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INTRACRANIAL ELECTROCORTICOGRAPHIC CORRELATES OF INTRINSIC BRAIN NETWORKS

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Purpose:

Analyzing patterns of intracranial electroencephalographic (EEG) recordings can provide insight into how temporal and spatial components of brain activity are related on a trial-by-trial basis. Research on fMRI resting state networks has clarified the role of the default mode network (DMN) in internally directed cognition (e.g., mind-wandering), and the frontoparietal network (FPN) in externally directed cognition (e.g., working memory tasks); however, the relation of these networks to similar functional properties of neuroelectric activity is not yet understood. Recently, it has been suggested that the scalp EEG phenomena of alpha event-related desynchronization (ERD; 8-13 Hz) and theta-band event-related synchronization (ERS; 3-7 Hz) during simple cognitive tasks might represent neuroelectric parallels of DMN down-regulation and FPN activity, respectively. This study addressed this question by investigating task-related patterns of alpha ERD and theta ERS at intracranial sites within the DMN and FPN networks while participants completed multiple trials of the Multi-Source Interference Task (MSIT), containing three levels of task difficulty.

Understanding the parallels between electrophysiology and neural networks will allow for a greater understanding of cognitive processing at the neural level. In utilizing technology with better spatiotemporal resolution (Kim et al., 1997), constructs such as cognitive performance can be more accurately characterized in the brain through the dimensions of frequency, time, and space. Finally, understanding how these processes occur can result in valuable insight on potential classification and treatment for certain clinical diagnoses such as Epilepsy, Alzheimer's, or ADHD. For example, a decline in overall theta power within the frontoparietal network could represent a biomarker for the onset of Alzheimer's Disease if these variables were found to be related. Understanding the neural mechanisms associated with clinical diagnoses could provide new insight for improvement of classification and treatment practices.

Background:

Brain-behavior relations were studied anatomically up until the early 2000s when the discovery of a baseline system known as the default mode network changed our understanding of the neuroanatomical basis of cognition (Raichle et al., 2001). Since this discovery, recent research has shined a light on the role of many neural networks in relation to cognitive functioning and human behavior. Rather than thinking about the brain modularly (i.e., this part of the brain is responsible for this function), we are now starting to view brain activity more holistically. Neural activity is correlated less with individual neurons firing, and more with complexes of interconnected neurons that form what are now termed neural networks. This thesis sought to analyze the connection between neural networks and electrophysiological measures to better understand cognitive performance.

Default Mode and Frontoparietal Networks

The default mode network (DMN) is correlated with brain regions including the medial temporal lobe, the medial prefrontal cortex, and the posterior cingulate cortex (Yeo et al., 2011). This network is known to be involved in non-task specific activity, or more colloquially, mind wandering. Non-task specific activity, or mind wandering, refers to when the brain is not actively engaged in a specific task such as remembering a phone number, but rather left to daydream or engage in “shower thoughts”. Past literature has found a link between deactivation of the DMN and goal-driven behavior such as working memory (Anticevic et al., 2010). The temporal and spatial patterns of DMN activation and deactivation provide us with insight on what the brain is doing while not engaged in task-based behavior and how this connects to information processing. Deactivation of the DMN likely gives room for resources and energy to be utilized in other networks during task-driven behavior for increased performance and processing.

The frontoparietal network (FPN) is associated with brain regions including the rostro- and dorsolateral prefrontal cortex, the anterior insula, the dorsal anterior cingulate cortex, and the anterior inferior parietal lobule (Yeo et al., 2011). In contrast to the DMN, the circuitry within these regions has been correlated with functions such as visuospatial analogical reasoning and active information processing (Watson & Chatterjee, 2012). The FPN activity is related to goal-driven behavior (Marek & Dosenbach, 2018), meaning that tasks involving more attention and active information processing, such as working memory tasks, will likely correspond with this network. The contrast between the FPN and DMN in neural network activation and associated task engagement could be relevant to mechanisms of cognitive performance. More precisely, it was hypothesized that, during performance of the MSIT, alpha-band desynchronization would be observed in DMN areas of the brain, and theta-band synchronization would be observed in FPN areas of the brain.

Methods:

Participants

This study examined the intracranial EEG patterns of 8 patients who underwent presurgical mapping for treatment of epilepsy. Participants were recruited from Columbia University in New York and Massachusetts General Hospital in Boston and were screened for participation based on three factors. Only patients who were undergoing neurosurgical monitoring for treatment of medically refractory epilepsy, over 18 years old, and judged to have an IQ above 70 by a neuropsychologist were eligible for participation. Roughly half of the participants were female (42%), and half male (58%). All participants had grid or depth electrodes implanted surgically for specific clinical purposes (see Figure 1).

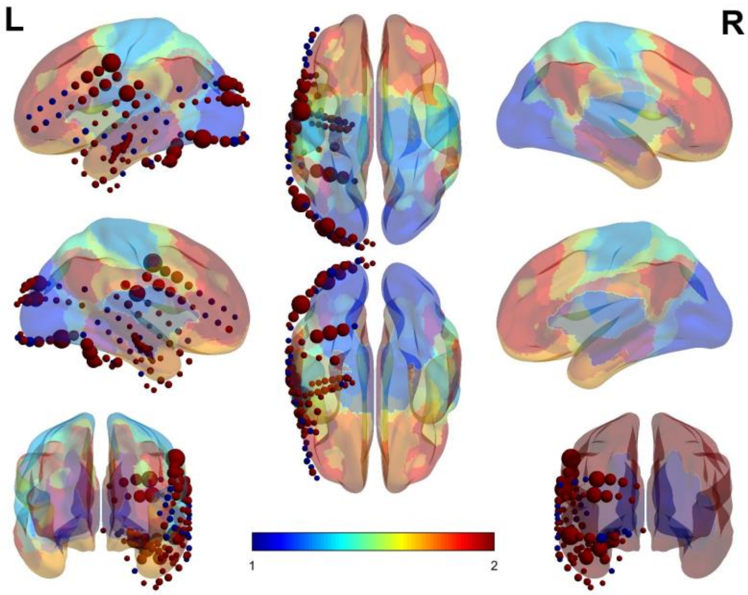

Figure 1. The above image displays the distribution of electrodes for a single participant. The colored brain regions indicate a neural network parcellation (Yeo et al., 2011).

Procedure

With electrodes implanted in the brain for presurgical mapping of epilepsy, all participants consented to complete a simple cognitive task under electroencephalographic (EEG) recording after pre-screening as described above. Participants completed the Multisource Interference Task (MSIT), a visuospatial cognitive task described in more detail below. In total, recordings were obtained from 1899 electrocorticography sites or depth electrodes.

Measures

Task

Participants completed the MSIT (similar to the Stroop task), which manipulates spatial and numerical interference to produce three levels of task difficulty (Bush & Shin, 2006). For each trial, participants were asked to identify a target based on a stimulus sequence of three numbers. To answer correctly, the participant had to press one of three buttons corresponding to the target identity: 1, 2, or 3. Some trials provided spatial or numeric interference by having incongruence between the target identity and the spatial position or numeric identity. For example, if the prompt asked for which number was different, both sequences of “112” and “121” would be followed by a correct response of pushing the second button, indicating the number “2”. In this scenario, the first sequence has spatial interference in that the number “2” is in the third position. An example of numeric interference would be a prompt asking for the number in the third position of either sequence above.

Data Processing

Prior to analyses, the raw EEG data was pre-processed to remove noisy channels and epochs. First, noisy channels were identified and removed by visual inspection. Next, line noise was removed with a band stop filter (at 60 Hz), and all trials were demeaned, and re-referenced to a common average. Finally, noisy trials were identified and removed by visual inspection. This pre-processing resulted in cleaned epochs ranging from -3000 to +3000 milliseconds relative to the onset of the stimuli. The epochs were then convolved with a series of Morlet wavelets – there were a total of 23 wavelets ranging from 3-14 Hz in 0.5 Hz intervals and each wavelet was fixed to five cycles. The result of the convolution was a complex time-frequency representation of the brain activity associated with each trial from -3000 ms pre-stimulus to +3000 ms post-stimulus and from 3 to 14 Hz. Each of these complex matrices was then multiplied by its complex conjugate to obtain the power of the signal in time-frequency space. For each trial, we then averaged over the frequency bands comprising the conventional theta (3-7 Hz) and alpha (8-13 Hz), producing theta and alpha power.

We then extracted pre-and post-stimulus data. The interval from -1.0 to -0.5 seconds was defined as the pre-stimulus interval, and +0.5 to +2.0 seconds was defined as the post-stimulus interval. Theta-band task-related power change was calculated as the average voltage over the post-stimulus period minus the average voltage in the pre-stimulus period for each trial. The same process was completed for calculation of alpha-band. The final data were single values for theta- and alpha-band task-related power change, averaged over trials within conditions and networks, where positive values indicate ERS, and negative values indicate ERD.

Results:

To better understand the role of neural networks in cognitive information processing, we measured the electrophysiologic patterns occurring in the brain as participants completed the MSIT, a visuospatial cognitive task. Specifically, after exclusion of data due to incomplete datasets, we assigned all electrodes to one of four neural networks (the DMN, FPN, dorsal attention, and visual networks) based on their relative location in the brain, and then analyzed reaction times according to trial difficulty. We were most interested in the default mode (DMN) and frontoparietal networks (FPN), as they have been linked to temporal patterns of theta and alpha rhythms in past literature (Scheeringa et al., 2009).

We predicted that task performance, in terms of reaction time, would show a positive relationship with task difficulty. Additionally, we hypothesized that theta-band ERS, defined as a positive change in theta power from pre- to post-stimulus, would be seen in the FPN, and alpha-band ERD, defined as a decrease in alpha power from pre- to post-stimulus, would be seen in the DMN. We conducted several repeated measures analyses of variance (ANOVA) to evaluate the factors of neural network identity and task difficulty, and then conducted exploratory follow-up analyses to investigate whether there was evidence for specific effects of task difficulty within four neural networks to be replicated in future work.

Reaction Time Results

As predicted, a positive relationship between reaction time and task difficulty was observed [$F(1.15, 8.05) = 16.11$, $p = 0.003$, $\eta^2 = 0.697$]. In contrast, the results did not support our specific hypotheses regarding expected power differences between the DMN and FPN. However, exploratory analyses suggest there may be significant differences between levels of task difficulty within the default mode, frontoparietal, dorsal attention, and visual networks in replication with a larger sample size.

Theta-band Results

In conducting a two-way ANOVA with factors of neural network (four levels) and task difficulty (low, medium, and high) assessed within subjects, we found no main effect of either neural network [$F(1.65, 11.54) = 1.52$, $p = 0.256$] or task difficulty [$F(1.30, 9.10) = 4.27$, $p = 0.061$], nor an interaction [$F(2.50, 17.47) = 1.50$, $p = 0.251$], on change in theta power. Despite the lack of observed omnibus effects, we conducted several exploratory pair-wise comparisons to support the development of future hypotheses. More precisely, we observed that within the frontoparietal and dorsal attention networks, higher difficulty levels showed a greater decrease in theta power than the lowest task difficulty level ($p = 0.048$, 95% CI for mean difference [-46.73, -0.24]; $p = 0.053$, 95% CI for mean difference [-46.27, 0.38]). Because differences in theta power change were observed between specific difficulty levels of the MSIT, these exploratory findings suggest that within the frontoparietal and dorsal attention networks, there may be a trend of decreasing theta ERS with increased task difficulty.

Alpha-band Results

Similar to theta-band results, a two-way ANOVA (4 x 3) assessed within subjects showed no main effect of either neural network [$F(1.30, 9.13) = 1.46$, $p = 0.268$] or task difficulty [$F(1.12, 7.84) = 4.17$, $p = 0.073$] on change in alpha power, and no interaction [$F(2.00, 14.02) = 2.46$, $p = 0.122$]. Once again, although we found no omnibus effects, we conducted several exploratory pair-wise comparisons to direct hypotheses for future research. Specifically, we found that within the frontoparietal network, the lowest difficulty level had a mean change in alpha power that was greater than the middle difficulty level ($p = 0.035$, 95% CI for mean difference [1.588, 33.330]), and the highest difficulty level ($p = 0.025$, 95% CI for mean difference [3.539, 38.665]). Within the dorsal attention network, the lowest difficulty level had a mean change in alpha power that was greater than the middle difficulty level ($p = 0.022$, 95% CI for mean difference [5.101, 48.444]). In looking at the effects of task difficulty on change in alpha power, dependent on neural network, these exploratory results suggested that the frontoparietal network showed a potential alpha event-related desynchronization (ERD) within-subjects, increasing with greater task difficulty, and the dorsal attention network showed a potential alpha event-related synchronization (ERS), decreasing with greater task difficulty. However, replication in an independent dataset with a larger sample size is needed to confirm these hypotheses.

Conclusions:

Although the results of this study are limited by variability between participants and lack of experimental control over electrode placement, the exploratory findings regarding theta and alpha power suggest that there may be important information to be learned about cognitive performance within the default mode, frontoparietal, visual and dorsal attention networks through intracranial technology. More precisely, the overall increase in alpha power within the visual network across the presentation of a visual stimulus, in combination with the overall increase in theta power within the dorsal attention network, could suggest that fluctuations in brain frequency-band power during cognitive tasks are more present in these networks than the frontoparietal network.

Despite the lack of observed main effects of neural network or task difficulty, this thesis supports the method of using intracranial electroencephalography as a tool to study neural network activity. Not only do these findings provide evidence for an effective method of understanding neural patterns of information processing, but also a potential solution to the problem of spatial and temporal resolution (Kim et al., 1997). Intracranial EEG is advantageous in that electrodes are placed directly into the brain, leading to fewer obstacles associated with the skin and skull barrier. The support for using intracranial data to understand neural network activity, which is more commonly studied with imaging technology such as fMRI, has important implications for improvement of data resolution in future research and clinical practices.

Ultimately, the findings presented in this study could also be pertinent to clinical practice. With a better understanding of how frequency band-specific patterns represent mechanisms of neural networks, scientists could be provided with additional resources to diagnose and treat psychiatric conditions and have a better understanding of the underlying neural mechanisms involved with these conditions. For example, decreased theta synchronization within control networks such as the dorsal attention network could provide valuable information about the onset of a clinical diagnosis such as Alzheimer's Disease.

This study provides valuable insight into where scientists can focus their specific research questions surrounding information processing, both spatially and temporally. With these findings, it is likely that there are important mechanisms of information processing to be uncovered within the default mode, frontoparietal, visual and dorsal attention networks. Likewise, parallel change in reaction time and theta power as task difficulty increased suggests a link between cognitive and behavioral measures of engagement. With replication, these findings could permit a reinterpretation of previous literature on frequency-band synchronization and desynchronization in relation to neural network activity and support new ways to study these networks using neuroelectric recordings.

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