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# Eye closure causes widespread low-frequency power increase and focal gamma attenuation in the human electrocorticogram

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HIGHLIGHTS

- Eye closure is known to have dramatic effects on the EEG, particularly in the $\alpha$ (8–12 Hz) band; to elucidate its effect on the brain, we recorded electrocorticograms (ECoG) from epilepsy patients undergoing invasive monitoring while they sequentially closed and opened their eyes.
- In addition to finding the expected increase in $\alpha$-range power over occipital cortex, we found that eye closure causes an anatomically widespread power increase for a broad range of low frequencies (2–30 Hz).
- At high frequencies eye closure causes an anatomically focal power decrease over occipital cortex and Brodmann areas 8 and 9.

ABSTRACT

*Objective:* We sought to characterize the effects of eye closure on EEG power using electrocorticography (ECoG). Specifically, we sought to elucidate the anatomical areas demonstrating an eye closure effect, and at which frequencies this effect occurs.
*Methods:* ECoG was recorded from 32 patients undergoing invasive monitoring for seizure focus localization. Patients were instructed to close and open their eyes repeatedly. ECoG power was compared in the epochs following eye closure and opening, for various frequency bands and brain regions.
*Results:* We found that at low frequencies, eye closure causes widespread power increases involving all lobes of the brain. This effect was significant not only in the $\alpha$ (8–12 Hz) band but in the $\delta$ (2–4 Hz), $\theta$ (4–8 Hz), and $\beta$ (15–30 Hz) bands as well. At high frequencies, eye closure causes comparatively focal power decreases over occipital cortex and frontal Brodmann areas 8 and 9.
*Conclusions:* Eye closure (1) affects a broad range of frequencies outside the $\alpha$ band and (2) involves a distributed network of neural activity in anatomical areas outside visual cortex.
*Significance:* This study constitutes the first large-scale, systematic application of ECoG to study eye closure, which is shown to influence a broad range of frequencies and brain regions.


## 1. Introduction

Eye closure is the single most effective behavioral modulator of the human electroencephalogram (EEG), an effect as old as EEG itself (Berger, 1929). This effect is qualitatively described by a transition from low-amplitude, non-rhythmic electrical activity

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to high-amplitude, oscillatory activity during the period of eye closure. The early, now classic, investigations describing this effect identified the frequency band of the oscillatory component during eye closure as the "alpha" wave (Berger, 1929); these studies isolated the effect specifically to visual stimulation (Adrian and Matthews, 1934) and also provided evidence that $\alpha$ oscillations originated in the occipital lobes (Adrian and Yamagiwa, 1935). Additional studies confirmed this effect and provided evidence on its ubiquity and reliability (Jasper, 1936; Smith, 1938; Jasper and Andrews, 1938).

The studies that followed up on these basic findings can be divided into two lines of research: those recording non-invasively from human participants and those recording invasively from animal models. In the first, the principal questions were whether the eyes-closed condition modulated (1) spectral activity outside of the $\alpha$ band and (2) regional activations outside of visual cortex. Using scalp EEG, it was indeed found that activity outside of the $\alpha$ band, namely in the $\delta$, $\theta$, and $\beta$ bands, was also modulated by the eyes-closed condition (Chapman et al., 1962; Glass and Kwiatkowski, 1970; Härdle et al., 1984). In addition, the temporal and parietal lobes displayed eyes-closed related activity, albeit at different resonant frequencies than the visual cortical $\alpha$ modulation (Mundy-Castle, 1957; Volavka et al., 1967; Legewie et al., 1969). Despite these advances, however, this line of research was severely limited by the poor spectral and spatial resolution of scalp EEG. For example, it was not possible in the early scalp recordings to relate $\gamma$ activity to the eyes-open condition, despite the fact that $\gamma$ activity has been explicitly related to visual processing (Jensen et al., 2007). As a result of these technical limitations, modern research has focused on the higher-level cognitive correlates of $\alpha$ activity (Mantini et al., 2007; Klimesch et al., 1996; VanRullen et al., 2005; Busch et al., 2009; Jensen et al., 2012). As a result, many basic electrophysiological properties of eye closure in humans remain unknown.

The second line of research responded to the inherent limitations of using scalp studies to investigate visual cortical $\alpha$-activity. To overcome these limitations, these studies investigated the $\alpha$ rhythm using invasive electrophysiology in animal models, opening the skull to obtain direct recordings from neural tissue (reviewed in Lopes da Silva, 1991). Using this approach, early studies suggested that the $\alpha$ rhythm emerged from sub-cortical structures, namely the lateral geniculate nucleus, the pulvinar and the reticular activating system (Andersen and Andersen, 1968). However, it was soon appreciated that cortical generators uniquely contributed to the $\alpha$ effect (Lopes da Silva et al., 1973; Lopes da Silva and van Leeuwen, 1977; Bollimunta et al., 2008; Bollimunta et al., 2011). Despite the advances from this line of research, it remains a challenge to apply these findings directly to the human brain. In particular, recordings in animal models are usually performed using micro-electrodes confined to highly specific regions of the thalamus and visual cortex. Therefore, the question of precisely which anatomical regions (outside of the visual cortex) respond to eye closure has largely been unexplored.

To overcome the challenges of each of these lines of research, it is necessary to record invasively electrophysiological activity directly from the human brain as participants close and open their eyes. Such recordings can be ethically obtained from neurosurgical patients undergoing invasive monitoring for seizure localization in the setting of pharmacologically-refractory epilepsy. Indeed, intracranial EEG, or electrocorticography (ECoG), has been used to elucidate the neural activity of a variety of motor, sensory, and cognitive phenomena (Jacobs and Kahana, 2010; Lachaux et al., 2012), but has yet to be systematically applied to the most basic of all electrophysiological behavioral effects: human eye closure. By recording directly from the surface of the brain, much like the animal models described above, ECoG can localize cortical eye closure effects with maximal anatomical precision. In addition, ECoG has the potential to record high-frequency activity ($\gamma$) in the absence of muscular artifact that occurs at the scalp (Yuval-Greenberg et al., 2008).

In this study, we examined the effect of eye closure on ECoG power during a simple eye closure/eye opening task. In it, we sought to examine both the spatial distribution of cortical responses to eye closure and opening, as well as which frequencies participated in the response.

## 2. Materials and methods

### 2.1. Participants

32 patients (13 female, 4 left-handed; Table 1) with pharmacologically-refractory epilepsy underwent a surgical procedure in which electrodes were implanted subdurally on the cortical surface; many of these patients received implants deep within the brain parenchyma as well. In each case, the clinical team determined the placement of the electrodes so as to best localize epileptic foci. Data were collected at the Hospital of the University of Pennsylvania (Philadelphia, PA) and Thomas Jefferson University Hospital (Philadelphia, PA). Our research protocol was approved by the institutional review board at both hospitals and informed consent was obtained from the participants and their guardians.

### 2.2. Behavioral task

Each patient participated in a suite of oculomotor tasks lasting, in total, 5–10 min (Fig. 1A, top panel). These tasks engaged the facial and extraocular muscles as well as the systems subserving saccades and smooth pursuit. The first and last elements in this suite were an alternating series of instructions for the patient to close and open his or her eyes. In the current paper, we have analyzed data only from these two elements, hereafter referred to as the eye-closure task. In the eye-closure task, asterisks are drawn on the screen at the 12, 3, 6 and 9 o'clock positions, and the pre-recorded words "close" and "open" are played in sequence 5 times (Fig. 1A, bottom-panel). The duration of the "close" and "open" clips are approximately 1480 and 1400 ms, respectively. Each word is followed by a delay interval of 5000 ms + uniformly-distributed jitter drawn from the interval $[0, 300]$ ms.

### 2.3. ECoG recordings

Data from our 32 patient database were collected over a 6-year period in collaboration with 2 different hospitals. Whereas each hospital used the same general implantation procedures and data-acquisition techniques, our analysis had to account for technical details that varied by institution. Electrocorticography (ECoG) data were recorded using a Nicolet, Grass Telefactor, or Nihon-Khoden EEG system. Depending on the amplifier and the discretion of the clinical team, the signals were sampled at 400, 500, 512, 1000, or 2000 Hz. Signals were referenced to a common electrode placed either intracranially or on the scalp or mastoid process. All recorded traces were re-sampled at 256 Hz, and a fourth order 2-Hz stop-band Butterworth notch filter was applied at 60 Hz to eliminate electrical line noise. The experimental laptop sent ±5 V analog pulses, via an optical isolator, into a pair of open lines on the clinical recording system to synchronize the electrophysiological recordings with behavioral events.

We collected electrophysiological data from a total of 3333 subdural and depth electrodes (1614 left-hemispheric; 1719 right hemispheric). Subdural electrodes were arranged in both grid and