Reconfiguration of Brain Network Between Resting State and P300 Task

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Abstract—Previous studies have explored the power spectra from the resting-state condition to the oddball task, but whether significant difference in the brain network exists is still unclear. This article aims to address how the brain reconfigures its architecture from a resting-state condition (i.e., baseline) to the P300 task in the visual oddball task. In this article, electroencephalograms (EEGs) were collected from 24 subjects, who were required to only mentally count the number of target stimuli; afterward, EEG networks constructed in different bands were compared between baseline and task to evaluate the reconfiguration of functional connectivity. Compared with the baseline, our results showed the significantly enhanced delta/theta functional connectivity and decreased alpha default mode network in the progress of brain reconfiguration to the task. Furthermore, the reconfigured coupling strengths were found to relate to P300 amplitudes, which were then regarded as features to train a classifier to differentiate the brain states and the high and low P300 groups with an accuracy of 100% and 77.78%, respectively. The findings of this article help us understand the updates in functional connectivity from resting state to the oddball task, and the reconfigured network structure has the potential for the selection of good subjects for P300-based brain–computer interface.

Index Terms—Brain network, brain reconfiguration, P300, rhythmic activity.

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I. Introduction

In recent years, the P300, a positive deflection in the human event-related potential (ERP), has been widely investigated by various neuroimaging technologies, including electroencephalogram (EEG) and functional magnetic resonance imaging (fMRI). The P300 is usually evoked by the presence of the target stimulus in the oddball task, in which two types of the stimulus (i.e., target and standard) are presented to individuals randomly. In this task, individuals are required to only respond to multiple target stimuli (e.g., counting the number or pressing a button), once they notice the appearance of the target stimulus, as correctly and quickly as possible, while omitting standard ones. The P300 is correlated with various cognitive functions, such as attention and decision making, and is also regarded as a biomarker to evaluate the degree to which the information can be processed by the brain in individual subjects [1]–[3], which has been widely used in multiple aspects, including clinical diagnosis [4]–[6], cognitive neuroscience [7], and brain–computer interface (BCI) [8]–[11]. The P300 is usually characterized quantitatively by its amplitude and latency, and both show huge variability across individuals [12], [13]. However, it is still unclear that the mechanism underlying the individual variability of the P300.

Heretofore, multiple regions in the brain, such as prefrontal, frontal, and parietal, have been demonstrated to play important roles in the generation of the P300 [14]–[16], while lesions in a certain part of these areas, such as frontal lobe, might result in its deficit, such as the decreased amplitude [17], [18]. Essentially, the specified brain activities in multiple bands, including delta, theta, and alpha bands, are closely related to the cognitive process and the P300 [19]–[24]. The brain and its functions work daily within a large-scale complex network, the information is, therefore, processed between the regions that are specialized, spatially distributed but functionally coupled in the brain [25], [26]. The network neuroscience thus raises a “bridge” between the brain network and cognitive architecture [27], [28]. For example, higher intelligence is unveiled to correlate with a more efficient information transfer in the brain [29], and the larger response in steady-state visually evoked potential-based studies is also clarified to be correlated with a better network structure [30], [31]. In fact, the generation of the P300 is also attributed to the inter-regional brain activity [32]–[34], and our studies on either resting-state [35] or oddball task [36], [37] have consistently found a close
relationship between the long-range connectivity of prefrontal and parietal/occipital lobes and the P300, which can also be validated by the synchronized activity that originates from the frontal-posterior network [38]. Herein, the brain network analysis is widely adopted to investigate the neural mechanism that accounts for the generation of the P300 [32], [34]; and multiple methods including the coherence and Granger causality, are usually applied in brain network studies [39]–[42].

Our brain is not idle, even at rest [43]. The spontaneous brain activity at rest may reflect the brain potential for the efficient information processing during task [44], [45], and be potentially applied to investigate the pathophysiological mechanisms of different diseases, such as epilepsy and Alzheimer’s disease [46]–[50]. In fact, both spontaneous activity (e.g., spectral power and network metrics) [35], [51] and task metrics [36], [38] help to deepen our knowledge of the P300. However, previous studies merely focus on either resting state or stimuli task to investigate the P300, few studies have considered the relationship between the two states, and most importantly, it is still left unveiled how the brain reorganizes from a resting state to fulfill the needs of the P300. Therefore, in this article, we assumed that the efficient reconfiguration from a resting state to an oddball task in the brain is highly associated with the information processing of the P300. We then collected the resting-state and P300 task EEG data sets of 24 subjects who participated in our oddball P300 tasks. By exploring the functional networks between the resting state and P300 task in different bands, we evaluated the updates of functional connectivity in the progress of brain reconfiguration from resting state to P300 task and, finally, investigated the potential relationships between the P300 and the reconfigured networks.

II. METHODS

A. Participants

Twenty-four healthy right-handed postgraduate students (males, the age range of 22–27 years) were compensated financially to participate in our experiment after providing their signed written informed consent. Of note, none of them had a history of substance abuse and a personal or family history of psychiatric or neurological disease. This experiment has been approved by the Institution Research Ethics Board of the University of Electronic Science and Technology of China.

B. Experimental Procedures

In the preparation stage, all subjects were asked to remain relaxed and focus their attention on the center of the computer screen. They were also required to refrain from extensive head motion, to avoid moving their body during the whole experiments. Then, we collected EEG data sets in a standard protocol that consists of a 4-min eyes-closed resting-state condition and following 3-times P300 tasks (Fig. 1), which was also depicted as follows.

Before tasks, a 4-min resting-state EEG was recorded. After a 1-min short break, the tasks started. We measured 150 trials, including 120 standard stimuli and 30 target stimuli, in each time of the P300 task. In each trial of P300, a bold cross appeared as a cue to remind them to focus their attention on the screen. Two hundred and fifty milliseconds later, a thin cross lasting 500 ms appeared to inform subjects that a (target or standard) stimulus came out randomly. A stimulus was then presented and lasted 500 ms. Meanwhile, to circumvent the motor effect, once they noticed the appearance of the target stimulus, they will mentally count its number as quickly and correctly as possible, rather than pressing a button [52]–[54].

In this article, the target stimulus was the combination of the downward-oriented triangle with a thin cross in its center, and the standard stimulus was the combination of the upward-oriented triangle with a thin cross in its center. After a 1-s break, a next P300 trial initiated. When one P300 loop completed, subjects were required to verbally speak out the total number of target stimuli that they had counted.

C. EEG Data Acquisition

The resting and task EEG data sets were recorded with 64 Ag/AgCl electrodes that are positioned in compliance with the international 10/20 system and digitized with a sampling rate of 500 Hz (Brain Products GmbH) and online bandpass filtering of 0.01–100 Hz. During EEG recordings, the electrodes FCz and AFz were set as the reference and ground, respectively. Meanwhile, the vertical and horizontal electrooculogram were separately recorded with two additional electrodes to monitor their eye movements. Of note, we ensured that the impedances of all electrodes were consistently maintained below 5 kΩ.

D. EEG Data Analysis

To investigate the specified reconfiguration in different bands from a resting-state condition to an oddball stimulus task in the brain, we first estimated the resting and task EEG time-frequency distributions (TFDs) and then extracted the P300 amplitudes for all subjects. Thereafter, the functional networks of all subjects per brain state were built, and we finally probed the relationship between the P300 amplitude and brain network reconfiguration.

1) Time-Frequency Analysis: The nearby electrodes acquire a similar contribution from cortical sources and also capture a similar activity. In this article, to reduce the effect
of volume conduction, following the procedure in related studies [55]–[57], the sparse electrodes, 21 out of 64 channels, (i.e., Fpz/1/2, Fz/3/4/7/8, Cz/3/4, T7/8, Pz/3/4/7/8, and Oz/1/2) were extracted and used in this article [35], [56]. Then, raw resting and task 21-channel EEG data sets were preprocessed using procedures, including reference electrode standardization technique (REST) rereferencing [58, 59], [1, 13] Hz bandpass filtering, 2.25-s data segmentation, and artifact-trial removing (±75 μV as the threshold).

After preprocessing, for the resting and task data, 116.17 ± 51.27 and 59.92 ± 21.71 artifact-free trials across subjects were left, respectively. Herein, to acquire the matched trials across subjects, following the minimum trial number suggested (i.e., 20 or more) [60], for each subject, the k-medoid clustering algorithm [61] was used to extract the matched trials among all artifact-free trials. In specific, based on the clustering results, only the trial in the center of each cluster was extracted and then used in any further analysis. Meanwhile, considering the small sample size, although three subjects had rest or task trials less than 20 (but exceeding 16), they were also included in further analysis, which led to the 26.19 ± 2.86 (Mean ± STD) trials of resting state and 26.31 ± 2.09 trials of task state across subjects.

Then, for each subject, the TFDs of both resting and task brain states were calculated using the extracted 2.25-s-length epochs, covering the whole trial periods, which were acquired by using the "wavemenu" (Wavelet Toolbox) in MATLAB (v2014a, The MathWorks Inc., Natick, MA, USA). In specific, for each subject, we first imported the resting or task single-trial data into the toolbox, and the parameters were then set to be cmor1-1.5 for wavelet basis and 512 for wavelet scale. Afterward, the TFDs of each resting or task 2.25-s-length epoch would be then calculated, and after acquiring the TFDs for all resting or task trials, we finally trial-averaged the TFDs across these trials to acquire the TFDs per brain state for each subject.

2) P300 Amplitude: P300 activity varies in time-frequency amplitude and topography [62], [63]. Brain activity within the low-frequency band, e.g., delta and theta, is demonstrated to underlie the P300 [19]–[24]. Herein, procedures, including REST rereferencing, [1, 13] Hz bandpass filtering, [−200 800] ms data segmentation (0 ms represents the onset of the stimulus), [−200 0] ms baseline correction, artifact-trial removing (±75 μV as the threshold), and trials averaging. Based on the averaged ERP, the P300 amplitude was calculated within a time interval of [250 ms, 600 ms] after the onsets of the target stimulus. To access a reliable estimation of the P300 amplitude for each subject, the mean of amplitudes was calculated across the five electrodes over posterior areas (i.e., CPz/1/2, Cz, and Pz) that have been demonstrated with significant P300s. Of note, to reduce the noise effect, the P300 amplitude was finally defined as the averaged amplitude within the time window of ±10 ms with the largest positive peak at the center.

3) Brain Network: Given that the brain activity in the delta, theta, and alpha bands is found to be related to the P300, exploring the corresponding functional network in the frequency domain in the brain seems to be helpful to deepen our knowledge of the P300. In essence, coherence is also a correlation coefficient quantitatively computed between the activities at two EEG sites in the frequency domain [64]; at frequency f, it actually measures the proportion of the variance of the EEG signal x(t) that can be accounted for by a best-fit linear relationship with the signal y(t). In this article, for each pair of EEG signals, x(t) and y(t), the coherence is expressed as follows:

\[
C_{xy}(f) = \left| R_{xy}(f) \right|^2 = \frac{\left| P_{xy}(f) \right|^2}{P_{xx}(f)P_{yy}(f)}
\]

where \(C_{xy}(f)\) and \(R_{xy}(f)\) represent the coherence value and complex correlation coefficient between x(t) and y(t) at frequency f, respectively. \(P_{xy}(f)\) represents the cross-spectrum of x(t) and y(t) at frequency f, and \(P_{xx}(f)\) and \(P_{yy}(f)\) represent the auto-spectrum at frequency f of x(t) and y(t) estimated from the Welch-based spectrum, respectively. For each frequency bin f, the \(C_{xy}(f)\) is acquired by squaring the magnitude of the complex correlation coefficient R, which returns a real value within the range of [0, 1].

Afterward, relying on the calculated \(C_{xy}(f)\) at each frequency bin f, the 21×21 adjacency matrix for each segment is acquired by averaging the \(C_{xy}(f)\) within the frequency range of interest (i.e., 1–8 and 8–13 Hz), which will be further trial-averaged across all segments to develop a final matrix for each subject under each condition. That is, for either 1–8 or 8–13 Hz, we would acquire an EEG brain network per brain state (i.e., the resting or P300 task).

A clear P300 can be efficiently evoked, only when subjects quickly and correctly respond to the targets while omitting the standards. Since we aimed to explore the neural reconfiguration of brain responses when the brain involves in responding to the required manners (i.e., mentally counting the target number), to uncover the neural support of the variability of the P300 across subjects, in this article, only the resting and target networks were, therefore, constructed.

To illustrate the brain reconfiguration in different bands, the paired t-test is adopted to statistically capture the topological differences between resting and task and to mark the edges significantly reconfigured (enhanced or suppressed), when the brain transits from resting state (i.e., baseline) to P300 task. In specific, for either frequency band, we statistically compared the networks between resting and task (i.e., 24×21×21 of resting versus 24×21×21 of the task) by using a paired t-test, resulting in a 21×21 matrix whose elements denote the significant (p < 0.05) or insignificant (p > 0.05) differences between two conditions. If a network edge significantly reconfigures, it will be kept; by contrast, if not, it will be discharged. Moreover, to exclude the artificial linkages, the false discovery rate (FDR) correction will be further used in the multiple correction procedure.

4) Outlier Subjects Removing Strategy: When exploring the relationship between the P300 amplitude and reconfigured coupling strength, there exist some outlier subjects whose data obviously deviates from the data center. In order to obtain a robust representative knowledge, the outlier subjects were discerned based on the Malahanobis distance [65]. In specific, based on the correlation between the reconfigured
coupling strengths of 1–8 Hz and P300 amplitudes, one subject having the largest Mahalanobis distance to the data center was excluded; and in order to keep the sample consistency, when investigating the relationship for 8–13 Hz, this subject was also excluded, that is, 23 subjects were included in the correlation and classification analyses.

5) Correlation Analysis: In this article, the Pearson’s correlation was used to assess the two potential relationships: one is the correlation between the two reconfigured coupling strengths in the different bands, and the other is the relationship between the P300 amplitude and the brain reconfiguration of distinct bands.

6) Classification Based on Reconfigured Coupling Strengths: Afterward, we intended to investigate if these reconfigured coupling strengths in different bands were helpful for the classification process with two different strategies. One was to classify the different brain states (i.e., resting state and P300 task), and the other was to categorize subjects into the low- or high-amplitude group. For the first strategy, based on the statistically tested network structure between the two states, we separately extracted the mean of reconfigured coupling strengths for the resting state and P300 task per band per subject. With respect to the second strategy, we calculated the reconfigured coupling strengths by averaging the coupling difference of the significantly reconfigured network edges from baseline to P300 task. In this article, of 23 subjects, nine subjects with the highest and nine subjects with the lowest amplitudes were included in both classification strategies.

For both 1–8 and 8–13 Hz, prior to the classification, we first explored the potential differences of reconfigured coupling strengths for the first and second strategies by using the paired and independent t-test, respectively. Thereafter, the calculated reconfigured coupling strengths were applied to both strategies, to discriminate the resting and task for the first strategy and to classify the high- and low-amplitude subjects for the second strategy, by using the linear discriminant analysis (LDA).

III. RESULTS

A. Specific Rhythmical Brain Reconfiguration

We first investigated the TFDs per subject before averaging the TFDs across subjects. Then, we found the intersubject variability of the TFDs in 1–8 Hz for the P300 task and in 8–13 Hz for the resting state. Of them, most of the subjects showed a similar pattern of the time–frequency activities, whose TFDs strength varied across subjects, and when looking at the other electrodes, this article illustrated a similar distribution for both states. Thereafter, to visually display the specified brain activity, Fig. 2 shows the grand-averaged TFDs on electrode Pz, since the P300 evoked by the target stimulus is prominently over the parietal region [14]; in specific, the alpha rhythm plays the dominated role in baseline spontaneous activity (i.e., resting state). By contrast, the alpha activity is attenuated in the stimulus task where the task activity in 1–8 Hz of delta and theta bands is surprisingly enhanced.

The topological differences reflecting the reconfiguration from resting state to P300 task in 1–8 and 8–13 Hz are displayed in Fig. 3, from which, we could see that in 1–8 Hz, the couplings between brain areas, including frontal/prefrontal and parietal lobes, are enhanced ($p < 0.05$, FDR correction), when the brain switches from baseline to P300 task. By contrast, the decreased default mode network (DMN)-like topology appears within this progress in the alpha band ($p < 0.05$, FDR correction).
Moreover, Fig. 4 displays the scalp topographies of the nodal degree corresponding to the reconfigured network structures for both 1–8 and 8–13 Hz. Specifically, in 1–8 Hz, multiple brain regions, especially the prefrontal and parietal lobes [Fig. 4(a)], clearly had the relatively large nodal degree; by contrast, the frontal and occipital lobes showed the large regional degree in the alpha band [Fig. 4(b)].

B. Correlations Between Brain Reconfiguration and P300 Amplitudes

Given the reconfigured coupling strengths from baseline to P300 task had been acquired for all subjects, the moderate linear relationships between the P300 amplitudes and reconfigured coupling strengths in 1–8 and 8–13 Hz are shown separately in Fig. 5, which illustrated that the increased coupling strengths in 1–8 Hz are positively related to the P300 amplitudes \(r = 0.483, p = 0.020\); by contrast, the decreased coupling strengths in the alpha band are negatively correlated with the P300 amplitudes \(r = -0.492, p = 0.017\).

C. Classification Based on Reconfigured Coupling Strengths in Different Frequency Bands

Given the potential relationships between the reconfigured coupling strengths and P300 amplitudes were found in Fig. 5, we then investigated if these reconfigured coupling strengths in 1–8 and 8–13 Hz could classify the different conditions in the two classification strategies.

For the first strategy, Fig. 6(a) shows the statistical differences of reconfigured coupling strengths in 1–8 and 8–13 Hz between the two states. In specific, the significantly larger reconfigured coupling strengths in 1–8 Hz \(t = 311.016, p = 0.000\) and smaller reconfigured coupling strengths in 8–13 Hz \(t = -15.895, p = 0.000\) were found for the P300 task, compared to that of the resting state. Moreover, the classification in Fig. 6(b) achieved a classification accuracy of 100% when differentiating the two brain states.

With respect to the second strategy, Fig. 7(a) displays the differences of reconfigured coupling strengths from resting to P300 task in 1–8 and 8–13 Hz between two groups, and for high-amplitude subjects, the significantly larger increased coupling strengths \(t = 1.904, p = 0.047\) in 1–8 Hz and smaller decreased coupling strengths \(t = -2.636, p = 0.015\) in the alpha band were found when compared to that of low-amplitude subjects. Meanwhile, for the classification in Fig. 7(b), only 4 out of 18 subjects were falsely classified into the opposite group, which achieved a classification accuracy of 77.78%.

IV. DISCUSSION

Previous studies have demonstrated that the specified brain activities in the delta, theta, and alpha bands significantly relate to the P300 [19]–[24]. Since no target information is received by the brain, the alpha rhythm plays the dominant role in the spontaneous brain activity at rest. Thus, the TFDs showed in Fig. 2(b) demonstrates a larger magnitude in the alpha band spanned across the whole duration. However, when subjects were required to perform the tasks, much target information is needed to be processed. The brain thus involves such functions, including attention, signal matching, and decision making, to process this information, which is accomplished by the specified activity in the delta and theta bands. Herein, Fig. 2(a) demonstrates the enhanced brain activity in the delta and theta bands during the P300 tasks. As a consequence, the brain activity in the alpha band is attenuated and suppressed (i.e., alpha event-related desynchronization) [20], [22]. We thus assumed that the specified reconfigured couplings from baseline to P300 task in different bands are governed by the needs of information processing in the brain, and the differentiable network topology could, therefore, account for the underlying mechanism of the generation of the P300.

In this article, the specified network topologies in different bands that reflect the reallocation of limited brain resources, are given in Figs. 3 and 4. The opposite reconfiguration patterns of specified brain activity that is related to the P300 are found in different frequency bands, and the metrics quantitatively evaluating both increased topologies in 1–8 Hz and decreased topologies in 8–13 Hz are further demonstrated to relate to the P300 (Fig. 5). The P300 is attributed to the involvement of such brain functions, such as attention and decision making [2], [66], [67], that function on the large-scale network in the brain [38], [68]–[70]. As illustrated, the interactions between frontal (also prefrontal) and parietal lobes play crucial roles in the generation of the P300, and the reduced amplitudes are observed in frontal-lobe lesioned patients [18]. In 1–8 Hz, the network edges between prefrontal and parietal lobes, that had the larger nodal degree in 1–8 Hz [Fig. 4(a)], are enhanced [Fig. 3(a)]. While in the alpha band, such a notion of alpha suppression as decreased DMN-like topology, along with the relatively larger regional degree in frontal and occipital lobes [Fig. 4(b)], is found, which has also been clarified by previous studies [20], [22]. DMN is deactivated in tasks and is thereby negatively correlated with the task [71], [72].

The brain works daily in a balanced way to effectively process information. A marginally significantly negative relationship between the increased coupling strengths in 1–8 Hz and decreased coupling strengths in 8–13 Hz is found in this article, i.e., the stronger the negative network reconfigures
in 8–13 Hz, the stronger the positive network reconfigures in 1–8 Hz. That is, during the oddball task, the interactions between prefrontal/frontal and parietal lobes in 1–8 Hz, which are the main generators of the P300 [14], [35], [73], are enhanced; whereas to compensate for this increased task activity, the alpha activity is inversely suppressed, which corresponds to the decreased DMN.

The close relationships between the reconfigured coupling strengths in different bands and P300 amplitudes could be found from Fig. 5. Theoretically, the reconfigured coupling strengths represent quantitatively the adjustment degree of a brain network to fulfill the requirement for efficient information processing. The positive relationship [Fig. 5(a)] of increased strengths versus P300 amplitudes and negative relationship [Fig. 5(b)] of decreased strengths versus P300 amplitudes consistently demonstrate that a person who has the more efficient brain network reconfigured from baseline to P300 task might have the greater potential to evoke a clear P300 with the larger amplitude, when he (or she) participates in our P300 tasks.

In this article, this inference was finally investigated by the comparison of reconfigured coupling strengths of 1–8 and 8–13 Hz in two different strategies provided in Figs. 6 and 7. Both strategies showed the differences of the reconfigured network couplings between the related conditions [Figs. 6(a) and 7(a)], and both achieved an accuracy of 100% and 77.78% when classifying the two conditions, respectively. Therefore, the statistically tested network structure reconfigured from resting to the task is indeed helpful to identify the brain states of either resting or task, as well as classifying the high- and low-amplitude groups. That is, the classification of brain states effectively validated the stability of the identified reconfigured network structure in Fig. 3, and the classification between high- and low-amplitude groups further demonstrated that these reconfigured network structures are helpful to deepen our knowledge of the information processing of the P300, as well as the individual variability of the P300.

In this article, a fixed intertrial interval was designed, which might induce the anticipation effect in subjects, even if they cannot expect if the presented stimulus is a target. In a future
study, a random interval will be set to eliminate the anticipation effect. Another limitation might be the relatively small sample number included, and to guarantee the reliable findings, more subjects will be recruited in the future. Meanwhile, by averaging multiple trials, this article initially investigated the static reconfiguration of the brain networks from the resting state to the oddball task but ignored the intrinsic time-variant characteristics; in contrast, exploring the corresponding dynamic reconfiguration seems to be more helpful to investigate cognitive state transition, as well as the interindividual variations, by combining the available network methods, such as phase locking value, which will be our future work.

V. CONCLUSION

In this article, the brain network was found to be effectively reconfigured from resting state to stimulus task in different bands (i.e., delta/theta and alpha bands) in an efficient and balanced manner. Furthermore, the reconfigured network topologies in different bands were clarified to closely relate to the P300 evoked by the presence of the target stimulus. The findings of this article demonstrated that the reconfigured brain network structure has the potential for the selection of applicable users for P300-BCI, and is also helpful to deepen our knowledge of the generation and the individual variability of the P300.

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