover schedule was used.

The 3 nights in bed were recorded under complete darkness. During the night in the chair light intensity was very low ($\sim$ 3 lux). The chairs were economy class chairs from a commercial airline. The subjects were asked to fasten their seat belts to prevent them from sliding down. The back of the seat was put in a reclining position. In contrast to most economy seats in aircrafts, there was ample room for the subjects to stretch their legs. The subjects were monitored via a video camera on a TV monitor and also recorded on videotape.

Drug. The 0.25 mg tablet of triazolam (Halcion^R) corresponds to the hypnotic dose recommended by the manufacturer. The oral administration of triazolam or placebo occurred 15 min prior to bedtime.

Sleep recordings, EEG spectra and subjective sleep parameters. Sleep was polygraphically recorded and scored for 20-s epochs according to conventional criteria (Rechtschaffen and Kales 1968). Sleep latency was defined as the interval between lights-out and the first occurrence of stage 2, 3, 4, or rapid eye movement (REM) sleep. REM sleep latency represents the interval between sleep onset and the first occurrence of REM sleep. The method of all-night spectral analysis of the EEG was similar to the procedure described previously (Borbély et al. 1981; Brunner et al. 1990). The EEG signal (C3/A2 or C4/A1 derivation) was amplified with a time constant of 0.9 s. The combined action of the amplifier's 50-Hz notch filter and an analog low pass filter served to attenuate high frequency components (-3 dB at 27 Hz). After AD-conversion (128 Hz, 12 bit resolution) the EEG signal was digitally low pass filtered (-3 dB at 25 Hz, 24 dB/oct) and subjected to a Fast Fourier Transform routine. Spectra were computed for consecutive 4-s epochs and 0.25-Hz bands in the range of 0.25–25.0 Hz by applying a rectangular window. The values were then averaged for 20-s epochs after excluding 4-s epochs which were contaminated by visually scored artifacts [usually arising from movements; 2.3 $\pm$ 0.2 (SEM) percent of total sleep time were excluded]. The 20-s power spectra were matched with the 20-s sleep scores. In addition, values of adjacent frequency bands were collapsed into 0.5 Hz (in the range of 0.25–5.0 Hz) or 1.0-Hz (5.25–25.0 Hz) bins.

Subjective sleep parameters were assessed 10 min after awakening by a questionnaire and 100 mm visual analogue scales (VAS). These methods have proved sensitive to document the hypnotic action and residual effects of various benzodiazepine hypnotics on subjective parameters (Mattmann et al. 1982).

Statistics. Statistical significance of comparisons between conditions were assessed by one-way or two-way ANOVAs for repeated measures. In the ANOVAs for repeated measures the degrees of freedom were adjusted according to the Huynh-Feldt criterion but the original degrees of freedom are reported. Paired comparisons were made with the non-parametric Wilcoxon test or the parametric *t*-test. Some variables were log transformed, as indicated.

Results

Figure 1 illustrates for one subject the time course of slow-wave activity (power density in the 0.75–4.5-Hz range) and of the vigilance stages during baseline sleep in bed and during sleep in a sitting position after intake of placebo.

Sleep parameters (Table 1)

Placebo condition. Sleep in a sitting position (Sit-PL) was impaired in comparison with sleep in bed in the preceding night (BL-PL). Total sleep time and sleep efficiency were reduced, while wakefulness after sleep onset and the amount of stage 1 were increased. An inhibitory effect on REM sleep was evident from the prolonged REM sleep latency and its reduced amount. Recovery effects were seen during the following night in bed (Post-PL), in which stage 1 was significantly below baseline (BL-PL), whereas REM sleep was enhanced.

Triazolam condition. Sleep in a sitting position was also impaired under triazolam. In comparison with sleep in bed (BL-TR) total sleep time, sleep efficiency and REM sleep were reduced, whereas stage 1 and wakefulness after sleep onset were enhanced. In the following night in bed (Post-TR) total sleep time, sleep efficiency and stage 2 were higher than in the baseline night (BL-TR), while REM sleep latency was reduced.

Comparison of triazolam and placebo. There were no significant differences between any of the three corresponding nights of the placebo and triazolam condition. However, an analysis per thirds of the night (i.e. time in chair)

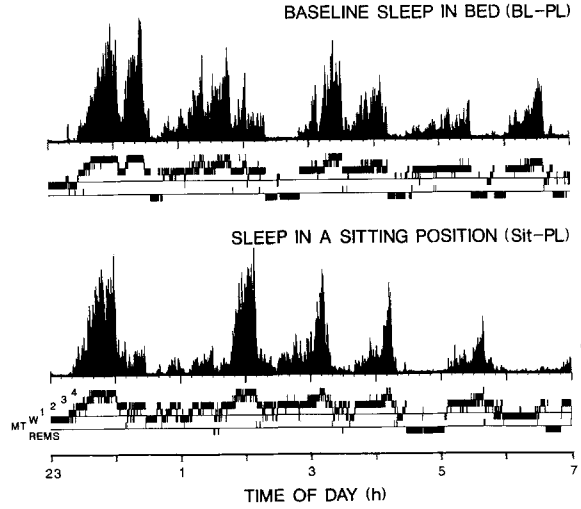

Fig. 1. Electroencephalographic slow-wave activity (0.75–4.5 Hz) and sleep stages in one subject during baseline sleep and sleep in a sitting position after intake of placebo. *W*, waking; *MT*, movement time. Data are plotted per 20-s epochs. Slow-wave activity values represent 3-point moving averages. Calibration mark at bottom right represents 100 $\mu V^2/Hz$

Table 1. Sleep parameters per sleep episode after intake of placebo or 0.25 mg triazolam before sleep in a sitting position (Sit-PL, Sit-TR), in the preceding baseline nights (BL-PL, BL-TR), and in the post-placebo (Post-PL) and post-triazolam (Post-TR) nights. Mean values (SEM in parentheses; $n = 8$) in minutes unless indicated otherwise. TIB, time in bed or time in chair respectively. There were no significant differences between corresponding nights of the two conditions. Values that differ significantly from the value of the corresponding baseline night are indicated by $*P < 0.05$; $**P < 0.01$ (paired t-test, two-sided). Pairwise comparisons were only made if a one-way ANOVA across the 3 consecutive nights in the placebo or triazolam condition showed a significant effect ($P < 0.05$)

Condition	BL-PL	Sit-PL	Post-PL	BL-TR	Sit-TR	Post-TR
Total sleep time (TST)	440.2 (8.5)	380.0** (17.6)	451.5 (6.0)	448.3 (3.0)	406.1* (11.8)	454.0* (3.0)
Sleep efficiency (% TST of TIB)	91.7 (1.8)	79.2** (3.7)	94.1 (1.3)	93.4 (0.6)	84.6* (2.4)	94.6* (0.6)
Sleep latency (to stage 2)	22.3 (4.6)	32.9 (8.6)	17.8 (6.0)	16.5 (2.6)	20.0 (3.1)	13.3 (2.9)
REMS latency (from stage 2)	95.3 (14.0)	156.2* (27.4)	70.4 (8.0)	81.7 (8.1)	115.1 (15.2)	67.8* (3.9)
Wakefulness after sleep onset	9.9 (5.0)	53.4** (11.6)	3.0 (1.1)	6.2 (2.0)	35.4* (12.1)	3.5 (1.1)
Stage 1	31.5 (2.9)	69.6* (10.0)	24.0* (3.4)	33.2 (3.8)	60.9* (8.7)	24.8 (2.0)
Stage 2	216.5 (10.6)	181.9 (17.7)	220.3 (10.4)	220.5 (8.0)	198.0 (16.1)	234.0** (7.9)
Stage 3	49.3 (5.5)	44.3 (3.7)	54.0 (4.8)	48.3 (3.0)	43.8 (2.9)	54.5 (5.8)
Stage 4	51.5 (11.2)	33.4* (7.7)	47.8 (8.2)	44.8 (6.9)	37.9 (6.4)	37.4 (7.6)
Slow wave sleep (SWS, stages 3 + 4)	100.9 (14.6)	77.6 (8.9)	101.8 (11.4)	93.1 (8.3)	81.7 (8.8)	91.9 (11.6)
REM sleep	91.3 (6.6)	50.8** (9.7)	105.5* (6.7)	101.5 (5.0)	65.5** (9.3)	103.4 (7.5)
Movement time	7.5 (1.0)	13.6 (2.6)	7.7 (1.3)	8.9 (1.5)	18.5 (5.3)	9.1 (1.4)

revealed differences between the triazolam (Sit-TR) and the placebo condition (Sit-PL). In the first third of the night, the precentages of stage 4 and SWS (stages 3 + 4) were higher after triazolam than after placebo [stage 4 as percent of total sleep time: 22.0 ± 4.4 (SEM) versus 13.7 ± 3.7; $P < 0.01$; paired t-test, two-sided], while the frequency of brief awakenings tended to be lower (number of isolated 20-s waking epochs per hour: 0.9 ± 0.4 versus 2.7 ± 0.8; $P < 0.1$; paired t-test, two-sided). Furthermore, the number of 20-s awakenings was negatively correlated with SWS in the first third of the night ($r = -0.56$, $P < 0.05$, $n = 16$; pooled data of the triazolam and the placebo condition). In the last third of the night, stage 4 tended to be lower in the drug condition as compared to the placebo condition ($0.6 \pm 0.4\%$ versus $4.2 \pm 1.8\%$; $P < 0.07$). There were no other significant differences in sleep parameters between corresponding thirds of the night.

Subjective sleep quality (Fig. 2)

Subjective sleep quality as assessed by the 100 mm visual analog scale (superficial versus deep sleep; restless versus quiet sleep) was significantly impaired for the placebo sitting condition, whereas the changes for the triazolam condition were not significant. Sleep was rated as deeper in the post-triazolam night than in the baseline night (BL-TR).

When comparing the two sitting conditions, sleep was rated as more quite after triazolam than after placebo. Significant differences were obtained neither between corresponding baseline nights nor between corresponding post-treatment nights.

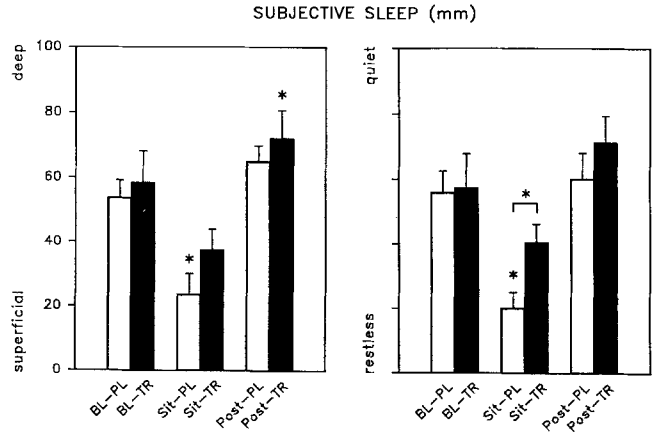

Fig. 2. Self-rated sleep quality in the morning (100 mm VAS; superficial vs deep sleep; restless vs quiet sleep) after baseline sleep in bed (BL-PL, BL-TR), after sleep in a sitting position with placebo (Sit-PL) or triazolam (Sit-TR), and after sleep in bed in the following night (Post-PL, Post-TR). Mean values with SEM ($n = 8$). *Asterisks* indicate significant differences from the corresponding baseline night, except for the asterisk above the bracket which refers to the Sit-PL - Sit-TR comparison ($P < 0.05$; Wilcoxon matched pairs, signed ranks test, two-sided)

EEG spectra

Comparison of triazolam and placebo. To visualize the effects of triazolam, EEG power spectra in the triazolam night were expressed relative to the placebo night. In nonREM sleep a broad and significant reduction of the values between the low delta range and the low alpha range was present (Fig. 3). An increase was seen in the

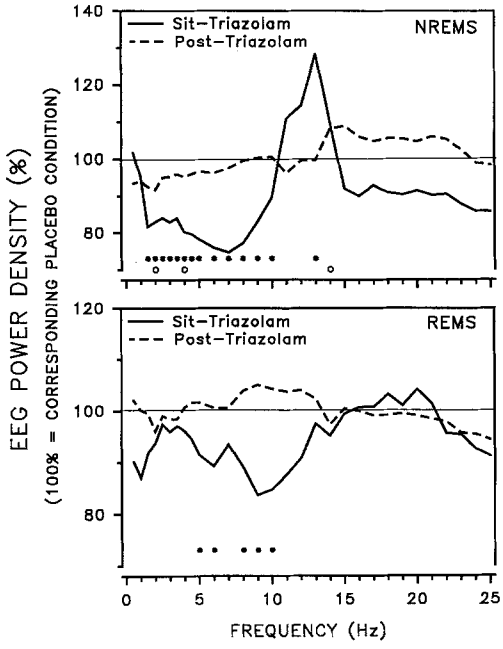

Fig. 3. Effect of triazolam on relative EEG power density in non-REM sleep and REM sleep: comparison to placebo. Spectra represent mean values ($n = 8$) for the drug night (*continuous line*) and post-drug night (*interrupted line*) computed for successive 0.5-Hz or 1-Hz bins. The values of the Sit-TR and Post-TR night were expressed as percentage of the Sit-PL and Post-PL night respectively. Significant deviations ($P < 0.05$; paired t-test on log transformed percentage values, two-sided) from the corresponding placebo value are indicated by *filled circles* for the drug night and *open circles* for the post-drug night. They are indicated at the upper limit of the bins

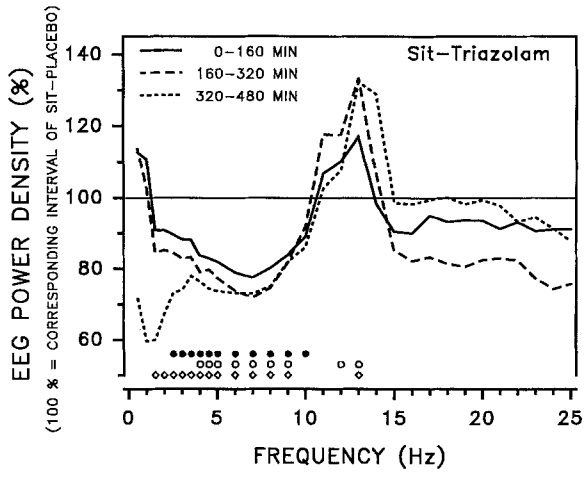

Fig. 4. Effect of triazolam on relative EEG power density in non-REM sleep, analyzed per thirds of the night (i.e. time in chair). The values of the drug night were expressed as percentage of the corresponding third of the placebo night. Significant deviations ($P < 0.05$; paired t-test on log transformed percentage values, two-sided) from the corresponding value in the placebo condition are indicated by *filled circles* for the first part, by *open circles* for the second part, and by *diamonds* for the third part of the night

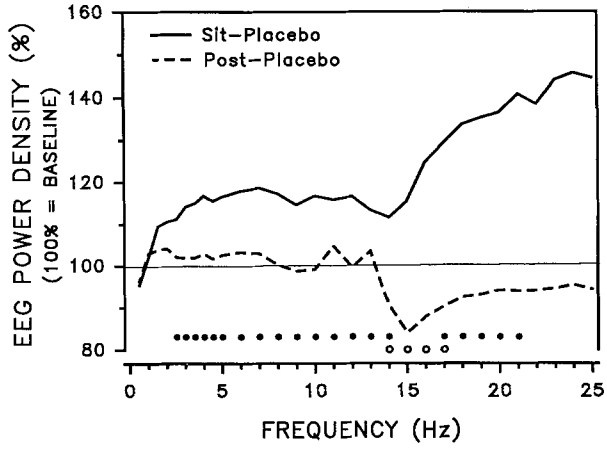

Fig. 5. Effect of posture on EEG power spectra in nonREM sleep. Power density in nonREM sleep for the sitting condition (Sit-PL) and the post-treatment night in bed (Post-PL) was expressed as percentage of the corresponding value for the preceding baseline night (BL-PL). Significant deviations ($P < 0.05$; paired t-test on log transformed percentage values, two-sided) from baseline are indicated by *filled circles* for the placebo night and *open circles* for the post-placebo night

12.25–13.0 Hz bin which is in the frequency range of sleep spindles. The changes in the triazolam night were less prominent for the REM sleep spectrum where only values of five bins in the theta and alpha range were significantly reduced.

In the post-triazolam night only minor deviations from the post-placebo values were observed for nonREM sleep and no significant effects for REM sleep (Fig. 3). The nonREM sleep spectra were reduced in two bins of the delta band and increased in the 13.25–14.0 Hz bin.

Time course of triazolam effects. To document the time course of the effects of triazolam on EEG power spectra in nonREM sleep, values were calculated by thirds of the night (i.e. time in chair). Comparison of thirds of the triazolam night with corresponding placebo values revealed that the changes persisted throughout the entire sleep episode (Fig. 4). Although in the third interval statistically significant differences extended over a broader frequency range, one-way ANOVAs on log-transformed percentage values did not yield a significant effect for the factor interval' in any frequency bin.

Comparison of sitting and recumbent sleep. EEG power density in nonREM sleep was higher for the sitting condition than for the recumbent condition. Thus a significant enhancement was found in the 2.25–21.0-Hz range in the placebo recordings as compared to the preceding baseline (Fig. 5). A two-factor repeated measures ANOVA with factors 'Condition' and 'Frequency bin' applied to the absolute values of the baseline night (BL-PL) and placebo night (Sit-PL) revealed a significant effect of 'Condition' ($F_{1,7} = 9.68$; $P < 0.02$) and 'Frequency bin' ($F_{29,203} = 462.0$; $P < 0.0001$) but no significant interaction between these two factors ($F_{29,203} = 2.30$; NS). In the post-placebo night power density reverted to baseline with the exception of the 13.25–17.0-Hz range in which the values were reduced.

Discussion

The sitting position impaired the objective and subjective sleep quality. Wakefulness after sleep onset was increased and thereby sleep efficiency and total sleep time were reduced. Further signs of impaired sleep quality were the increase in the amount of stage 1, the prolongation of REM sleep latency and the reduction of REM sleep. In the recovery night, some of the sleep parameters changed in the opposite direction which represents a compensatory response to the sleep deficit.

Although the mean values of the sleep parameters indicated that triazolam was able to attenuate the sleep impairment induced by the sitting position, the differences from the placebo condition were not significant. However, the ratings in the morning showed that sleep after triazolam was perceived as more quite. Moreover, the analysis by thirds of the night revealed that triazolam augmented the percentage of stage 4 and SWS in the first third of the night. This effect was offset by a trend in the opposite direction in the last third of the night, so that no significant differences were present for the entire sleep episode. The initial augmentation of SWS is in accordance with the data of Balkin et al. (1989) who reported a dose dependent increase of SWS when subjects were administered triazolam before sleeping in a sitting position. In contrast to the present data, the effect was observed for the entire sleep episode. The differences in the experimental setting may account for the different results. Thus the subjects recorded by Balkin et al. could sleep during daytime for 6 h in a well-lit, crowded room after a waking episode of 24 h, whereas our subjects had the opportunity to sleep during the night for 8 h in a dimly lit room after the habitual 16-h waking episode. In the previous study, both sleep efficiency (71.5 versus 79.2%) and SWS (35 min versus 77.6 min) after placebo were lower than in the present experiment. Nevertheless, in both studies, the benzodiazepine hypnotic induced a transitory or persistent increase in SWS under conditions of sleep impairment despite the fact that benzodiazepine receptor agonists are known to suppress SWS, when sleep is undisturbed (see Borbély et al. 1991). Apparently, the rise in SWS is an early sign of a drug-induced improvement of sleep continuity.

All-night spectral analysis of the sleep EEG revealed that triazolam reduced the power density of the nonREM sleep EEG in the low frequency range (up to 10 Hz), and enhanced EEG activity in the frequency range of sleep spindles. In a previous study (Borbély et al. 1985), a 0.5 mg dose of triazolam induced very similar, yet more prominent changes of the sleep EEG spectrum. Whereas the 0.25 mg dose in the present study reduced the nonREM sleep spectrum in the theta range by somewhat more than 20%, an almost 40% reduction had been observed for the higher dose. The effects on the REM sleep spectrum were also strikingly similar in the present and previous study, the maximum reduction occurring in both cases in the 9–10-Hz range. A dose-response relationship was also evident for REM sleep.

Computation of spectra by thirds of night allowed the time course of the pharmacological effect to be followed. Even though the elimination half life of triazolam is only 2–3 h, the spectral changes persisted unabated into the last third of the night. Similar findings had been obtained for the 0.5 mg dose of triazolam (Borbély et al. 1985) as well as for other rapidly eliminated benzodiazepine receptor agonists [midazolam (Trachsel et al. 1990); zolpidem (Brunner et al. 1991)]. These results indicate that cerebral functions are still altered at a time when the hypnotic effect has largely subsided. The study of the 0.5 mg dose of triazolam revealed not only persistent drug effects throughout the night but even a reduction of slow-wave activity in the subsequent drug-free night. Although in the present study the post-triazolam spectra of nonREM sleep deviated only little from the corresponding post-placebo level, some indication of a reduced delta activity was present.

Some of the effects of triazolam on the sleep EEG had been already recognized in early computer-aided studies (Johnson and Spinweber 1981; Johnson et al. 1983). They are strikingly similar to the EEG modifications induced by various other benzodiazepine hypnotics [flunitrazepam (Borbély et al. 1983, 1985), flurazepam (Johnson and Bickford 1976; Feinberg et al. 1979; Johnson et al. 1979, 1983; Azumi and Shirakawa 1982; Borbély et al. 1983, 1985), midazolam (Trachsel et al. 1990), nitrazepam (Azumi and Shirakawa 1982), temazepam (Dijk et al. 1989)], as well as by the non-benzodiazepine hypnotics zopiclone (Trachsel et al. 1990) and zolpidem (Brunner et al. 1991). Since the common property of these compounds is their agonistic action on the $GABA_A$-benzodiazepine receptor complex, their effect on the sleep EEG has been referred to as "spectral benzodiazepine signature" (Trachsel et al. 1990). Substances such as ethanol, whose hypnotic action is presumably mediated by different mechanisms, induced different changes of the sleep EEG (Dijk et al. 1992).

Unexpectedly, the analysis of the present data revealed that body position had a prominent effect on the EEG spectra. Power density in nonREM sleep was significantly higher when the subjects were sitting than when they were recumbent. Similar effects were observed in REM sleep (data not shown). The posture-induced effects differed from those induced by physiological manipulations (e.g. sleep deprivation; Borbély et al. 1981; Dijk et al. 1991) or pharmacological compounds (see above), in that the spectra were altered similarly over a broad frequency range. The posture-induced effects were also present in the triazolam night in which they appeared to be additive to the drug-induced effects. This was evident when the spectral values of the triazolam night (Sit-TR) were expressed relative to those of baseline sleep in bed (data not shown). The posture-dependent effects on the EEG may be associated with differences in hemodynamics. Further experiments are required to investigate this intriguing observation.

We conclude that a 0.25 mg dose of triazolam does not prevent a posture-induced sleep disturbance, but attenuates the impairment of subjective sleep quality. The drug induced changes in the sleep EEG which are typical for benzodiazepine receptor agonists. These changes were not reflected by the distribution of sleep stages based on conventional scoring criteria. The study provides further evidence for the usefulness of computer-aided EEG analysis in pharmacological sleep studies.

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References

Azumi K, Shirakawa S (1982) Characteristics of spindle activity and their use in evaluation of hypnotics. Sleep 5:95–105

Balkin TJ, O'Donnell VM, Kamimori GH, Redmond DP, Belenky G (1989) Administration of triazolam prior to recovery sleep: effects on sleep architecture, subsequent alertness and performance. Psychopharmacology 99:526–531

Borbély AA, Åkerstedt T, Benoit O, Holsboer F, Oswald I (1991) Hypnotics and sleep physiology: a consensus report. Eur Arch Psychiatry Clin Neurosci 24:13–21

Borbély AA, Baumann F, Brandeis D, Strauch I, Lehmann D (1981) Sleep deprivation: effect on sleep stages and EEG power density in man. Electroenceph Clin Neurophysiol 51:483–493

Borbély AA, Mattmann P, Loepfe M, Fellmann I, Gerne M, Strauch I, Lehmann D (1983) A single dose of benzodiazepine hypnotics alters the sleep EEG in the subsequent drug-free night. Eur J Pharmacol 89:157–161

Borbély AA, Mattmann P, Loepfe M, Strauch I, Lehmann D (1985) Effect of benzodiazepine hypnotics on all-night sleep EEG spectra. Hum Neurobiol 4:189–194

Brunner DP, Dijk DJ, Tobler I, Borbély AA (1990) Effect of partial sleep deprivation on sleep stages and EEG power spectra: evidence for nonREM and REM sleep homeostasis. Electroenceph Clin Neurophysiol 75:492–499

Brunner DP, Dijk DJ, Münch M, Borbély AA (1991) Effect of zolpidem on sleep and sleep EEG spectra in healthy young men. Psychopharmacology 104:1–5

Dijk DJ, Beersma DGM, Daan S, van den Hoofdakker RH (1989) Effects of seganserin, a 5-HT_2 antagonist, and temazepam on human sleep stages and EEG power spectra. Eur J Pharmacol 171:207–218

Dijk DJ, Brunner DP, Borbély AA (1991) EEG power density during recovery sleep in the morning. Electroenceph Clin Neurophysiol 78:203–214

Dijk DJ, Brunner DP, Aeschbach D, Tobler I, Borbély AA (1992) The effects of ethanol on human sleep EEG power spectra differ from those of benzodiazepine receptor agonists. Neuropsychopharmacology 7:225–232

Feinberg I, Fein G, Walker JM, Price LJ, Floyd TC, March JD (1979) Flurazepam effects on sleep EEG. Arch Gen Psychiatry 36:95–102

Johnson LC, Bickford RG (1976) Effect of flurazepam on sleep spindles and K-complexes. Electroenceph Clin Neurophysiol 40:67–77

Johnson LC, Spinweber CL (1981) Effect of a short-acting benzodiazepine on brain electrical activity during sleep. Electroenceph Clin Neurophysiol 52:89–97

Johnson LC, Seales DM, Naitoh P, Church MW, Sinclair M (1979) The effects of flurazepam hydrochloride on brain electrical activity during sleep. Electroenceph Clin Neurophysiol 47:309–321

Johnson LC, Spinweber CL, Seidel WF, Dement WC (1983) Sleep spindle and delta changes during chronic use of a short-acting and a long-acting benzodiazepine hypnotic. Electroenceph Clin Neurophysiol 55:662–667.

Mattmann P, Loepfe M, Scheitlin T, Schmidlin D, Gerne M, Strauch I, Lehmann D, Borbély AA (1982) Day-time residual effects and motor activity after three benzodiazepine hypnotics. Arzneimittelforschung 32:461–465

Rechtschaffen A, Kales A (1968) A manual of standardized terminology, techniques and scoring systems for sleep stages of human subjects. Brain Information Service/Brain Research Institute, Los Angeles, pp 1–60

Trachsel L, Dijk DJ, Brunner DP, Klene C, Borbély AA (1990) Effect of zopiclone and midazolam on sleep and EEG spectra in a phase-advanced sleep schedule. Neuropsychopharmacology 3:11–18