Alcohol and Sleep I: Effects on Normal Sleep

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This review provides a qualitative assessment of all known scientific studies on the impact of alcohol ingestion on nocturnal sleep in healthy volunteer's. At all dosages, alcohol causes a reduction in sleep onset latency, a more consolidated first half sleep and an increase in sleep disruption in the second half of sleep. The effects on rapid eye movement (REM) sleep in the first half of sleep appear to be dose related with low and moderate doses showing no clear trend on REM sleep in the first half of the night whereas at high doses, REM sleep reduction in the first part of sleep is significant. Total night REM sleep percentage is decreased in the majority of studies at moderate and high doses with no clear trend apparent at low doses. The onset of the first REM sleep period is significantly delayed at all doses and appears to be the most recognizable effect of alcohol on REM sleep followed by the reduction in total night REM sleep. The majority of studies, across dose, age and gender, confirm an increase in slow wave sleep (SWS) in the first half of the night relative to baseline values. The impact of alcohol on SWS in the first half of night appears to be more robust than the effect on REM sleep and does not appear to be an epiphenomenon REM sleep reduction. Total night SWS is increased at high alcohol doses across gender and age groups.

Key Words: Alcohol Provocation Test, Alcohol Challenge, Polysomnography, Sleep Physiology.

HISTORICAL OVERVIEW

THE USE OF a presleep dose of alcohol (alcohol provocation, alcohol induction, alcohol challenge) has formed part of the clinical and research study of sleep and other medical conditions for more than a century. The earliest known publication of a study of the impact of alcohol on nocturnal sleep dates back to 1883 when Mönninghof and Piesbergen conducted an *observational* study of sleep depth in response to alcohol and exercise. They measured sleep depth by determining the intensity of a graded auditory stimulus necessary to awaken the subject. Following the ingestion of small doses of alcohol they found that the relative soundness of sleep was less than when no exercise or alcohol ingestion preceded the sleep period. When larger doses of alcohol were given then sleep was much sounder at the beginning, but more restless later and its total duration was longer. These observations remain relevant to sleep science today (Mullen et al., 1933).

In 1961, Nathaniel Kleitman suggested that hypnotics and alcohol suppress rapid eye movement (REM) sleep (Kleitman, 1961). Two years later the REM suppressing effects of a presleep dose of alcohol was objectively confirmed using polysomnography (PSG). This placebo controlled study refined the alcohol sleep study protocol by formalizing the acclimatizing of subjects to the novel sleep laboratory environment and the recording of a baseline night (Gresham et al., 1963). Table 1 summarizes the milestones in alcohol and sleep research and the pioneering contributors to this field.

METHODOLOGY

This review focuses primarily on the sleep laboratory studies where alcohol (syn. EtOH) has been directly administered prior to nocturnal sleep to assess its physiological impact on sleep variables in healthy volunteers and control samples as measured by PSG. To provide a comprehensive view of the impact of alcohol on physiological sleep, we have included a summary of studies where alcohol has been administered in the afternoon to assess its immediate effects on an afternoon nap and its delayed effects on nocturnal sleep.

The majority of studies testing the impact of alcohol on physiological sleep have measured nocturnal *s*leep parameters following a single prebedtime dose of alcohol in the period prior to the usual sleep period.

A few studies have used *repeated or consecutive* dosing procedures to measure the effects of *short-term* daily alcohol consumption on sleep parameters. Other studies have administered alcohol in the afternoon (or evening) and then measured its *immediate* impact on an afternoon nap or its *delayed* impact on nocturnal sleep.

Other methods employed to assess the acute response to alcohol include *staged studies* and cross-over studies with a period of days between study nights. Incremental *acute dosing* studies, where various acute (single) doses are administered usually have a minimum of 24 to 48 hours alcohol free period between alcohol testing.

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Table 1. Milestones in Alcohol and Sleep Research

Publication year and author	Study description	Main findings and milestones
Mullen and colleagues (1933)	High dose acute study	1. Alcohol causes reduction in motility and temperature in first half of night 2. Alcohol causes increased motility and temperature in second half of night 3. Alcohol reduces latency to sleep onset
Gresham and colleagues (1963)	High dose acute study	1. Suppression of rapid eye movement (REM) sleep over 5 hour period 2. Reduction in sleep onset latency 3. Introduction of acclimatization night to alcohol and sleep research
Yules and colleagues (1966)	High dose acute study	1. REM sleep suppression in first half of sleep 2. REM sleep rebound in second half of sleep 3. Slow wave sleep (SWS) constant 4. Increase in Stage 2 sleep "compensates" for reduced REM sleep 5. Impact of alcohol is predominantly on duration of sleep stages rather than shifts in sleep stages
Yules and colleagues (1966)	Consecutive high dose study	1. Reduction in total REM sleep for the first 5 nights of alcohol dosing and then returned to and exceeded prestudy levels in subsequent alcohol nights 2. REM levels remained above control levels in the alcohol free "recovery" period—REM sleep "recovery" is predominantly in second half of sleep period
Yules and colleagues (1967)	Afternoon dosing studies (acute and consecutive high dose)—4 hours prior to sleep	1. Impact of alcohol on nocturnal sleep is similar but less pronounced then nocturnal dosing 2. Increase in SWS rather than Stage 2 sleep in first half of sleep
Knowles and colleagues (1968)	Acute and consecutive dosing at low and high dose (27 "virtual" nights) in a single subject	1. Low dose suppresses REM sleep in first half of night 2. High dose alcohol suppresses total REM sleep 3. Alcohol is eliminated in a linear fashion during sleep

The most commonly used protocol when assessing the *acute* nocturnal effects of a *single dose* of alcohol is to conduct an alcohol free baseline and/or acclimatization and/or placebo night (sometimes 2 or more nights) followed by an alcohol induction night. Alcohol administration usually commences within 100 minutes of bedtime and completes about 15 to 30 minutes prior to PSG recording.

Alcohol Dosages and Levels

An alcohol *dose* has traditionally been described in milligrams of pure EtOH per kilogram of the subject's weight (expressed as mg/kg). Alcohol *levels* prior to bedtime or sleep testing have used either breath alcohol *concentration* (expressed as BrAC and in grams per 100 ml or g%) or blood alcohol *levels* (expressed as BAL and in milligrams per 100 ml or mg/dl or mg%) prior to bedtime to provide a measure of the actual alcohol levels just prior to sleep testing.

In this review, we use alcohol *dosage* in mg/kg, breath alcohol concentrations in g% and blood alcohol levels in mg% (Arnedt et al., 2011; Feige et al., 2006; Gresham et al., 1963; Prinz et al., 1980; Roehrs et al., 1991, 1999; Stone, 1980; Williams et al., 1983; Yules et al., 1966).

Based on the dosage schedules and grading systems employed in the majority of studies examined the division into *low, moderate*, and *high* dose, studies has been pegged at the following levels:

1. *Low dose alcohol studies* have used alcohol of between 0.15 and 0.49 mg/kg which is about 1 to 2 standard drinks,
2. *Moderate dose studies* have used a dosage range from 0.5 to 0.74 mg/kg equivalent to between 2 and 4 standard drinks, and
3. *High dose studies* have used EtOH doses of ≥ 0.75 mg/kg which equates to more than 4 standard drinks.

Inclusion Criteria

Examination of all available English language medical databases from 1960 to the present, including Medline, EMBASE, The Royal Society of Medicine, British Medical Association, and The Royal College of Psychiatrists online libraries were accessed. This revealed a total of 153 studies where alcohol had been directly tested on sleep of human participants in various conditions and times of day. Full text versions of all these 153 publications were examined and *27 publications* fulfilled the *initial* criteria for inclusion in the *nocturnal dosing* group. Some of these 27 published works had a single *experiment (study)* as part of the protocol and others had more than 1 type of experiment. Where data appeared incomplete or where more detail or clarification on methodology or dosing, etc., was required, the papers' lead author and/or researcher were contacted directly to clarify.

Nocturnal Dosing Studies

The studies are further divided into the following 2 types:

1. *Acute single dose studies* which are then subdivided into low, moderate, and high dose studies and further divided according to age group and gender, and
2. *Consecutive or repeated dose studies* are divided according to dosage, gender, and age groups.

Acute Single Dose Studies. The primary inclusion criteria for this review are:

1. Studies where a single dose of alcohol had been administered prior to the *nocturnal* sleep period in healthy volunteers and/or control samples,
2. *At least 1* alcohol free (acclimatization/baseline/placebo) night *preceded* the alcohol provocation night,
3. Data are provided for all sleep stages, with statistical analysis, and
4. Data are provided for at least one half of the night and/or the full night.

Control data and acute alcohol night (alcohol "night 1") data from repeated dosing studies fulfilling the inclusion criteria have been included where they provide information on the acute impact of alcohol on physiological nocturnal sleep in healthy volunteers and/or normal controls.

Consecutive Nightly Dose Studies. Studies where daily consecutive nocturnal alcohol provocation has been utilized are included in this review as they provide additional data on the short-term effects of nightly alcohol consumption on PSG measured sleep variables in healthy volunteers and control samples.

Afternoon Alcohol Dosing Studies

There have been only a few studies identified that have measured the effects of afternoon alcohol administration on PSG recorded sleep and a commentary on these findings is included for completeness (Landolt et al., 1996; Rouhani et al., 1989; Smith and Smith, 2003; Van et al., 1995; Yules et al., 1967).

Exclusion Criteria

Studies where alcohol has been administered to participants who have been sleep deprived, where alcohol has been administered to gauge its impact on daytime sleepiness and/or performance have been excluded. Similarly, studies on patient groups with medical disorders, those with sleep disorders (snoring, sleep apnea), neurological and psychiatric disorders such as alcohol dependence syndrome have not been included here and will form part of a separate review on alcohol and sleep disorders and dysfunctions.

From the initial short-list of 27 publications, 7 were *completely* excluded from the data analysis due to methodological limitations, duplication of data, incomplete data, and other issues affecting the veracity of the data (Chan et al., 2011; Gresham et al., 1963; Knowles et al., 1968; Kobayashi et al., 1998; Stone, 1979; Williams and Salamy, 1972; Yules et al., 1966).

Sleep Stage Terminology and Data

We use both, the current and previous sleep stage terminology for the purposes of this review. Non-REM sleep is listed as Stages N1, N2, and N3 with slow wave sleep (SWS) (N3) incorporating the previously labeled Stage 3 and Stage 4. We use the terms SWS and N3 interchangeably to denote Stage N3 (SWS). Where studies have shown an impact on 1 specific Non-REM sleep stage (e.g., Stage 4) we highlight this in the tables for completeness and to maintain continuity.

Values for sleep architecture variables are provided in percent terms only. Where the researchers have reported sleep stage data in minutes we have converted these into percentages. Some variables, such as sleep onset latency (SOL) and REM onset latency (ROL) are reported in minutes only. Only the mean value is displayed for all variables in the tables to enable a uniform approach throughout.

RESULTS

From a total of 153 peer-reviewed publications where alcohol had been administered prior to sleep, 20 *publications* fulfilled the inclusion criteria for this review. These 20 publications contain a total of 38 *sleep laboratory experiments (studies)* with a total sample size of 517 participants. Fifty-one percent of the sample is made up of young adult males ($n = 262$) and young adult females make up 44% ($n = 227$).

Table 2 summarizes the distribution of the total sample of *nocturnal single and consecutive alcohol dosing studies* by type of study, gender, and age group. Where possible, data are presented by gender. In some studies, data have not been reported by gender and these studies have been grouped into a "mixed gender" group.

Table 3 summarizes the 20 publications and the 38 sleep laboratory studies by decade, year of publication, first author, type of study, gender and age distribution, and the timing of alcohol dosing interval prior to PSG.

Sleep and alcohol research has traditionally focused on changes in certain sleep variables and the timing of these changes. The variables most affected by alcohol were thought to be SOL, wake after sleep onset (WASO—an indicator of sleep continuity or sleep disruption), SWS (Stage N3), and REM sleep changes—distribution of REM sleep, REM sleep onset latency (ROL), and the percentage of total REM sleep. The early finding linking ingestion of high doses of alcohol to REM sleep suppression in the *first half* of sleep encouraged researchers to report sleep data for the first 2 to 4 hours of sleep in addition to all night sleep parameters. We continue this trend in our data analysis and reporting (Yules et al., 1966).

The Impact of a Single Dose of Alcohol on Nocturnal Sleep

Table 4 provides a summary of findings for the impact of alcohol on *the first half of sleep* compared to baseline values across all dosage ranges. Table 5 summarizes the *all night sleep data* compared to baseline data across all dosage ranges.

Table 2. Summary of Acute and Consecutive Alcohol Dose Studies

	Acute single dose studies				Consecutive dose studies			
	Low	Moderate	High	Total	Low dose	High dose	Total	Total (*N*)
Number of studies (experiments)								
Young adult males	3	4	9	16	0	2	2	18
Young adult females	2	2	2	6	0	0	0	6
Young adult mixed groups	1	4	5	10	1	1	2	12
Older adult males	0	0	1	1	0	0	0	1
Older adult females	0	0	1	1	0	0	0	1
Total	6	10	18	34	1	3	4	38
Sample sizes								
Young adult males	27	45	175	241	5	20	25	266
Young adult females	19	38	160	217	5	5	10	227
Older adult males	0	0	20	20	0	0	0	20
Older adult females	0	0	8	8	0	0	0	8
Total	46	83	363	492	10	25	35	517

Low Dose Alcohol and Sleep

There are 5 publications identified with a total of 6 sleep laboratory studies using a low dose of prebedtime EtOH. All of the studies were in young adults with 3 having a male only sample, 2 with an exclusively female sample, and 1 with a mixed gender group making up a total sample size of 46 subjects (19 female). All 6 studies provide data for the entire night but only 4 studies report data for the first half of sleep.

First Half of Sleep Data. Of the 4 studies reporting first half of sleep data, *all* show a reduction in SOL and in WASO compared to baseline data confirming the long held view that low doses of alcohol shorten the latency to sleep and consolidate sleep in the first sleep period. Three of the 4 studies show an increase in Stage N3, the single study in an all male sample reports a statistically significant increase in SWS and both female only studies confirm an increase in N3. The single study in a mixed gender sample reports a *decrease* in N3 (Feige et al., 2006). The majority of studies therefore report an increase in N3 in the first half of sleep and this effect applies to both gender groups.

Both studies that report a reduction in REM sleep in the first half of sleep come from female only samples and of the 2 studies that report an increase in REM sleep, 1 is from a male only sample and the other a mixed gender group. This apparent conflicting data highlights the variable effects of low doses of alcohol on REM sleep architecture (Feige et al., 2006).

All Night Sleep Data. All night effects of low dose alcohol include an *increase* in total REM sleep percentage as a proportion of total sleep time in 5 of 6 studies, an increase in the latency to REM onset (ROL) in 4 of 6 studies. In 4 of the 6 studies, a reduction in total N3 is reported. All night WASO is increased in 5 of 6 studies confirming alcohol's sleep disruptive effects in the second half of sleep.

Moderate Dose Alcohol and Sleep

There are a total of 9 publications with 10 sleep laboratory studies testing a single moderate dose of alcohol in young healthy adults and/or social drinkers. Four studies are in male only samples, 2 in all female samples, and 4 in mixed gender groups. Five of the studies report data for the first half of sleep and all 10 studies reported data for the full night.

First Half of Sleep Data. Data presented for the first half of sleep mirrors the findings in subjects taking low doses of alcohol. When compared to baseline data, the 2 most significant findings with moderate alcohol doses is a reduction in SOL and WASO confirming that low and moderate doses of alcohol shorten the time to fall asleep and provide a more consolidated first half of sleep.

Four of the 5 studies report an *increase* in SWS compared to baseline values. REM sleep is reported as *increased* in 3 of the 5 studies with only 2 studies reporting a *reduction* in first half REM sleep. The *only* statistically significant findings for SWS and REM sleep come from a single study in an all female sample. In this study, SWS is increased by 4.9% compared with baseline and REM sleep is reduced by 5.77% (Williams et al., 1983). The majority of studies report an increase in SWS in the first part of sleep at moderate doses of alcohol.

All Night Sleep Data. Of the 10 studies reporting all night data, 4 are in all male groups, 2 in all female samples and 4 in mixed gender samples with a total sample size of 81 (38 female). There are no clear gender specific changes in any of the sleep parameters apparent from the data examined. Four of the 7 studies that published data on WASO reported small nonsignificant increases in WASO. Five of the 7 studies reporting data on ROL confirmed a nonsignificant increase and the remaining 2 a nonsignificant decrease in the latency to the first REM sleep episode.

Table 3. Alcohol and Nocturnal Sleep List of Publications and Studies

Study number	Publication year and author by decades	Type of study	Males	Females	Alcohol dose (g/kg)	Dose timing (minutes)	Additional comments
	1970s						
1	1a. Rundell and colleagues (1972)	Acute high dose	10	0	0.9	30	
2	1b. Rundell and colleagues (1972)	Acute high dose	7	0	0.9	30	Alcohol night 1 of chronic dose study
3	1c. Rundell and colleagues (1972)	Consecutive high dose	7	0	0.9	30	1 acclimatization night followed by 2 placebo nights and then 3 consecutive nights with alcohol
	1980s						
4	1a. Stone (1980)	Acute low dose	6	0	0.16	60	Placebo controlled study with acclimatization and 3 doses separated by 7 days
5	1b. Stone (1980)	Acute low dose	6	0	0.32	60	
6	1c. Stone (1980)	Acute moderate dose	6	0	0.64	60	
7	2a. Prinz and colleagues (1980)	Acute high dose	5	0	0.8	60	
8	2b. Prinz and colleagues (1980)	Consecutive high dose	5	0	0.8	60	2 baseline nights followed by 12 consecutive nights of alcohol administration (nights 1, 11, and 12 recorded) and then 1 night of withdrawal
9	3a. MacLean and Cairns (1982)	Acute low dose	10	0	0.25	45	Placebo night preceding alcohol night with 5 days between dosing
10	3b. MacLean and Cairns (1982)	Acute moderate dose	10	0	0.5		
11	3c. MacLean and Cairns (1982)	Acute high dose	10	0	0.75		
12	3d. MacLean and Cairns (1982)	Acute high dose	10	0	1.0		
13	4. Scrima and colleagues (1982)	Acute high dose	4	2	0.8	30	Control sample with acclimatization night preceding alcohol night
14	5a. Williams and colleagues (1983)	Acute moderate dose	0	11	0.5	45	Adaptation night then 3 alcohol nights with 5 alcohol free nights intervening
15	5b. Williams and colleagues (1983)	Acute high dose	0	11	0.75	45	
16	6. Block and colleagues (1985)	Acute high dose	0	8	1	30	Postmenopausal females—a group of 10 participants excluded as no baseline data preceded alcohol ingestion
17	7a. Block and colleagues (1986)	Acute high dose	20	0	1	30	Young males
18	7b. Block and colleagues (1986)	Acute high dose	20	0	1	30	Older males
19	7c. Block and colleagues (1986)	Acute high dose	0	20	1	30	Premenopaual females
	1990s						
20	1. Roehrs and colleagues (1991)	Acute high dose	5	0	0.8	30	Data from control (nonsleep deprived) sample
21	2. Dijk and colleagues (1992)	Acute moderate dose	8	0	0.6	45	1 subject 0.68 g/kg
22	3. Roehrs and colleagues (1999)	Acute moderate dose	6	3	0.5	60	Control data from insomnia study
	2000s						
23	1. Kobayashi and colleagues (2002)	Acute high dose	10	0	0.8	60	Polysomnography and correlation dimension analysis of data
24	2a. Smith and Smith (2003)	Acute moderate dose	1	4	0.7	30	Total sample of 15 divided into 3 groups 5 with 2 alcohol groups and
25	2b. Smith and Smith (2003)	Acute moderate dose	1	4	0.7	30	1 nonalcohol control group. Alcohol group A contained "inexperienced" drinkers and alcohol group B had "more experienced" drinkers
26	2c. Smith and Smith (2003)	Acute high dose	1	5	0.9	45	High dose study
27	3a. Miyata and colleagues (2004)	Acute low dose	0	7	0.28	30	Alcohol sensitive group (n = 6) excluded
28	3b. Miyata and colleagues (2004)	Acute moderate dose	0	7	0.69	30	
29	4. Bazil and colleagues (2005)	Acute moderate dose	3	9	0.5	45	Control group in gabapentin clinical trial
30	5a. Van Reen and colleagues (2006)	Acute low dose	0	7	0.49	60	All female sample
31	6a. Feige and colleagues (2006)	Acute low dose	5	5	0.3	30	
32	6b. Feige and colleagues (2006)	Acute high dose	5	5	1	30	
33	6c. Feige and colleagues (2006)	Consecutive low dose	5	5	0.3	30	
34	6d. Feige and colleagues (2006)	Consecutive high dose	5	5	1	30	
	2010s						
35	7. Rohsenow and colleagues (2010)	Acute high dose	37	58	1.1–1.2	60	
36	8. Arnedt and colleagues (2011)	Acute high dose	34	59	1.1–1.2	60	Largest study of its kind, robust support for dose dependent increase in total N3
37	9a. Sagawa and colleagues (2011)	Acute moderate dose	10	0	0.5	100	Study to gauge nocturnal autonomic effects of alcohol ingestion
38	9b. Sagawa and colleagues (2011)	Acute high dose	10	0	1	100	

Table 4. First Half of Sleep Data for Single Nocturnal Dose Alcohol

Publication year and author	Dose (g/kg)	Blood alcohol levels (mg%)	Breath alcohol concentration (g%)	Timing (mins)	Sample size	% Difference in N3	*p*-Value	% Difference in Stage REM	*p*-Value	Difference in SOL (mins)	*p*-Value	Difference in WASO (%)	*p*-Value
(A) Low dose studies													
Males													
MacLean and Cairns (1982)	0.25	8	NR	47	10	0.80%	<0.05	0.10%	NS	−7.3	<0.05	−2	<0.05
Females													
Miyata and colleagues (2004)	0.28	NR	NR	30	7	1.50%	NS	−0.10%	NS	−1.1	NS	−5.20%	NS
Van Reen and colleagues (2006)	0.49	NR	0.043	60	7	7.50%	<0.001	−4.16%	<0.001	−1	NS	−1.76%	NS
Mixed gender groups													
Feige and colleagues (2006)	0.3	30	NR	30	10 (5 F)	−1.57%	0.425	3.58%	0.111	−1.75	NS	−0.19%	NS
(B) Moderate dose studies													
Males													
MacLean and Cairns (1982)	0.5	30	NR	47	10	−0.40%	NS	0.70%	NS	−16	<0.05	−4.70%	NS
Sagawa and colleagues (2011)	0.5	37	NR	100	10	2.10%	NS	0.30%	NS	−2.9	NS	−2.28%	NS
Females													
Williams and colleagues (1983)	0.5	NR	0.05	45	11	4.90%	<0.05	−5.77%	<0.05	−10.2	<0.05	NR	NR
Miyata and colleagues (2004)	0.69	NR	NR	30	7	3.50%	NS	0.50%	NS	−1.7	NS	NR	NR
Mixed gender groups													
Roehrs and colleagues (1999)	0.5	NR	0.043	60	9 (3 F)	0.42%	NS	−2.16%	NS	−1.8	<0.05	NR	NR
(C) High dose studies													
Males													
Rundell and colleagues (1972)	0.9	75	NR	30	10	2.40%	NS	−3%	<0.01	NR	NR	2.10%	NS
Rundell and colleagues (1972)	0.9	77	NR	30	7	3.40%	NS	−6.90%	<0.05	NR	NR	−0.4	NS
Prinz and colleagues (1980)	0.8	80.5	NR	60	5	10.40%	<0.05	−9.36%	NS	NR	NR	1.65%	NS
MacLean and Cairns (1982)	0.75	59	NR	47	10	4%	<0.05	0.40%	NS	−16	<0.05	−4.20%	NS
MacLean and Cairns (1982)	1	74	NR	47	10	5.60%	<0.05	−2%	NS	−13.2	<0.05	−5.50%	NS
Sagawa and colleagues (2011)	1	99	NR	100	10	5.47%	NS	−5.45%	<0.05	−4.2	NS	−3.55%	NS
Females													
Williams and colleagues (1983)	0.75	NR	0.081	45	11	8.00%	<0.05	−7.05%	<0.05	−11.8	<0.05	NR	NR
Mixed gender groups													
Feige and colleagues (2006)	1	100	NR	30	10 (5 F)	11.03%	0.00	−2.62%	NS	−6.55	0.165	−1.45%	NS
Arnedt and colleagues (2011)	1.1–1.2	NR	0.11	60	92 (59 F)	1.10%	<0.001	0.60%	NS	NR	NR	−1.40%	<0.001

% Difference in N3 refers to the change in percentage of slow wave sleep (SWS) as a proportion of first half of sleep compared to baseline values.
% Difference in Stage rapid eye movement (REM) refers to the change in percentage of REM sleep as a proportion of first half of sleep compared to baseline values.
SOL, sleep onset latency—difference compared to baseline night in minutes (mins).
WASO, wake after sleep onset—percent difference as a proportion of first half sleep compared to baseline night.
NR, not reported; NS, not significant.

Table 5. All Night Sleep Data for Single Nocturnal Dose Alcohol

Publication year and author	Dose (g/kg)	Blood alcohol levels (mg%)	Breath alcohol concentration (g%)	Timing (mins)	Sample size	%Difference in N3	*p*-Value	% Difference in Stage REM	*p*-Value	Difference in WASO	*p*-Value	ROL difference	*p*-Value
(A) Low dose studies													
Males													
Stone (1980)	0.16	6.25	NR	30–60	6	−1.90%	<0.05	1%	NS	2.50%	< 0.05	21.9 mins	NS
Stone (1980)	0.32	26.5	NR	30–60	6	−5%	<0.05	2.60%	NS	0.10%	NS	7 mins	NS
MacLean and Cairns (1982)	0.25	8	NR	47	10	1.90%	NS	1.60%	NS	NR	NR	−9.4	NS
Females													
Miyata and colleagues (2004)	0.28	NR	NR	30	7	−2.80%	NS	0.90%	NS	−3.10%	NS	−54.1	NS
Van Reen and colleagues (2006)	0.49	NR	0.043	60	7	1.67%	NS	−2.53%	0.039	1.35%	NS	19 mins	NS
Mixed gender groups													
Feige and colleagues (2006)	0.3	30	NR	30	10 (5 F)	−0.68%	0.412	0.20%	NS	0.98%	NS	13.9 mins	NS
(B) Moderate dose studies													
Males													
Stone (1980)	0.64	51.4	NR	30–60	6	−1.90%	<0.05	1.10%	NS	0.10%	NS	24.5 mins	NS
MacLean and Cairns (1982)	0.5	30	NR	47	10	1.40%	NS	0.40%	NS	NR	NR	4.2 mins	NS
Dijk and colleagues (1992)	0.6	NR	0.061	45	8	0.03%	NS	−0.46%	NS	0.03%	NS	−7.5	NS
Sagawa and colleagues (2011)	0.5	37	NR	100	10	−1.81%	NS	−2.41%	NS	1.10%	NS	−1.5	NS
Females													
Williams and colleagues (1983)	0.5	NR	0.054	45	11	0.30%	NS	−0.70%	<0.05	NR	NR	17 mins	NS
Miyata and colleagues (2004)	0.69	NR	NR	30	7	−5.50%	NS	1.00%	NS	1.30%	NS	60.5 mins	NS
Mixed gender groups													
Roehrs and colleagues (1999)	0.5	NR	0.043	60	9 (3 F)	0.10%	NS	−0.50%	<0.03	−0.8	NS	13.9 mins	NS
Smith and Smith (2003)	0.7	NR	NR	30	5 (4 F)	3.20%	NS	−1.20%	NS	2.20%	NS	NR	NR
Smith and Smith (2003)	0.7	NR	NR	30	5 (4 F)	−2.03%	NS	−5.10%	NS	−0.45%	NS	NR	NR
Bazil and colleagues (2005)	0.5	NR	NR	45	12 (9 F)	−0.10%	NS	−1.35%	NS	NR	NR	NR	NR
(C) High dose studies													
Males													
Rundell and colleagues (1972)	0.9	75	NR	30	10	2%	NS	−3%	<0.01	0.80%	NS	NR	NR
Rundell and colleagues (1972)	0.9	77	NR	30	7	0.60%	NS	−11.40%	<0.01	1.10%	NS	NR	NR
MacLean and Cairns (1982)	0.75	59	NR	47	10	0.00%	NS	−0.30%	NS	NR	NR	3.2 mins	NS
MacLean and Cairns (1982)	1	74	NR	47	10	2.40%	NS	−2.10%	NS	NR	NR	8.9 mins	NS
Block and colleagues (1986)	1	62	NR	30	20	4.10%	NS	−2.15%	NS	NR	NR	NR	NR
Roehrs and colleagues (1991)	0.8	NR	0.06	30	5	−1.90%	NS	−4.50%	<0.01	0.40%	NS	2.4 mins	NS
Kobayashi and colleagues (2002)	0.8	NR	NR	60	10	−0.90%	NS	−1.45%	NS	5.50%	NS	41 mins	<0.05
Arnedt and colleagues (2011) (Male Data)	1.1–1.2	NR	0.11	60	34	1.60%	<0.05	−0.65%	<0.001	0.30%	<0.01	34.8 mins	<0.001
Sagawa and colleagues (2011)	1	99	NR	100	10	−0.87%	NS	−6.21%	<0.001	0.84%	NS	85.5 mins	<0.05
Females													
Williams and colleagues (1983)	0.75	NR	0.081	45	11	−1.00%	<0.05	−3.50%	<0.05	NR	NR	31.5 mins	NS
Block and colleagues (1986)	1	75	NR	30	20	1.50%	NS	−1.40%	NS	NR	NR	NR	NR
Arnedt and colleagues (2011) (Female Data)	1.1–1.2	NR	0.11	60	59	2%	<0.05	−3.90%	<0.001	3.70%	<0.001	29.6 mins	<0.001
Mixed gender groups													
Scrima and colleagues (1982)	0.8	NR	NR	30	6 (2 F)	7%	<0.07	0%	NS	NR	NR	59 mins	<0.05

Continued.

Table 5. (Continued)

Publication year and author	Dose (g/kg)	Blood alcohol levels (mg%)	Breath alcohol concentration (g%)	Timing (mins)	Sample size	%Difference in N3	*p*-Value	% Difference in Stage REM	*p*-Value	Difference in WASO	*p*-Value	ROL difference	*p*-Value
Smith and Smith (2003)	0.9	NR	NR	45	6 (5 F)	7.59%	NS	−7.53%	NS	−0.56%	NS	NR	NR
Feige and colleagues (2006)	1	100	NR	30	10 (5 F)	4.46%	NS	−1.15%	0.514	0.59%	NS	26.45 mins	NS
Rohsenow and colleagues (2010)	1.1–1.2	NR	0.11	60	95 (58 F)	1.90%	<0.002	−4.40%	<0.001	NR	NR	NR	NR
Older males													
Block and colleagues (1986)	1	70	NR	30	20	4.60%	NS	−5.40%	NS	NR	NR	NR	NR
Older females													
Block and colleagues (1985)	1	88	NR	30	8	9.13%	NS	−7.51%	NS	NR	NR	NR	NR

% Difference in N3 refers to the change in percentage of slow wave sleep (SWS) as a proportion of total night sleep compared to baseline values.
% Difference in Stage REM refers to the change in percentage of REM sleep as a proportion of total night sleep compared to baseline values.
SOL, sleep onset latency—difference compared to baseline night in minutes (mins).
WASO, wake after sleep onset—percent difference as a proportion of first half sleep compared to baseline night.
ROL, REM onset latency—the time from sleep onset to the first REM period. The difference is between baseline and alcohol night expressed in minutes from sleep onset.
NR, not reported; NS, not significant.

Fifty percent of studies report an increase in total night N3 and the other half report a decrease or no change in total N3. There is no clear trend on the effects of moderate doses of alcohol on all night N3 changes. Seven of the 10 studies report a reduction in the total percentage of REM sleep with 2 studies showing a statistically significant reduction.

High Dose Alcohol and Sleep

There are 13 publications reporting data on the impact of a single high dose of alcohol on physiological sleep and from these there are 18 studies. In addition, 1 publication reports male and female data separately for the first half of sleep providing a further 2 gender specific data sets (Arnedt et al., 2011).

Ten studies report data in young adult males, 3 on young adult females, 5 studies report data for young adult mixed gender groups, 1 study is in older male participants, and 1 in a postmenopausal female group. Of these 20 studies and/or data sets, 9 have data for the first half of sleep and 18 on all night sleep variables.

First Half of Sleep Data. The impact of a high dose of alcohol on the first half of sleep is more consistent across age, gender, and type of study. All 9 studies report an increase in SWS (N3) and a reduction in SOL. Eight of 9 studies confirm a reduction in REM sleep percentage with 1 study showing a nonsignificant increase of 0.4%. Sleep is more consolidated in the first half of sleep as reflected by 6 of the studies showing a decrease in WASO. These findings are in keeping with most of the previous reviews on the subject (Lands, 1999; Roehrs, 2010; Roehrs and Roth, 2001).

All Night Sleep Data. Seventeen of the 18 studies show a reduced total night REM sleep percentage compared to baseline data and 14 of the 18 studies show an increase in total SWS following administration of a high dose of alcohol. One recent study confirms the increase in all night N3 to be more robust for their female subgroup (Arnedt et al., 2011). All 10 studies reporting data on REM sleep latency confirm an increase in the latency to the first REM sleep period (ROL).

The Impact of Repeated Doses of Alcohol on Nocturnal Sleep

We identified 5 publications with 6 studies where consecutive dosing procedures were used to assess the impact of nocturnal alcohol administration on sleep parameters (Feige et al., 2006; Knowles et al., 1968; Prinz et al., 1980; Rundell et al., 1972; Yules et al., 1966).

Three early studies provide detailed data only for REM sleep changes, all showing a reduction in REM sleep in the first half of sleep at low doses (Knowles et al., 1968) and reduction on all night REM sleep percentage at high doses with a trend to adaptation to baseline levels of REM after repeated doses (Rundell et al., 1972; Yules et al., 1966). All these early studies had significant methodological limitations

and no generalizations can be made based on this data alone. In the 1980 study conducted by Prinz and colleagues, a single night's data in a 9 night consecutive dosing schedule was used to assess the "chronic" impact of high dose alcohol on the first half of sleep. They found a significant reduction in first half REM sleep and no change in SWS. No data was presented for all night sleep changes (Prinz et al., 1980).

The study by Feige and colleagues (2006) provide data on the impact of low and high consecutive doses of alcohol on PSG recorded sleep. With low dose alcohol, effects on sleep parameters were negligible for both whole nights and half-nights indicating that during short-term use, low dose alcohol consumption did not disturb objectively measured sleep patterns. High dose alcohol ingestion provided a more distinct pattern with a significant shortening of sleep latency especially on the second night of alcohol ingestion and a reduction in whole night REM percentage. Furthermore, they found that repeated ingestion of high dose alcohol exerted its effect on sleep mainly in the first part of the night, with a significant reduction percentage of Stage 1 sleep, a reduced number of wake periods, increased SWS, and decreased REM.

Afternoon Alcohol Dosing Studies

Immediate Effects of Alcohol on an Afternoon Nap. Of the 2 studies identified, 1 tested the impact of low dose alcohol on an afternoon nap and the other a high dose effect (Rouhani et al., 1989; Van et al., 1995). Compared to baseline values, *low dose* alcohol caused a statistically significant reduction in REM sleep percentage, SWS, and SOL. WASO was increased as was Stage 1 light sleep. The total sleep time for the alcohol group was reduced (at 64 minutes) compared to the control group. As this was a single study no clear conclusions can be generalized from this data (Rouhani et al., 1989). The *high dose* study by Fiona Van and colleagues (1995) confirmed a statistically significant increase in SWS (specifically Stage 4 sleep) in all subjects compared to baseline values. REM sleep was absent in 6 of 8 subjects and SOL significantly reduced (Van et al., 1995).

Nocturnal Effects of Afternoon and Evening Alcohol Dosing. Three publications containing 4 studies have described the experimental impact of afternoon alcohol dosing on nocturnal PSG recorded sleep (Landolt et al., 1996; Smith and Smith, 2003; Yules et al., 1967).

In the single and repeated high dose studies where alcohol was administered 4 hours prior to nocturnal PSG (an evening dose), REM reduction in the first part of sleep was present but of a lesser magnitude when compared with nocturnal alcohol dosing. The delay in REM sleep onset (ROL) was similarly of lesser magnitude and both these effects were maintained for the first 3 nights of repeated alcohol dosing. When alcohol was administered for a fourth and fifth night, no further depression below control levels occurred and when alcohol administration was stopped, REM time increased to above control levels with the highest on the first postalcohol night and progressively decreased to control levels over the following 4 postalcohol nights. Non-REM sleep stage effects were variable and different in the 4 subjects (Yules et al., 1967).

The study by Landolt and colleagues (1996) provides insufficient data to reach any meaningful conclusions. Another study measuring the impact of alcohol on memory, compared afternoon alcohol dosing to nocturnal dosing in the absence of control group data (Smith and Smith, 2003). The afternoon dose was given 5 hours before nocturnal sleep recording and data was compared to subjects who received a nocturnal alcohol dose. The nocturnal group showed a significant reduction in REM density, increases in total SWS, and a reduction in total REM compared to the afternoon alcohol group in response to high dose alcohol.

DISCUSSION

Previous reviews on the subject of the impact of alcohol on PSG recorded sleep have examined several parameters and reached similar conclusions. The areas of agreement have been that alcohol reduces the latency to persistent sleep, suppresses REM sleep particularly in the first part of sleep, and increases SWS in the first part of sleep. Alcohol reduces WASO in the first half of sleep but increases it in the latter part of the night in keeping with the metabolic elimination of alcohol (Lands, 1999; Roehrs, 2010; Roehrs and Roth, 2001). Our review has for the first time divided all the data by dosage, gender, and age and found the following.

Sleep Onset Latency

We have found that SOL is reduced at all dosages in all studies and appears to be the single most robust effect of alcohol on nocturnal sleep.

Wake After Sleep Onset

In keeping with the findings in previous reviews, WASO is reduced in the first half of sleep and increased for total sleep time in the majority of studies across dose, gender, and age (Lands, 1999; Roehrs, 2010; Roehrs and Roth, 2001).

Slow Wave Sleep (N3, SWS)

One area of debate and sometimes controversy has been the issue of the impact of alcohol on SWS. For the first time, all the available data are presented here and based on the findings from all available studies, and in the majority, alcohol clearly increases SWS in the first part of sleep *at all doses*, across gender and ages.

Data for the impact of alcohol on total night SWS display a dose dependent effect with low doses showing no clear trend, moderate doses show a trend toward an increase in SWS and with high doses there is a significant and clear effect

of increasing total SWS. This effect is consistent across gender and age groups.

REM Sleep Parameters

REM sleep percentage in the first half of sleep shows no definite trend either to increase or decrease following low doses of alcohol. With ingestion of a moderate dose a similar equivocal effect is seen. It is here that our data differs from the established view. REM sleep suppression has always been thought of as a primary effect of alcohol ingestion at all dosages. The data presented here shows strong effect on REM sleep reduction only with high doses of alcohol. This is unlike the impact of alcohol on SWS where all dosages caused an increase in first half SWS.

The most substantive impact of alcohol on REM sleep is the *reduction in all night REM sleep percentage* at moderate and high doses of alcohol but not at low doses. The reduction in total REM sleep in response to an alcohol load appears to be more robust than the "suppression" of REM sleep percentage in the first half of sleep. Moreover, the increase in the time to first REM period (ROL) appears to mirror the effect on total REM percentage rather that the REM "suppression" of the first sleep period.

The concept of REM sleep being "absorbed" by SWS seems as pertinent today than it did in the 1960s (Yules et al., 1967). The data supporting an increase in SWS, particularly in the first half of sleep, appears to be more robust than the data on reduction in first half REM sleep at all dosage levels.

The reduction in *total* REM sleep and the delay in REM sleep onset are both clearly dose dependent and appear to be a direct effect of alcohol on REM sleep physiology.

CONCLUSION

The impact of a single dose of alcohol on nocturnal sleep parameters in healthy volunteers and control samples is to reduce SOL, provide a more consolidated sleep in the first part of the night with more disruption in the second half of the night. SWS is increased in the first half of the night at all dosages and the increase in total night SWS is consistently found at higher doses. The reduction in total night REM sleep percentage and the delay in ROL appear to be the most significant and consistent effects of alcohol on REM sleep. REM sleep reduction in the first part of sleep is a particular effect of high dose alcohol ingestion. Further studies are needed to assess the impact of repeated nightly alcohol consumption on sleep and on the immediate and delayed effects of afternoon alcohol intake on sleep parameters.

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