Alcohol and Sleep Review: Flawed Design, Methods, and Statistics Cannot Support Conclusions

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To the Editor:

IN A RECENT publication, Ebrahim and colleagues state in their abstract that they have provided an assessment of "all known scientific studies of the effects of alcohol on the nocturnal sleep of healthy volunteers" (Ebrahim et al., 2013, p. 539). Our review of this article found it to be seriously flawed by research design and statistical problems.

Ebrahim and colleagues (2013) selected 20 published articles concerned with the effects of alcohol on sleep in humans. Numerous articles were excluded from consideration. Within these articles are 38 groups of subjects based on other criteria such as sex or dose of alcohol administered. Although all sleep stages were addressed, Ebrahim and colleagues (2013) focus on the effects of alcohol on slow-wave sleep (SWS); variously known as or abbreviated as SWS, deep sleep, Stages 3 + 4. Current nomenclature combines stages 3 and 4 sleep and renames them "N3"(Iber et al., 2007).

As noted in their conclusion,

> 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. (Ebrahim et al., 2013, pp. 547–548)

RESEARCH DESIGN

The 20 studies selected vary widely with regard to methods and subjects. They also differ in results. The majority of studies were underpowered with 28 of the 38 groups of subjects studied including 10 or fewer subjects. It would appear that only a meta-analysis research design could deal with problems of small sample size, differing results of studies, and result in better estimates of effect size (Sacks et al., 1987).

STATISTICAL SIGNIFICANCE

Ebrahim and colleagues (2013) rely on statistically nonsignificant results. These errors can be clearly seen in Tables 4 and 5, particularly with regard to SWS (N3) where NSs can be easily counted. They frequently report "increases" in N3 percentage or minutes when the tabular data indicate there was no statistically significant difference (ns) between normal and alcohol conditions. In the results and discussion, "increases" and statistically significant increases are combined to support a conclusion that alcohol increases SWS.

> ....the increase in total night SWS is consistently found at higher doses. (Ebrahim et al., 2013, p. 548)

These "increases" are reported even though the original published articles make no such claims.

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ARITHMETIC INSTEAD OF STATISTICS

In Tables 4 and 5, the authors do not present the actual summary data—means, standard deviations (SD), ranges, etc.—for each study even though these key data were available for all studies in the original publications. Instead, Ebrahim and colleagues (2013) have created their own nonstatistical measure—"% difference N3"—based on a comparison of group means—alcohol versus no alcohol—by simple division or simple subtraction. The standard deviations are not accounted for. The "%N3" difference cannot determine whether differences in data are due to random variation or not.

A review of the original studies showed that 13 of the 20 studies included means and SDs as a percentage of total sleep time. The remaining 7 studies presented summary data in minutes. In the studies using a percentage of total sleep time, Ebrahim and colleagues (2013) simply subtracted %N3 during the alcohol condition from the %N3 during the control normal sleep condition. Standard deviations were ignored. In the studies presenting summary data in minutes, Ebrahim and colleagues (2013) simply divided minutes of N3 in the control normal sleep condition by minutes of N3 in the alcohol condition to produce %N3 difference. Again standard deviations were ignored. If the "% difference N3" was a positive number following subtraction or division, the authors determined it to be an "increase." If the resulting product of division or subtraction was "negative," it was determined to be a "decrease."

For example, here are the data from 2 articles included in Ebrahim and colleagues' (2013) review.

Feige and colleagues (2006) report a nonsignificant decrease in SWS% on the first alcohol night compared to baseline.

	Baseline	Alcohol Night 1	
SWS (%SPT)	13.41 ± 7.01	12.72 ± 7.17	0.412 (NS)

Ebrahim and colleagues (2013) noted a % difference of −0.68%. This is simply 13.41 to 12.72 and reported as a decrease.

Block and colleagues (1986) reported in their original article the N3% data for the following group of young women subjects as a percentage of total sleep time (Stage 3 + 4 = N3 using current nomenclature):

	Placebo	Alcohol	*p* Value
Stage 3%	3.6 ± 1.8	3.8 ± 1.7	NS
Stage 4%	22.6 + 9.1	23 + 8.3	NS

Ebrahim and colleagues (2013) added 3 + 4 to get total SWS or N3% and then subtracted placebo from alcohol to report an "increase" of 1.50%. As noted, Block reported these findings as nonsignificant.

In the absence of the appropriate statistical tests and findings of statistical significance, these "increases" and "decreases" cannot be distinguished from otherwise random variation in the data and should be reported as such.

SUMMARY OF ALCOHOL EFFECTS ON N3 SLEEP

Ebrahim and colleagues (2013) reviewed the effect of alcohol on N3 for the first half of the night versus for the entire night.

Effects of Alcohol on N3 Sleep for the First Half of the Night

A review of all studies for N3 at all alcohol dosage levels during the first half of the sleep period showed statistically significant, but small increases in 9 of 18 studies (Table 4). In some studies noted, there was a statistically significant increase in N3 in the first half of the night but not across the entire night. This suggests some change in the timing of N3. Alternative explanations other than the direct effect of alcohol include the result of intervening periods of rapid eye movement sleep delayed or suppressed by alcohol. None of the studies used an ABA design or presented alcohol on the first night or in a crossover design that might have assisted in determining whether this increase in SWS was a direct effect of alcohol or an epiphenomena of other uncontrolled factors.

Effects of Alcohol on N3 Sleep During the Entire Night

In effects of alcohol on of all night, %N3 showed that 7 of the 37 studies showed a statistically significant difference of %N3 between alcohol and no alcohol. This can be clearly seen by simply counting the NSs that appear in Table 5. However, 4 of these 7 studies showed a statistically significant *decrease* in % of N3.

Alcohol, Sleep Deprivation, N3, Sleepwalking, and Criminal Defense

Whether or not alcohol increases SWS is of more than academic interest.

Alcohol-intoxicated individuals charged with criminal acts have employed the "alcohol-induced sleepwalking defense for criminal behavior" (Ebrahim and Fenwick, 2008; Pressman et al., 2007, p. 198). While voluntary intoxication is not a complete defense, a finding of sleepwalking may result in an acquittal. This defense hypothesizes that alcohol acts as a trigger for sleepwalking violent behavior via an increase in SWS. Sleep laboratory studies have reported that increased SWS following sleep deprivation increases the probability of sleepwalking episodes and related sleep disorders in predisposed individuals (Joncas et al., 2002; Zadra et al., 2008). However, the reported % of SWS after sleep deprivation in sleepwalkers and normal controls is much higher than that reported in any of the studies reviewed by Ebrahim and col-

leagues (2013). In the absence of reliable scientific evidence, both the recently published International Classification of Sleep Disorders (ICSD-3) and the DSM-5 no longer list alcohol as a trigger for sleepwalking (American Academy of Sleep Medicine, 2014; American Psychiatric Association, 2013). Additionally, the ICSD-3 states that in the presence of alcohol intoxication, sleepwalking should not be diagnosed.

In summary, the research design, results, and interpretation of this study are faulty. A detailed biostatistical review of the methods and analysis is clearly required to correct these errors. A meta-analysis design would appear to be required to account for small sample size, differing results of studies, and to achieve better estimates of effect size. Inclusionary and exclusionary requirements should be carefully examined. Means and standard deviations should be included in tabular data reported for each study. Numerical "increases" or "decreases" resulting from simple division or subtraction as well as statements of simple "majority" in the absence of statistical significance testing are inconsistent with generally accepted statistical procedures. For these reasons, no conclusions regarding the relationship of alcohol to SWS or to sleep in general can be drawn from this article at this time.

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