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Effects of Abstinence From Smoking on Sleep and Daytime Sleepiness*

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This study examined the effect of smoking abstinence on sleep quality, daytime sleepiness, and mood in 18 subjects (10 men and 8 women) aged 35 to 49 years who had smoked at least 20 cigarettes per day for more than 2 years. Subjects were studied on two consecutive weeks following an adaptation night. During week 1 (study nights 1, 2, and 3), the subjects smoked as usual. Smoking abstinence was mandatory during week 2 beginning 3 h prior to night 4 and ending after the final tests on night 6. Complete sleep monitoring each night was followed by multiple sleep latency tests (MSLTs) throughout the day. Psychomotor tests and mood observations were performed throughout the day between the MSLTs. The results of testing when the subjects smoked were compared with those during nonsmoking days and nights. Nights 1 and 4 were considered adaptation nights and not included in the analysis. Overnight studies showed a significant increase in the number of relative arousals (a change in sleep stage to wake, stage 1 sleep, or movement), stage changes, and awakenings during smoking cessation. The MSLT latency to stage 1 sleep decreased during smoking cessation. Also during abstinence, the subjects reported that they felt more irritable, had increased feelings of anxiety, felt greater tension, and had more cravings for cigarettes. We conclude that smoking cessation is associated with increased daytime sleepiness and impaired mood. The daytime sleepiness may be due to the combination of sleep disturbance and withdrawal of the nicotine normally provided through smoking.

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METHODS

The subjects were recruited with an advertisement in a local newspaper. The target population was men and women aged 35 to 55 years who had smoked cigarettes for at least 5 years and were currently smoking at least 20 cigarettes a day. Potential subjects filled out a questionnaire concerning symptoms of depression; the use of medication, alcohol, illegal drugs; and prior or current medical illness. If the questionnaire indicated

Effects of Abstinence From Smoking on Sleep and Sleepiness (Prosise et al)
depresion, use of illegal substances, use of stimulant or hypnotic medication, daily consumption of alcohol, or evidence of a high consumption of caffeine (more than four cups of coffee daily), the subjects were excluded. The study group consisted of 18 smokers (10 men and 8 women) aged 35 to 49 years (mean, 41.3 years) who had smoked 20 to 45 (mean, 32) cigarettes per day and had smoked for 17 to 38 years (mean, 23.6 years). One subject was a paraplegic. Subjects gave written informed consent before participating in the study. The study was approved by our institution’s human studies committee. The Fagerstrom tolerance questionnaire was administered to assess the tolerance to nicotine. The possible score ranges from 0 to 11 with a score of 6 or greater indicating a high probability of tolerance to nicotine.

After an adaptation night, computer practice tests, and a sleep history, the subjects were studied on two consecutive weeks: week 1—nights 1, 2, 3, and week 2—nights 4, 5, 6 (and the following days). The subjects were allowed to smoke normally during week 1 and were required to abstain from smoking during week 2 (from 3 h before bedtime on night 4 until the end of day 6). The first 12 subjects were studied on an additional 2 nights (nights 7 and 8) on which smoking was optional. Ten subjects smoked during this time and because the data did not differ from the first three nights of smoking, the final two nights were dropped from the protocol.

Subjects were permitted to smoke in one separate, designated room measuring 5.4 m². This room was removed from the study area. Urine cotinine analyses were performed on the final six subjects to confirm smoking abstinence during the nonsmoking period. Urine was collected throughout the final day of the study and analyzed for each of the six subjects as a pooled sample. The urine was immediately stored at −70°C until analyses were performed by radioimmunoassay method.

Polysomnographic recordings were made each night using standard methods with a polygraph (Grass model 7BD, Quincy, Mass) including the following: central and occipital EEG, electro-oculogram (EOG), mentalis and anterior tibialis electromyogram (EMG), ECG, and oronasal airflow (measured with a Grass model ONT2 thermistor). Chest and abdominal movements were detected with respiratory inductive plethysmography (Respitrace, Ardsley, NY) and arterial oxygen saturation was monitored with a pulse oximeter (Ohmeda, Madison, Wis).

Following each night, the subjects performed a series of psychomotor tests and mood observations alternating with multiple sleep latency testing (MSLT) throughout the day. Sleep latency testing was conducted at 10 AM, 12 noon, 2 PM, 4 PM, and 10 PM. During the MSLT, the EEG, EOG, and chin EMG were monitored for 20 min or until the subject reached 1 min of stage 2 or rapid eye movement (REM). The latency to stage 1 was defined as total minutes from lights out to the first epoch of stage 1 sleep.

Tests of performance and mood and a questionnaire assessing symptoms of smoking withdrawal (Smokecheck) were administered by a computerized test battery system at 9 AM, 11 AM, 3 PM, and 9 PM. The performance tests included a 30-min version of the Wilkinson vigilance test,12 short-term word memory—scored for number of words correctly recalled,13 proof-reading—the number of lines of text with double words that were correctly identified, and a memory and search task (MAST) test that asks subjects to remember 1, 3, or 5 letters and identify lines of letters containing the target letters.14,15 These tests were chosen because they have been used with sleep loss assessment14,15 and in assessment of performance changes after smoking cessation.16 In the vigilance, proof reading, and MAST tests, the ability of the subjects to detect target and reject nontarget stimuli was expressed by computing the discrimination index (A’). The A’ is a nonparametric index based on signal detection theory16 that is computed from the number of hit and false alarm responses as a fraction of the total number of target and nontarget stimuli presented. It estimates the area under the curve (usually 0.5 to 1) generated by plotting hit probability vs false alarm probability for different values of response bias using a single point on the curve. This controls for changes in hit rate due to changes in response bias.

The number of lines the subjects scored in the MAST and proof reading tests (in a set time) were also analyzed. The profile of mood states (POMS) determined the degree of tension, depression, anger, vigor, fatigue, or confusion experienced by the subjects.17 The degree of anxiety was assessed by the state portion of the State-Trait Anxiety Inventory (STAI) developed by Spielberger and associates.18 This examination was performed at 8 AM and 11 PM and consisted of 20 multiple-choice questions. Each answer was scored on a scale of 1 to 4 and the possible score ranged from 20 to 80 with a higher score indicating more anxiety. The Smokecheck questionnaire consisted of a list of smoking cessation symptoms based on nine withdrawal symptoms identified by Cummings et al.,14 including coughing, irritability, sleeplessness, dizziness, constipation, tightness in chest, sleepiness, fatigue, restless, sores in mouth, and tobacco cravings. Subjects responded for each symptom on a scale of 1 to 5 (5 being most intense) and also stated the total number of cigarettes smoked since last questioned. The amount of cigarettes smoked was also continuously monitored and recorded by the technicians.

Data Analysis And Statistical Analysis

Sleep was staged in 30-s epochs using standard criteria.11 Total sleep time (TST) and the sleep period time (SPT) were determined. The SPT was defined as the time from the first epoch of any stage of sleep until the final awakening. The times spent in each sleep stage in minutes and as a percentage of TST and SPT were also calculated. An arousal was defined as a sudden change in the EEG such as EEG speeding or a burst of alpha wave activity for at least 5 s. Movement time was defined as an epoch more than 50 percent unreadable due to movement artifact. A relative arousal was defined as a change in sleep stage, stage 1, or movement. Leg movement scoring criteria included an initial increase in leg EMG to at least double the background EMG lasting 0.5 to 5 s. An apnea was defined as an absence of airflow at the nose and mouth for 10 s or more. A hypopnea was defined as a decrease in airflow of 50 percent or greater from the baseline lasting 10 s or longer. The apnea + hypopnea index was defined as the sum of the number of apneas and hypopneas per hour of sleep.

The original study group consisted of ten men and eight women. One woman was dropped from the study when she became ill during the second week of testing. One man was dropped when urine cotinine values suggested that he had been smoking during the nonsmoking week. The data from the 16 remaining subjects were analyzed by the repeated measures analysis of variance19 using a statistical package (2V) (BMDP Statistical Software, Los Angeles). Smoking vs nonsmoking conditions were analyzed by comparing the mean results of nights 2 and 3 and the following days (smoking) with the mean of nights 5 and 6 and the following days (nonsmoking). The time of day was also included as a factor in the analysis of the MSLT results. When we reviewed the time course of the performance data, we noted an increase over the first week (days 1 to 5) with a plateau during day 3 and an early fall during day 4 (first nonsmoking day) with a subsequent return toward the day 3 results. Therefore, we compared the mean test values on days 2 and 3 (smoking) with nonsmoking test values at the different times on day 4 and the mean values on days 5 and 6 using a © 1994 American College of Chest Physicians
Table 1—Sleep Data*

<table>
<thead>
<tr>
<th></th>
<th>Smoker</th>
<th>Nonsmoker</th>
<th>F(1,15)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST, min</td>
<td>381±53</td>
<td>378±40</td>
<td>0.17</td>
<td>0.69</td>
</tr>
<tr>
<td>Stage 1, %SPT</td>
<td>11±5</td>
<td>12±51</td>
<td>0.14</td>
<td>0.30</td>
</tr>
<tr>
<td>Stage 2, %SPT</td>
<td>47±9</td>
<td>44±11</td>
<td>1.65</td>
<td>0.21</td>
</tr>
<tr>
<td>Stage 3, %SPT</td>
<td>5±3</td>
<td>5±2</td>
<td>0.18</td>
<td>0.68</td>
</tr>
<tr>
<td>Stage 4, %SPT</td>
<td>9±7</td>
<td>9±8</td>
<td>0.38</td>
<td>0.55</td>
</tr>
<tr>
<td>Stage REM, %SPT</td>
<td>21±6</td>
<td>21±5</td>
<td>0.11</td>
<td>0.74</td>
</tr>
<tr>
<td>WASO, min</td>
<td>24±17</td>
<td>32±25</td>
<td>1.48</td>
<td>0.24</td>
</tr>
<tr>
<td>Stage changes, No.</td>
<td>114±32</td>
<td>133±46</td>
<td>7.38</td>
<td>0.02</td>
</tr>
<tr>
<td>Arousal index, No./h</td>
<td>11.8±5.8</td>
<td>12.2±6.8</td>
<td>0.17</td>
<td>0.68</td>
</tr>
<tr>
<td>Relative arousals</td>
<td>27±10</td>
<td>34±20</td>
<td>5.87</td>
<td>0.00</td>
</tr>
<tr>
<td>Awakenings, No.</td>
<td>11±7</td>
<td>18±16</td>
<td>6.66</td>
<td>0.02</td>
</tr>
<tr>
<td>Latency to sleep</td>
<td>12±10</td>
<td>8.7±8</td>
<td>1.78</td>
<td>0.20</td>
</tr>
</tbody>
</table>

*Values are means±SD. WASO = wake after sleep onset; smoking—average of nights 2, 3; nonsmoking—average of nights 5, 6.

RESULTS

The age of the subjects (n=16) ranged from 35 to 49 years with a mean (± SD) of 41.6±5.0 years. The mean of the weights expressed as a percentage of mid range ideal weight was 112.0±22.8. Two of the women were quite obese (172 percent and 167 percent of ideal weight). The subjects had been smoking between 20 and 50 cigarettes per day for at least 2 years. The subjects' scores on the Fagerstrom nicotine tolerance questionnaire ranged from 8 to 10 with a mean of 8.7±0.79 indicating a high probability of tolerance to nicotine. During the three nights when smoking was permitted, the subjects smoked an average of 24.3 cigarettes per day with a range of 12 to 57 per day.

The night time sleep data (Table 1) indicate that the TST and the sleep stage percentages (percent SPT) were similar between smoking and nonsmoking weeks; however, a greater number of relative arousals (p<0.05), an increased number of stage changes (p<0.02), and an increased number of awakenings (p<0.02) were present during smoking abstinence.

The mean apnea + hypopnea indices on smoking and nonsmoking nights were 5.2±6.8 and 4.2±5.6 events per hour of sleep, respectively (p=NS). Only one very obese female subject (172 percent of ideal body weight) had an apnea + hypopnea index above 15 events per hour. Her apnea + hypopnea index did not differ on smoking and nonsmoking nights (20.6 vs 21.3 events per hour). Her MSLT tests showed sleep latencies above 15 min in both the smoking and nonsmoking conditions. The mean index of periodic leg movements (PLMs) was slightly but not significantly higher on nonsmoking nights (4.8±8.1) compared with smoking nights (3.0±5.6 events per hour of sleep).

The mean latency to stage 1 sleep during the daytime naps decreased 3 min during smoking cessation (from 14±3 to 11±4 min, F(1,15)=7.65, p<0.02). The mean values of each subject for smoking and nonsmoking nights are shown in Figure 1. A significant time of day effect was also noted (F(4,60)=9.96, p<0.0001); however, there was no significant interaction with the smoking/nonsmoking condition (F(4,60)=0.27). Post-hoc analysis of the time of day effect with the Student-Newman-Keuls method showed for both the smoking and nonsmoking conditions that only the first nap differed significantly from the others (shorter sleep latency) at a p=0.05 level.

Mood was impaired during smoking cessation. Subjects reported (POMS) increased tension (F(1,15)=7.85, p<0.02) during the nonsmoking week. On the Smokecheck questionnaire the subjects also reported increased feelings of irritability (F(1,15)=10.7, p<0.006) as well as the expected increased cravings to smoke (F(1,15)=5.5, p<0.04) when they stopped smoking. The STAI also showed a higher anxiety score during smoking cessation (F(1,15)=7.1, p<0.02), although the increase in the anxiety score was relatively small (30.2±6.8 vs 32.4±6.9).

The tests of performance revealed a significant drop in the number of lines examined in a fixed period of time in the MAST test (Fig 2) on the first test period of day 4 (the first nonsmoking day). This was approximately 12 h since smoking abstinence had begun. The A' of the MAST test was not altered by smoking cessation. Although the A' on the vigilance test also showed a fall from day 3 to day 4, the change was not statistically significant. There
was no evidence of a decrement in the other performance tests during the nonsmoking week. Thus, despite the changes in mood and tendency to fall asleep, we found that smoking abstinence impaired performance only slightly.

DISCUSSION

The major finding of this study is that abstinence from smoking acutely impairs sleep quality and increases daytime sleepiness. Smoking abstinence increased the number of sleep stage changes, awakenings, and relative arousals during the night. As expected, mood was also impaired and cigarette craving increased. Although smoking abstinence did not radically alter the total amount of sleep or percentage of sleep stages, it was associated with a decreased latency to sleep during daytime naps (MSLT).

Our data support the findings of many questionnaire studies with respect of symptoms of sleep disturbance and daytime sleepiness. It might be argued that the sleep differences reported herein are actually conservative estimates as the initial nights in the sleep laboratory were smoking nights. However, we found no difference in any sleep variable between the first and third weeks of testing for the ten subjects who completed three weeks of testing and chose to smoke during week 3.

Our results with respect to sleep quality during smoking cessation do differ from those found by Soldatos and coworkers. This may be due to the fact that our group of subjects was older and had normal baseline nocturnal sleep latencies. In addition, we looked for more subtle evidence of nocturnal sleep disturbance such as the number of sleep stage changes. The effect of smoking cessation may vary with the population studied. For example, the effects of smoking cessation could differ in a population with no insomnia. We attempted to select subjects with no history of underlying sleep disturbance.

The increase in daytime sleepiness during smoking abstinence could be due to both the increase in sleep disturbance and to the withdrawal of the stimulant nicotine. During tobacco abstinence in awake subjects, subtle EEG changes have been seen as early as 29 h after smoking cessation and may last in some subjects up to 7 days. The changes in EEG include a decrease in alpha and beta frequency and an increase in theta power. Indeed, sleep onset is associated with a decrease in the amount of alpha activity and an increase in theta. Small doses of nicotine comparable to those obtained by smoking induce changes in central nervous system activity, indicating an increase of cortical arousal. Nicotine replacement therapy can also reverse the EEG changes seen during smoking abstinence. Thus, nicotine withdrawal may directly increase daytime sleepiness. It was not the goal of this study to separate the effects of nicotine withdrawal and sleep disturbance on the daytime sleepiness. We believed that is was important to first demonstrate that smoking abstinence (both behavioral and physiologic components) was associated with sleep disturbance and daytime sleepiness.

Although we found evidence of mood impairment during smoking cessation, there was only minimal evidence of changes in performance tests between smoking and nonsmoking weeks. This may indicate that although mood was affected, it was not enough to affect the motivation or ability to work. Myrsten and coworkers also found minimal changes in performance during smoking cessation despite impairment of mood. In contrast, Snyder et al did find evidence of performance decrements using a computerized assessment battery of two- and six-letter search (a variation of the MAST test), logical reasoning, digit recall, and serial addition/subtraction that peaked at 24 to 48 h after tobacco withdrawal. They found mainly an increase in response time, but also a reduction in accuracy in the last two tests. The finding of an increase in response time on the MAST test is equivalent to our finding of a decrease in the number of lines examined in a fixed time.

The minimal changes in performance despite an increased tendency for daytime sleepiness in our subjects could be attributed to a greater sensitivity of the MSLT to detect preceding sleep disturbance. It might also be maintained that the lack of performance decrement in performance tests during non-
smoking weeks could be due to a learning effect because subjects had 3 days of testing in the smoking condition before the nonsmoking week. While some subjects showed increases in performance over day 2, the test scores had reached a plateau by the end of day 3. When we examined the performance data of the ten subjects in whom a third week of testing was performed (smoking), we still could not demonstrate additional evidence of performance differences between smoking and nonsmoking weeks.

It might also be argued that the abstinence from smoking was too brief to induce performance deficits. This seems unlikely because definite deficits in mood and sleep were documented and the performance deficits documented by Snyder et al peaked at 24 to 48 h after smoking cessation.

Our study does not provide information on the effects of longer-term smoking abstinence on sleep and performance. Future study is needed to determine how long the changes in sleep and daytime sleepiness persist during smoking cessation. In addition, we had a quantitative method to detect smoking during the nonsmoking condition in only six of our subjects. One should note that even urine cotinine analysis cannot exclude low levels of smoking. However, the fact that we documented definite changes in the nonsmoking week suggests that our subjects either did not smoke or smoked at low levels.

The findings of our study are relevant with respect to understanding the tobacco withdrawal syndrome and designing approaches to increase the probability of successful smoking cessation. We have documented that abstinence from smoking does in fact disturb sleep and increase daytime sleepiness. Thus, measures designed to improve sleep quality during acute withdrawal such as benzodiazepines might decrease the symptoms of tobacco withdrawal. With the advent of nicotine replacement therapy in the form of a sustained-release patch, the possibility of reducing the physiologic component of nicotine withdrawal is now more practical. However, nicotine replacement therapy can itself disturb sleep. This has resulted in the development of a 16-h nicotine patch (instead of 24 h). However, to our knowledge, neither 16 nor 24 hours of nicotine replacement has been compared with placebo with respect to quantitative measures of sleep quality and daytime sleepiness during abstinence from tobacco. Our study shows that the amount of sleep disturbance by nicotine replacement during smoking cessation must be evaluated with the knowledge that sleep is disturbed by abstinence from tobacco alone.

In summary, this study shows that smoking cessation is associated acutely with sleep disturbance and increased daytime sleepiness. The increased daytime sleepiness could be secondary to either the nocturnal sleep disturbance or the withdrawal of nicotine. The existence of poor sleep and daytime sleepiness secondary to cessation of smoking suggests that at least some individuals may have difficulty in withdrawing from cigarettes as a consequence of disturbed sleep and daytime mood. If sleep were improved during smoking cessation, residual effects of poor sleep on alertness and mood might be reduced and the probability of continued smoking cessation increased.

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