ALCOHOLISM CLINICAL & EXPERIMENTAL RESEARCH

The Acute Effects of Alcohol on Sleep Electroencephalogram Power Spectra in Late Adolescence

Julia K. M. Chan, John Trinder, Ian M. Colrain, and Christian L. Nicholas

Background: Alcohol's effect on sleep electroencephalogram (EEG) power spectra during late adolescence is of interest given that this age group shows both dramatic increases in alcohol consumption and major sleep-related developmental changes in quantitative EEG measures. This study examined the effect of alcohol on sleep EEG power spectra in 18- to 21-year-old college students.

Methods: Participants were 24 (12 female) healthy 18- to 21-year-old social drinkers. Participants underwent 2 conditions: presleep alcohol and placebo, followed by standard polysomnography with comprehensive EEG recordings.

Results: After alcohol, mean breath alcohol concentration at lights-out was 0.084%. Interaction effects indicated simultaneous increases in frontal non-rapid eye movement sleep (NREM) delta ($p = 0.031$) and alpha ($p = 0.005$) power in the first sleep cycles following alcohol consumption which was most prominent at frontal scalp sites ($p < 0.001$). A decrease in sigma power ($p = 0.001$) was also observed after alcohol.

Conclusions: As hypothesized, alcohol increased slow wave sleep-related NREM delta power. However, there was a simultaneous increase in frontal alpha power. Results suggest that alcohol may exert an arousal influence which may compete with the sleep maintenance influence of increased delta activity. The phenomenon is similar to, or the same as, alpha-delta sleep which has been associated with the presence of disruptive stimuli during sleep. This may have negative implications for the impact of presleep alcohol consumption on sleep and consequent daytime functioning.

Key Words: Alcohol, Sleep, Adolescence, Sleep Electroencephalogram, Power Spectra, Sleep Architecture.

ALCOHOL CONSUMPTION IS prevalent within the general community with around 80% of people having consumed alcohol at some point in their lives (Maxwell, 2008). Alcohol can affect a variety of biological systems including neural processing and can have serious medical consequences if consumed to excess (Harper et al., 2003; Kril et al., 1997; Pfefferbaum et al., 1988). It is also associated with increased likelihood for risky sexual practices, physical injury, and motor vehicle accidents (Abbey et al., 2005; NHMRC, 2009; Wechsler et al., 2000). Problem or binge drinking is a prominent feature of late adolescence (Bonomo et al., 2004; Wechsler et al., 2000), and animal models indicate that alcohol consumption at this age may increase vulnerability to alcohol-related neuronal disruptions (Crews et al., 2006).

In adults, alcohol initially acts as a sedative, decreasing sleep onset latency. Alcohol also promotes slow wave sleep (SWS) and its associated delta frequency electroencephalogram (EEG) activity and inhibits rapid eye movement (REM) sleep (Chan et al., 2013; Landolt et al., 1996a; MacLean and Cairns, 1982; Roehrs et al., 1989; Rundell et al., 1972; Williams et al., 1983). These effects are most consistently seen during the first half of the sleep period when blood alcohol levels are at their highest (Aldrich, 1998; Chan et al., 2013; Feige et al., 2006; Rundell et al., 1972; Stone, 1980; Vitiello, 1997; Williams et al., 1983). The second half of the sleep period, when blood alcohol levels fall substantially, is associated with marked sleep disruption (Aldrich, 1998; Chan et al., 2013; Vitiello, 1997; Williams et al., 1983). Alcohol-related sleep architecture effects are thought to be closely linked to alcohol's effects on gamma-aminobutyric acid (GABA) and glutamate neurotransmitter systems, both of which are intricately involved in sleep regulation and the occurrence of different EEG frequencies (Amzica and Steriade, 1998; Roehrs and Roth, 1995, 2001; Steriade et al., 1993b).

Computerized analysis of the sleep EEG may reveal subtle effects of alcohol that vary according to brain region but are not evident from manual scoring of the polysomnography. Rundell and colleagues (1972) conducted an automated period analysis of EEG in the first half of the night and reported decreases in beta activity along with increases in "alphoid" activity (first derivative of the zero crossing count within the alpha frequency band). Dijk and colleagues (1992) observed increases in delta power in a single central derivation which

From the Melbourne School of Psychological Sciences (JKMC, JT, IMC, CLN), The University of Melbourne, Parkville, Victoria, Australia; and Human Sleep Research Program (IMC), SRI International, Menlo Park, California.

Received for publication April 3, 2014; accepted October 27, 2014.

Reprint requests: Christian L. Nicholas, PhD, Melbourne School of Psychological Sciences, The University of Melbourne, Parkville, Vic. 3010, Australia; Tel.: +61-3-8344-3935; Fax: +61-3-93476618; E-mails: cln@unimelb.edu.au; clinch@gmail.com

DOI: 10.1111/acer.12621

is consistent with increased SWS and also observed decreases in sigma power (typically associated with sleep spindles in stage 2 non-rapid eye movement [NREM] sleep [N2 sleep]) in the first 2 hours of the sleep period. Van Reen and colleagues (2006) reported that a low dose of alcohol (mean breath alcohol concentrations [BrACs] of 0.044% at bedtime) was associated with increased 3 Hz and alpha frequency 9 to 11 Hz activity in anterior derivations (Fz/Cz) with no difference in posterior derivations (Pz/Oz) during NREM sleep compared to baseline (in women aged 22 to 25 years), suggesting that the impact of alcohol on the sleep EEG differs according to brain region. Landolt and colleagues (1996a) also conducted spectral analysis; however, their alcohol dose (BrACs of 0.055) and timing of alcohol administration (6 hours before bedtime) made it likely that alcohol was eliminated prior to bedtime, and as such their results more accurately represent withdrawal from acute alcohol consumption, but arguably bear little relevance to the effects of acute administration on sleep EEG. Given that these studies differed in alcohol dose (0.49 to 0.90 g/kg body weight), timing (35 to 90 minutes prior to sleep), analysis methods, and results, it is difficult to determine whether there is a consistent effect of alcohol on power spectra on the basis of these studies.

Significant reductions in EEG delta frequency activity and power occur with normal development between the ages of 12 and 16, with continued reductions at a slower rate through late adolescence and into the third decade of life (Carskadon et al., 2001; Feinberg and Campbell, 2010; Feinberg et al., 2011). Changes in sleep are thought to be related to the development of neural systems, with myelination and synaptic pruning commencing prior to the emerging sleep changes but continuing across the second decade of life until after the age of 21, which roughly corresponds with the tail end of persisting changes in sleep (Feinberg et al., 2011; Sowell et al., 2004). Only 2 studies have assessed alcohol-related sleep effects in late adolescents (Chan et al., 2013; Williams et al., 1983). Both studies found that sleep architecture effects appear broadly consistent with the adult literature (Chan et al., 2013; Williams et al., 1983). They reported increased SWS and decreased REM sleep in the first half of the sleep period (particularly in the first sleep cycles; Chan et al., 2013) and decreased SWS along with increased sleep disruption in the second half of the sleep period, particularly in late sleep cycles (Chan et al., 2013; Williams et al., 1983).

This study sought to characterize the effects of acute alcohol consumption on sleep EEG power spectra in 18- to 21-year-old men and women. We aimed to extend upon previously published findings (Dijk et al., 1992; Landolt et al., 1996b; Rundell et al., 1972; Van Reen et al., 2006) by providing a comprehensive description of EEG effects across multiple sleep cycles and at several different scalp sites. Consistent with the adult literature, we tested 2 hypotheses. First, that alcohol consumption would promote NREM sleep-related delta activity early in the sleep period, especially at frontal scalp sites where delta activity is dominant. Second, that alcohol consumption would be associated with decreased NREM sleep-related delta activity and elevated high frequency activity in later sleep cycles.

MATERIALS AND METHODS

Sleep architecture information from this data set has previously been published. A more detailed description of the methodology can be found in that paper (Chan et al., 2013).

Participants

Participants were 24 (12 female) volunteers aged between 18 and 21 years, with a mean age of 19.1 ± 1.0 years and a mean body mass index of 22.0 ± 2.3 kg/m^2. Participants were recruited through advertisement and attended a face to face screening interview for medications, health problems, a family history of alcoholism, as well as recent (past 30 days) and lifetime alcohol consumption (Pfefferbaum et al., 1988). Potential participants were excluded if they reported, sleep disorders, erratic or irregular sleep wake schedules (habitual bedtimes after 1 AM and any differences in bedtime >3 hours more than twice a week [e.g., those associated with shift work]), habitual short sleepers (<6 hours), any substantial period of binge drinking in their lifetimes, current use of medications known to affect sleep, or a first degree family history of alcoholism. Participants were all healthy light drinkers who consumed <7 standard drinks per week over the previous 30 days (NHMRC, 2009). The protocol conformed to the Declaration of Helsinki and had prior approval of the local Human Subjects Ethics Committee. Participant informed consent was obtained prior to the screening interview.

General Laboratory Procedures

Participants attended 3 nonconsecutive nights (1 adaptation/screening night and 2 experimental nights) within a 2 week period at the Melbourne School of Psychological Sciences Sleep Laboratory, The University of Melbourne, Australia. Experimental nights were counterbalanced across beverage conditions (no condition order effects were observed): one involved presleep alcohol administration dosed to obtain a peak BrAC of 0.1% (vodka and orange juice) and the other involved a placebo beverage (orange juice with a straw dipped in vodka). Participants were informed prior to the study that they would be receiving alcohol on one of the experimental nights and thus were blind to the experimental condition at the time of alcohol administration. All beverages were mixed to produce a total volume adjusted for body mass such that a 70 kg person would receive 400 ml. For alcohol beverages, the dose of vodka was determined according to Curtain and Fairchild's (2003) method using each individual's height, weight, and percentage total body water (which largely accounts for gender differences in body composition) obtained from commercially available bathroom scales (Tanita BC541 Innerscan; Tanita Australia Kewdale WA, Australia).

Female participants were tested during the midfollicular phase of their menstrual cycle. For those who were on oral contraceptives, experimental nights were scheduled during their week of placebo pills (Baker and Driver, 2007; Baker et al., 2001).

Participants maintained their regular sleep wake schedule for 1 week prior the first night in the laboratory and throughout the duration of the experiment as assessed by sleep diary (actigraphy was not available), refrained from alcohol for 48 hours before the sessions and from food and caffeine after lunchtime on the day of the sessions. All sessions started 5 hours before habitual bedtimes, with lights-out being at their normal bedtime. On arriving at the laboratory, participants were breathalyzed (Alchosense Precision,

Andatech® Pty. Ltd. Vermont VIC, Australia) and all had a BrAC of 0.00%. Participants then received a standardized evening meal and then recording instrumentation was attached. Beverages were consumed evenly over a period of 30 minutes, starting 1 hour before lights-out.

Measurements and Recordings

On all 3 nights, standard Compumedics respiratory equipment and leg electromyograms (EMGs; Compumedics Ltd., Abbotsford, Australia) assessed the presence of sleep disordered breathing and periodic limb movements (Chan et al., 2013).

Electrophysiological Measures. On all nights, 11 EEG (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, O2—from the International 10/20 system; Jasper, 1958) electrodes, left and right eye electrooculogram (EOG), submental (chin) EMG, and electrocardiograph (ECG) were recorded to a single forehead reference.

Data Acquisition. All signals were acquired using an ambulatory sleep system (Siesta Unit, Compumedics Ltd., Abbotsford, Australia), with EEG, EOG, EMG, and ECG signals being sampled continuously at 512 Hz. All signals were displayed continuously and filtered optimally for visual scoring according to standard guidelines (AASM, 2007).

Data Reduction and Statistical Analyses

Data recorded on the adaptation night were visually scored for sleep disordered breathing or periodic limb movements according to American Academy of Sleep Medicine (AASM) criteria (AASM, 2007), and 1 participant with mild sleep disordered breathing was excluded. Sleep polysomnography data were visually scored independently by 2 researchers according to AASM guidelines for sleep staging, EEG events, and arousals (AASM, 2007). Differences were resolved by an independent adjudicator. All scorers were blinded to beverage condition.

Sleep cycle length was scored using rules based on Trinder and colleagues (1982). This method was adopted because young subjects frequently have rudimentary first REM periods which are not always reflected in an epoch scored as REM sleep (Chan et al., 2013; Trinder et al., 1982).

Power spectral analysis was conducted using Curry 7® software (Compumedics Neuroscan™, Abbotsford, Australia). EEG data were digitally re-referenced to a linked ears reference and bandpass filtered with a zero phase Hann filter between 0.3 and 30 Hz (0.6 and 8 Hz slopes, respectively). Differences in EEG power were assessed within 5 EEG frequency bands [delta (0.5 to 4 Hz), theta (4 to 8 Hz), alpha (8 to 12 Hz), sigma (12 to 16 Hz), and beta (16 to 32 Hz)] over sleep cycles and across the night for each sleep stage. The power spectral analysis used fast Fourier transforms decomposing each EEG time series into composite sine and cosine waves of different frequencies. Power values, measured as the squared EEG amplitude (μV^2) within each 0.125 Hz frequency bin, for each of the 5 EEG frequency bands were calculated by integrating the area under the power spectral distribution for that frequency band. Power values were calculated for arousal and artifact free, 5-second EEG segments and then averaged across each 30-second sleep epoch; these values were averaged for each sleep stage within each sleep cycle across the night.

As an initial omnibus analysis, spectral data for each frequency band were analyzed using a sex (men vs. women) by condition (alcohol vs. placebo), by sleep stage (NREM vs. REM sleep), by sleep cycle (1, 2, 3, and 4), and by electrode site (Fz, Cz, Pz, and O2) mixed-model analysis of variance (ANOVA), the specific results of these analyses can be found in the Online Supplement. Statistical analyses to test the specific hypotheses are outlined below, with planned comparisons controlling for multiple comparisons.

Hypothesis 1. Alcohol consumption will promote NREM sleep-related delta activity early in the sleep period, especially at frontal scalp sites. Delta activity in NREM sleep was analyzed using a condition (alcohol vs. placebo) by sleep cycle (1, 2, 3, and 4) and by electrode site (Fz, Cz, Pz, and O2) mixed-model ANOVA. The hypothesis was tested by evaluating the condition by cycle by site interaction term, with planned comparisons testing Fz against other sites and cycle 1 against cycles 2, 3, and 4 on the alcohol–placebo interaction data.

Hypothesis 2. Alcohol consumption will lead to decreased NREM sleep-related delta activity and elevated high frequency activity in later NREM sleep cycles. The spectral data from NREM sleep for each frequency band were analyzed using a condition (alcohol vs. placebo) by sleep cycle (1, 2, 3, and 4) mixed-model ANOVA. The hypothesis was tested by evaluating the condition by cycle interaction term, with planned comparisons testing cycle 4 against cycles 1, 2, and 3.

Only Fz, Cz, Pz, and O2 scalp sites were included in analyses as no laterality effects were predicted (Oz was not recorded). The site, cycle, and condition by cycle main effects and interactions were tested for sphericity and when violated, *F*-values were tested against Hyund–Feldt corrected degrees of freedom. Nineteen of the 22 participants had 4 complete sleep cycles in both alcohol and placebo conditions. To account for the absence of a fourth cycle in the remaining 3 participants, the data were analyzed in 2 ways: once with 19 participants (excluding the 3 without 4 cycles) and once interpolating missing data from the remaining 3 participants (as per Chan et al. 2013). In the interpolated data set, missing data were substituted (1 value for each of the 3 participants) with values based on the group mean for the fourth cycle, scaled according to the relationship of each subject's values for the first 3 cycles to the mean of the other 20 participants. No differences in the pattern of results or the number of significant effects were noted, and therefore, the interpolated data set (with adjusted degrees of freedom) are reported.

RESULTS

On alcohol nights, mean alcohol dose was 0.828 (±0.085 g/kg) (mean ± SD) resulting in a mean BrAC at lights-out of 0.084 (±0.016%) compared with 0.00% on placebo nights, $t(23) = 25.49$, $p < 0.001$. Mean BrAC levels at lights-out were higher in men than in women, men = 0.090 ± 0.02% and women = 0.077 ± 0.01%, $t(22) = 2.247$, $p = 0.035$. There were no differences between men and women for alcohol consumption in the 30 days prior to study participation, men = 2.35 ± 1.63 and women = 3.88 ± 2.66 standard drinks per week, $t(22) = 1.7$, $p = 0.103$, or for lifetime consumption of alcohol, men = 3.17 ± 4.167 and women = 6.87 ± 7.06 kg of alcohol, $t(22) = 1.564$, $p = 0.132$.

Omnibus Analyses of Spectral Data

As noted above the specific results of the initial omnibus analysis of spectral data for each frequency band can be found in the Table S1. In summary, however, there were significant main and interaction effects of stage, scalp site, and sleep cycle, not involving the alcohol condition that were

reflective of the normal sleep literature (Carskadon and Dement, 2005; Feinberg and Campbell, 2010). Delta, theta, and sigma power were greater and beta power less during NREM sleep compared to REM sleep. NREM delta and alpha power was maximal at Fz, whereas theta, beta, and sigma power were greatest at Cz. Sleep cycle effects indicated that delta, theta, and alpha activity was greatest in early sleep cycles. Stage by cycle by site interactions for delta, theta, and beta power, indicated that NREM versus REM and cycle effects were maximal at the sites at which the activity was most prominent. Likewise, NREM/REM and cycle differences for alpha power were more prominent over frontal scalp sites. In line with the decrease in delta power as the night progressed, stage by cycle by site interactions indicated that sigma power was maximal in the second part of the sleep period during NREM sleep and over central areas. Main effects of alcohol condition were observed for delta, alpha, and sigma power, with presleep alcohol increasing delta and alpha power and decreasing sigma power during sleep.

Hypothesis 1: Alcohol Consumption Will Promote NREM Sleep-Related Delta Activity Early in the Sleep Period, Especially at Frontal Scalp Sites

NREM delta power was higher in the alcohol condition compared to placebo at frontal scalp sites in the early sleep cycles (see Table 1). The 3-way ANOVA assessing hypothesis 1 demonstrated significant main effects for condition, $F(1, 21) = 10.59$, $p = 0.002$, sleep cycle, $F(3, 63) = 77.45$, $p < 0.001$, and scalp site, $F(3, 63) = 74.23$, $p < 0.001$, for NREM delta frequency power. Significant sleep cycle by scalp site, $F(9, 189) = 33.55$, $p < 0.001$, and condition by sleep cycle by scalp site, $F(9, 189) = 2.83$, $p = 0.031$, interactions were also observed with no condition by scalp site, $F(3, 63) = 1.28$, $p = 0.213$, interaction effect. Critically for hypothesis 1, the condition by cycle by site interaction term for delta activity was significant, $F(9, 189) = 2.83$, $p = 0.031$. The planned comparisons are presented in Table 2. All were significant ($p < 0.001$).

Hypothesis 2: Alcohol Consumption Will Lead to Decreased NREM Sleep-Related Delta Activity and Elevated High Frequency Activity in Later NREM Sleep Cycles

Mean values and main effects for the alcohol condition by sleep cycle analysis for delta, theta, alpha, sigma, and beta NREM EEG power can be seen in Tables 3 and 4, respectively. Critical to hypothesis 2, the condition by cycle interaction term was significant for delta, $F(3, 63)$ $F = 5.44$, $p = 0.012$, and alpha, $F(3, 63) = 9.73$, $p = 0.005$, but not for beta, $F(3, 63) = 0.24$, $p = 0.773$, sigma, $F(3, 63)$ 0.43, $p = 0.64$, or theta activity, $F(3, 63) = 3.29$, $p = 0.059$. Planned comparisons showed that delta activity was higher in cycle 1 and lower in cycle 4 in the alcohol condition compared to placebo with no difference between cycles 2 and 3. Planned comparisons also showed that alpha activity higher in cycles 1, 2, and 3 and lower in cycle 4 in the alcohol condition compared to placebo (see Table 5).

Although not directly hypothesized, another interesting aspect of the data arising from the present analysis was the simultaneous increase in both delta and alpha frequency EEG activity in the first sleep cycle at frontal scalp sites following alcohol. Indeed, there was a significantly higher levels of alpha [34.04 to 73.75 μV^2, 117% increase: $t(22) = -3.06$, $p = 0.006$] and delta [2,387.21 to 3,052.24 μV^2, 28% increase: $t(22) = -2.46$, $p = 0.023$] activity seen in the first sleep cycle at frontal scalp sites after alcohol consumption compared to placebo. This represented a 4-fold greater increase in alpha activity compared to the increase in delta activity after alcohol.

Table 1. Mean [Standard Error (SEM)] Delta Power (μV^2) During Non-Rapid Eye Movement Sleep After Alcohol and Placebo Across Fz (Top Panes) Cz, Pz (Middle Panes), and O2 (Bottom Panes) Electrode Sites from the First to Fourth Sleep Cycles (Left to Right Panes) Across the Night

Delta power (μV^2)				
	Fz – cycle 1	Fz – cycle 2	Fz – cycle 3	Fz – cycle 4
Placebo	2387.2 (192.5)	1481.5 (176.7)	1165.0 (121.6)	687.6 (72.9)
Alcohol	3052.2 (383.8)	1614.4 (230.5)	1280.1 (128.3)	546.1 (72.0)
	Cz – cycle 1	Cz – cycle 2	Cz – cycle 3	Cz – cycle 4
Placebo	1970.4 (137.6)	1212.9 (154.8)	975.0 (107.3)	611.1 (69.6)
Alcohol	2625.1 (226.2)	1441.5 (201.8)	1145.2 (117.5)	489.3 (66.3)
	Pz – cycle 1	Pz – cycle 2	Pz – cycle 3	Pz – cycle 4
Placebo	1700.1 (129.9)	956.3 (130.8)	773.6 (91.7)	459.4 (51.6)
Alcohol	2319.4 (249.0)	1192.0 (175.2)	936.3 (104.3)	372.8 (52.6)
	O2 – cycle 1	O2 – cycle 2	O2 – cycle 3	O2 – cycle 4
Placebo	693.7 (51.3)	405.1 (63.8)	338.6 (50.4)	192.2 (19.1)
Alcohol	961.4 (96.4)	495.1 (80.1)	383.0 (45.1)	173.8 (24.8)

Table 2. Planned Comparisons for Delta Activity in Non-Rapid Eye Movement Sleep Subsequent to the Condition (Alcohol vs. Placebo) by Sleep Cycle (1, 2, 3, and 4) and by Electrode Site (Fz, Cz, Pz, and O2) Mixed-Model ANOVA (Means and SEM in Table 1). Comparisons Tested Sleep Cycle 1 Against the Remainder of the Night's Cycles and Fz Against Other Sites on the Alcohol–Placebo Interaction Data

Comparison	*df*	*F*	*p*
Sleep cycle			
Cycle 1 versus cycle 2	1, 21	60.95	<0.001
Cycle 1 versus cycle 3	1, 21	86.67	<0.001
Cycle 1 versus cycle 4	1, 21	148.66	<0.001
Electrode site			
Fz versus Cz	1, 21	19.34	<0.001
Fz versus Pz	1, 21	32.79	<0.001
Fz versus O2	1, 21	83.38	<0.001

p-Values reported significant using Holm–Bonferroni correction for multiple comparisons.

DISCUSSION

Widespread differences in EEG power spectra were observed after alcohol consumption, indicating that alcohol had a major impact on EEG power. As predicted, and consistent with the previously reported increase in SWS in this data set (Chan et al., 2013), spectral analysis of the EEG found that alcohol consumption initially promoted delta activity, particularly at frontal scalp sites. This occurred at the expense of sigma power, which is generally associated with sleep spindles in N2 sleep. NREM delta frequency EEG activity was suppressed in the fourth sleep cycle in the alcohol condition relative to placebo. Contrary to hypothesis 2, an increase in high frequency EEG activity during NREM sleep was not observed in the later sleep cycles. Further to this, and of particular note, frontal alpha power during the first NREM sleep cycle was significantly elevated after alcohol consumption. There were minimal effects of alcohol on the theta and beta frequency bands.

The differences in alcohol doses, time of alcohol administration, EEG recording sites, and EEG analysis methods in the 3 previous studies evaluating the acute effects of alcohol on sleep EEG make comparison with present data challenging. Nonetheless, the increase in delta early in the night is consistent with Dijk and colleagues (1992) and to a limited extent (3 Hz only) with Van Reen and colleagues (2006). Consistent with present data, Van Reen and colleagues (2006) also showed a stronger delta effect at anterior sites. The absence of an alcohol-related effect on delta activity in the Rundell and colleagues (1972) study may have been due to their use of period amplitude rather than spectral analysis.

As noted above, the present data only partially supported the hypothesis that "alcohol consumption will lead to decreased NREM sleep-related delta activity and elevated high frequency activity in later sleep cycles during NREM sleep." Delta activity was suppressed in the fourth sleep cycle after presleep alcohol but high frequency activity was not specifically increased in late sleep cycles as might be expected in the presence of increased wakefulness and numbers of micro-arousals (Chan et al., 2013). Although it should be noted that alpha frequency activity was increased across the first 3 sleep cycles (and decreased in the fourth cycle) after alcohol, the increase, however, was largest in the first sleep cycle (discussed below). Of the 3 studies which have used quantitative EEG techniques to assess the effect of presleep alcohol on sleep EEG, only Van Reen and colleagues (2006) segmented the night into a series of consecutive (2-hour) epochs. This study did not report statistically significant increases in high frequency NREM sleep EEG power in 2-hour data blocks later in the night after alcohol. It should be noted that Van Reen and colleagues (2006) also did not observe increased micro-arousals late in the night following alcohol.

An increase in alpha activity was not found by Dijk and colleagues (1992), but was reported by Van Reen and colleagues (2006) and Rundell and colleagues (1972). Consistent with current data, Van Reen and colleagues (2006) showed this effect to be in frontal rather than occipital sites. This was visually discernable in current data (see Fig. 1). Of note, the

Table 3. Mean [Standard Error (SEM)] Spectral Data (μV^2) for ANOVAs for Alcohol Condition by Sleep Cycle Analysis for Delta, Theta, Alpha, Sigma, and Beta Non-Rapid Eye Movement Electroencephalogram Power (Statistics in Table 4)

	Cycle 1	Cycle 2	Cycle 3	Cycle 4
Delta power (μV^2)				
Placebo	2387.2 (191.9)	1481.4 (175.5)	1165 (119)	687.5 (76.2)
Alcohol	3052.2 (378.3)	1614.4 (226)	1280.1 (126.7)	546 (70.7)
Theta power (μV^2)				
Placebo	112.5 (7.1)	71.6 (5.7)	63.6 (4.4)	51 (3.6)
Alcohol	122.5 (12.3)	75.4 (6.8)	65.2 (5.3)	42.2 (4)
Alpha power (μV^2)				
Placebo	34 (4.4)	26 (2.7)	23.7 (2.1)	20.8 (2.1)
Alcohol	73.7 (16.5)	31.1 (3.4)	27 (2.7)	17.1 (2.1)
Sigma power (μV^2)				
Placebo	13.2 (1.1)	11.8 (1.1)	12.1 (1.1)	13.6 (1.2)
Alcohol	10.6 (1.1)	9.8 (1.1)	10.1 (1)	11.1 (1.2)
Beta power (μV^2)				
Placebo	4.5 (0.6)	3.8 (0.2)	4.1 (0.3)	4.4 (0.3)
Alcohol	4.1 (0.4)	3.7 (0.2)	3.8 (0.3)	4.4 (0.3)

Table 4. Statistical Main Effects and Interactions for Alcohol Condition by Sleep Cycle Analysis for Delta, Theta, Alpha, Sigma, and Beta Non-Rapid Eye Movement Electroencephalogram Power

	df	*F*	*p*
Delta power			
Condition	1, 21	3.791	0.065
Sleep cycle	3, 63	59.48	<0.001
Condition by sleep cycle	3, 63	5.44	0.012
Theta power			
Condition	1, 21	0.131	0.721
Sleep cycle	3, 63	76.163	<0.001
Condition by sleep cycle	3, 63	3.286	0.059
Alpha power			
Condition	1, 21	7.994	0.010
Sleep cycle	3, 63	12.499	0.002
Condition by sleep cycle	3, 63	9.731	0.005
Sigma power			
Condition	1, 21	13.448	0.001
Sleep cycle	3, 63	4.436	0.012
Condition by sleep cycle	3, 63	0.427	0.635
Beta power			
Condition	1, 21	0.900	0.354
Sleep cycle	3, 63	2.377	0.108
Condition by sleep cycle	3, 63	0.244	0.773

Table 5. Planned Comparisons Testing Cycle 4 Against Cycles 1, 2, and 3 for Alpha and Delta Frequency Bands. Mean [Standard Error (SEM)] Spectral Data (μV^2) for ANOVAs Where a Significant Condition (Alcohol vs. Placebo) by Sleep Cycle (1, 2, 3, and 4) was Observed is Presented

	Alcohol	Placebo	*p*
Alpha power μV^2			
Cycle 1	73.75 (16.6)	34.04 (4.4)	0.003
Cycle 2	31.10 (3.5)	26.07 (2.8)	0.021
Cycle 3	27.06 (2.7)	23.73 (2.1)	0.038
Cycle 4	17.17 (2.2)	20.84 (2.2)	0.007
Delta power μV^2			
Cycle 1	3052.24 (378.3)	2387.21 (191.9)	0.012
Cycle 2	1614.43 (226.0)	1481.47 (175.5)	ns
Cycle 3	1280.10 (126.8)	1165.00 (119.0)	ns
Cycle 4	546.09 (70.8)	687.55 (76.2)	0.017

p-Values reported significant using Holm–Bonferroni correction for multiple comparisons.

levels of alpha activity seen in the first sleep cycle at frontal scalp sites after alcohol consumption were 117% higher than after placebo, which is a 4-fold greater increase in alpha activity compared to the increase seen in delta activity after alcohol consumption (28% increase). This frontal topographical distribution of alpha activity during sleep is thought to be functionally different from alpha activity seen during quiet wakefulness, the latter being maximal over occipital regions. Frontal alpha EEG during sleep is thought to reflect a form of sleep disruption, distinct from the intrusion of wakefulness (Pivik and Harman, 1995). The alcohol-induced decrease in sigma associated with increased delta was reported by Dijk and colleagues (1992), but not seen in the other studies. The present data failed to show effects on beta activity reported by Rundell and colleagues (1972) (but not reported in other studies). The present data thus confirm increased frontal delta and alpha activity early in the night as the most consistent finding following acute alcohol administration and extend this finding into a younger age group than previously studied.

The increase in delta activity is consistent with alcohol's GABA agonistic properties. GABA-mediated hyperpolarization of cortical and thalamocortical neurons is thought to underlie the calcium channel-mediated burst firing that results in EEG delta activity. While alcohol does not lead to presynaptic GABA release in the thalamus or cortex, the way it does in some other brain regions (Kelm et al., 2011), it does enhance the function of GABA A receptors (Krystal et al., 2006).

Simultaneous frontal delta and alpha activity must be viewed as very different to enhancement of delta activity alone. This phenomenon has been previously described as alpha-delta sleep (Hauri and Hawkins, 1973). It has been hypothesized that alpha-delta sleep represents a form of endogenous arousal, reducing the restorative action of NREM sleep and manifesting in daytime symptoms in the subsequent waking period (Moldofsky, 2001b; Roizenblatt et al., 2001). This comes from observations that alpha-delta sleep is prevalent in patients who also experience sleep disruption and report waking up feeling unrefreshed (Mahowald and Mahowald, 2000; Menefee et al., 2000) and that alpha-delta activity can be induced in normal individuals with deep pain stimulation or selective deprivation of NREM stage 4 SWS (Moldofsky, 2001a). Whether induced in normal healthy controls or occurring in clinical populations, alpha-delta sleep is associated with the presence of a variety of negative symptoms, including headaches, musculoskeletal pain, and negative mood (Moldofsky, 2001a). The presence of alpha-delta sleep following high-dose alcohol consumption is therefore consistent with sleep acting less restoratively than normal, even in the first part of the night.

The observed decrease in sigma power, reflecting activity typical of sleep spindles following alcohol consumption, is in contrast to the spindle and sigma facilitation seen following administration of benzodiazepines (Johnson et al., 1983). This observation is consistent with recent data showing that alcohol facilitates benzodiazepine insensitive GABA A receptor subtypes (Krystal et al., 2006). Spindles are produced when thalamocortical cells become hyperpolarized resulting in low threshold spikes and the generation of spindle frequency activity in thalamic reticular cells (Steriade et al., 1993a). Further hyperpolarization leads to cessation of spindle activity and the development of delta frequency activity in thalamocortical neurons, reflected in cortical neurons and thus the scalp recorded EEG (Steriade et al., 1993a). Alcohol preferentially facilitates tonic GABAergic neurotransmission (Wei et al., 2004) and thus is likely to lead to delta production.

This study does have some limitations. First, although participants were blind to condition at the time of alcohol administration, the study did not assess the veracity of the

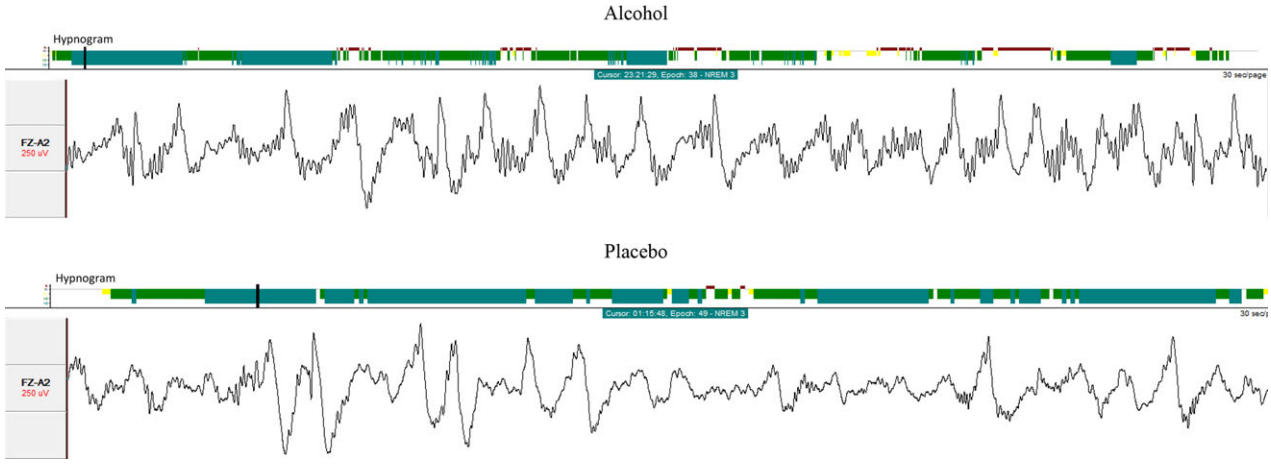

Fig. 1. Electroencephalogram recordings (30-second epoch) of Fz channels from a representative subject during slow wave sleep (SWS) in their first cycle after alcohol (top panel) and placebo (bottom panel) displaying the increase in alpha activity during SWS. Note: Vertical black line denotes where each 30-second epoch was located within each all-night hypnogram for the alcohol and placebo condition.

placebo, and the high dose of alcohol administered made it likely that participants were aware of which beverage contained alcohol (MacLean and Cairns, 1982). While participant awareness of alcohol has been shown to influence subjective ratings of sleep quality, we consider it unlikely to have affected the objective measures studied, it should also be noted that beverage condition order was counterbalanced across participants and no condition order effects were observed. However, it is nevertheless possible that participant expectation of having received the alcohol may have influenced some of these measures (Fratello et al., 2005). Second, the current study did not objectively measure sleeping habits prior to the adaptation night. As condition order was counterbalanced however, it is unlikely that there were any systematic differences in prestudy sleep between conditions. Third, although there were no alcohol-related sex differences observed in any aspect of these data, estimated lifetime consumption of alcohol was numerically higher for women than for men, which is uncharacteristic when compared to sex differences in the pattern of consumption in the broader population. It is likely that this was due to the recruitment of light drinkers, as light drinking young men were difficult to recruit compared to young women who drank regularly but at a responsible level. Further to this, as the current study was restricted to light drinking late adolescents without sleeping problems, findings cannot be readily generalized to more frequent drinkers, or those with abnormal sleep. Given that many late adolescents engage in binge drinking, further studies are needed to clarify the acute effects of alcohol in heavy or binge drinking cohorts, and in young people with sleeping problems (Bonomo et al., 2004; Wechsler et al., 1994). Finally, our sample was deliberately restricted to late adolescents due to the increase in alcohol consumption seen in this age group. As such, care should be taken when generalizing to older or heavier drinking cohorts. To address these issues, future research should include heavier drinkers either as a direct comparison group or as a large cohort with a wide range of drinking patterns, so this issue can be investigated as a continuum. Additionally, the interpretation of possible unique effects of alcohol in young adults is limited by the absence of an older comparison group.

In conclusion, as expected and in accordance with the sleep architecture literature, alcohol increased NREM sleep-related delta power after alcohol, particularly in the first sleep cycles and at frontal scalp sites where delta power is maximal. The increases in delta power were accompanied by a simultaneous promotion of alpha frequency activity. This may indicate the occurrence of an arousal influence which may compete with the sleep maintenance influence of delta activity. This may manifest in negative symptoms related to sleep disruption, or alpha-delta sleep, following alcohol and may have particular implications for the impact of presleep alcohol consumption on sleep and subsequent daily functioning.

ACKNOWLEDGMENTS

The project was supported by the Australasian Sleep Association (Rob Pierce Grant) and National Health & Medical Research Council (1012195) to CLN and NIH (AA017320; AA020565) to IMC.

REFERENCES

AASM (2007) The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. American Academy of Sleep Medicine, Westchester, IL.

Abbey A, Saenz C, Buck PO (2005) The cumulative effects of acute alcohol consumption, individual differences and situational perceptions on sexual decision making. J Stud Alcohol 66:82–90.

Aldrich MS (1998) Effects of alcohol on sleep, in *Alcohol Problems and Aging, Alcohol Problems and Aging* (Gomberg EL, Hegedus AM, Zucker RA eds), pp 281–300. National Institute of Health, Bethesda, MD.

Amzica F, Steriade M (1998) Electrophysiological correlates of sleep delta waves. Electroencephalogr Clin Neurophysiol 107:69–83.

Baker FC, Driver HS (2007) Circadian rhythms, sleep, and the menstrual cycle. Sleep Med 8:613–622.
Baker FC, Mitchell D, Driver HS (2001) Oral contraceptives alter sleep and raise body temperature in young women. Pflugers Arch 442:729–737.
Bonomo YA, Bowes G, Coffey C, Carlin JB, Patton GC (2004) Teenage drinking and the onset of alcohol dependence: a cohort study over seven years. Addiction 99:1520–1528.
Carskadon MA, Acebo C, Seifer R (2001) Extended nights, sleep loss, and recovery sleep in adolescents. Arch Ital Biol 139:301–312.
Carskadon MA, Dement WC (2005) Normal human sleep: an overview, in *Principles and Practice of Sleep Medicine, Vol. 4* (Kryger MH, Roth T, Dement WC, Roehrs T eds), pp 13–23. Elsevier Saunders, Philadelphia, PA.
Chan JKM, Trinder J, Andrewes HE, Colrain IM, Nicholas CL (2013) The acute effects of alcohol on sleep architecture in late adolescence. Alcohol Clin Exp Res 37:1720–1728.
Crews FT, Mdzinarishvili A, Kim D, He J, Nixon K (2006) Neurogenesis in adolescent brain is potently inhibited by ethanol. Neuroscience 137:437–445.
Curtin JJ, Fairchild BA (2003) Alcohol and cognitive control: implications for regulation of behavior during response conflict. J Abnorm Psychol 112:424–436.
Dijk DJ, Brunner DP, Aeschbach D, Tobler I, Borbely AA (1992) The effects of ethanol on human sleep EEG power spectra differ from those of benzodiazepine receptor agonists. Neuropsychopharmacology 7:225–232.
Feige B, Gann H, Brueck R, Hornyak M, Litsch S, Hohagen F, Riemann D (2006) Effects of alcohol on polysomnographically recorded sleep in healthy subjects. Alcohol Clin Exp Res 30:1527–1537.
Feinberg I, Campbell IG (2010) Sleep EEG changes during adolescence: an index of a fundamental brain reorganization. Brain Cogn 72:56–65.
Feinberg I, de Bie E, Davis NM, Campbell IG (2011) Topographic differences in the adolescent maturation of the slow wave EEG during NREM sleep. Sleep 34:325–333.
Fratello F, Curcio G, Ferrara M, Marzano C, Couyoumdjian A, Petrillo G, Bertini M, De Gennaro L (2005) Can an inert sleeping pill affect sleep? Effects on polysomnographic, behavioral and subjective measures. Psychopharmacology 181:761–770.
Harper C, Dixon G, Sheedy D, Garrick T (2003) Neuropathological alterations in alcoholic brains. Studies arising from the New South Wales tissue resource centre. Prog Neuropsychopharmacol Biol Psychiatry 27:951–961.
Hauri P, Hawkins DR (1973) Alpha-delta sleep. Electroencephalogr Clin Neurophysiol 34:233–237.
Jasper H (1958) Report of committee on methods of clinical exam in EEG. Electroencephalogr Clin Neurophysiol 10:370–375.
Johnson LC, Spinweber CL, Seidel WF, Dement WC (1983) Sleep spindle and delta changes during chronic use of a short-acting and a long-acting benzodiazepine hypnotic. Electroencephalogr Clin Neurophysiol 55:662–667.
Kelm MK, Criswell HE, Breese GR (2011) Ethanol-enhanced GABA release: a focus on G protein-coupled receptors. Brain Res Rev 65:113–123.
Kril JJ, Halliday GM, Svoboda MD, Cartwright H (1997) The cerebral cortex is damaged in chronic alcoholics. Neuroscience 79:983–998.
Krystal JH, Staley J, Mason G, Petrakis IL, Kaufman J, Harris RA, Gelernter J, Lappalainen J (2006) Gamma-aminobutyric acid type A receptors and alcoholism: intoxication, dependence, vulnerability, and treatment. Arch Gen Psychiatry 63:957–968.
Landolt HP, Dijk DJ, Achermann P, Borbely AA (1996b) Effect of age on the sleep EEG: slow-wave activity and spindle frequency activity in young and middle-aged men. Brain Res 738:205–212.
Landolt HP, Roth C, Dijk D-J, Borbely AA (1996a) Late-afternoon ethanol intake affects nocturnal sleep and the sleep EEG in middle-aged men. J Clin Psychopharmacol 16:428–436.
MacLean AW, Cairns J (1982) Dose-response effects of ethanol on the sleep of young men. J Stud Alcohol 43:434–444.
Mahowald ML, Mahowald MW (2000) Nighttime sleep and daytime functioning (sleepiness and fatigue) in less well-defined chronic rheumatic diseases with particular reference to the 'alpha-delta NREM sleep anomaly'. Sleep Med 1:195–207.
Maxwell JC (2008) Are we becoming more alike? Comparison of substance use in Australia and the United States as seen in the 1995, 1998, 2001 and 2004 national household surveys. Drug Alcohol Rev 27:473–481.
Menefee LA, Cohen MJ, Anderson WR, Doghramji K, Frank ED, Lee H (2000) Sleep disturbance and nonmalignant chronic pain: a comprehensive review of the literature. Pain Med 1:156–172.
Moldofsky H (2001a) Sleep and pain. Sleep Med Rev 5:385–396.
Moldofsky HK (2001b) Disordered sleep in fibromyalgia and related myofascial facial pain conditions. Dent Clin North Am 45:701–713.
NHMRC (2009) Australian Guidelines to Reduce Health Risks from Drinking Alcohol. National Health and Medical Research Council of Australia, Canberra, ACT.
Pfefferbaum A, Rosenbloom M, Crusan K, Jernigan TL (1988) Brain CT changes in alcoholics: effects of age and alcohol consumption. Alcohol Clin Exp Res 12:81–87.
Pivik RT, Harman K (1995) A reconceptualization of EEG alpha activity as an index of arousal during sleep: all alpha activity is not equal. J Sleep Res 4:131–137.
Roehrs T, Roth T (1995) Alcohol-induced sleepiness and memory function. Alcohol Health Res World 19:130–136.
Roehrs T, Roth T (2001) Sleep, sleepiness and alcohol use. Alcohol Res Health 25:101–109.
Roehrs T, Zwyghuizen-Doorenbos A, Timms V, Zorick F, Roth T (1989) Sleep extension, enhanced alertness and the sedating effects of ethanol. Pharmacol Biochem Behav 34:321–324.
Roizenblatt S, Moldofsky H, Benedito-Silva AA, Tufik S (2001) Alpha sleep characteristics in fibromyalgia. Arthritis Rheum 44:222–230.
Rundell OH, Lester BK, Griffiths WJ, Williams HL (1972) Alcohol and sleep in young adults. Psychopharmacologia 26:201–218.
Sowell ER, Thompson PM, Toga AW (2004) Mapping changes in the human cortex throughout the span of life. Neuroscientist 10:372–392.
Steriade M, McCormick DA, Sejnowski TJ (1993a) Thalamocortical oscillations in the sleeping and aroused brain. Science 262:679–685.
Steriade M, Nunez A, Amzica F (1993b) Intracellular analysis of relations between the slow (< 1 Hz) neocortical oscillation and other sleep rhythms of the electroencephalogram. J Neurosci 13:3266–3283.
Stone BM (1980) Sleep and low doses of alcohol. Electroencephalogr Clin Neurophysiol 48:706–709.
Trinder J, Stevenson J, Paxton SJ, Montgomery I (1982) Physical fitness, exercise, and REM sleep cycle length. Psychophysiology 19:89–93.
Van Reen E, Jenni OG, Carskadon MA (2006) Effects of alcohol on sleep and the sleep electroencephalogram in healthy young women. Alcohol Clin Exp Res 30:974–981.
Vitiello MV (1997) Sleep, alcohol and alcohol abuse. Addict Biol 2:151.
Wechsler H, Davenport A, Dowdall G, Moeykens B, Castillo S (1994) Health and behavioral consequences of binge drinking in college. A national survey of students at 140 campuses. JAMA 272:1672–1677.
Wechsler H, Lee JE, Kuo M, Lee H (2000) College binge drinking in the 1990s: a continuing problem. Results of the Harvard School of Public Health 1999 College Alcohol Study. J Am Coll Health 48:199–210.
Wei W, Faria LC, Mody I (2004) Low ethanol concentrations selectively augment the tonic inhibition mediated by delta subunit-containing GABAA receptors in hippocampal neurons. J Neurosci 24:8379–8382.
Williams DL, MacLean AW, Cairns J (1983) Dose-response effects of ethanol on the sleep of young women. J Stud Alcohol 44:515–523.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Delta power: *F*-statistics and effect size, power, and significance levels across Fz, Cz, Pz and O2 electrodes and the first 4 sleep cycles in NREM and REM sleep.

Table S2. Mean (standard error [SEM]) delta power during NREM and REM sleep after alcohol and placebo across Fz, (top panes) Cz, Pz (middle panes), and O2 (bottom panes) electrode sites from the first to fourth sleep cycles (left to right panes) across the night.

Table S3. Theta power: *F*-statistics and effect size, power, and significance levels across Fz, Cz, Pz, and O2 electrodes and the first 4 sleep cycles in NREM and REM sleep.

Table S4. Mean (standard error [SEM]) theta power during NREM and REM sleep after alcohol and placebo across Fz, (top panes) Cz, Pz (middle panes), and O2 (bottom panes) electrode sites from the first to fourth sleep cycles (left to right panes) across the night.

Table S5. Alpha power: *F*-statistics and effect size, power, and significance levels across Fz, Cz, Pz, and O2 electrodes and the first 4 sleep cycles in NREM and REM sleep.

Table S6. Mean (standard error [SEM]) alpha power during NREM and REM sleep after alcohol and placebo across Fz, (top panes) Cz, Pz (middle panes), and O2 (bottom panes) electrode sites from the first to fourth sleep cycles (left to right panes) across the night.

Table S7. Sigma power: *F*-statistics and effect size, power, and significance levels across Fz, Cz, Pz, and O2 electrodes and the first 4 sleep cycles in NREM and REM sleep.

Table S8. Mean (standard error [SEM]) sigma power during NREM and REM sleep after alcohol and placebo across Fz, (top panes), Cz, Pz (middle panes), and O2 (bottom panes) electrode sites from the first to fourth sleep cycles (left to right panes) across the night.

Table S9. Beta power: *F*-statistics and effect size, power, and significance levels across Fz, Cz, Pz, and O2 electrodes and the first 4 sleep cycles in NREM and REM sleep.

Table S10. Mean (standard error [SEM]) beta power during NREM and REM sleep after alcohol and placebo across Fz, (top panes) Cz, Pz (middle panes), and O2 (bottom panes) electrode sites from the first to fourth sleep cycles (left to right panes) across the night.