Adolescence and Parental History of Alcoholism: Insights from the Sleep EEG

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Background: Disrupted sleep is a common complaint of individuals with alcohol use disorder and in abstinent alcoholics. Furthermore, among recovering alcoholics, poor sleep predicts relapse to drinking. Whether disrupted sleep in these populations results from prolonged alcohol use or precedes the onset of drinking is not known. The aim of this study was to examine the sleep electroencephalogram (EEG) in alcohol-naïve, parental history positive (PH+), and negative (PH−) boys and girls.

Methods: All-night sleep EEG recordings in 2 longitudinal cohorts (child and teen) followed at 1.5 to 3 year intervals were analyzed. The child and teen participants were 9/10 and 15/16 years old at the initial assessment, respectively. Parental history status was classified by Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria applied to structured interviews (DIS-IV) resulting in 14 PH− and 10 PH+ children and 14 PH− and 10 PH+ teens. Sleep data were visually scored in 30-second epochs using standard criteria. Power spectra were calculated for EEG derivations C3/A2, C4/A1, O2/A1, O1/A2 for nonrapid eye movement (NREM) and rapid eye movement (REM) sleep.

Results: We found no difference between PH+ and PH− individuals in either cohort for any visually scored sleep stage variable. Spectral power declined in both cohorts across assessments for NREM and REM sleep in all derivations and across frequencies independent of parental history status. With regard to parental history, NREM sleep EEG power was lower for the delta band in PH+ teens at both assessments for the central derivations. Furthermore, power in the sigma band for the right occipital derivation in both NREM and REM sleep was lower in PH+ children only at the initial assessment.

Conclusions: We found no gross signs of sleep disruption as a function of parental history. Modest differences in spectral EEG power between PH+ and PH− children and teens indicate that a marker of parental alcohol history may be detectable in teens at risk for problem drinking.

Key Words: Sleep EEG, Adolescence, Children of Alcoholics, Spectral Analysis, Development.

ALCOHOL USE DISORDER affects an estimated 76.3 million people globally (WHO, 2004), and almost 80,000 people in the United States die per year from the consequences of alcohol consumption (Mokdad et al., 2004). Thus, much research has focused on identifying the factors that contribute to the emergence of this disorder (for a review, see Bierut, 2011). Such complex diseases as alcohol use disorder are caused by many genetic and environmental factors working together. For example, family, twin, and adoption studies have identified a genetic contribution to the development of alcohol dependence (Heath et al., 1997; Hesselbrock, 1995), with children of alcoholic (COA) parents at an increased risk for themselves developing alcohol dependence (Lieb et al., 2002; Merikangas et al., 1998).

Another factor contributing to alcoholism vulnerability may be sleep quality. An association between alcohol dependence and disrupted sleep has been well established. For example, among the most common complaints of alcoholics during acute consumption, withdrawal, and abstinence are difficulty falling asleep and reduced sleep duration (Brower, 2001). Furthermore, disrupted sleep may play an important role in susceptibility to relapse. Several studies have reported an association between objective and subjective measures of insomnia and relapse (Brower et al., 1998; Drummond et al., 1998; Foster and Peters, 1999; Foster et al., 2000). Support for the notion that sleep disturbances may precede alcoholism and thus constitute a vulnerability also comes from a laboratory study of nonalcoholic men (Roehrs et al., 1999). In this study, participants were given a choice between an alcoholic and nonalcoholic beverage before sleep. Individuals suffering from insomnia chose the alcohol beverage on 67% of experimental nights, while noninsomniacs chose the alcohol beverage on only 22% of experimental nights.

Brower (2001) has proposed a model that describes a reciprocal relationship between alcoholism and insomnia. In this

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model, individuals with sleep difficulties self-medicate by using alcohol's sedative effects to help them fall asleep. Although initially efficacious, increased tolerance leads to consumption of greater amounts of alcohol to achieve the same hypnotic effect. Chronic alcohol use, in turn, disrupts the brain systems involved in sleep regulation resulting in a cycle of greater sleep disruption, which leads to greater alcohol consumption. Thus, an individual may enter this cycle through a preexisting vulnerability, namely sleep difficulties.

Disrupted sleep may be a factor contributing to the increased risk of developing alcoholism previously observed in COAs as compared to children of nonalcoholics. Examining sleep in alcohol-naïve COAs provides an opportunity to assess whether sleep disruption may precede initiation of alcohol use. Two studies have examined the sleep and the sleeping electroencephalogram (EEG) in alcohol-naïve COAs. A study by Dahl and colleagues (Dahl et al., 2003) assessed sleep in 32 depressed youth ages 8 to 12 years; 18 had a parental history of alcoholism (PH+), and 14 had no such history (PH−). This study found no differences in sleep stage variables, such as sleep latency or total sleep time, between the 2 groups. Examination of the nonrapid eye movement (NREM) and rapid eye movement (REM) sleep EEG spectra showed that PH+ boys had greater power in the alpha band than PH− boys, while PH+ girls had lower alpha band power than PH− girls (i.e., a significant interaction of family history and sex). One limitation of this study was that these children were depressed, which is known to affect power in the alpha band. A second study compared the sleep EEG of thirteen 9/10-year-old children with a parental history of alcohol abuse/dependence to 17 children without a positive parental history (Tarokh and Carskadon, 2010b). Again, no differences in sleep stage variables were observed between the 2 groups; however, sleep EEG spectral analysis revealed modest differences between the groups. In this study, PH+ children exhibited less normalized power in the delta band and spindle range during NREM sleep than PH− children. Although this effect was apparent for the all-night spectrum, it was most pronounced in the first NREM sleep cycle.

The EEG spectrum provides a computationally derived estimate of cortical neuronal activity and thus may be a more sensitive measure of subtle differences between PH+ and PH− individuals than gross measures of visually scored sleep architecture. Indeed, the Collaborative Study of the Genetics of Alcoholism (COGA), a large multisite family study, found that the same GABRA2 gene was associated with Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) diagnosis of alcohol dependence and waking EEG beta power (Porjesz and Rangaswamy, 2007). Based on these findings, the authors proposed that the EEG might represent a useful endophenotype in the study of alcoholism. Examining the sleep EEG in children with a parental history of alcoholism, therefore, not only provides an opportunity to assess whether sleep is disrupted, but also whether cortical development follows a different trajectory in this population. In this study, we extend our previous study of a 1-time assessment in children (Tarokh and Carskadon, 2010b) by examining the sleep EEG longitudinally in children and teens with and without a parental history of alcoholism within the age range of 9 to 19 years.

MATERIALS AND METHODS

Participants

Two cohorts participated in this study. The child cohort included 24 children ages 9/10 years who were followed-up 1.5 to 3 years later. This cohort consists of a subset of participants reported in Tarokh and Carskadon (2010b) who were assessed longitudinally. Ten children (4 females) had a parental history of alcohol abuse and/or dependence (PH+) and 14 (4 females) did not (PH−). The teen cohort included 25 teens ages 15/16 years who were followed-up 1.5 to 3 years later. Of these teens, 10 (5 females) were PH+ and 15 (11 females) were PH−. Ages of both cohorts are reported in Table 1.

Participants were recruited using flyers, mailings to previous participants, and radio and newspaper advertisements. Exclusion criteria included self- or parent-reports of chronic or current medical illness, evidence of learning disabilities, sleep disorder, or personal or family history of psychopathology at a telephone screen or interview. Tanner staging, a measure of external primary and secondary sex characteristics, was performed by a physician and used to determine pubertal status. Tanner stages range from 1 to 5: Tanner stage 1 represents pre-pubertal status, while Tanner stage 5 represents sexual maturity (Table 1). We performed a chi-square test at each assessment to determine whether the distribution of pre/early pubertal (Tanner 1 and 2) and mid/late pubertal (Tanner 3, 4, or 5) was different between PH+ and PH− children. We found no difference at the initial ($\chi^2(1) = 0.11$, ns) or the follow-up assessments ($\chi^2(1) = 1.31$, ns). All participants in the teen cohort were post-pubertal (Tanner 5).

Participants' alcohol use was assessed at both sessions with a 1-month time-line follow-back interview (Sobell and Sobell, 1992). Only participants who reported either no experience with alcohol, experience with alcohol only in small quantities for religious observance, or <1 standard drink per month on average (drinking ≤ 2 standard drinks on a given occasion and never having been drunk) were included in this analysis. Using these criteria, 8 participants in the teen cohort were excluded from the analysis.

Parental History of Alcohol Abuse or Dependence

Parental history of alcohol abuse/dependence was determined using DSM-IV criteria applied to structured interviews. Both parents were interviewed with the diagnostic interview schedule (DIS-IV; Robins et al., 2000) when possible. When one parent was unavailable for interviewing, the available parent was interviewed regarding alcohol use in the absent parent only if they reported good recent knowledge about the other parent.

Procedure

Participants spent at least 1 week on a stabilized sleep schedule before each in-laboratory session. This schedule allotted at least 10 hours time in bed (TIB) for the child cohort and 9 hours TIB for the teen cohort. Compliance to the sleep schedule was verified by phone calls to the laboratory's time-stamped answering machine at bed and rise times, sleep diaries, and continuous wrist actigraphy. Participants were medication free and healthy on study days. Participants slept in individual darkened and temperature controlled rooms, where all-night polysomnography was recorded for 2 nights, an adaptation night followed by a baseline night.

Table 1. Sleep Stage Variables

	PH+		PH−				
Sleep variable	Initial	Follow-up	Initial	Follow-up	Time	PH	PH × time
Children							
Age	10.2 (0.65)	12.4 (0.84)	10.1 (0.51)	12.5 (0.66)	<0.0001	0.98	0.79
Tanner stage 1/2	9	7	11	6			
Tanner stage 3/4/5	1	3	2	7			
Stage 1	38 (11)	29 (10)	32 (12)	41 (14)	0.95	0.34	0.01
Stage 2	191 (64)	226 (37)	205 (43)	249 (33)	0.004	0.16	0.71
Slow wave sleep	237 (64)	191 (36)	223 (39)	157 (53)	0.0003	0.10	0.51
REM sleep	102 (18)	121 (20)	108 (22)	114 (23)	0.06	0.91	0.29
WASO	22 (21)	12 (19)	11 (11)	13 (14)	0.38	0.34	0.22
Sleep latency	11 (12)	12 (10)	11 (5)	17 (18)	0.61	0.26	0.84
Total sleep time	568 (26)	566 (18)	568 (17)	562 (22)	0.47	0.69	0.77
Total recording time	607 (12)	599 (2)	600 (6)	600 (1)	0.04	0.13	0.05
Teens							
Age	15.6 (0.29)	17.7 (0.42)	15.8 (0.52)	18.4 (0.58)	<0.0001	0.92	0.79
Stage 1	33 (8)	42 (11)	33 (10)	39 (11)	0.009	0.65	0.67
Stage 2	233 (36)	255 (31)	219 (43)	260 (33)	0.003	0.63	0.37
Slow wave sleep	151 (27)	114 (30)	164 (38)	119 (31)	0.0001	0.34	0.63
REM sleep	101 (18)	104 (25)	100 (17)	105 (37)	0.61	0.96	0.93
WASO	11 (15)	12 (8)	9 (11)	14 (29)	0.61	0.99	0.74
Sleep latency	10 (5)	9 (6)	8 (5)	9 (6)	0.74	0.56	0.56
Total sleep time	517 (20)	515 (10)	516 (9)	523 (46)	0.75	0.68	0.62
Total recording time	543 (10)	540 (<1)	540 (<1)	551 (33)	0.47	0.44	0.23

Age = mean age (standard deviation) in years. Tanner stage 1/2 = number of participants who were Tanner 1 or 2. Tanner stage 3/4/5 = number of participants who were Tanner 3, 4, or 5. Mean and standard deviation in minutes of sleep stage variables based on visual scoring. Slow wave sleep, minutes of stage 3 and 4 sleep; REM, rapid eye movement; WASO, wake after sleep onset measured from first occurrence of 1.5 minutes of stage 1 or first stage 2 to final awakening; Sleep latency = time in minutes to first 1.5 consecutive minutes of stage 1 or first stage 2. Significance values are based on a 2 (time; initial vs. follow-up) by 2 (parental history; positive vs. negative) ANOVA. Time = main effect of time; PH = main effect of parental history; PH × time = interaction of parental history and time. Significant values at alpha = 0.05 are shaded in gray (extra cells grayed).

Data from the baseline night are reported here for all participants except for 2 PH− teens whose adaptation night was used at the follow-up assessment because of extended bouts of wakefulness (67 minutes) on the baseline night resulting from an acute event in the laboratory.

Polysomnography Recording

Polysomnographic recordings included 2 central (C3/A2 and C4/A1) and 2 occipital (O2/A1 and O1/A2) EEG derivations, right and left electro-oculogram, electromyogram (EMG; mentalis, submentalis), and electrocardiogram. Respiration (oral/nasal thermocouple) and leg EMG recordings on the adaptation night confirmed that all participants were free of sleep-related breathing abnormalities or periodic limb movements. Electrode impedance values were always below 10 kΩ. Because of equipment upgrades during the study, recordings were performed on 2 different systems. All initial recordings, with the exception of 5 children and 2 teens, were performed using the Albert Grass Heritage System (Astromed, Grass, West Warwick, RI) with GAMMA software. Those EEG signals were digitized online (12 bit AD converter; Butterworth filter, −12 dB/octave; low-pass filter, −6 dB at 35 Hz; time constant 1.0 second) with a sampling rate of either 100 or 128 Hz. The remaining initial recordings and all follow-up recordings were performed using the TWin system (Astromed) using TWin AS40 bedside amplifiers, from which the signals were collected digitally with a sampling frequency of 400 Hz and filtered offline (high-pass EEG filter 0.3 Hz; low-pass filter 35 Hz). We tested whether the output of the 2 systems was comparable by inputting a calibration signal 25 μV in amplitude into both systems simultaneously. The signals were within a microvolt of one another at frequencies from 0.6 to 16 Hz, after which small discrepancies emerged. Therefore, we restrict our analyses to frequencies below 16 Hz.

Power Spectral Analysis

Polysomnographic recordings were sleep stage scored according to the criteria of Rechtschaffen and Kales (1968), with intra- and inter-rater reliability of at least 86%. Epochs with artifacts were rejected using a semi-automated procedure based on power in the 0.6- to 4.6-Hz and 20- to 40-Hz bands and confirmed by visual inspection. Epochs were rejected when power in the delta band exceeded 2.5 times or power in the beta band exceed 2 times the power calculated using a moving average determined over fifteen 30-second epochs. Accuracy of artifact rejection was confirmed by visual inspection. Power spectra were calculated for each 30-second epoch (Hanning window, average of six 5-second epochs; frequency resolution = 0.2 Hz) using MATLAB (The MathWorks Inc., Natick, MA). All-night power spectra were calculated separately for NREM and REM sleep. Because of individual variability in absolute sleep EEG power, we also examined normalized sleep EEG power by dividing power at each frequency bin by the maximum power across bins (always located at the lowest frequency bin, 0.6 Hz) for each individual.

Statistics

Data from the 2 cohorts were analyzed separately. For each cohort, a 2 × 2 ANOVA with factors parental history (positive vs. negative) and assessment (initial vs. follow-up) was used to assess statistical significance of sleep stage variables. To reduce the number of multiple comparisons, the sleep EEG spectra were binned into the following frequency bands: delta (0.6 to 4.8 Hz), theta (5 to 8.4 Hz), alpha (8.6 to 10.8 Hz), and sigma (11 to 16 Hz).

Bootstrap analysis with 5,000 iterations was used to assess statistical significance of the EEG power spectra. The bootstrap is a nonparametric test in which a distribution of values is obtained by

random shuffling of the data, and the application of the bootstrap to sleep EEG data has been described in depth in the study by (Tarokh and Carskadon, 2010b). Because only 2 distributions can be compared with the bootstrap, we compared PH+ and PH− participants for each frequency band at the initial and follow-up session separately (e.g., PH+ children at the initial session compared with PH− children at the initial session). Furthermore, we combined data from PH+ and PH− participants to determine whether a change in power occurred across assessments independent of parental history status. To assess whether the rate of change in power between assessments differed in PH+ and PH− individuals, we calculated the rate of power change within an individual as:

$$P_{\Delta} = \frac{P_F - P_I}{A_F - A_I}. \quad (1)$$

In this equation, P_F is average power in a given band at the follow-up session, while P_I is power in a given band at the initial session. A_F and A_I are age (in years) at the final and initial sessions, respectively. We performed a bootstrap analysis comparing the rate of change, P_{Δ}, in PH+ and PH− participants. Statistical analyses were performed with alpha set to 0.05.

RESULTS

Sleep Stage Variables

We observed a decrease in the minutes of slow wave sleep (SWS) and a concurrent increase in the minutes of stage 2 sleep with maturation in both cohorts independent of parental history status (main effect of time; Table 1). A significant increase in stage 1 sleep was also found in the teen group, independent of parental history. The statistically significant finding for total recording time in the child cohort is not functionally meaningful (7 minute difference). We did not observe a main effect of parental history for any sleep stage variable or cohort examined or any interaction of parental history and time (Table 1).

Power Spectra: Children

We observed a decline in sleep EEG power with increasing age during NREM and REM sleep in both cohorts irrespective of PH status (main effect of time) (Fig. 1 NREM; Fig. 2 REM; Fig. 3 P_{Δ}). This effect was present in all bands for C3/A2, O2/A1, and O1/A2 and restricted to the delta, theta, and alpha bands for derivation C4/A1 for NREM sleep. For REM sleep, an effect of assessment occurred in all bands for C3/A2 and O2/A1 and in the delta, theta, and sigma bands for C4/A1 and O1/A2.

With regard to parental history of alcoholism, significant effects during NREM sleep were restricted to derivation O2/A1, where we found significantly lower EEG power for PH+ and PH− children at the initial session for all frequency bands (delta: $p = 0.04$; theta: $p = 0.02$; alpha: $p = 0.02$; sigma: $p = 0.01$). A similar finding was present for REM sleep, where we observed less power for PH+ children compared with PH− children in O2/A1 for the delta ($p = 0.04$) and sigma ($p = 0.01$) bands at the initial session. Conversely, in the right central derivation, we observed greater EEG power for PH+ as compared with PH− children for the theta ($p = 0.04$) and alpha ($p = 0.049$) bands at the initial assessment. We found no differences between the groups at the follow-up assessment.

The rate of change, P_{Δ}, was slower for PH+ compared with PH− children in the right occipital derivation (O2/A1) for all frequency bands for NREM (delta: $p = 0.03$; theta: $p = 0.01$; alpha = 0.02; sigma: $p = 0.01$) and REM (delta: $p = 0.03$; theta: 0.01; alpha = 0.02; sigma: 0.01) sleep. Similarly, during NREM sleep, PH+ children exhibited a slower rate of change in the left occipital derivation (O1/A2) for the theta ($p = 0.04$), alpha ($p = 0.009$), and sigma ($p = 0.02$) bands and in the left central derivation (C3/A2) for the delta ($p = 0.048$) and sigma ($p = 0.04$) bands. For REM sleep in addition to the lower rate of change for O2/A1 in all bands, the rate of change was also lower for C4/A1 in the theta ($p = 0.049$) and alpha ($p = 0.036$) and in derivation O1/A2 in the delta band ($p = 0.045$).

Our analysis of normalized power revealed lower power from PH+ children compared with PH− children in the delta band during NREM sleep for the left occipital derivation. No differences were observed in normalized REM sleep spectra.

Power Spectra: Teens

As in the child cohort, we observed a decline in power with maturation in both groups at all derivations during NREM and REM sleep independent of parental history (Fig. 4 NREM; Fig. 5 REM; Fig. 6 P_{Δ}). This effect was significant in all frequency bands for derivations C3/A2, C4/A1, and O2/A1 in both states. For derivation O1/A2, a maturational decline in power occurred in the delta and theta bands for both sleep states.

PH+ teens exhibited less power than PH− teens at both assessments for derivations C3/A2 (initial: $p = 0.03$; follow-up: $p = 0.03$) and C4/A1 (initial: $p = 0.04$; follow-up: $p = 0.04$) during NREM sleep in the delta band. We found no difference in the rate of change, P_{Δ}, for any derivation or frequency between PH+ and PH− teens for NREM sleep. During REM sleep, PH+ teens exhibited less delta power than PH− teens for C3/A2 ($p = 0.04$) band for the follow-up session and for C4/A1 ($p = 0.04$) during the initial session. Similarly, PH+ children exhibited greater power in the alpha band for O2/A1 at follow-up. Furthermore, during REM sleep, the rate of change was slower in the theta band for PH+ as compared to PH− teens in the right central derivation ($p = 0.04$).

We found no differences in the normalized sleep EEG spectra between PH+ and PH− teens for any frequency or either sleep state.

DISCUSSION

This study included 2 longitudinal cohorts to examine the sleep EEG of children and teens with and without a

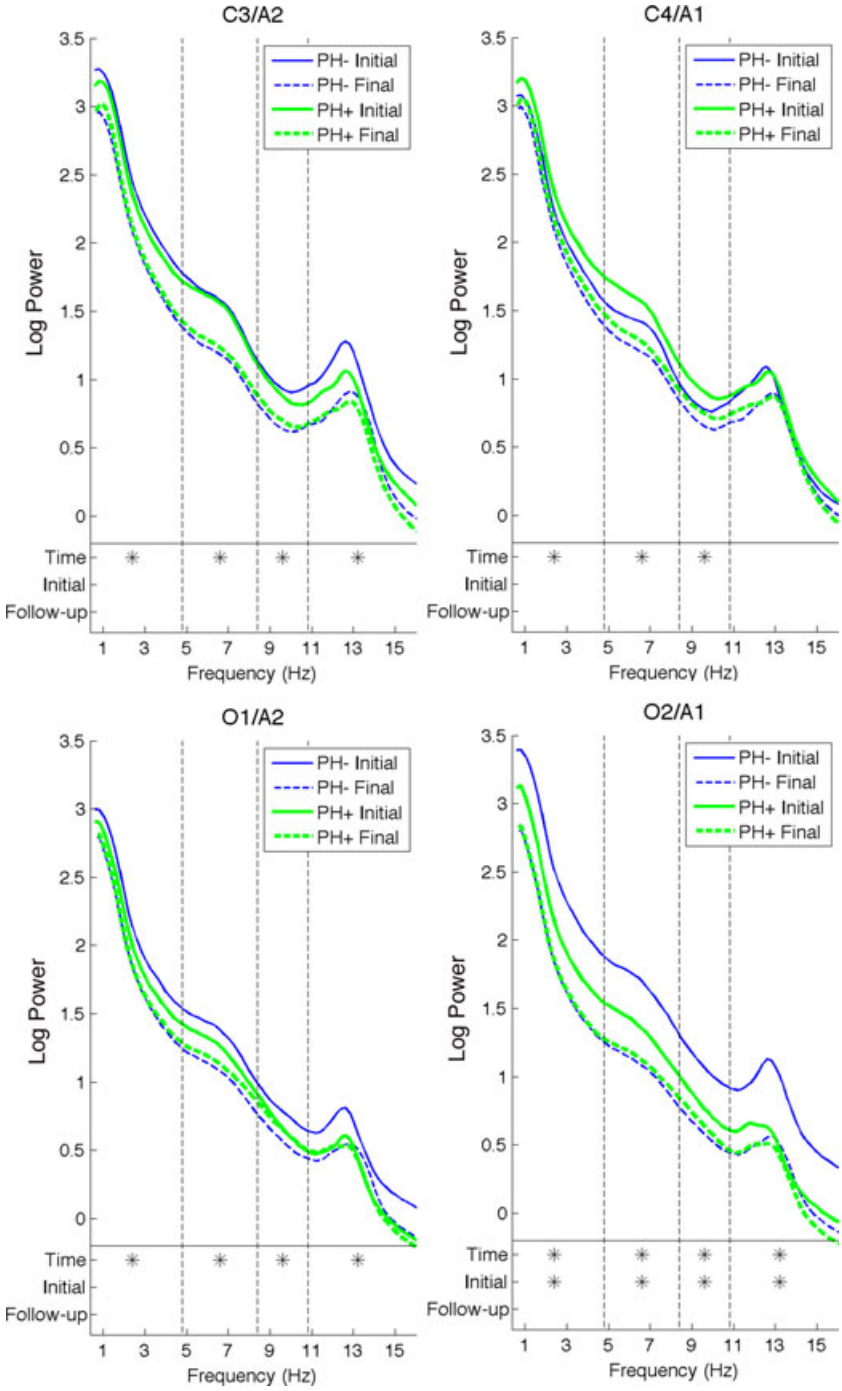

Fig. 1. Child cohort all-night nonrapid eye movement sleep spectra. Average spectra of log power at 2 central (C3/A2 and C4/A1) and 2 occipital (O2/A1 and O1/A2) derivations. Parental history positive children (PH+) are shown in grey, while parental history negative children (PH−) are in black. Initial sessions are depicted with a solid line, while follow-up sessions are shown with a dashed line. The vertical lines divide the spectra into 4 bands: delta (0.6 to 4.8 Hz), theta (5 to 8.4 Hz), alpha (8.6 to 10.8 Hz), and sigma (11 to 16 Hz). An asterisk shows significance ($p < 0.05$) at the bottom of each plot. Time = significant difference between assessments, Initial = significant difference between PH+ and PH− participants for the initial assessment, Final = significant difference between PH+ and PH− children for the follow-up assessment.

parental history of alcohol abuse/dependence. By examining the sleep EEG under controlled conditions in a population at increased risk for alcohol abuse/dependence, we hoped to ascertain whether sleep disturbances precede alcohol use and thus serve as a predictive marker or perhaps as a trigger to initiate alcohol consumption for its hypnotic affects. We found no signs of parental history-associated gross sleep disturbance, such as increased waking after sleep onset, reduced total sleep time, or increased sleep latency.

Abstinent adult alcoholics exhibit increased REM sleep duration compared with controls, which persists even after long periods of abstinence, raising the question of whether this REM sleep increase results from disrupted brain

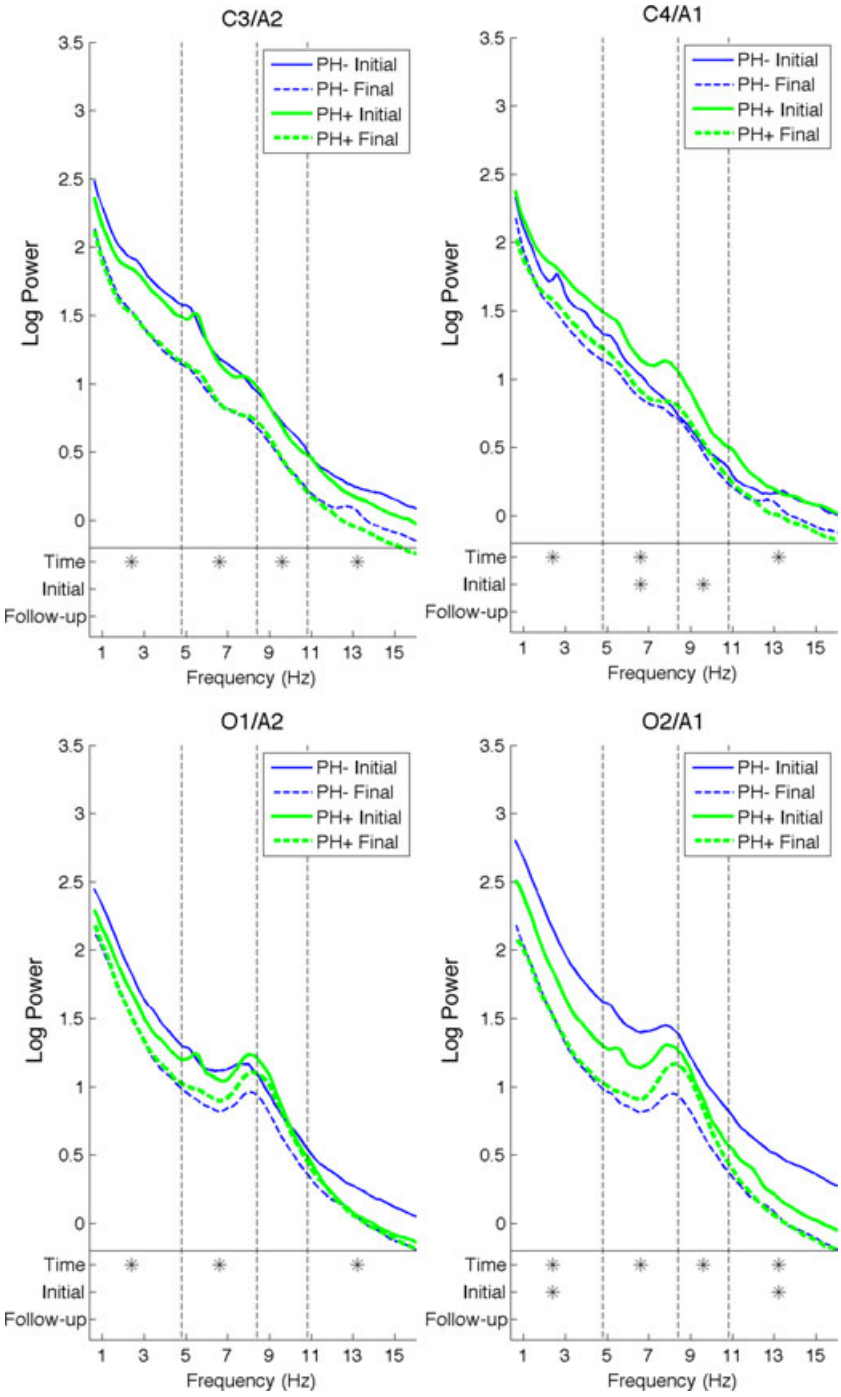

Fig. 2. Child cohort all-night rapid eye movement sleep spectra. For details, see Fig. 1 legend.

neurophysiology because of alcohol abuse or predates alcohol use (Colrain et al., 2009; Drummond et al., 1998; Feige et al., 2007; Gann et al., 2001; Gillin et al., 1990; Thompson et al., 1995). We found no signs of differential amounts of REM sleep in either children or teens, supporting the hypothesis that the increased REM sleep observed in abstinent alcoholics is because of prolonged alcohol abuse.

The lack of significant differences in sleep stage variables between PH+ and PH− children and teens aligns with previous sleep EEG studies (Dahl et al., 2003; Tarokh and Carskadon, 2010b), which also reported no differences between PH+ and PH− children. When considering negative findings in studies with small sample sizes, however, the possibility that individual variability may mask group differences should be taken into account. Indeed, the PH+ children showed a trend for lower amounts of SWS, although no such trend was apparent in the teen cohort.

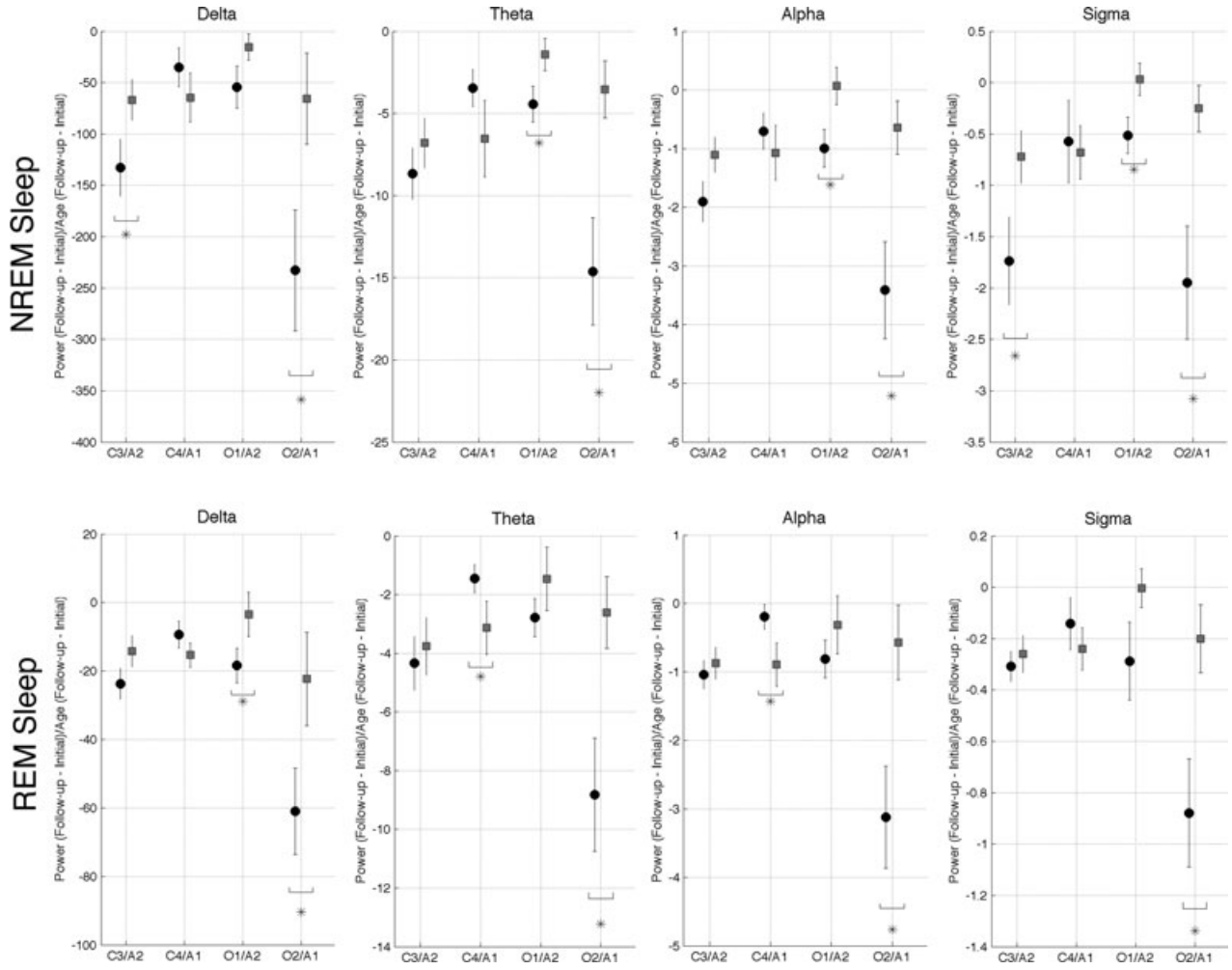

Fig. 3. Child cohort rate of change for nonrapid eye movement (NREM) and rapid eye movement (REM) sleep. Rate of change in power between assessments measured in microvolt squared per year, as defined in Eq. (1). PH+ children are shown in grey squares while PH− children are shown as black circles. Significance, $p < 0.05$, indicated with an asterisk.

Independent of parental history status, we observed an expected age-related reduction in minutes of SWS and an increase in minutes of stage 2 sleep (e.g., Tarokh and Carskadon, 2010a; Tarokh et al., 2011c) within child and teen cohorts. With regards to sleep EEG power spectra, the reduction in power that we observed between assessments in both cohorts was found in all derivations, most frequencies, and both NREM and REM sleep. This finding is in line with a number of studies (e.g., Campbell et al., 2011; Kurth et al., 2010; Tarokh et al., 2011a) and is thought to reflect the synaptic pruning that occurs in the healthy adolescent cortex during this period (Feinberg, 1982). Evidence for an association between age-related decline in gray matter volume and waking and sleeping EEG power in adolescents (Buchmann et al., 2010; Whitford et al., 2007) indicates that a common mechanism such as synaptic pruning could underlie both processes.

We observed modest differences in several sleep EEG spectral measures between PH+ and PH− children/teens. Our interpretation of the parental history findings derives from several assumptions about the sleep EEG. Sleep EEG recordings of several hours in duration allow for reliable measures of cortical activity during 2 brain states (NREM and REM sleep), each of which has distinct neurophysiological and neurochemical underpinnings (for a review, see Hobson and Pace-Schott, 2002). Thus, the sleep EEG provides a window on the developing brain, enabling us to examine whether gross cortical differences exist in PH+ and PH− children and teens. Thus, differences between PH+ and PH− participants found in both NREM and REM sleep EEG spectra are driven by neuroanatomical differences between the groups.

Our main finding with regards to parental history in the child cohort was lower state-independent sigma (11 to 16 Hz) and delta (0.6 to 4.8 Hz) EEG power at derivation O2/A1 for PH+ children at the initial assessment with no difference at the follow-up assessment. The absence of observed differences between child groups at the follow-up assessment indicates that the rate of change in power was significantly slower in PH+ compared with PH− children. One explanation

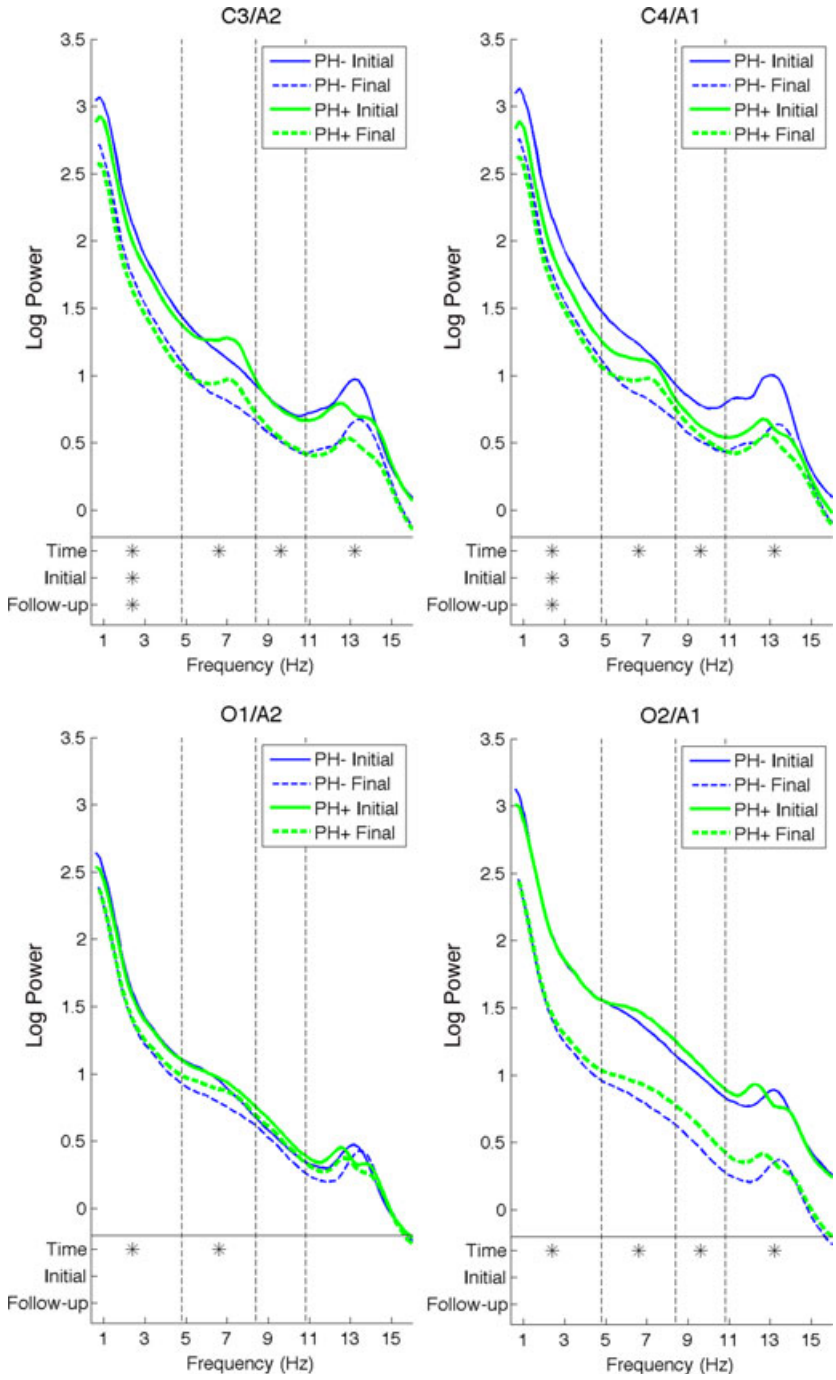

Fig. 4. Teen cohort all-night nonrapid eye movement sleep spectra. For details, see Fig. 1 legend.

for the difference at the initial assessment may be that synaptic pruning occurred earlier in PH+ children resulting in reduced sleep EEG power. An alternate hypothesis is that PH+ children never achieve the same plateau as PH− children in sleep EEG power (and thus synaptic sprouting) before synaptic pruning commenced. We note that this effect was restricted to the right occipital derivation. One magnetic resonance imaging study in youth ages 11 to 15 years with and without a family history of alcoholism reported that children with a positive family history had lower fractional anisotropy (FA) in the right but not left optic radiation than those with a negative family history (Herting et al., 2010). FA is a measure of axon fiber bundle diameter, myelination, and coherent fiber organization. The same regional anatomical differences may underlie our finding. Several reports that link structure to EEG power support this hypothesis. For example, Colrain and colleagues (2011) showed that myelin degradation, as measured through fractional diffusivity, is associated with low delta power during task performance; others show positive correlations between FA and gray

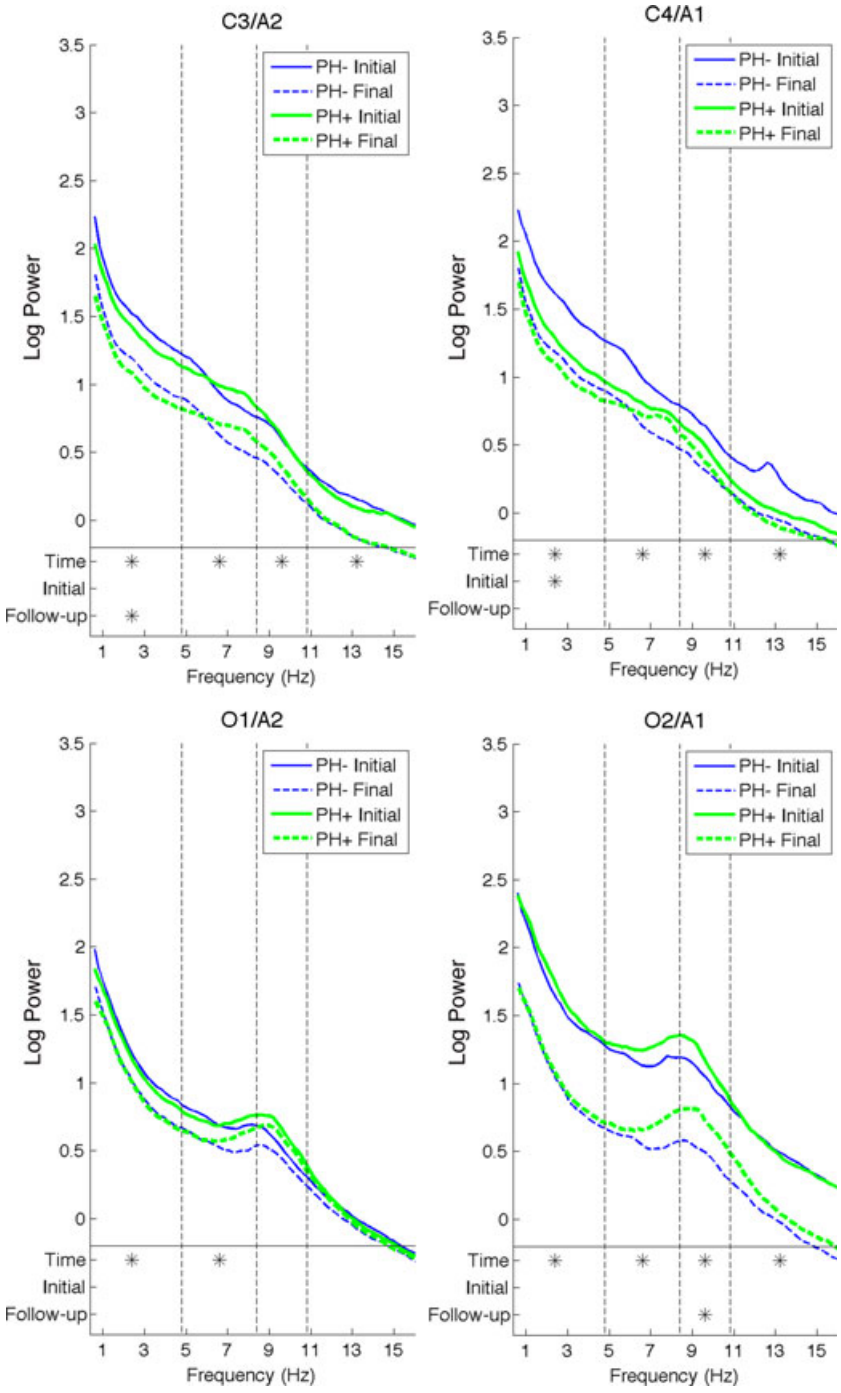

Fig. 5. Teen cohort all-night rapid eye movement sleep spectra. For details, see Fig. 1 legend.

matter thickness (Kochunov et al., 2007), and associations between gray matter thickness and EEG power (Whitford et al., 2007). By inference, FA values may be positively associated with EEG power, and our data may indicate relative paucity in right occipital cortical structure in PH+ children.

The child cohort includes a subset of participants whose initial assessment was reported in the Tarokh and Carskadon study (2010b). As in the earlier analysis, PH+ children exhibit lower normalized delta power in the left occipital derivation when compared with PH− children. Unlike the earlier study, we no longer observed a difference in the sigma band, most likely because the previous sigma effect was limited to 1-Hz frequency bin rather than a larger band as in the current analysis. On the other hand, the significant difference in absolute power between PH+ and PH− children at the initial assessment was not captured in the normalized data used in the previous analysis. Furthermore, we were unable to replicate the findings of Dahl and colleagues (2003) of greater

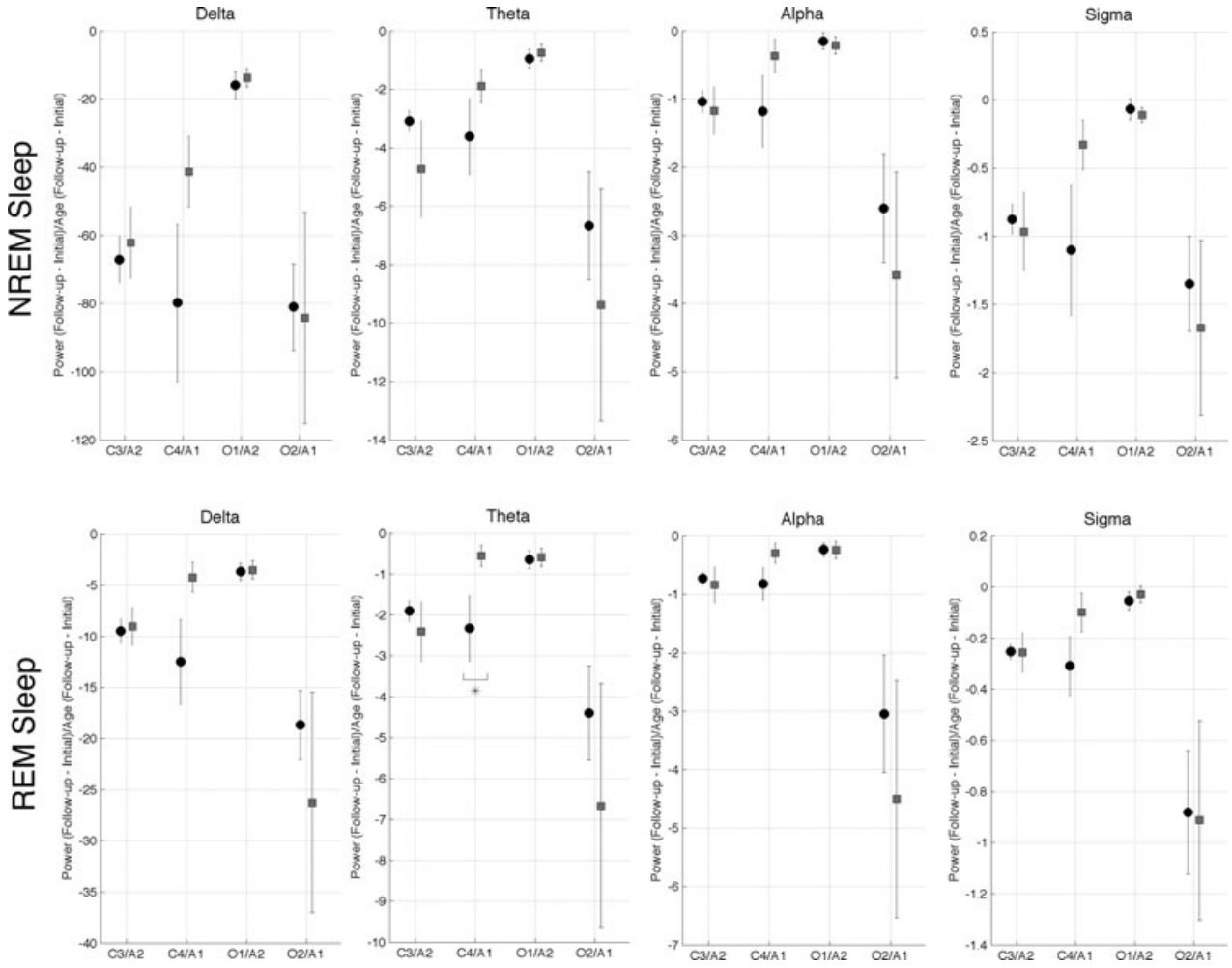

Fig. 6. Teen cohort rate of change for nonrapid eye movement (NREM) and rapid eye movement (REM) sleep. For details, see Fig. 3 legend.

power in PH+ boys in the alpha band (7.5–11 Hz) for the first and second NREM period and across the entire night for derivation C3 and C4. Although we were underpowered to examine the influence of sex, we did not observe a difference in the child cohort between PH+ and PH− individuals for these derivations in any frequency band. We note that the Dahl and colleagues' study (2003) was performed in depressed children over a broad age range (8 to 16 years), possibly influencing the results.

Our main parental history finding in the teen cohort showed lower delta power in PH+ teens than PH− teens in the central derivations at both assessments during NREM sleep. Several studies of abstinent alcoholic adults show that NREM delta power is diminished as compared with nonalcoholic adults (Colrain et al., 2009; Gillin et al., 1990; Irwin et al., 2000; Kurella et al., 1990). State-dependent neurophysiology may account for the differences observed only in NREM sleep in previous studies of alcoholics and at both assessments in our study. Thus, lower NREM delta power in PH+ compared with PH− teens may indicate that NREM delta power may herald alcoholism in offspring of alcoholics. Support for this notion can be inferred from a study by Colrain and colleagues (2009) wherein NREM delta power in 42 abstinent alcoholics was not correlated with either days of sobriety or estimated alcohol consumption before abstaining. If diminished NREM delta power predates alcoholism rather than arises from drinking, one would not expect NREM delta power to be correlated with alcohol use. Moreover, similar to our study in alcohol-naïve adolescents, Colrain and colleagues (2009) reported lower NREM delta power in abstinent alcoholics compared with controls in frontal and central and not occipital derivations. Indeed, waking EEG studies have identified a link between EEG oscillations and genes associated with alcoholism. For example, the COGA project found significant linkage between delta and theta oscillations and the CHMR2 gene, which is associated with a diagnosis of alcohol dependence (Porjesz and Rangaswamy, 2007). The sleeping EEG is a heritable trait (Ambrosius et al., 2008; De Gennaro et al., 2008) and stable across adolescent development (Tarokh et al., 2011b); thus, a genetic predisposition toward alcoholism may be reflected in the sleep EEG spectrum.

Several limitations of this study are important to note. First, our sample size limited our ability to examine sex differences. Second, although the bootstrap analysis minimizes the false positive rate, it does not have a formal correction for multiple comparisons. Even so, group differences were modest. Future studies with larger sample sizes are required to confirm these results. Furthermore, we do not know whether any of these participants will develop alcohol abuse disorder; such knowledge might increase our ability to use this type of data for predicting alcohol problems. Finally, although the parents of PH+ participants met the DSM-IV criteria for a lifetime history of alcohol abuse/dependence, they did not meet criteria for current illness. Despite these limitations, this longitudinal study showed no distinctions of parental history for gross signs of sleep stage disturbance and thus did not support the notion that sleep disruption might be present in alcohol-naïve offspring and potentially precede the onset of alcohol abuse/dependence. On the other hand, spectral analysis showed modest differences between young participants with and without a parental history of alcohol problems, perhaps indicating that differences in brain structure and function are a consequence of this family history.

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