

Full Spectrum EEG Response to Eyes Open Versus Eyes Closed in Children and The Development of The Alpha Rhythm

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Abstract

This report examines spectrum-wide (1 to 100 Hz) differences in electroencephalogram (EEG) power between eyes open (EO) and eyes closed (EC) conditions in children. A high density (60 electrode) system was used to measure EEG power at 4, 5, 7, 9, and 11 years of age. Results showed spatial and frequency band differences as a function of age. Specifically, 1) the alpha peak shifts from 8 Hz at 4 years to 9 Hz at 11 years, 2) EC results in increased power at lower frequencies but decreased power at higher frequencies for all ages, 3) the sign change for the difference between EO and EC occurs in a narrow band of frequencies which changes across childhood, 4) at 4 and 5 years, EC increases lower frequency power most prominently over posterior regions; 5) in contrast, at all ages, EC decreases power above 30 Hz most prominently over anterior regions. These results extend previous findings to show EO/EC differences in higher frequencies and to the presence of developmental changes across childhood. This report demonstrates that the simple EO/EC task can provide important information about maturation of brain states and can be done with a very brief, minimal protocol.

Introduction

In humans, as in all primates, more cortical surface area is devoted to visual processing than to any other sensory modality. As a result, it is not surprising that profound differences in brain activity occur depending on whether the eyes are open or closed. These modalities allow the indirect quantification of diverse mechanisms attributable to the eyes opening and closure task. Such differences can be measured with electroencephalography (EEG) or functional magnetic resonance imaging (fMRI) (eg. Nunez, 2001; Xu, 2014). Thus, the “task” of opening or closing the eyes has emerged as a practical, noninvasive, and sensitive measure of brain function (Barry, 2007).

Traditionally, the signature brain response to eyes closed (EC) state has been the increase in EEG power in the alpha band (8 to 12 Hz), most prominent over posterior scalp regions (Berger H, 1929; Nunez PL, 2006). This increase in alpha activity during EC is thought to reflect increased global synchronization of neuronal activity, with global desynchronization and decreased alpha activity accompanying the eyes open (EO) state (Klimesch, 1999). Alpha desynchronization may be mediated by cortical and thalamo-cortical interactions from increased visual stimulation and increased autonomic arousal (Barry, Clarke, Johnstone, & Brown, 2009; Bellato, Arora, Kochhar, Hollis, & Groom, 2020).

EEG responses to EO/EC have been studied in relation to a number of clinical conditions. In a study of adolescents, alpha power during EC was reduced in individuals with autism spectrum disorder and attention deficit hyperactivity disorder compared to typically developing controls (Bellato et al., 2020). Another study in adults found an association between autism traits, including social rigidity, and alpha power in the parietal scalp region during the EC condition (Carter Leno, Tomlinson, Chang, Naples, & McPartland, 2018). In adults with schizophrenia, auditory steady state responses were dependent upon EO/EC state (Griskova-Bulanova, Dapsys, Maciulis, & Arnfred, 2013).

Other studies have focused on characterization of EO/EC in healthy individuals. Most of those studies have been in adults (Barry, Clarke, Johnstone, Magee, & Rushby, 2007; Chapman, Armington, & Bragdon, 1962; Geller et al., 2014; Glass & Kwiatkowski, 1970; Xu et al., 2014). We found only two studies in which EEG responses to an EO/EC paradigm were assessed in children. Barry and colleagues showed that in 8 to 10-year-old children there were significant differences in EEG activity from 1.5 to 25 Hz in the EO vs EC conditions using a 19-electrode system (Barry et al., 2009). Johnstone and coauthors recorded EEG with a single electrode device in 7 to 12-year-old participants and similarly found significant frontal EO vs EC differences from 0.5 to 25 Hz (Johnstone et al., 2020). Thus, differential responses to the EO vs EC conditions can provide markers of neurobehavioral disorders and maturation.

We explored using EEG responses to the simple manipulation of opening and closing the eyes to elucidate differences in neuronal networks across development. The purpose of this current study was to examine spectrum-wide differences (i.e. not limited to the alpha band and inclusive of the gamma band) in EEG power between the EO and EC conditions in a cross-sectional study of young children using a high density (60 electrode) EEG system. EEG was recorded as part of an ongoing follow-up of subjects originally enrolled in the Prenatal Alcohol in SIDS and Stillbirth Safe Passage cohort (Dukes et al., 2014). These follow-up assessments occurred as part of the PASS-ECHO (Environment Influences on Child Health Outcomes) study in South Dakota (Gillman et al., 2018). Here we present results in children at 4, 5, 7, 9, and 11 years of age.

Methods

Participants

Data were collected as part of the Environmental Influences on Childhood Outcomes (ECHO) longitudinal study in South Dakota (PASS-ECHO). This study assesses multiple factors that influence health outcomes in children from fetal, infancy (1 month, 1 year), early childhood (2, 3, 4, 5 years) to late childhood (7, 9, and 11 years of age). Demographics are shown in Table 1. EEG studies were conducted at the Avera Center for Pediatric and Community Research (CPCR), in Sioux Falls and Rapid City, SD. Recordings were collected from September 2018 through March 2020. Informed consents to collecting infant and child brain activity using EEG were procured as part of consent for the main study. Written informed consent was obtained from the parents of all participants. Institutional Review Board approval was obtained from New York State Psychiatric Institute, Columbia University, Avera Health and the Western Institutional Review Board. All research was performed in accordance with the relevant guidelines/regulations of those institutions. In total, across all ages, 549 children were studied. Exclusion criteria for enrollment in the ECHO study were: parent unable to provide informed consent; health care provider advises against participation; major neurologic or developmental deficit, diagnosed by a pediatrician according to parental report.

EEG Recording

Baseline EEG was collected at 4, 5, 7, 9, and 11 years of age. Children were seated in front of a computer screen and were asked to fixate on a central crosshair. The research assistant ensured the child remained calm with minimal distractions. EEG was then collected for up to 3 minutes using a 64-channel Geodesic Sensor Net System (EGI, Inc., Eugene, OR). The nets had the four face channels (E61-E64) removed to measure heart rate and respiration. Children were asked to keep their eyes open for 30 sec and then closed for 30 sec. There were 3 EO/EC repetitions. EEG data were referenced to the single vertex electrode, Cz, and sampled at 500 Hz. Impedances were checked prior to collection and recording was started when they reached values below 50 kOhms. EEG data were exported from Netstation to raw binary format and imported into MATLAB for pre-processing to remove artifacts

EEG Processing

As a first step, raw data were filtered to remove line noise. A 16,000-point finite-impulse response 4 Hz wide notch filter was applied at the line noise frequency (60 Hz) and its first three harmonics (120 Hz, 180 Hz, 240 Hz), with 36 to 100 dB power reduction within the notches. In the second step ECG artifact was removed from each electrode/channel, using a recently developed method that mimics ballistocardiogram removal from EEG recorded during MRI. This method removes ECG artifact by using a simultaneously recorded ECG signal to precisely identify the times of each R wave peak, and then signal average the EEG over small windows (± 60 ms) centered on those times, deriving a channel-specific template that is then subtracted from each channel.

EEG power spectra were calculated for each 30 second epoch in each condition and then averaged within conditions. Spectra were computed using the Welch method, averaging over fast Fourier transforms (FFTs) taken on 1 second segments. Data were demeaned and a Hanning window was applied prior to computing the FFT for each second. To minimize effects of eye-movement artifact, data from the four leads closest to the eyes were removed. Leads and epochs contaminated by movement-related or other sources of electrical artifact were identified using multiple criteria on a second by second basis to data from each lead. Criteria for each second were (cf. Isler et al., 2006): standard deviation of voltage less than $40 \mu\text{V}$ (to remove noisy leads) and greater than $0.000001 (10^{-6}) \mu\text{V}$ (to remove disconnected leads); sample-to-sample change less than $25 \mu\text{V}$ (to screen out sudden movements); absolute value of voltage less than $100 \mu\text{V}$; log-log spectral slope of raw data between 20 and 120 Hz greater than -0.1 (to screen for muscle artifact which has a white noise spectrum). If more than nine leads had artifact during any one second, that second was excluded from subsequent analyses. Remaining data were re-referenced to the average over all leads at each sample. Finally, base 10 log power was the average of the squared FFT's over the accepted seconds, requiring at least 15 acceptable seconds per 30-second epoch for each lead as a minimum inclusion threshold. Finally, to be included in the analyses a participant must have had acceptable data in both eye conditions.

Statistical Analyses

To explore whether EO vs EC state power differences were a wide-spread phenomenon, power spectra were first averaged over all electrode locations for each condition and age group. At each age, averaged spectra were then tested for eye state differences with paired t-tests at each frequency. Subsequently, to determine the spatial underpinnings of the averaged spectra, paired t-tests between EC and EO were performed at each electrode location. Effects of multiple comparisons were controlled for using a False Discovery Rate (FDR) of 10%. Two-dimensional spatial maps were then used to show the t-statistic for each location where the p-value was less than the critical p-value determined by FDR. FDR was applied across frequencies for spatially averaged spectra and across electrodes for spatial maps.

Results

Table 1 summarizes the number of participants at each age.

Table 1: Demographic information of study participants

Age	Mean Age	IQR Age	N total	N male	N female
4	4.24	0.30	92	48 (52.17%)	44
5	5.20	0.23	144	69 (47.92%)	75
7	7.23	0.25	138	69 (50.00%)	69
9	9.25	0.24	60	29 (48.33%)	31
11	11.24	0.17	52	29 (55.78%)	23

There were significant differences in EEG power in the EO versus the EC conditions across considerable portions of the spectrum and across all ages. At low frequencies, eye closure resulted in increased power, while at higher frequencies eye closure resulted in decreased power. Lack of significant differences between conditions was limited to the spectral band where this transition occurs, near to and right above the well-known alpha peak. These spectral features are exemplified in Figure 1. The Left Panels of Figure 1 display the EO and EC spatially-averaged spectra for participants from 4 (Top Panels) to 11 (Bottom Panels) years of age. The Right Panels of Figure 1 show the power difference between the two conditions (EO-EC) for the same participants. In this representation, we defined the transition frequency as intersection of the spectral difference and the zero blue horizontal line. For frequencies below the transition frequency, the difference (EO-EC) is negative, thus on average the power associated with the EC condition is greater than that of EO, while the opposite is found for frequencies above the transition frequency. To ensure that high frequency differences in spatially averaged spectra were not driven by microsaccades, which primarily contaminate the frontal channels, spectra were separately averaged only within parietal regions not expected to contain microsaccade related activity and results nearly identical to those presented in Figure 1 were obtained (see Supplemental Figure 1).

Overall, we found that decreases in EEG power become more pronounced with age, while increases are comparable across ages. Additionally, at 4 years of age, the transition frequency is a narrow band from 9 to 15 Hz, while at 11 years of age it is a discrete frequency of around 32 Hz. This is related to the evidence that the alpha peak at 4 years of age occurs at 8 Hz; by 11 years of age, it occurs at 9 Hz and is associated with a much larger difference (~two-fold larger) between EO and EC.

To illustrate these changes with age, Figure 2 expands on the EO/EC differences visualized in Figure 1 considering all five ages and with a focus on three specific frequency bands; 7 to 9, 19 to 21, and 99 to 101 Hz. The panels are labeled with the central frequencies of these bands. At 8 Hz (Left Panel), for all ages, EO power is significantly lower than power during the EC condition. The magnitude of these differences shows a minimal change as a function of age. On the other hand, the directional differences in the Middle Panel of Figure 2, show how the transition frequency varies with age. At 4 and 5 years of age, in the frequency interval 19-21 Hz, power in the EO condition is higher than for EC. At 7 and 9 years of age the difference between the two conditions is not significant and by 11 years of age the EO has significantly lower power. For higher frequencies bands EO power is significantly greater than EC power for all ages (see 100 Hz example, Right Panel of Figure 2).

The above results were obtained by averaging power over all electrodes. To determine if there is spatial variation in those results, we examined EC vs EO differences at each electrode location. Power was averaged in 3 Hz wide bins and 3 frequency bins (8, 20 and 100 Hz) are displayed in Figure 3 for the different ages, namely 4, 5, 7, 9, and 11 years. As shown in the Left Panel of Figure 3, at 4 years of age the overall greater power seen in the EC condition at 8 Hz is driven by electrodes in the posterior area of the brain, predominantly located in the occipital regions. At older ages, the greater power associated with EC condition becomes a widespread phenomenon not exclusively associated with the posterior area of the brain.

The distribution of the EO versus EC difference in the band 19-21 Hz highlights a progressive spatial differentiation. Specifically, at 4 years of age the power associated with EO is greater than EC (frequencies above the transition band) and spatially confined in the frontal regions of the brain. On the other hand, the posterior regions of the brain are responsible for the greater power of EC at 11 years of age. The electrode configurations for the remaining age groups are associated with intermediate spatial patterns.

Lastly, at 100 Hz, overall greater power seen in the EO condition is driven by frontal, parietal, and temporal regions (third column). Differences at 100 Hz (and above, not shown) are associated with a spatial organization consistent with those of lower frequencies from 30 to 50 Hz, supporting evidence for the frontal, parietal, and temporal distribution of power differences above the transition frequency. The described findings for the frequency band 99-101 Hz are consistent across ages.

Discussion

This study reports spectrum-wide (2-250 Hz) differences in EEG power between eyes open (EO) and eyes closed (EC) brain states in a cross-sectional study of children at 4, 5, 7, 9, and 11 years of age. The principal results are that: 1) the alpha band spectral peak increases from 8 Hz at 4 years of age to 9 Hz at 11 years of age; 2) eye closure results in increased power at lower frequencies but decreased at higher frequencies; 3) the change in sign for the difference between EO and EC conditions occurs in a narrow band of 'transitional' frequencies; 4) the transitional frequencies change across childhood, from a center frequency of 9 Hz at 4 years of age to a center frequency of 32 Hz at 11 years of age; 5) at 4 and 5 years of age, eye closure increases lower frequency power most prominently over posterior regions; 6) reduced power at higher frequencies with eye closure is most prominent over anterior regions.

The earliest normative studies of EEG power in response to eye closure focused solely on the alpha band (Chapman, Shelburne, & Bragdon, 1970). Subsequent work with adults explored frequency bands outside of alpha, such as the beta band (14 to 30 Hz) (Barry et al., 2007; Glass & Kwiatkowski, 1970). Those studies found increased beta power in response to eye closure. Barry et al. (Barry et al., 2009) studied children aged 8 to 12 and found a similar increase in beta power with eye closure. Our findings for the *older children* are consistent with these adult findings however, we found that at earlier ages beta power decreases with eye closure. Recently, Johnstone et al. (Johnstone et al., 2020) reported a developmental increase in frontal alpha power in children from 7 to 12 years old, but no developmental change in beta power. However, akin to Barry et al., they defined the beta band as 12.5 to 25 Hz. In contrast to both the Barry and Johnstone studies, we examined 3 Hz wide bands across the same beta range and found mixed effects dependent upon both age and frequency (Supplemental Figure 2).

The results we have presented used spectra averaged over three 30-second epochs in each eye condition. We investigated whether we would obtain the same, or very similar results, if we only used one epoch in each condition. Therefore, we repeated all analyses using just the first epoch in each condition. Indeed, we found that, in general, using only one epoch in each condition replicates our initial results (see Supplemental Figures 3 through 6). This suggests that the amount of data needed to observe the described eye closure effect is minimal. This characteristic may be important to some deployments of the eye-closure paradigm.

To our knowledge, this is the first study in children to test for EEG differences induced by eye closure in the gamma band and higher frequencies (above 30 Hz) using scalp EEG. Decreased power in response to eye closure occurred over the entire range of high frequencies from 30 to 200 Hz. Interestingly, one recent study of eye closure used EEG data from adult patients with intracranial electrodes implanted for seizure localization (Geller et al., 2014). Convergent with our results, they reported that eye closure resulted in widespread increased power at lower frequencies but decreased power over a broad frequency range above 30 Hz. Further, the higher frequency effects were limited to occipital regions and two focal frontal areas.

Barry et al (Barry et al., 2007) interpreted their findings as follows: widespread increases in power at lower frequencies with eye closure reflects a decrease in global arousal, while more localized higher frequency

power reflects cortical activation and visual processing. This view has some support in the results reported by Geller 2014 (Geller et al., 2014) discussed previously. Furthermore, a recent study of eye closure using fMRI network analyses showed that networks active during EC had higher global efficiency, while networks active during EO had higher local clustering (Xu et al., 2014). Additional studies have demonstrated associations between increased alpha power during the EC condition and increased autism traits in typically developing adults (Carter Leno et al., 2018) suggesting a potential relationship between global arousal and behavioral rigidity.

One limitation of our study, especially regarding the transition frequencies and spatial location of differences between EO and EC, is that these current results were cross-sectional. It would be important to track individuals' trajectories over time to validate the hypothesis of variation in transition frequencies with age are related to neurobehavioral functions. Further studies that would link these differences to neurodevelopmental measures are expected to offer a likely biomarker of neurodevelopmental risk. A second limitation of our very high frequency results is their origin in scalp EEG, which is predominately susceptible to muscle artifact at those frequencies. However, muscle artifact has a flat spectrum (Nunez, 2006), and the lack of any clear break in the log-log slopes of our power spectra argue against that explanation.

Assessments of different brain states, e.g. sleep states or evoked response states, provide good markers of brain maturation and capacities. However, these types of assessments either require long periods of data acquisition or equipment that allows precise linkage of stimuli presentation and brain activity making these approaches difficult for large cohort studies. We are now initiating studies in which this challenge is being used for remote, in home assessment.

This current report demonstrates that the simple challenge of opening and closing the eyes can provide important information about the maturation of brain states and can be done with a very brief, minimally demanding protocol. In conclusion, the present work demonstrates EO/EC elicits changes in EEG spectra not confined to lower frequencies and which change as function of age during childhood.

Declarations

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Conflict of Interest Statement:

None of the authors have potential conflicts of interest to be disclosed.

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Figures

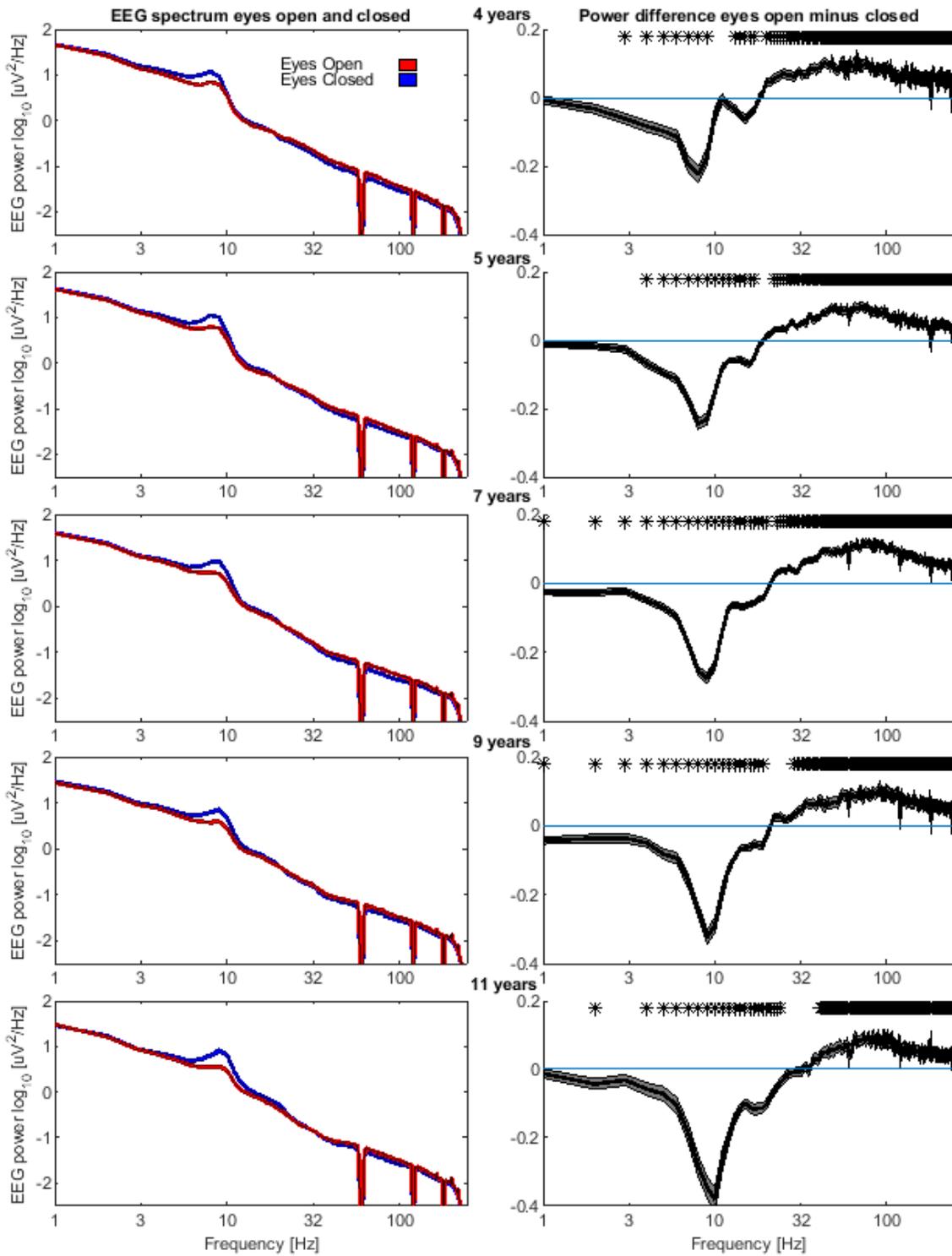


Figure 1

The effects of eye opening and closure in participants of all ages. Left Panel: Spatially-averaged EEG power spectra are shown in \log_{10} power, \log_{10} frequency format with mean values (solid line) and \pm standard error (shading). EC and EO spectra are shown in blue and red, respectively. Right Panel: Differences (EO-EC) between spatially-averaged EEG power spectral amplitudes are shown with mean

values (solid line) and \pm standard error (shading). Paired t-tests at each frequency were applied. Asterisks identify frequencies where differences remained significant after applying a 10% false discovery rate.

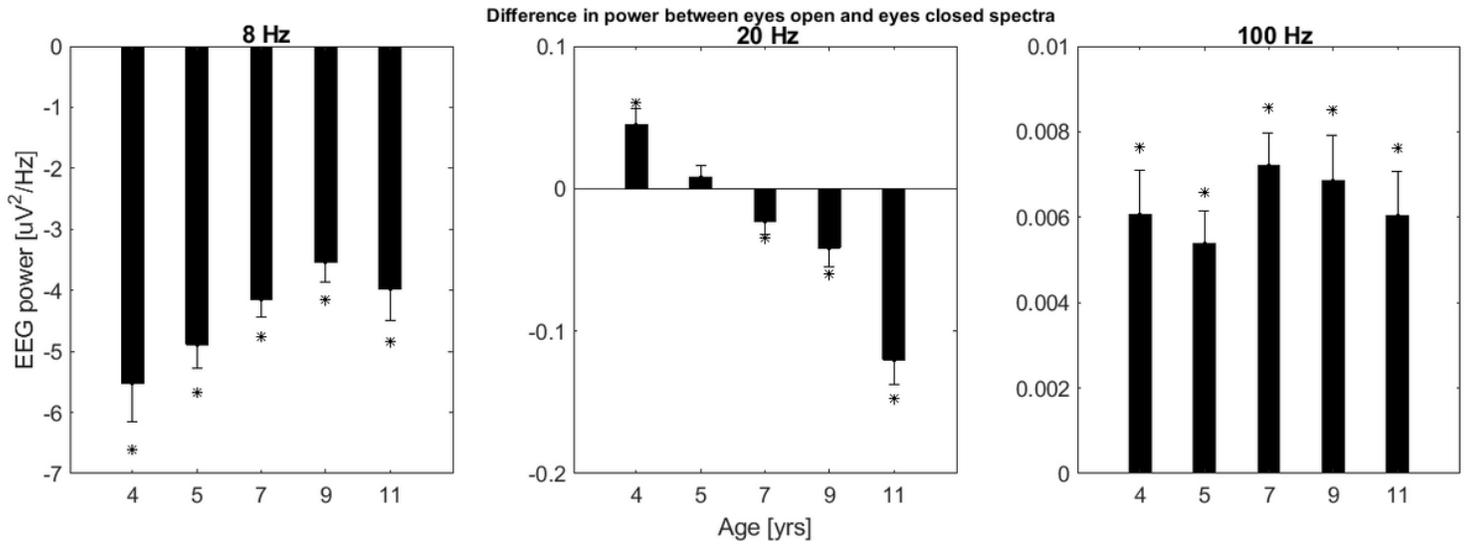


Figure 2

Developmental changes of differences between spatially-averaged spectral bands (EO - EC) are shown with bar plots at each of the five ages. Bands were 3 Hz wide, (subpanels, labeled by center frequency, 8, 20, and 100 Hz). Bands with significant EC vs EO differences are marked with asterisks, all of which remained significant after applying a Bonferroni adjustment to alpha.

Spatial distribution of significant differences in power between eyes open and eyes closed

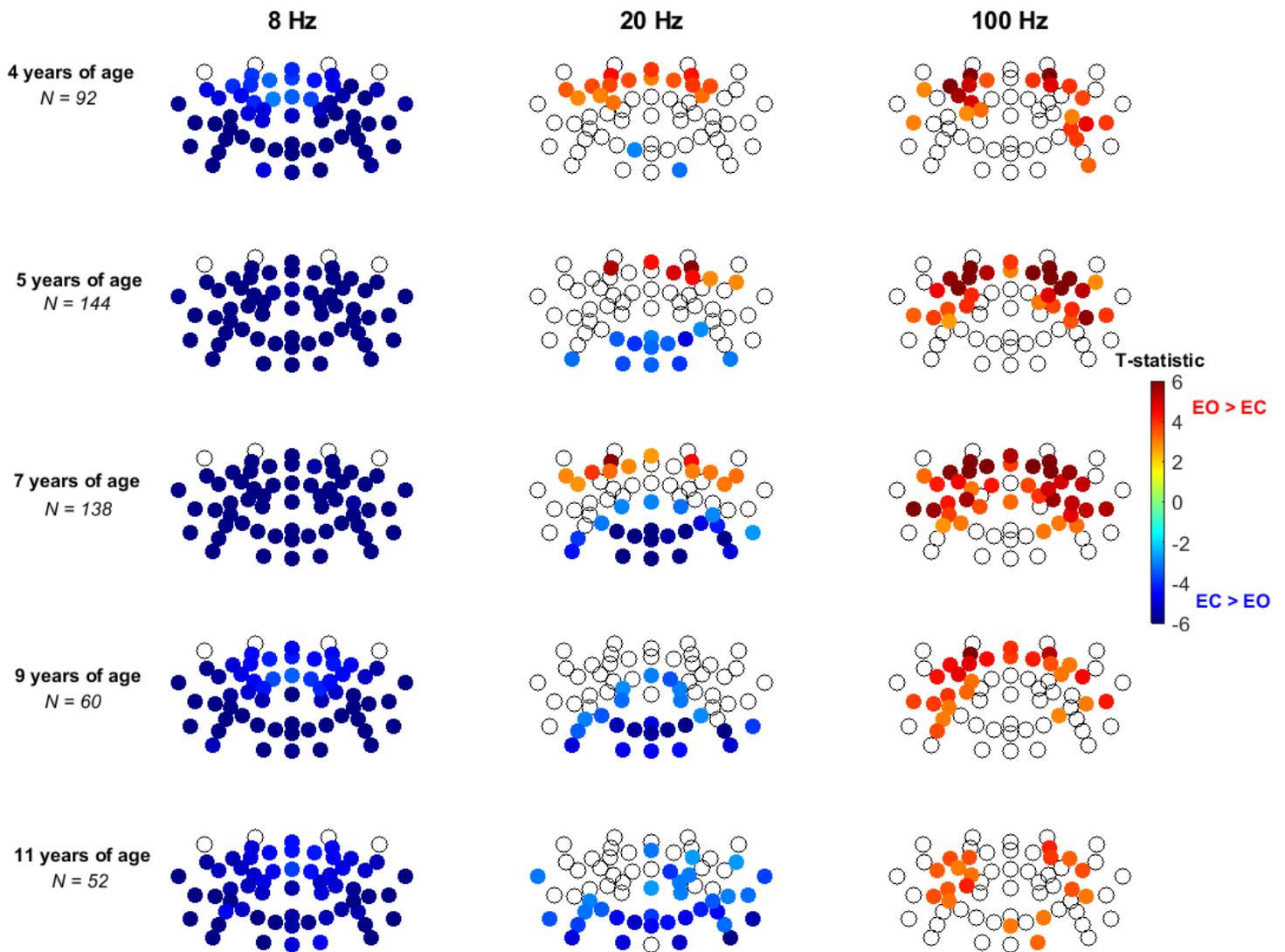


Figure 3

Spatial dependence of EO - EC spectral band differences, colored according to the associated T-statistic (transparent portion of the color bar indicates not significant T-statistic values) at each electrode location for 3 Hz wide bands. Electrodes are colored if associated with a statistically significant difference after performing a 10% false discovery rate (FDR) correction.

Supplementary Files

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