NeuroImage 183 (2018) 897–906

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

The frequency of alpha oscillations: Task-dependent modulation and its functional significance

Immanuel Babu Henry Samuel, Chao Wang, Zhenhong Hu, Mingzhou Ding *

J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, USA

ARTICLE INFO

Keywords:
Alpha oscillation
Alpha frequency
Alpha power
Working memory
Alpha modulation
Alpha source
Simultaneous EEG-fMRI

ABSTRACT

Power (amplitude) and frequency are two important characteristics of EEG alpha oscillations (8–12 Hz). There is an extensive literature showing that alpha power can be modulated in a goal-oriented manner to either enhance or suppress sensory information processing. Only a few studies to date have examined the task-dependent modulation of alpha frequency. Instead, alpha frequency is often viewed as a trait variable, and used to characterize individual differences in cognitive functioning. We performed two experiments to examine the task-dependent modulation of alpha frequency and its functional significance. In the first experiment, high-density EEG was recorded from 21 participants performing a Sternberg working memory task. The results showed that: (1) during memory encoding, alpha frequency decreased with increasing memory load, whereas during memory retention and retrieval, alpha frequency increased with increasing memory load, (2) higher alpha frequency prior to the onset of probe was associated with longer reaction time, and (3) higher alpha frequency prior to the onset of cue or probe was associated with weaker early cue-evoked or probe-evoked neural responses. In the second experiment, simultaneous EEG-fMRI was recorded from 59 participants during resting state. An EEG-informed fMRI analysis revealed that the spontaneous fluctuations of alpha frequency, but not alpha power, were inversely associated with BOLD activity in the visual cortex. Taken together, these findings suggest that alpha frequency is task-dependent, may serve as an indicator of cortical excitability, and along with alpha power, provides more comprehensive indexing of sensory gating.

1. Introduction

EEG alpha rhythm (8–12 Hz) is prominent over occipital-parietal cortices in humans during restful wakefulness. Like any oscillatory activity, alpha can be characterized by its amplitude (power) and frequency. Since its initial discovery by Berger (1929), extensive evidence has accumulated to suggest that alpha oscillations are involved in cognitive processing, including attention and working memory (Fink et al., 2005; Jensen et al., 2002; Jensen and Tesche, 2002; Klimesch et al., 1997). In particular, alpha power is considered a reliable indicator of cortical excitability (Jensen and Mazaheri, 2010; Lange et al., 2013) and can be modulated by higher-order brain areas to functionally inhibit or facilitate sensory information processing according to behavioral goals (Liu et al., 2014; Mulholland, 1968; Rajagovindan and Ding, 2011; Wang et al., 2016).

Alpha frequency, in contrast, has been viewed mainly as a trait variable. Individual differences in alpha frequency have been linked to differences in cognitive capabilities (Anokhin and Vogel, 1996; Grandy et al., 2013). An existing theory postulates that alpha frequency is a manifestation of an internal brain clock controlling the speed of information processing (Klimesch et al., 1996); the faster the internal clock (higher individual alpha frequency), the faster the information and cognitive processing (e.g., in memory retrieval and cognitive control). In addition, alpha frequency is known to change systematically over the lifespan (Bernhard and Skoglund, 1939), and is subject to the impact of neurological disorders (Bonanni et al., 2008). Perceptually, individual differences in alpha peak frequency has been shown to predict the temporal windows of the double-flash illusion, suggesting that the peak alpha frequency is the "fingerprint" that drives cross-modal impact on visual perception (Cecere et al., 2015). Similarly, the phasic differences of alpha rhythm has been shown to impact visual perception of rapid sequential stimuli (Minami and Amano, 2017; Valera et al., 1981).

To what extent alpha frequency can be modulated in a task-dependent manner? If such modulation occurs, what is the associated functional significance? These questions have yet to be fully addressed. Two earlier studies by Osaka and by Earle reported inconclusive findings. Osaka

---

* Corresponding author.
E-mail address: mding@bme.ufl.edu (M. Ding).

https://doi.org/10.1016/j.neuroimage.2018.08.063
Received 19 January 2018; Received in revised form 17 August 2018; Accepted 25 August 2018

showed that alpha frequency increased with task difficulty (Osaka, 1984), but Earle reported that while in some tasks alpha frequency increased when task difficulty increased, in other tasks, the opposite was observed (Earle, 1988). Haegens et al., using an n-back working memory task, found that alpha frequency increased with task difficulty, i.e., higher working memory load was accompanied by higher alpha frequency (Haegens et al., 2014). A more recent study reported that alpha frequency changes according to the types of visual perception such as temporal stimulus integration and temporal stimulus segregation (Wutz et al., 2018). Despite these advances, many questions remain; in particular, the functional and behavioral relevance of alpha frequency modulation by task conditions remains to be further elucidated. Some of the tasks used in previous studies have temporally overlapping cognitive processes. For example, in the n-back task used by Haegens et al. (2014), cognitive processes such as sensory encoding, memory retention and memory retrieval are difficult to separate temporally, and each process may have a differential effect on alpha frequency (Jensen et al., 2002).

Alpha frequency modulation may also be considered in the context of how alpha interacts with other neural processes, such as theta oscillations (Sauseng et al., 2005; Scheeringa et al., 2009), beta oscillations (Yuan et al., 2010), and gamma oscillations (Voytek et al., 2010). In particular, in light of the proposal that gamma cycles are embedded within alpha (Osipova et al., 2008; Roux and Uhlhaas, 2014), alpha frequency modulation may become a means to flexibly increase and decrease the number of gamma cycles accommodated within a cycle of alpha to either facilitate or inhibit sensory processing.

In this study, we considered task-dependent modulation of alpha frequency, its functional significance, and the underlying neural correlates by conducting two experiments. In the first experiment, high-density EEG (128 channels) was recorded from 21 subjects performing a Sternberg working memory task. In this task, memory related cognitive processes such as encoding, retention and retrieval are well separated in time, making it well-suited for analyzing modulations of alpha frequency by distinct cognitive processes. Alpha frequency was estimated during different stages of the task and compared across memory loads. Functional significance was further assessed by correlating the modulations of alpha frequency with behavioral performance and other neural variables such as event-related brain responses. In the second experiment, we examined the neural sources underlying the modulation of scalp level alpha variables, namely, alpha power and alpha frequency. Simultaneous EEG-fMRI was recorded from a cohort of 59 subjects at rest. Utilizing the naturally occurring fluctuations of alpha frequency and alpha power, we examined the possible neural underpinnings of alpha frequency modulation and alpha power modulation by correlating them with the simultaneously recorded fMRI BOLD (Blood Oxygen Level Dependence) fluctuations from different regions of the visual cortex as well as the entire brain.

2. Materials and methods

2.1. Experiment 1

2.1.1. Procedure and paradigm

The experimental protocol was approved by the Institutional Review Board of the University of Florida (UF IRB). Twenty-one healthy individuals (age: 20 to 34; 3 women) with normal or corrected-to-normal vision gave written informed consent and participated in the study. On each trial of the working memory task, a digit set (cue set) of 1, 3 or 5 distinct numerical digits (0–9) was displayed for 1s (encoding). This was followed by a 3s period during which the subjects held the cue set in working memory while fixating on a cross on the computer screen (retention). At the end of the retention period, a probe digit was

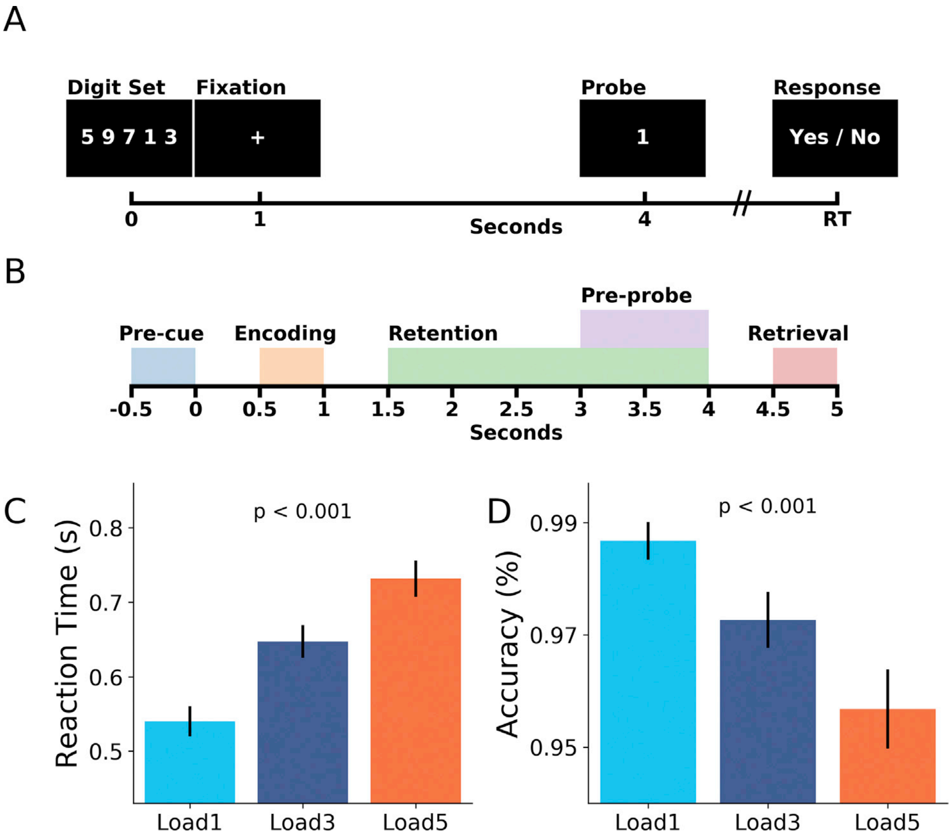

Fig. 1. Paradigm and behavioral results. (A) Schematic illustration of the working memory task. Depicted is a trial where the memory load is 5 and a yes answer is the correct response. (B) Definition of time periods of analysis for pre-cue, encoding, retention, pre-probe, and retrieval. (C) Reaction time. (D) Accuracy. (The p-values in C and D were obtained from a mixed-effects linear model fit on the behavioral data.)

presented, and the subject was instructed to indicate whether it belonged to the cue set with a button-press response (retrieval). The inter-trial-interval between the button-press and the onset of the next cue set was 2s. Schematically illustrated in Fig. 1A is a trial with a cue set containing 5 digits (memory load 5) and the correct response is 'yes' since the probe digit is present in the cue set.

2.1.2. Data acquisition and preprocessing

High-density EEG was acquired using a 128-channel BioSemi System. The data was band-pass filtered between 0.3Hz and 40Hz, down-sampled to 200 Hz, average referenced, projected to the standard 81-channel montage using BESA 6.0, and epoched from −0.5s to 5s. Here 0s denoted the onset of the cue set, 1s the cue offset, and 4s the probe onset. Noisy epochs were rejected. Independent Component Analysis (ICA) implemented in EEGLAB was further applied to the EEG data and the components containing eye-blink artifacts and electrode noise were removed (Delorme and Makeig, 2004).

For analysis, the encoding period is defined as the time interval between 0.5s and 1s, the retention period between 1.5s and 4s, and the retrieval period between 4.5s and 5s (Fig. 1B). In these definitions, the 0.5s time interval immediately following stimulus onset and offset was removed from analysis, to avoid the influence of the trial-to-trial variability of evoked response on spectral estimations (Wang et al., 2008; Wang and Ding, 2011). ERPs were also removed before calculation of any spectral measures to reduce spectral contributions from evoked responses. To investigate the impact of alpha frequency preceding probe onset on neural activity evoked by probe processing, a fourth time period of 3s–4s, which was the interval immediately preceding the onset of the probe stimulus, was defined as the pre-probe time period. To investigate the impact of alpha frequency preceding cue onset on cue-evoked neural response, a fifth time period, the pre-cue period, was further defined to be −0.5s to 0s. These pre-stimulus periods were defined in such a way that neural activities in these periods were expected to have an impact on the early stimulus-evoked neural responses.

2.1.3. Estimation and analysis of alpha power and alpha frequency

The channels of interest were occipital and parietal-occipital channels, including PO9, PO7, PO3, POz, PO4, PO8, PO10, O1, Oz, O2, O9, O10, and Iz. For a given time period of analysis (Fig. 1B), a Fourier-based periodogram method ("scipy.signal.periodogram," n. d.) was applied to the data of each channel to estimate the power spectra. The power spectra were normalized by dividing average baseline alpha power (pre-cue period) and then averaged across channels. To maintain consistency in the spectral resolution across different functional states, for each of the five time periods defined above that were longer than 0.5s, the time period was divided into 0.5s windows with 50% overlap and the spectrum was estimated for each window after detrending and zero-padding to the length of nfft = 1000 and averaged across windows. Alpha frequency was calculated according to (Klimesch et al., 1993):

$$\text{Alpha Frequency} = \frac{\sum_{f=8}^{12} (Power(f) \times f)}{\sum_{f=8}^{12} Power(f)}$$

Alpha frequency, along with alpha power in the 8–12 Hz band, were compared across memory loads for each of the three cognitive states: encoding, retention and retrieval. A mixed-effects model was used to test for significant effects of memory load, in which alpha frequency or alpha power was taken as the dependent variable, with subjects as the random factor. To test whether alpha power modulation by memory load and alpha frequency modulation by memory load were related, the alpha variables were plotted against the memory load, and the slope of the linear least squares fit was taken as the load modulation index of that alpha variable. The load modulation indices of alpha power and alpha frequency were then correlated to determine their relationship.

2.1.4. Assessment of functional significance of alpha frequency modulation

As a first step to assess the functional significance of alpha frequency modulation we utilized the naturally occurring variability in behavioral performance to sort trials. Since the accuracy was over 95%, there were too few error trials to perform a convincing accuracy-related analysis, and consequently, reaction time (RT) was chosen as the behavioral measure for our analysis. For an individual subject, according to z-scored reaction time (RT), within each memory load, trials were divided into a fast RT group ($z < 0$) and slow RT group ($z > 0$). During the retention and retrieval time periods, alpha frequencies of the fast RT trials were averaged across memory load and compared to that of the slow RT trials averaged across memory load. To verify the findings, a full statistical model with alpha power, alpha frequency and memory load as the independent variables and reaction time as the dependent variable was also implemented.

We next examined the impact of pre-probe (3s–4s) alpha frequency on early probe-evoked neural responses quantified by global field power (GFP) (Lehmann and Skrandies, 1980; Murray et al., 2008). GFP at a given instant of time is defined as the standard deviation of EEG data across all scalp channels and is commonly used to measure the strength of stimulus processing. For probe processing, since the ERP component P1 is the early neural response evoked by the probe stimulus, we set the time period of interest (TOI) to be between 80 ms and 120 ms relative to probe onset, which approximates the onset and offset of the probe-evoked P1 component. Similar to RT, the trials were grouped based on z-scored single-trial GFP during the TOI, into a high response group ($z > 0$) and a low response group ($z < 0$) for each memory load. The pre-probe alpha frequency from high response trials averaged across memory load and that from low response trials averaged across memory load were compared. Given that differences in early visual sensory processing can give rise to differences in late higher-order processing (Wiens et al., 2011), we further examined the relation between alpha frequency during the retrieval period and the early probe-evoked response defined above. The same analysis was also done for the pre-cue period to test the effect of pre-cue alpha frequency on the early cue-evoked neural responses (80 ms–120 ms relative to cue-onset) and how alpha frequency during the encoding period relates to early cue-evoked responses. Similar to the analysis on alpha frequency and reaction time, a full statistical model with alpha power, alpha frequency and load as the independent variables and early stimulus-evoked neural response as the dependent variable was also implemented to further examine the relation between alpha frequency before and after a stimulus (cue or probe) and stimulus-evoked response.

2.2. Experiment 2

2.2.1. EEG acquisition and preprocessing

Much like alpha power, even at rest, alpha frequency is expected to fluctuate naturally. To shed further light on the functional significance of alpha frequency modulation, we collected simultaneous EEG-fMRI data from a different cohort of 59 subjects (age: 17 to 31; 20 women) in an eyes-closed resting state condition, and performed EEG-informed fMRI analysis. Written informed consent approved by UF IRB was obtained from these participants before recording. For EEG data acquisition, a 32-channel MRI-compatible EEG system was used (Brain Products, Germany). Thirty one sintered Ag/AgCl electrodes were applied in the standard 10–20 montage. One additional electrode was placed on the subject's upper back to record electrocardiogram (ECG) which was needed for removing scanner artifacts. Impedance from the thirty one scalp channels were kept low (<10kOhms) for optimal signal to noise ratio. The EEG data was sampled at 5 kHz, digitized to 16 bit and transferred to a recording computer through an optic fiber cable. The EEG data acquisition system and the scanner's internal clock were synchronized to ensure successful removal of gradient artifacts during preprocessing.

EEG data was preprocessed off-line to remove MR related gradient artifacts and cardio-ballistic artifacts using Brain Vision Analyzer 2.0. To remove gradient artifact, a template of the artifact generated using a sliding window across 41 consecutive TRs was subtracted from the raw data. To remove the cardio-ballistic artifact, an average artifact template was generated for every 21 consecutive heart beat event identified by R peaks and subtracted from the data. The data was then down-sampled to 250 Hz, average referenced, and epoched into 1 TR (1.98s) time segments relative to scan onset pulse obtained from the MR scanner. Since the data was recorded in an eyes-closed resting state, eye-blink related ICA correction was not performed.

2.2.2. *FMRI acquisition and preprocessing*

Functional MRI scans were recorded on a 3-T Phillips Achieva whole-body MRI system (Phillips Medical Systems). T2* weighted echo planar imaging (EPI) sequence was used to obtain 212 functional volumes (session duration ~ 7mins) with echo time (TE) = 30 ms, repetition time (TR) = 1980 ms and flip angle = 80°. Each functional volume consisted of 36 axial slices (field of view: 224 mm, matrix size: 64 × 64; slice thickness: 3.5 mm; voxel size: 3.5 mm × 3.5 mm x 3.5 mm). The preprocessing for fMRI data was carried out within SPM which included slice timing, realignment to mean image, normalization to the MNI template and re-sampling to voxel size of 3 mm × 3 mm x 3 mm. Normalized volumes were spatially smoothed using 8 mm FWHM (Full Width at Half Maximum) Gaussian kernel.

2.2.3. *EEG-informed fMRI analysis*

Alpha power and alpha frequency was obtained for each epoch of 1 TR in duration, and averaged across the occipital and parietal-occipital channels of interest, including POz, O1, O2, and Oz. To quantify the intrinsic alpha frequency variations within subjects, the mean, minimum and maximum alpha frequency was obtained for each subject; population means and standard deviations were calculated. Alpha power and alpha frequency time series with a sampling rate of 1 TR was convolved with the hemodynamic response function (HRF). A GLM analysis was applied at the single subject level to examine the relationship between alpha power/frequency and BOLD time series from multiple visual cortical regions, including V1d, V1v, V2d, V2v, V3d, V3v, V4 and IPS, defined by a recently published visuo-topic atlas (Wang, Mruczek, Arcaro and Kastner, 2015). Second level statistical tests were done on the correlation maps obtained from the single subject analysis. Specifically, the mean of the correlation map within the ROIs were obtained for each subject and a *t*-test was done to obtain group level significance for each ROI. Because there are multiple visual regions within the atlas, we applied the false discovery rate (FDR) method to cope with the resulting multiple comparison problem (Genovese et al., 2002). In the GLM model, 6 motion regressors were included to remove the effects of head movement during the scan and a constant regressor was added to remove the temporal mean. For the exploratory whole brain analysis, the correlation maps for single subject analysis were taken over the whole brain and a voxel-wise second-level *t*-test followed by cluster enhancement (FSL-TFCE) was done to identify group-level associations between BOLD fluctuations and alpha power/frequency fluctuations.

3. Results

3.1. *Experiment 1*

3.1.1. *Behavioral results*

Behavioral measures were analyzed using a mixed-effects linear model with performance metrics as the dependent variable, memory load (1, 3 and 5) as the independent variable, and subjects as the random effects. As shown in Fig. 1C and D, reaction time was significantly slower for higher memory load ($p < 0.001$), whereas accuracy was significantly lower for higher memory load ($p < 0.001$), in agreement with previous studies of the same paradigm (Jensen and Lisman, 1998; Sternberg, 1969).

3.1.2. *Alpha power and frequency modulation by working memory load*

Power spectra for the three memory loads during encoding were shown in Fig. 2A. A mixed-effects linear model showed that both alpha frequency (Fig. 2B) and alpha power (Fig. 2C) decreased with increasing memory load ($p < 0.001$). To test whether alpha power modulation and alpha frequency modulation by memory load are related, a modulation index as described in the methods section (2.1.3) was defined for each alpha variable at the individual subject level. As shown in Fig. 2D, the lack of correlation ($r = 0.168$, $p = 0.468$) between alpha power modulation index and alpha frequency modulation index suggests that the two alpha characteristics were modulated independently by memory load. For retention, both alpha power and alpha frequency increased with memory load (Fig. 2F and G, $p < 0.001$ and $p = 0.002$, respectively), and their modulation indices at individual subject level were again uncorrelated (Fig. 2F, $r = -0.187$, $p = 0.417$). For retrieval, as shown in Fig. 2J and K, whereas alpha frequency increased with increase in memory load ($p < 0.001$), there was no load dependent alpha power modulation ($p = 0.116$). As with encoding and retention, during retrieval, there was no relation between alpha frequency modulation and alpha power modulation (Fig. 2L, $r = 0.156$, $p = 0.5$).

3.1.3. *Effect of alpha frequency modulation on behavioral performance*

We tested the impact of alpha frequency modulation during retention on reaction time. Trials were divided into fast RT trials and slow RT trials for each memory load. Power spectra were estimated for each RT group, averaged across loads, and shown in Fig. 3A. The slow RT trials were associated with a significantly higher ($p = 0.012$) alpha frequency than the fast RT trials, as shown in Fig. 3B, suggesting that higher alpha frequency during retention may impede probe processing and lead to increased reaction time. Alpha frequency during retrieval and RT, in contrast, were not associated ($p = 0.962$), as shown in Fig. 3C and D. A full statistical model on the effects of alpha frequency on behavioral performance in which alpha power and memory load were also co-variates showed similar effects, namely, the higher the retention period alpha frequency the longer the reaction time. These results were included in the supplementary material (Supplementary Table S1-S2).

3.1.4. *Effect of alpha frequency modulation on stimulus-evoked neural responses*

The functional role of alpha frequency modulation was further tested by examining the impact of pre-stimulus alpha frequency on stimulus-evoked responses. For probe-evoked responses, the Global Field Power (GFP) during 80 ms–120 ms after probe-onset was calculated for each trial, and grouped into low response trials (see Fig. 3E for probe-evoked ERP for low response group) and high response trials (see Fig. 3F for probe-evoked ERP for high response group) within each memory load and averaged across memory load. The pre-probe alpha frequency of low response trials was significantly higher than that of high response trials ($p = 0.001$; Fig. 3G). Similar results were found for cue-evoked response where the pre-cue alpha frequency of low cue-evoked response trials was significantly higher than that of high cue-evoked response trials ($p = 0.047$; Fig. 3G). These findings give support to the idea that high alpha frequency prior to stimulus onset impedes sensory processing of the stimulus. During post-stimulus periods, the low response trials had a higher alpha frequency compared to the high response trials ($p = 0.009$ for encoding and $p = 0.023$ for retrieval; Fig. 3G). A full statistical model on the effects of alpha frequency on early evoked response in which memory load and alpha power were also co-variates showed similar effects for encoding, pre-probe and retrieval time periods, namely, higher alpha frequency was associated with lower early stimulus-evoked neural response, but for pre-cue, the effect was not statistically significant. These results were included in the supplementary material (Supplementary Table S3-S6).

3.2. *Experiment 2*

The possible neural substrate underlying alpha frequency modulation

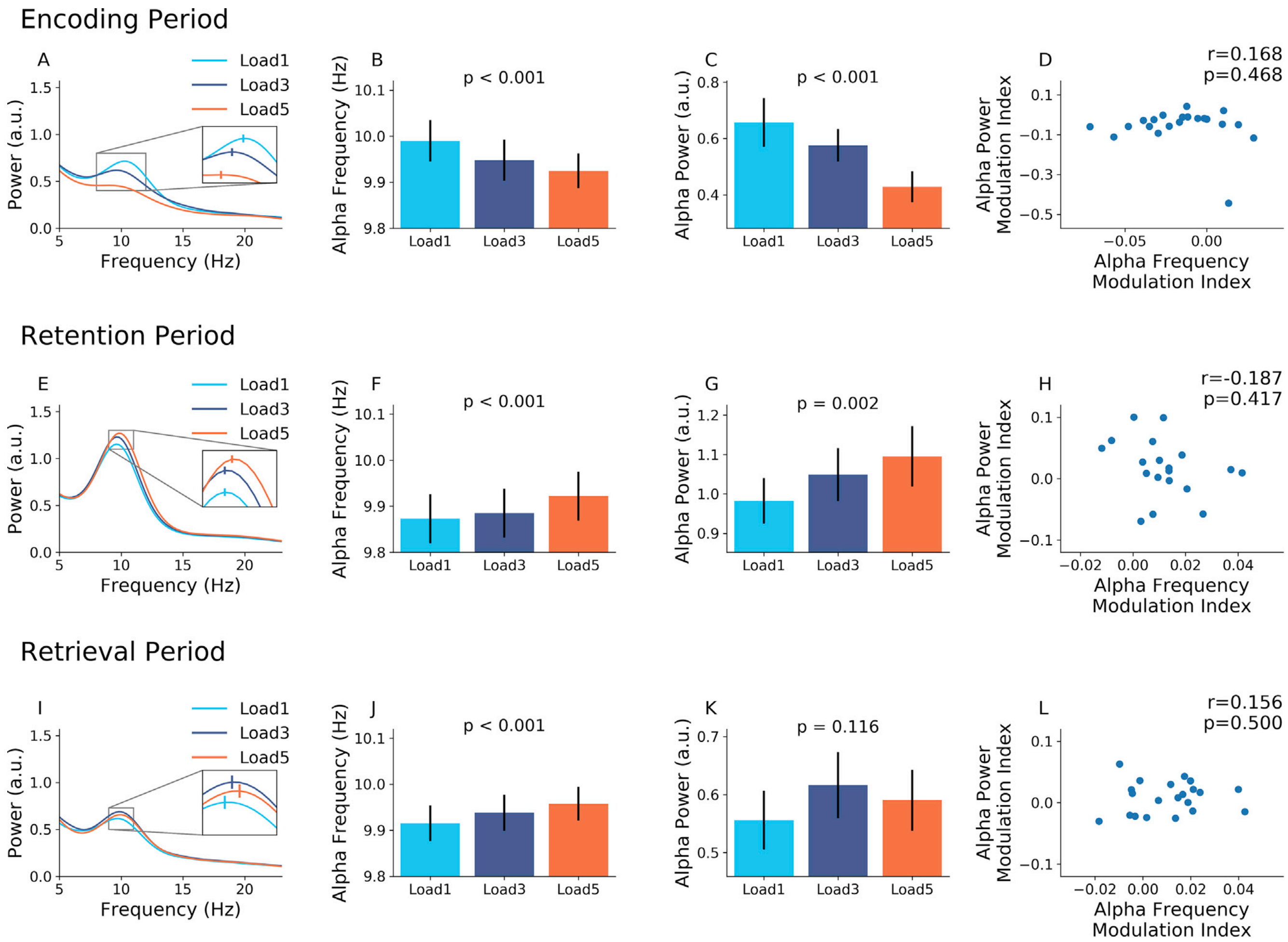

Fig. 2. Memory load modulation of alpha power and alpha frequency during different stages of working memory processing. A–D: encoding. E–H: retention. I-L retrieval. (The p-values in B, C, F, G, J and K are obtained from the mixed-effects linear model fit on the alpha power and alpha frequency.)

was investigated by recording simultaneous resting-state EEG and fMRI from 59 healthy subjects. For this cohort, the mean alpha frequency was 9.976 ± 0.233Hz, the minimum alpha frequency was 9.208 ± 0.249 Hz and the maximum alpha frequency was 10.713 ± 0.222 Hz. For 56 out of 59 subjects, alpha frequency fluctuations were normally distributed, according to the Shapiro test (Shapiro and Wilk, 1965). The alpha power and alpha frequency time series sampled at the resolution of 1 TR were then convolved with a hemodynamic response function (HRF) and used in a generalized linear-regression Model (GLM) with both alpha power and alpha frequency as regressors to identify voxels in the brain whose BOLD activity co-varies with the alpha variables. Fig. 4A shows temporal variation in alpha frequency for a representative subject, and 4B shows the HRF convolved alpha frequency time series and the BOLD time series from a visual voxel. Defining visual cortical regions according to a recently published visuo-topic atlas in Fig. 4C (Wang et al., 2015), the GLM analysis revealed that alpha power was not correlated with BOLD activities in the visual ROIs (Fig. 4D), whereas the alpha frequency was inversely correlated with BOLD activity in V2d, V2v, V3d, V3v, V4 and IPS ROIs (Fig. 4E), indicating that higher alpha frequency was associated with lower BOLD activity in these visual areas ($p < 0.05$ controlling for multiple comparisons with false discovery rate).

Association between alpha variable fluctuation and BOLD activity from the whole brain was examined in an exploratory analysis. As shown Fig. 5A, alpha frequency was positively associated with BOLD activity in posterior cingulate cortex (PCC), lateral parietal cortex (lateral PC), and anterior cingulate cortex (ACC), and negatively associated with visual and sensorimotor areas. In Fig. 5B, alpha power was seen to be negatively associated with BOLD activity in the lateral frontal cortex (lateral FC), cuneus, sensorimotor areas and medial prefrontal cortex (mPFC).

4. Discussion

4.1. Main findings

We performed two experiments to examine the task-dependent modulation of alpha frequency and its functional significance as well as its neural substrate. In the first experiment, the analysis of EEG recorded from healthy subjects performing a Sternberg working memory task shows that: (1) alpha power decreased with memory load during encoding, increased with memory load during retention, and had no systematic relationship with memory load during retrieval, (2) alpha frequency decreased with increasing memory load during encoding, and increased with memory load during both retention and retrieval, (3) alpha power modulation by memory load and alpha frequency modulation by memory load were not correlated, (4) higher alpha frequency during retention was associated with slower reaction time, and (5) higher alpha frequency prior to cue onset and prior to probe onset was associated with smaller cue-evoked and probe-evoked neural responses. In the second experiment, analysis of simultaneous EEG-fMRI recordings from subjects in an eyes-closed resting state condition shows that: (1) alpha frequency fluctuations but not alpha power fluctuations were negatively associated with BOLD activity in the visual cortex and (2) the alpha power and alpha frequency fluctuations were associated with BOLD from different cortical structures. Collectively, these results suggested that (1)

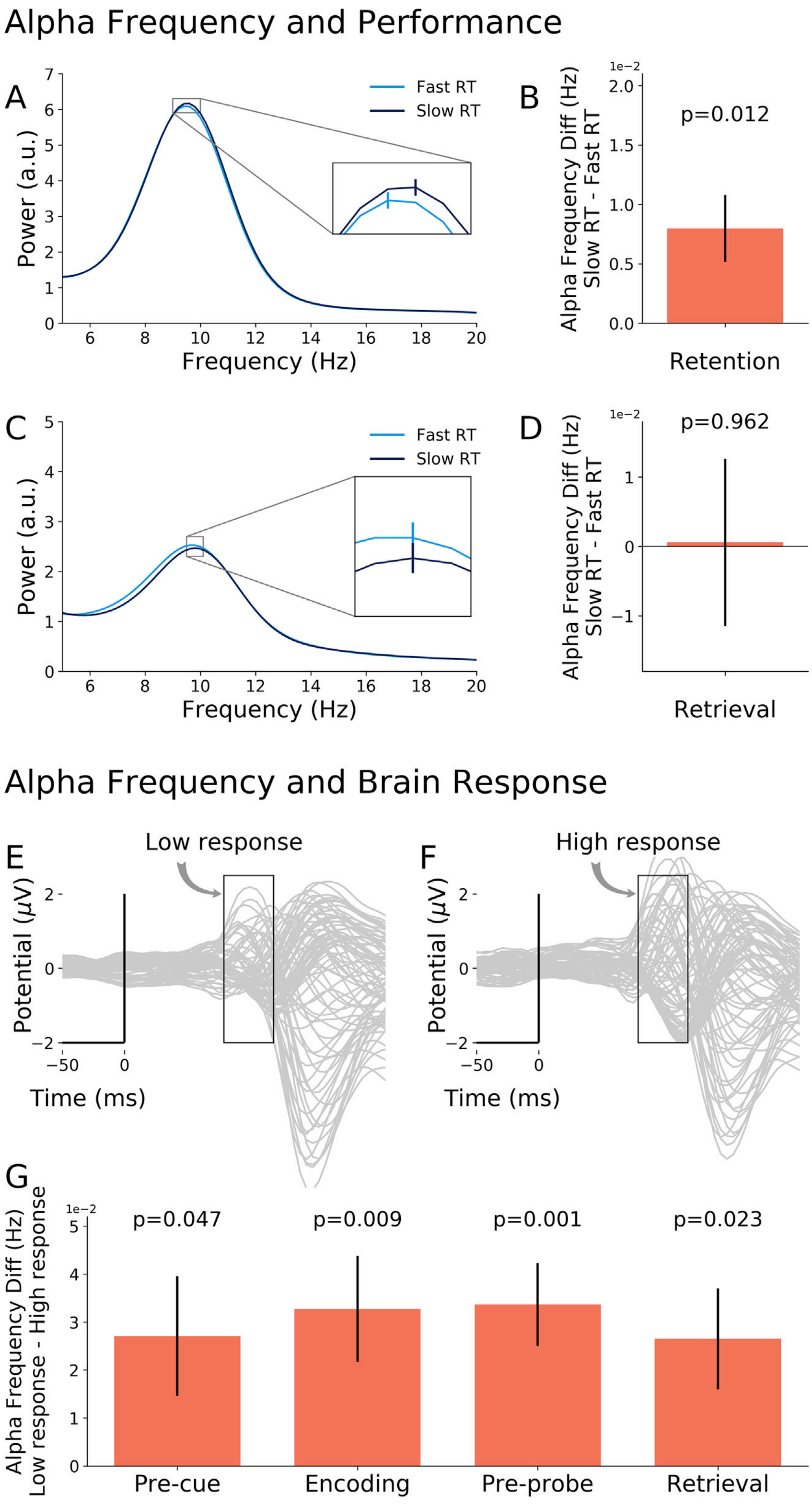

Fig. 3. Functional significance of alpha frequency modulation. Association of alpha frequency with RT during retention and retrieval (A-D): (A) Power spectra of fast RT and slow RT trials during retention time period and (B) alpha frequency difference between fast RT and slow RT trials during retention time period; (C) power spectra of fast RT and slow RT trials during retrieval and (D) alpha frequency difference between fast RT and slow RT trials during retrieval. Relation between alpha frequency and early stimulus-evoked responses (E-G): (E) and (F) Probe-evoked ERPs of low response trials and high response trials; (G) alpha frequency difference between high response trials and low response trials during pre-cue, encoding, pre-probe and retrieval period. Note: For pre-cue and encoding, the cue-evoked responses were considered.

alpha frequency was task-dependent and modulated by memory load in distinct fashions in different stages of the working memory task, (2) alpha frequency were inversely related to visual cortical excitability and could be modulated by higher-order brain networks in a goal-oriented fashion to enhance or suppress sensory processing, (3) alpha frequency and alpha power may be modulated by different brain structures, and (4) alpha frequency, along with alpha power, provides a more comprehensive indexing of task-dependent sensory gating.

4.2. Alpha frequency as a trait variable

Historically, alpha frequency has been mainly studied as a trait variable (Klimesch et al., 1990). Higher individual alpha frequency (IAF) correlates with better memory performance (Angelakis et al., 2004; Clark et al., 2004; Klimesch et al., 1993; Lebedev, 1994; Saletu and Grünberger, 1985), larger vocabulary (Angelakis et al., 2004), faster reaction time (Klimesch et al., 1996), better temporal resolution in visual perception

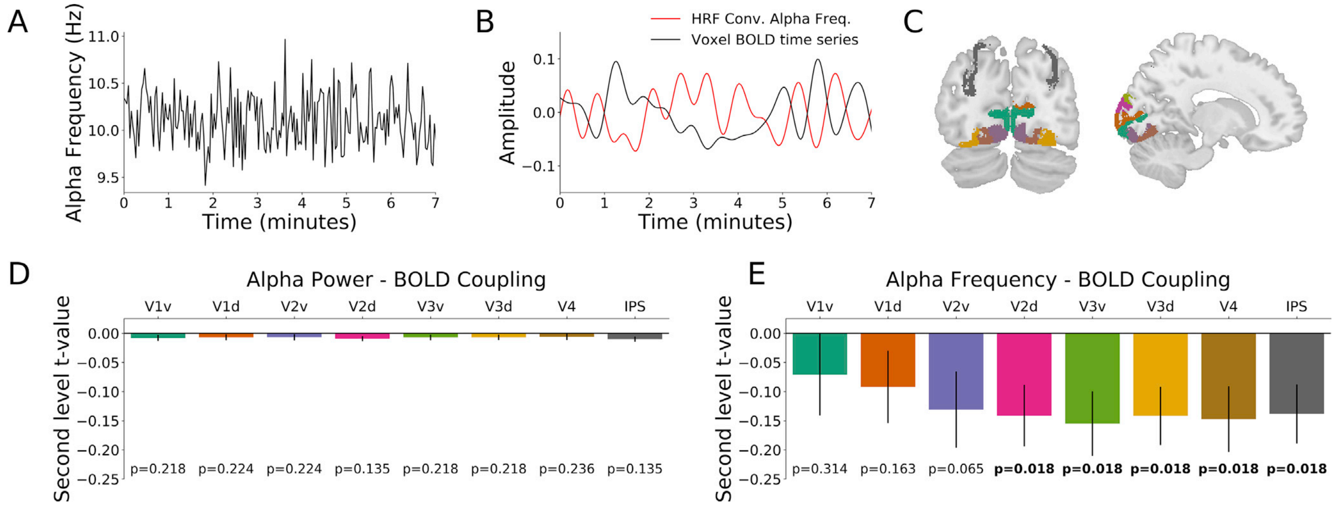

Fig. 4. Alpha variable fluctuations and BOLD activity. (A) Alpha frequency time series for a representative subject during resting state. (B) HRF-convolved alpha frequency time series and BOLD time series from a voxel in visual cortex (18, −79, −10) of a representative subject. (C) Regions of interest (ROIs) in the visual cortex. (D) Association between alpha power fluctuation and BOLD activity from different visual ROIs at the group level. (E) Association between alpha frequency fluctuation and BOLD activity from different visual ROIs at the group level. FDR-corrected p-values were given.

(Samaha and Postle, 2015), and stronger response control (Angelakis et al., 2004). Further, higher IAF is associated with better cognitive abilities in the realm of fluid intelligence and working memory capacity (Klimesch et al., 1990). Additionally, IAF decreases in normal aging (Köpruner et al., 1984; Li et al., 1996; Roubicek, 1977), and is lower in patients suffering from disorders such as mild traumatic brain injury (Lewine et al., 2007; Lewine et al., 1999; Tarapore et al., 2013), Parkinson's disease (Soikkeli et al., 1991), dementia (Soikkeli et al., 1991), and Alzheimer's disease (Penttilä et al., 1985). Since many of these brain disorders are coupled with declined cognition, lower alpha frequency is seen as an indicator of reduced cognitive functioning. Theoretical models explain these associations by positing that alpha frequency is a measure of the speed of the brain's internal clock (Treisman et al., 1990); individuals with higher alpha frequency have faster speed of neural information processing.

4.3. Task-dependent modulation of alpha frequency

Osaka (1984) was among the first to investigate whether alpha frequency is task-dependent and showed that alpha frequency increased when human subjects performed a complex addition task relative to a simple addition task (Osaka, 1984). Earle (1988) later found that in certain tasks alpha frequency increased with increase in task difficulty, but in other tasks, alpha frequency decreased when task difficulty was increased (Earle, 1988). A more recent study using an N-back task ($N = 0$ and $N = 2$) reexamined this issue and showed that the more difficult 2-back condition has higher alpha frequency relative to the easier 0-back condition (Haegens et al., 2014). Because in the N-back task, encoding, retention and retrieval may be overlapped in time, it is difficult to relate alpha frequency modulation to a specific working-memory related cognitive operation. In addition, how alpha frequency modulation impacts behavior or other neural variables remains unclear. Klimesch et al. (1996), noting the lack of any relationship between reaction time and alpha frequency within individuals, argued that task-dependent changes in alpha frequency are not real.

In this work we employed a working memory task where encoding, retention and retrieval are temporally separated to examine the task-dependent modulation alpha frequency (Jensen and Lisman, 1998; Sternberg, 1969). During encoding, higher memory load was associated with lower alpha power and alpha frequency, whereas during retention, higher memory load was associated with higher alpha power and alpha frequency. For alpha power, it is well-established that its decrease following stimulus onset reflects the opening of the sensory space for information processing, and higher memory load trials have increased demand for sensory processing, leading to more decrease of alpha power (Stipacek et al., 2003). Alpha frequency decrease with increasing memory load during encoding suggests that it plays a similar role of indexing sensory processing demand considering that higher memory load is associated with a larger array of digits in the present paradigm.

During retention, alpha power increases with increasing memory load, a highly replicated finding which has been interpreted as reflecting sensory inhibition to protect information held online from sensory interference (Jensen et al., 2002; Worden et al., 2000). Alpha frequency similarly increased with memory load during retention. For retrieval, while there was no systematic relationship between alpha power and memory load, alpha frequency was again systematically increased with increasing memory load. In both retention and retrieval, a parsimonious interpretation of the alpha frequency increase with memory load is that it, like alpha power increase during retention, is a marker of increased sensory inhibition (see below).

While associations between memory load and alpha power have been shown across the different temporal stages previously (Jensen et al., 2002; Klimesch et al., 2005; Meltzer et al., 2007), the present findings of alpha frequency modulation by memory load during different stages of working memory have not been demonstrated before, and may lead to novel hypotheses. In particular, given that increased alpha frequency is thought to facilitate top-down modulated inter-regional coupling of alpha rhythm (Sauseng et al., 2005), one may predict that during retention and retrieval, higher memory load is associated with stronger alpha-mediated posterior functional connectivity. In this manner, the modulation of the alpha frequency during each stage namely encoding, retention and retrieval, is consistent with the corresponding goals of each working memory stage.

It is worth noting that the aforementioned internal clock theory of alpha frequency developed to explain the relation between cognitive ability and individual alpha frequency appears to be not applicable to explain the findings on the task modulation of alpha frequency. Specifically, according to the internal clock theory, encoding of higher memory load cues should be associated with increase in alpha frequency to better meet the demand of increased sensory information processing, whereas during retention, the higher memory loads, requiring reduced processing of sensory information processing to prevent interference, should be accompanied by reduced alpha frequency; in both cases, these predictions are not compatible with the empirical observations reported here.

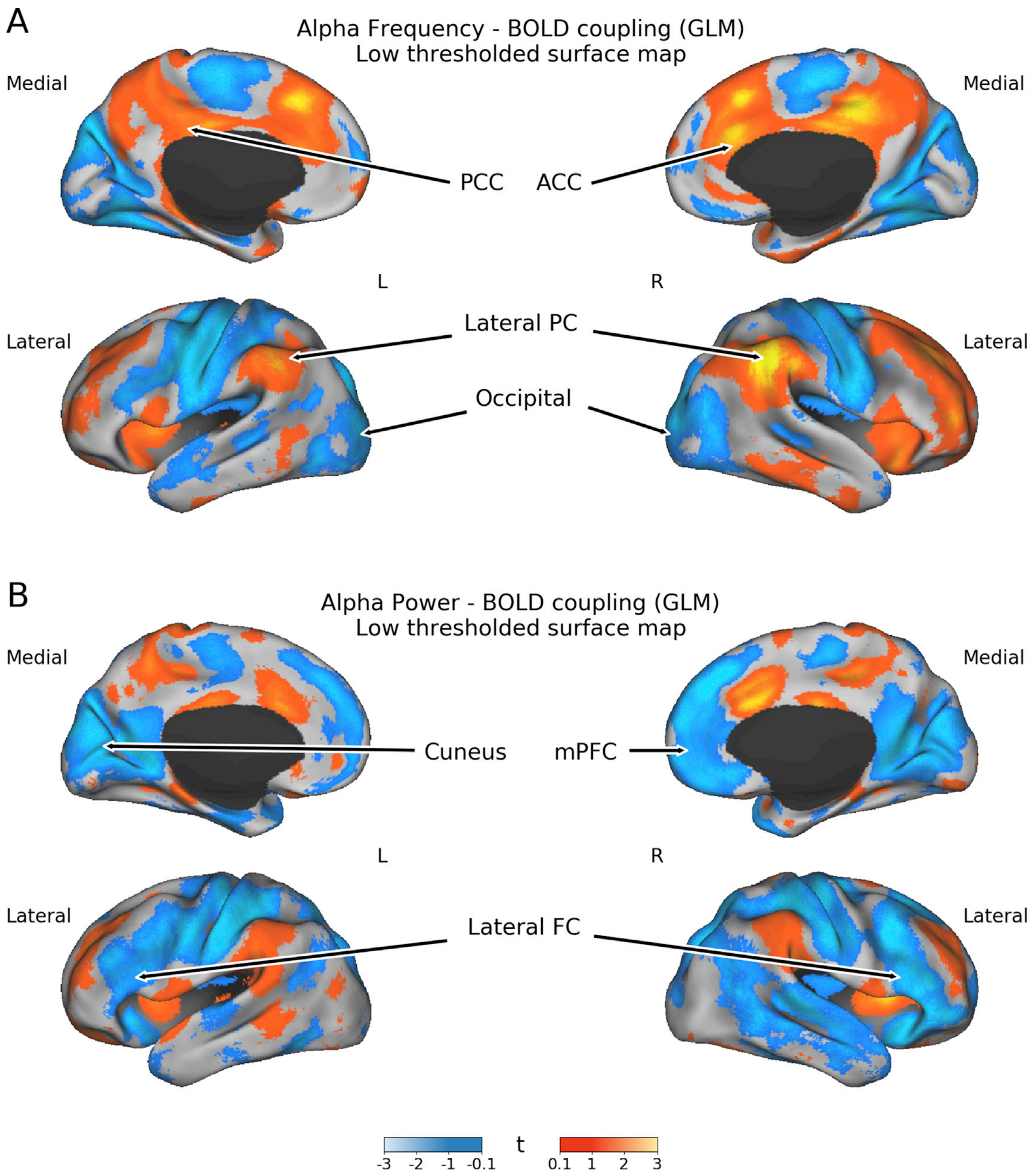

Fig. 5. Exploratory whole brain analysis. (A) Low-threshold maps of alpha frequency - BOLD coupling. (B) Low-threshold maps of alpha power - BOLD coupling. ACC – anterior cingulate cortex, FC - frontal cortex, mPFC - medial pre-frontal cortex, PC – parietal cortex, PCC - posterior cingulate cortex.

4.4. *Functional role of alpha frequency modulation*

In the foregoing we interpreted alpha frequency increase and decrease as reflecting sensory inhibition and facilitation (disinhibition). The potential function of alpha frequency modulation was further tested by analyzing the effect of alpha frequency variation on reaction time and stimulus-evoked brain responses. Dividing the trials into fast reaction time trials and slow reaction time trials within each memory load, it was shown that when subjects responded slower, the alpha frequency during retention was higher. Furthermore, higher pre-cue alpha frequency and pre-probe alpha frequency was associated with lower early cue-evoked and probe-evoked responses, respectively. Along with decreasing alpha frequency with increasing demand of sensory processing during encoding, these results suggest that alpha frequency may provide an index of cortical excitability, namely, increased alpha frequency reflects decreased cortical excitability and reduced sensory information processing and vice versa. In addition, lower probe-evoked responses were followed by higher alpha frequency during the retrieval period. This result, along with the finding that alpha frequency during retrieval increases with memory load, supports the notion that sensory cortex is inhibited in this time period to guard the retrieval process taking place in higher-order structures against sensory interference (Pinal et al., 2014). Interestingly, in the same time period, alpha power is not systematically associated with memory load, highlighting the important contribution of alpha frequency modulation during retrieval. It is worth noting that similar increase in alpha frequency following smaller early cue-evoked neural responses were observed, indicating that within a given memory load, the same interpretation given above to the relation between retrieval period alpha frequency and probe-evoked neural response applies to the relation between encoding period alpha frequency and cue-evoked neural response.

The above hypothesis that alpha frequency reflected cortical inhibition was further tested in the second experiment in which simultaneous EEG and fMRI was recorded during resting state. Correlating the naturally occurring fluctuations of alpha frequency and alpha power with BOLD signals using a general linear model approach with both alpha frequency and alpha power as regressors, we found that alpha frequency and BOLD in visual cortex were inversely associated, indicating that BOLD activity is lower during the time period where alpha frequency is higher. While the exact neurophysiological meaning of the BOLD is still under investigation (Ekstrom, 2010; Heeger et al., 1999; Logothetis and Wandell, 2004), the general consensus is that higher BOLD level indicates stronger neural activity (Koós and Tepper, 1999). Following this understanding, higher alpha frequency is associated with a state of lower activity in the visual cortex, whereas lower alpha frequency is associated with a state of higher activity in the visual cortex, which is consistent with our interpretation of alpha frequency modulation during different stages of the working memory task in the first experiment. The fact that alpha power was not associated with BOLD activity in the visual areas in our analysis appears to run counter to previous reports that alpha power is negatively correlated with BOLD from visual cortex (Gonçalves et al., 2006; Laufs et al., 2006; Mo et al., 2013). This may be due to the fact that these studies do not use alpha frequency as a co-variate. Without considering this factor the GLM model may be underdetermined.

From Fig. 4E, alpha frequency-BOLD coupling is stronger in the extra-striate cortex (V3, V4, IPS), but weaker in V1. One possible reason could be the difference in cell types across the different visual ROIs with higher order regions containing larger neurons responsible for integrating information from early visual areas (Collins et al., 2016); larger cells may produce stronger fields. Another reason could be the difference in how anterior higher-order (frontal and parietal) brain regions project to different visual ROIs. Extra-striate areas such as V2, V3 and V4 receive stronger projections from higher order areas and consequently may be more susceptible to top-down inhibitory control signals leading to stronger BOLD deactivation (Stanton et al., 1995). Thirdly, the role of acetylcholine in modulating alpha frequency is intriguing. Prior research has shown that increased cholinergic concentration is related to increase in oscillation frequency (Fellous and Sejnowski, 2000). It is known that cholinergic input has inhibitory functions (Gulledge and Stuart, 2005; Phillis and York, 1967). Higher order visual areas like V2 are suggested to have more evident cholinergic modulation than V1 (Disney et al., 2006). We recognize that these ideas are quite speculative. Much more research is needed to better understand the relationships we report here.

4.5. *Relationship between alpha power and alpha frequency*

Memory load modulation of alpha power and alpha frequency is quantified by their respective load modulation indices. As seen in Fig. 2, across subjects, the two indices are not correlated with one another, suggesting that each alpha variable can be independently tuned functionally. This appears to be supported by the alpha-BOLD coupling analysis in Experiment 2 where alpha power and alpha frequency fluctuations are shown to be correlated with BOLD from different brain networks. As seen in Fig. 5, whereas alpha frequency is positively coupled with regions of DMN, alpha power is negatively coupled with lateral prefrontal cortex. At first glance, these findings appear to be incompatible with the finding that alpha power and alpha frequency are related within a subject (Nelli et al., 2017). The following considerations may reconcile the diverse findings. At the single trial level, there is no straightforward relationship between alpha power and alpha frequency (see Figure S1 for an illustration). Even if there is, one can understand the independent modulation of alpha power and alpha frequency by examining a simple statistical model in which at the individual subject level: $AF = a \times Load + e_1$ and $AP = b \times Load + e_2$, where alpha frequency (AF) and alpha power (AP) vary from trial to trial, driven by the random variables e_1 and e_2. Each subject has constant modulation indices a and b which vary from subject to subject. AF and AP being correlated at the single trial level implies that e_1 and e_2 are correlated random variables. Across subjects, variations of the random variables a and b can be independent from each other, as we reported here.

Disclosure of interest

The authors report no conflicts of interest.

Acknowledgment

This work was supported by US National Institutes of Health grant MH112206 and US National Science Foundation grant BCS1439188.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.neuroimage.2018.08.063.

References

Angelakis, E., Lubar, J.F., Stathopoulou, S., 2004. Electroencephalographic peak alpha frequency correlates of cognitive traits. Neurosci. Lett. 371 (1), 60–63. https://doi.org/10.1016/j.neulet.2004.08.041.

Anokhin, A., Vogel, F., 1996. EEG alpha rhythm frequency and intelligence in normal adults. Intelligence 23 (1), 1–14.

Berger, H., 1929. Über das Elektrenkephalogramm des Menschen. Archiv für Psychiatrie und Nervenkrankheiten 87 (1), 527–570. https://doi.org/10.1007/BF01797193.

Bernhard, C.G., Skoglund, C.R., 1939. On the alpha frequency of human brain potentials as a function of Age1. Skandinavisches Archiv Für Physiologie 82 (2), 178–184. https://doi.org/10.1111/j.1748-1716.1939.tb00458.x.

Bonanni, L., Thomas, A., Tiraboschi, P., Perfetti, B., Varanese, S., Onofrj, M., 2008. EEG comparisons in early Alzheimer's disease, dementia with Lewy bodies and Parkinson's disease with dementia patients with a 2-year follow-up. Brain 131 (3), 690–705. https://doi.org/10.1093/brain/awm322.

Cecere, R., Rees, G., Romei, V., 2015. Individual differences in alpha frequency drive crossmodal illusory perception. Curr. Biol. 25 (2), 231–235. https://doi.org/10.1016/j.cub.2014.11.034.

Clark, C.R., Veltmeyer, M.D., Hamilton, R.J., Simms, E., Paul, R., Hermens, D., Gordon, E., 2004. Spontaneous alpha peak frequency predicts working memory performance across the age span. Int. J. Psychophysiol. 53 (1), 1–9.

Collins, C.E., Turner, E.C., Sawyer, E.K., Reed, J.L., Young, N.A., Flaherty, D.K., Kaas, J.H., 2016. Cortical cell and neuron density estimates in one chimpanzee hemisphere. Proc. Natl. Acad. Sci. U.S.A. 113 (3), 740–745. https://doi.org/10.1073/pnas.1524208113.

Delorme, A., Makeig, S., 2004. EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. J. Neurosci. Meth. 134 (1), 9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009.

Disney, A.A., Domakonda, K.V., Aoki, C., 2006. Differential expression of muscarinic acetylcholine receptors across excitatory and inhibitory cells in visual cortical areas V1 and V2 of the macaque monkey. J. Comp. Neurol. 499 (1), 49–63. https://doi.org/10.1002/cne.21096.

Earle, J.B., 1988. Task difficulty and EEG alpha asymmetry: an amplitude and frequency analysis. Neuropsychobiology 20 (2), 96–112. https://doi.org/10.1159/000118482.

Ekstrom, A., 2010. How and when the fMRI BOLD signal relates to underlying neural activity: the danger in dissociation. Brain Res. Rev. 62 (2), 233–244. https://doi.org/10.1016/j.brainresrev.2009.12.004.

Fellous, J.-M., Sejnowski, T.J., 2000. Cholinergic induction of oscillations in the hippocampal slice in the slow (0.5–2 Hz), theta (5–12 Hz), and gamma (35–70 Hz) bands. Hippocampus 10 (2), 187–197.

Fink, A., Grabner, R.H., Neuper, C., Neubauer, A.C., 2005. EEG alpha band dissociation with increasing task demands. Cognit. Brain Res. 24 (2), 252–259.

Genovese, C.R., Lazar, N.A., Nichols, T., 2002. Thresholding of statistical maps in functional neuroimaging using the false discovery rate. Neuroimage 15 (4), 870–878.

Gonçalves, S.I., de Munck, J.C., Pouwels, P.J.W., Schoonhoven, R., Kuijer, J.P.A., Maurits, N.M., et al., 2006. Correlating the alpha rhythm to BOLD using simultaneous EEG/fMRI: inter-subject variability. Neuroimage 30 (1), 203–213. https://doi.org/10.1016/j.neuroimage.2005.09.062.

Grandy, T.H., Werkle-Bergner, M., Chicherio, C., Lövdén, M., Schmiedek, F., Lindenberger, U., 2013. Individual alpha peak frequency is related to latent factors of general cognitive abilities. Neuroimage 79, 10–18.

Gulledge, A.T., Stuart, G.J., 2005. Cholinergic inhibition of neocortical pyramidal neurons. J. Neurosci. 25 (44), 10308–10320.

Haegens, S., Cousijn, H., Wallis, G., Harrison, P.J., Nobre, A.C., 2014. Inter- and intra-individual variability in alpha peak frequency. Neuroimage 92, 46–55. https://doi.org/10.1016/j.neuroimage.2014.01.049.

Heeger, D.J., Boynton, G.M., Demb, J.B., Seidemann, E., Newsome, W.T., 1999. Motion opponency in visual cortex. J. Neurosci. 19 (16), 7162–7174.

Jensen, O., Gelfand, J., Kounios, J., Lisman, J.E., 2002. Oscillations in the alpha band (9–12 Hz) increase with memory load during retention in a short-term memory task. Cerebr. Cortex 12 (8), 877–882.

Jensen, O., Lisman, J.E., 1998. An oscillatory short-term memory buffer model can account for data on the Sternberg task. J. Neurosci. 18 (24), 10688–10699.

Jensen, O., Mazaheri, A., 2010. Shaping functional architecture by oscillatory alpha activity: gating by inhibition. Front. Hum. Neurosci. 4.

Jensen, O., Tesche, C.D., 2002. Frontal theta activity in humans increases with memory load in a working memory task. Eur. J. Neurosci. 15 (8), 1395–1399.

Klimesch, W., Doppelmayr, M., Pachinger, T., Russegger, H., 1997. Event-related desynchronization in the alpha band and the processing of semantic information. Cognit. Brain Res. 6 (2), 83–94. https://doi.org/10.1016/S0926-6410(97)00018-9.

Klimesch, W., Doppelmayr, M., Schimke, H., Pachinger, T., 1996. Alpha frequency, reaction time, and the speed of processing information. J. Clin. Neurophysiol. 13 (6), 511–518.

Klimesch, W., Schack, B., Sauseng, P., 2005. The functional significance of theta and upper alpha oscillations. Exp. Psychol. 52 (2), 99–108.

Klimesch, W., Schimke, H., Ladurner, G., Pfurtscheller, G., 1990. Alpha frequency and memory performance. J. Psychophysiol. Retrieved from http://psycnet.apa.org/psycinfo/1991-21873-001.

Klimesch, W., Schimke, H., Pfurtscheller, G., 1993. Alpha frequency, cognitive load and memory performance. Brain Topogr. 5 (3), 241–251.

Koós, T., Tepper, J.M., 1999. Inhibitory control of neostriatal projection neurons by GABAergic interneurons. Nat. Neurosci. 2 (5), 467–472. https://doi.org/10.1038/8138.

Köpruner, V., Pfurtscheller, G., Auer, L.M., 1984. Quantitative EEG in normals and in patients with cerebral ischemia. Prog. Brain Res. 62, 29–50.

Lange, J., Oostenveld, R., Fries, P., 2013. Reduced occipital alpha power indexes enhanced excitability rather than improved visual perception. J. Neurosci. 33 (7), 3212–3220. https://doi.org/10.1523/JNEUROSCI.3755-12.2013.

Laufs, H., Holt, J.L., Elfont, R., Krams, M., Paul, J.S., Krakow, K., Kleinschmidt, A., 2006. Where the BOLD signal goes when alpha EEG leaves. Neuroimage 31 (4), 1408–1418. https://doi.org/10.1016/j.neuroimage.2006.02.002.

Lebedev, A.N., 1994. The neurophysiological parameters of human memory. Neurosci. Behav. Physiol. 24 (3), 254–259.

Lehmann, D., Skrandies, W., 1980. Reference-free identification of components of checkerboard-evoked multichannel potential fields. Electroencephalogr. Clin. Neurophysiol. 48 (6), 609–621. https://doi.org/10.1016/0013-4694(80)90419-8.

Lewine, J.D., Davis, J.T., Bigler, E.D., Thoma, R., Hill, D., Funke, M., et al., 2007. Objective documentation of traumatic brain injury subsequent to mild head trauma: multimodal brain imaging with MEG, SPECT, and MRI. J. Head Trauma Rehabil. 22 (3), 141–155.

Lewine, J.D., Davis, J.T., Sloan, J.H., Kodituwakku, P.W., Orrison Jr., W.W., 1999. Neuromagnetic assessment of pathophysiologic brain activity induced by minor head trauma. Am. J. Neuroradiol. 20 (5), 857–866.

Li, D., Sun, F., Jiao, Y., 1996. Frontal EEG characters in aging and the correlativity with some cognitive abilities. Acta Psychol. Sin. 28 (1), 76–81.

Liu, Y., Bengson, J., Huang, H., Mangun, G.R., Ding, M., 2014. Top-down modulation of neural activity in anticipatory visual attention: control mechanisms revealed by simultaneous EEG-fMRI. Cerebr. Cortex 26 (2), 517–529.

Logothetis, N.K., Wandell, B.A., 2004. Interpreting the BOLD signal. Annu. Rev. Physiol. 66 (1), 735–769. https://doi.org/10.1146/annurev.physiol.66.082602.092845.

Meltzer, J.A., Zaveri, H.P., Goncharova, I.I., Distasio, M.M., Papademetris, X., Spencer, S.S., et al., 2007. Effects of working memory load on oscillatory power in human intracranial EEG. Cerebr. Cortex 18 (8), 1843–1855.

Minami, S., Amano, K., 2017. Illusory jitter perceived at the frequency of alpha oscillations. Curr. Biol. 27 (15), 2344–2351 e4. https://doi.org/10.1016/j.cub.2017.06.033.

Mo, J., Liu, Y., Huang, H., Ding, M., 2013. Coupling between visual alpha oscillations and default mode activity. Neuroimage 68 (Suppl. C), 112–118. https://doi.org/10.1016/j.neuroimage.2012.11.058.

Mulholland, T., 1968. The concept of attention and the EEG alpha-rhythm. Electroencephalogr. Clin. Neurophysiol. 24 (2), 188.

Murray, M.M., Brunet, D., Michel, C.M., 2008. Topographic ERP analyses: a step-by-step tutorial Review. Brain Topogr. 20 (4), 249–264. https://doi.org/10.1007/s10548-008-0054-5.

Nelli, S., Itthipuripat, S., Srinivasan, R., Serences, J.T., 2017. Fluctuations in instantaneous frequency predict alpha amplitude during visual perception. Nat. Commun. 8 (1) https://doi.org/10.1038/s41467-017-02176-x.

Osaka, M., 1984. Peak alpha frequency of EEG during a mental task: task difficulty and hemispheric differences. Psychophysiology 21 (1), 101–105.

Osipova, D., Hermes, D., Jensen, O., 2008. Gamma power is phase-locked to posterior alpha activity. PLoS One 3 (12), e3990. https://doi.org/10.1371/journal.pone.0003990.

Penttilä, M., Partanen, J.V., Soininen, H., Riekkinen, P.J., 1985. Quantitative analysis of occipital EEG in different stages of Alzheimer's disease. Electroencephalogr. Clin. Neurophysiol. 60 (1), 1–6.

Phillis, J.W., York, D.H., 1967. Cholinergic inhibition in the cerebral cortex. Brain Res. 5 (4), 517–520.

Pinal, D., Zurrón, M., Díaz, F., 2014. Effects of load and maintenance duration on the time course of information encoding and retrieval in working memory: from perceptual analysis to post-categorization processes. Front. Hum. Neurosci. 8. https://doi.org/10.3389/fnhum.2014.00165.

Rajagovindan, R., Ding, M., 2011. From prestimulus alpha oscillation to visual-evoked response: an inverted-U function and its attentional modulation. J. Cognit. Neurosci. 23 (6), 1379–1394. June, 2010.

Roubicek, J., 1977. The electroencephalogram in the middle-aged and the elderly. J. Am. Geriatr. Soc. 25 (4), 145–152. https://doi.org/10.1111/j.1532-5415.1977.tb00282.x.

Roux, F., Uhlhaas, P.J., 2014. Working memory and neural oscillations: alpha–gamma versus theta–gamma codes for distinct WM information? Trends Cognit. Sci. 18 (1), 16–25. https://doi.org/10.1016/j.tics.2013.10.010.

Saletu, B., Grünberger, J., 1985. Memory dysfunction and vigilance: neurophysiological and psychopharmacological aspects. Ann. N. Y. Acad. Sci. 444 (1), 406–427.

Samaha, J., Postle, B.R., 2015. The speed of alpha-band oscillations predicts the temporal resolution of visual perception. Curr. Biol. 25 (22), 2985–2990. https://doi.org/10.1016/j.cub.2015.10.007.

Sauseng, P., Klimesch, W., Doppelmayr, M., Pecherstorfer, T., Freunberger, R., Hanslmayr, S., 2005a. EEG alpha synchronization and functional coupling during top-down processing in a working memory task. Hum. Brain Mapp. 26 (2), 148–155.

Sauseng, P., Klimesch, W., Schabus, M., Doppelmayr, M., 2005b. Fronto-parietal EEG coherence in theta and upper alpha reflect central executive functions of working memory. Int. J. Psychophysiol. 57 (2), 97–103. https://doi.org/10.1016/j.ijpsycho.2005.03.018.

Scheeringa, R., Petersson, K.M., Oostenveld, R., Norris, D.G., Hagoort, P., Bastiaansen, M.C.M., 2009. Trial-by-trial coupling between EEG and BOLD identifies networks related to alpha and theta EEG power increases during working memory maintenance. Neuroimage 44 (3), 1224–1238. https://doi.org/10.1016/j.neuroimage.2008.08.041.

scipysignalperiodogram (n.d.). Retrieved May 2, 2018, from https://docs.scipy.org/doc/scipy/reference/generated/scipy.signal.periodogram.html.

Shapiro, S.S., Wilk, M.B., 1965. An analysis of variance test for normality (complete samples). Biometrika 52 (3/4), 591–611.

Soikkeli, R., Partanen, J., Soininen, H., Pääkkönen, A., Riekkinen, P., 1991. Slowing of EEG in Parkinson's disease. Electroencephalogr. Clin. Neurophysiol. 79 (3), 159–165.

Stanton, G.B., Bruce, C.J., Goldberg, M.E., 1995. Topography of projections to posterior cortical areas from the macaque frontal eye fields. J. Comp. Neurol. 353 (2), 291–305. https://doi.org/10.1002/cne.903530210.

Sternberg, S., 1969. Memory-scanning: mental processes revealed by reaction-time experiments. Am. Sci. 57 (4), 421–457.

Stipacek, A., Grabner, R.H., Neuper, C., Fink, A., Neubauer, A.C., 2003. Sensitivity of human EEG alpha band desynchronization to different working memory components and increasing levels of memory load. Neurosci. Lett. 353 (3), 193–196. https://doi.org/10.1016/j.neulet.2003.09.044.

Tarapore, P.E., Findlay, A.M., LaHue, S.C., Lee, H., Honma, S.M., Mizuiri, D., et al., 2013. Resting state magnetoencephalography functional connectivity in traumatic brain injury: clinical article. J. Neurosurg. 118 (6), 1306–1316.

Treisman, M., Faulkner, A., Naish, P.L.N., Brogan, D., 1990. The internal clock: evidence for a temporal oscillator underlying time perception with some estimates of its characteristic frequency. Perception 19 (6), 705–742. https://doi.org/10.1068/p190705.

Valera, F.J., Toro, A., Roy John, E., Schwartz, E.L., 1981. Perceptual framing and cortical alpha rhythm. Neuropsychologia 19 (5), 675–686. https://doi.org/10.1016/0028-3932(81)90005-1.

Voytek, B., Canolty, R.T., Shestyuk, A., Crone, N., Parvizi, J., Knight, R.T., 2010. Shifts in gamma phase–amplitude coupling frequency from theta to alpha over posterior cortex during visual tasks. Front. Hum. Neurosci. 4. https://doi.org/10.3389/fnhum.2010.00191.

Wang, C., Rajagovindan, R., Han, S.-M., Ding, M., 2016. Top-down control of visual alpha oscillations: sources of control signals and their mechanisms of action. Front. Hum. Neurosci. 10.

Wang, L., Mruczek, R.E.B., Arcaro, M.J., Kastner, S., 2015. Probabilistic maps of visual topography in human cortex. Cerebr. Cortex 25 (10), 3911–3931. https://doi.org/10.1093/cercor/bhu277.

Wang, X., Chen, Y., Ding, M., 2008. Estimating Granger causality after stimulus onset: a cautionary note. Neuroimage 41 (3), 767–776.

Wang, X., Ding, M., 2011. Relation between P300 and event-related theta-band synchronization: a single-trial analysis. Clin. Neurophysiol. 122 (5), 916–924.

Wiens, S., Sand, A., Olofsson, J.K., 2011. Nonemotional features suppress early and enhance late emotional electrocortical responses to negative pictures. Biol. Psychol. 86 (1), 83–89. https://doi.org/10.1016/j.biopsycho.2010.11.001.

Worden, M.S., Foxe, J.J., Wang, N., Simpson, G.V., 2000. Anticipatory biasing of visuospatial attention indexed by retinotopically specific-band electroencephalography increases over occipital cortex. J. Neurosci. 20 (RC63), 1–6.

Wutz, A., Melcher, D., Samaha, J., 2018. Frequency modulation of neural oscillations according to visual task demands. Proc. Natl. Acad. Sci. Unit. States Am. 201713318. https://doi.org/10.1073/pnas.1713318115.

Yuan, H., Liu, T., Szarkowski, R., Rios, C., Ashe, J., He, B., 2010. Negative covariation between task-related responses in alpha/beta-band activity and BOLD in human sensorimotor cortex: an EEG and fMRI study of motor imagery and movements. Neuroimage 49 (3), 2596–2606. https://doi.org/10.1016/j.neuroimage.2009.10.028.