

A Comparative Model: Reaction Time Performance in Sleep-Disordered Breathing Versus Alcohol-Impaired Controls

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Objectives/Hypothesis: Patients with sleep-disordered breathing have reaction time deficits that may lead to catastrophic accidents and loss of life. Although safety guidelines do not exist for unsafe levels of sleepiness, they have been established for unsafe levels of alcohol consumption. Since reaction time performance is altered in both, we prospectively used seven measures of reaction time performance as a comparative model in alcohol-challenged normal subjects with corresponding measures in subjects with sleep-disordered breathing. **Study Design:** Institutional Review Board-approved, nonrandomized prospective controlled study. **Methods:** Eighty healthy volunteers (29.1 ± 7.5 y of age, 56.3% female subjects) performed four reaction time trials using a psychomotor test at baseline and at three subsequent rising alcohol-influenced time points. The same test without alcohol was given to 113 subjects (47.2 ± 10.8 y of age, 19.3% female subjects) with mild to moderate sleep-disordered breathing. **Results:** Mean blood alcohol concentrations (BACs) in the alcohol-influenced subjects at baseline and three trials were 0, 0.057, 0.080, and 0.083 g/dL. The sleep-disordered subjects had mean respiratory disturbance indices of 29.2 events per hour of sleep. On all seven reaction time measures, their performance was worse than that of the alcohol subjects when BACs were 0.057 g/dL. For three of the measures, the sleep-disordered

subjects performed as poorly as or worse than the alcohol subjects when alcohol levels were 0.080 g/dL. These results could not be explained by sex or age differences. **Conclusion:** The data demonstrate that sleep-disordered subjects in this study (with a mean age of 47 y) with mild to moderate sleep-disordered breathing had worse test reaction time performance parameters than healthy, nonsleepy subjects (with a mean age of 29 y) whose BAC is illegally high for driving a commercial motor vehicle in California. This comparative model points out the potential risks of daytime sleepiness in those with sleep-disordered breathing relative to a culturally accepted standard of impairment. **Key Words:** Sleep-disordered breathing, alcohol drinking, psychomotor performance, reaction time, blood alcohol concentration, polysomnography.

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INTRODUCTION

Sleep-disordered breathing (SDB) is associated with hypoxemia and repetitive arousals that fragment sleep. Daytime fatigue and sleepiness, with subsequent deterioration of neurobehavioral functions, are a consequence of SDB.¹⁻⁵ The quality of life is subsequently altered with an awake somatic loss of well-being and altered daytime performance.^{6,7} The daytime sleepiness may be sufficient to result in catastrophic events to life, property, and the environment.⁸⁻¹³ Young et al.¹⁴ reported that the prevalence of SDB in conjunction with hypersomnolence in 30- to 60-year-old individuals was 2% in women and 4% in men. Thus pathologic sleepiness and related performance decrements affect an active group of the population of the United States. Individual common sense has not resulted in the self-limiting of strategic activities while sleepy, nor are there safety-related guidelines established for unsafe levels of sleepiness. This is not to say that other investigators have not suggested countermeasures following separate studies on sleep deprivation and simulated driving performance in SDB.¹⁵⁻¹⁷ Even though data from such studies were compelling, the effects of pathologic sleepiness may not be universally appreciated. This, we postu-

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late, is due in part to the lack of a simple comparative model. Sleepiness, whether from experimental sleep loss or from sleep-disordered breathing, can cause deterioration of reaction time (RT) as a result of slowing of cognitive functions.¹⁸⁻²¹ Decades ago, it had also been established that RTs deteriorated with increasing blood alcohol concentrations (BACs).²²⁻²⁵ In both situations these decrements in neurobehavioral function alter performance.²⁶⁻²⁸ Previous investigations have emphasized the relationship of alcohol and performance decrements to injury, death, and property loss associated with driving a motor vehicle. As a result of these findings, legal limits for blood alcohol levels were established for public health and safety. Since legal limits are already established for alcohol-impaired driving, it may be possible to construct a comparative model to correlate RT delays in alcohol-challenged subjects with those attained from subjects who are sleepy because of the effects of SDB.

MATERIALS AND METHODS

Study Design

This nonrandomized, prospective investigation was designed to assess RT performance impairments in patients with SDB to those in healthy young adults challenged with alcohol. University Institutional Review Board approval was attained for this investigation.

Research Subjects

Alcohol control group. Eighty healthy subjects were recruited with no history of snoring or sleep disorders, or drug or alcohol abuse. Inclusion criteria limited the study to adult cohorts (ages 21-60 y) who were light drinkers (wine or one hard-alcohol drink with dinner, or occasional weekend drinking) or very moderate drinkers (one to two drinks daily). Subjects who used alcohol on a more extensive basis (three drinks or more daily and drinking on the weekends) were excluded.

Sleep group. One hundred fifty-three patients with reported fatigue or sleepiness during the daytime with symptoms of SDB, or both, were recruited for this study and underwent RT testing. One hundred thirteen of these patients were accepted into this investigation after documentation of SDB by nocturnal polysomnography. Forty patients were excluded because of insufficient total sleep time of less than 240 minutes or no rapid eye movement (REM) sleep as similarly described by Young et al.¹⁴ In addition, those with split night studies were excluded. These excluded patients did not differ significantly from the overall group in age, sex, body mass index, or severity of SDB. All performed RT testing during the same circadian time sequence (1,000-1,300 h) and before polysomnographic recording.

Control: practice learning effect. A separate, healthy, nonsleepy, nonsnoring group (nonalcohol, n = 11) completed a 10-minute psychomotor vigilance task (PVT) test four times in succession, with a 5-minute rest between each session, to assess the potential for a learning or fatigue effect associated with repeated testing of RTs. The time of day of testing was the same as in the sleep-disordered group.

Evaluation

History and physical examinations were performed on all subjects, along with an Epworth Sleepiness Scale (ESS)²⁹⁻³² before entry into the study. Polysomnography was performed on the

sleep-disordered group. The following variables were monitored during nocturnal sleep: electroencephalogram, electrooculogram, snoring microphone, chin and leg electromyograms, electrocardiogram (modified V2 lead), airflow, thoracic and abdominal efforts, pulse oximetry, and intraesophageal pressure (Pes).

Testing

Breath ethanol testing. An Intoxilyzer, model 5000 (CMI, Inc., Owensboro, KY), using infrared alcohol detection technology (U.S. measurements, U.S. Department of Transportation [DOT]-approved), was used for all breath alcohol concentration (BrAC) measurements (grams of alcohol per 210 liters of breath), which is considered by DOT to be equivalent to BAC measurements (grams of alcohol per 100 milliliters of blood). Instrument standardization was calibrated against a known alcohol control (0.100 g/210 L), using a wet bath simulator, before and after each testing session (Toxitest II, CMI, Inc.).

Sleep activity monitoring. In normal subjects an actigraph worn on the dominant wrist was used to study the rest-activity cycle (sleep-wake cycle). (Ambulatory Monitoring, Inc., Ardsley, New York). Actigraphy and concurrent nightly sleep logs were recorded 3 days before testing the alcohol-influenced group and control test subjects, to ensure that they were not sleep deprived before the test date.³³⁻³⁵

Reaction time testing. All study subjects performed simple visual RT testing according to the schedules described below, using a PVT instrument.³⁶ A commercially available PVT instrument was used (Ambulatory Monitoring, Inc.). This handheld, portable, microprocessor-controlled instrument has been previously designed and validated to be highly sensitive to a sustained attentional process that is fundamental to normal alert neurobehavioral functioning.³⁶⁻³⁹ A performance trial consists of responding to a bright red light (light-emitting diode [LED]-digital counter) by pressing a response button as soon as the light stimulus is seen. The response stops the LED (1 s) and displays the RT in milliseconds (ms). The interstimulus interval varies randomly from 2 to 10 seconds over a 10-minute task duration with approximately 80 to 90 responses per trial. Data were maintained by solid-state storage and later downloaded to a personal computer. Each subject was instructed on the proper use of the PVT. Two trials were given for practice, and to extinguish any learning effect.

Procedure: alcohol group. All subjects were instructed not to eat past midnight, except for water, and commenced testing at 11:00 A.M. the next day, after 3 nights of full sleep (mean sleep time, 455 ± 57 min/night by actigraphy). Quiet, separate rooms were used and monitored by closed-circuit television. A baseline BrAC measurement was taken before ingestion of alcohol. Eighty percent of a calculated 1.0-g/kg dose of 80-proof (40% ethanol)

TABLE I.
Characteristics of 80 Alcohol-Challenged Subjects and of 113 Sleep-Disordered Subjects.

Variable	Alcohol-Challenged Subjects (N = 80)	Sleep-Disordered Subjects (N = 113)
Age (y)	29.1 ± 7.5	47.2 ± 10.8
Women (%)	56.3	19.5
Body mass index (kg/m ²)	23.4 ± 3.2	31.4 ± 7.4
Epworth Sleepiness Scale*	5.7 ± 3.4	11.5 ± 4.7

*Epworth Sleepiness Scale reflects the patient-reported chance of dozing in specific situations as well as daytime sleepiness (range 0-24, nonsleepy normal controls 5.9 ± 2.2).²⁹

Data are mean ± standard deviation for continuous parameters and percent for dichotomous variables.

TABLE II.
Polysomnographic Results of Patients With Sleep-Disordered Breathing (N = 113)

Variable	Value
Total sleep time (TST) (min)	327 ± 98
Sleep efficiency index (SEI)*	0.76 ± 0.14
Sleep latency (SL)†	14.4 ± 15.8
Apnea index (AI)‡	16.1 ± 23.2
Hypopnea index (HI)§	13.8 ± 16.1
Respiratory disturbance index (RDI)¶	28.7 ± 28.2
Nadir oxygen saturation (SaO ₂ %)	83.5 ± 9.8%
Maximal intraesophageal negative pressure (-cm H ₂ O)	-36.4 ± 28.0
Stage 1-4 sleep (min)	275 ± 80
REM sleep (min)	47.5 ± 28.4

*Total time asleep/total time in bed.

†Time in minutes from lights out to first sleep.

‡The number of apneas (cessation of breathing for ≥10 seconds) per hour of sleep.

§The number of hypopneas (reduction of respiratory airflow by 50% vs. prior recordings accompanied by an oxygen desaturation of 4%) per hour of sleep.

¶The number of apneas plus hypopneas per hour of sleep.

vodka, mixed with orange juice to a total volume of 200 mL, was initially used as the loading dose of ethanol to reach a BAC of less than the final target peak BAC of 0.08 g/dL. The fractionation of the loading dose (1.0 g/kg) was performed to limit, over the three trials, the possibility of dose-related nausea or vomiting. This dose, combined with a 20% supplemental dose given after the second PVT test, was sufficient to raise the respective BACs in incremental levels from a baseline BrAC of zero through a mean of 0.80 g/210 L of breath. Control for alcohol in the mouth was accomplished by rinsing the mouth vigorously and brushing the teeth with water, followed by a 2-minute wait before BrAC testing. Before ingestion of alcohol, a baseline 10-minute PVT trial was administered. PVT was performed and recorded only over the rising range of the BrAC for all three trials.⁴⁰⁻⁴² Each subject was allowed 10 minutes to ingest the initial ethanol dose. Fifteen

minutes to 20 minutes elapsed, after the start of the first drink, before the first BrAC measurement was taken, and then the subject immediately started PVT testing. At completion of the PVT (10 min) a second BrAC measurement was taken for a total time for completion of the first trial of less than 30 minutes. The mean of the two BrAC levels were recorded and used for analysis to more accurately depict the BrAC during testing. This method and test timing were used for all additional alcohol dosages, PVTs, and BrACs during the investigation.

Data Analysis

Polysomnography. Polygraphic recordings were scored following the international criteria of Rechtschaffen and Kales⁴³ for sleep staging and using the international definitions of sleep apnea and obstructive, mixed, and central apnea. The most negative inspiratory Pes was identified during each recording.

Psychomotor vigilance test metrics. Seven PVT RT measures were tabulated. These measures were the mean RT in milliseconds during the testing period, the maximum RT during the period; the number of times the subject required at least 500 milliseconds to respond (defined as PVT lapses or microsleep episode); the standard deviation (SD) of the RTs to all stimuli during the testing session; the mean of the 10 fastest RTs; the mean of the reciprocal of the RT (1/RT) measured in seconds; and the mean of the reciprocal of the 10 slowest RTs measured in seconds. Following the suggestion of Dinges et al.,²¹ reciprocals were used for the latter two measures because the reciprocals were more normally distributed than the variables themselves. These outcome measures are all summary RT statistics that reflect the time it took for subjects to respond to approximately 80 to 90 stimuli during each 10-minute testing period.

Statistical analysis. Comparisons between male and female sleep-disordered subjects were performed using χ^2 tests for dichotomous variables and, depending on distributional characteristics, using Student *t* tests or Wilcoxon's test for continuous variables. Repeated-measures analysis of variance (ANOVA) was used to evaluate changes over time in the seven measures of RT in the alcohol-challenged subjects. Regression residuals and influence statistics suggested that for three of the outcome measures, the model fit was compromised by a small number of

TABLE III.
Characteristics of Sleep-Disordered Breathing Subjects by Sex.

Variable	Women (N = 22)	Men (N = 91)	P Value
Age (yr)	47.5 ± 7.7	47.2 ± 11.5	.918
Body mass index (kg/m ²)	31.2 ± 7.7	31.5 ± 7.4	.870
Epworth Sleepiness Scale (range 0-24)*	12.9 ± 2.8	11.1 ± 5.0	.083‡
Polysomnographic results			
Total sleep time (TST)†	343 ± 83	323 ± 102	.406
Sleep latency (SL)†	19.0 ± 18.2	13.4 ± 15.2	.157
Apnea index (AI)†	3.5 ± 5.2	19.1 ± 24.8	.000‡
Hypopnea index (HI)†	8.2 ± 10.5	15.1 ± 17.0	.008‡
Respiratory disturbance index (RDI)†	11.9 ± 14.9	32.7 ± 29.2	.0001‡
Nadir oxygen saturation (SaO ₂ %)	89.2 ± 5.7%	82.2 ± 10.1%	.0003‡
Maximal intraesophageal negative pressure (-cmH ₂ O)	-29.9 ± 17.1	-38.5 ± 30.6	.182‡
Stage 1-4 sleep (min)	287 ± 65	272 ± 83	.444
REM sleep (min)	53.2 ± 29	46.0 ± 28	.313

*See Table I for definition.

†See Table II for definition.

‡P value based on Wilcoxon's test. Unpaired *t* tests were used for other variables.

TABLE IV.
Breath Alcohol Concentrations and Subject Responses During Each Trial Stage.

Variable	Alcohol Subjects (N = 80)				P Value Comparing Alcohol Subjects Over Time	Sleep Subjects (no alcohol) (N = 113)
	Baseline	Trial 1 With Alcohol*	Trial 2 With Alcohol*	Trial 3 With Alcohol*		
All subjects						
Breath alcohol concentration†	0 ± 0	0.057 ± 0.02	0.080 ± 0.01	0.083 ± 0.01		0.0 ± 0
Mean reaction time (ms)	241 ± 25	263 ± 43	276 ± 53	283 ± 51	<.0001	266 ± 39
SD of reaction time‡	48 ± 21	53 ± 24	61 ± 28	63 ± 26	<.0001	60 ± 26
Maximum reaction time (ms)	480 ± 137	511 ± 149	548 ± 169	554 ± 166	.003	566 ± 207
No. of times RT > 500 ms	0.49 ± 1.1	0.84 ± 1.9	1.26 ± 2.7	1.65 ± 3.2	.004	1.24 ± 1.9
Mean: 10 fastest times (ms)	194 ± 16	203 ± 19	206 ± 24	210 ± 29	<.0001	205 ± 24
Mean of the reciprocal of RT/1,000 ms§	4.31 ± 0.4	4.00 ± 0.5	3.86 ± 0.5	3.78 ± 0.5	<.0001	3.97 ± 0.5
Mean of the reciprocal of the 10 slowest RT/1,000 ms¶	3.13 ± 0.5	2.91 ± 0.5	2.74 ± 0.5	2.64 ± 0.5	<.0001	2.81 ± 0.5
Men only						
Breath alcohol concentration†	0 ± 0	0.056 ± 0.02	0.080 ± 0.01	0.083 ± 0.01		
Mean reaction time (ms)	236 ± 19	251 ± 26	264 ± 36	271 ± 38	<.0001	
SD of reaction time ‡	48 ± 17	48 ± 14	58 ± 18	61 ± 20	.0006	
Maximum reaction time (ms)	495 ± 145	488 ± 114	556 ± 163	561 ± 152	.045	
No. of times RT > 500 ms	0.40 ± 0.6	0.49 ± 0.8	0.91 ± 1.2	1.20 ± 1.6	.004	
Mean: 10 fastest times (ms)	192 ± 13	199 ± 16	203 ± 23	207 ± 28	<.0001	
Mean of the reciprocal of RT/1,000 ms§	4.39 ± 0.3	4.14 ± 0.4	3.99 ± 0.5	3.91 ± 0.5	<.0001	
Mean of the reciprocal of the 10 slowest RT/1,000 ms¶	3.19 ± 0.4	3.02 ± 0.4	2.85 ± 0.5	2.73 ± 0.4	<.0001	
Women only						
Breath alcohol concentration†	0 ± 0	0.059 ± 0.02	0.080 ± 0.01	0.084 ± 0.01		
Mean reaction time (ms)	246 ± 28	272 ± 50	285 ± 62	292 ± 58	<.0001	
SD of reaction time‡	48 ± 24	57 ± 29	63 ± 33	66 ± 30	.001	
Maximum reaction time (ms)	469 ± 131	528 ± 171	541 ± 174	550 ± 178	.033	
No. of times RT > 500 ms	0.56 ± 1.4	1.11 ± 2.5	1.53 ± 3.4	2.00 ± 4.0	.037	
Mean: 10 fastest times (ms)	195 ± 18	207 ± 20	209 ± 25	213 ± 29	<.0001	
Mean of reciprocal of RT/1,000 ms§	4.24 ± 0.4	3.90 ± 0.5	3.75 ± 0.5	3.67 ± 0.5	<.0001	
Mean of reciprocal of 10 slowest RT/1,000 ms¶	3.09 ± 0.5	2.82 ± 0.5	2.66 ± 0.5	2.56 ± 0.5	<.0001	

*Mean of breath alcohol at start and at end of each PVT test trial (1-3).

†Number of grams of alcohol per 210 liters of breath (BrAC, g/210 L) equivalent to blood alcohol concentration of grams of alcohol per 100 milliliters of blood (BAC, g/dl).

‡Standard deviation of the mean reaction time. The standard deviation is computed for each subject, and tabulations reflect the average standard deviation for all subjects.

§Computed by first translating each reaction time (RT) into seconds by dividing the number of milliseconds by 1,000 (1 sec). For each 10-minute PVT trial, the mean of the reciprocal of all reaction times (measured in seconds) is computed to generate a single mean value for the given PVT. The tabulated mean of the reciprocal of RT/1,000 is then computed as the mean of these values for all subjects.

¶Computed precisely as was described above except that only the 10 slowest reaction times for a given PVT are included in the computation.

It is important to keep in mind that when reciprocals are used, slower reaction times are associated with lower values.

Values are mean ± standard deviation. P values are based on repeated measures analysis of variance testing the equality of mean values during the four tests.

extreme outliers. For these outcome measures (maximum RT, the SD of RT, and the number of cases where the response time exceeded 500 ms), the outlying values were truncated and set equal to the maximum nonoutlying value. This adjustment was required for, at most, 4 of the 320 measurements collected during four time points.

RESULTS

Table I summarizes basic demographic characteristics of the 80 alcohol-challenged subjects (alcohol group), along with both the demographic and polysomnographic status (Table II) of the 113 SDB subjects (sleep group).

