

Effective Connectivity Measuring of ERP Signals in Recognition Memory Process by Generalized Partial Directed Coherence

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Abstract—Various processes occur in recalling in brain and it is necessary to investigate memory brain function. Dual process theory separates recollection from familiarity in recognition memory. By comparing individuals with respect to normal state and with impairment, one can understand performance of memory. Comparison of two conditions infers that particular brain mechanism is being affected from impairment. In this study, we use the data in which recollection has been affected more than familiarity by midazolam drug. To investigate this difference, connectivity between Brain regions is estimated. Multivariate autoregressive models (MVAR) is used for determination of Granger causality to estimate effective connectivity in time-frequency domain. In this regard, we use GPDC method. Results show specific connectivity between parietal and frontal that is evidence of recollection to continue process and familiarity compensation in failing of recollection.

Keywords—brain connectivity; recognition memory; GPDC; MVAR; Granger causality

I. INTRODUCTION

Recognition memory is about stimulus event that has been previously experienced and truly judged. In two decades, cognitive neuroscientists have become more interested in it. Dual-process models, hypothesizing that recognition memory is based on distinct retrieval processes. event-related brain potentials (ERPs), are used to separate familiarity and recollection [1]. Previous studies assign ‘parietal’ to the recollection and ‘mid-frontal’ to the familiarity by the use of neuroimaging [2].

Midazolam includes benzodiazepine that causes to amnesia, and may be used to separate recollection from familiarity [3]. Hirshman et al. solicited subjects to report their recognition judgments basis in terms of “remembering” (i.e., recollection) or “knowing” (i.e., familiarity lacking recollection), the results exhibited that midazolam affected recollection greater than familiarity.

Several studies using functional magnetic response suggested that parietal and prefrontal cortices related to recollection [4], [5]. whereas medial temporal related to familiarity [6]. other researcher reported ERPs peaks at 400 ms in prefrontal and at ~600 ms in parietal, suggested that ~400 ms

peak associated with familiarity, despite ~600 ms one related to recollection [7]–[9].

Over the past two decades, neuroimaging was dominant in systems neuroscience. Scientists expect that over the next two decades neuroimaging of dynamic and connectivity will play a major role in revealing the brain's function and operation [10].

Granger introduced the mathematical definition of causality that time series $x_i(t)$ is granger-cause $x_j(t)$ if past knowledge of $x_j(t)$ improve prediction of $x_i(t)$ significantly [11]. Granger causality principle can be considered by multivariate autoregressive model (MVAR). Several measures are defined in the context of Multivariate Autoregressive Model and based on Granger causality principle (e.g.: Granger Causality Index (GCI), Directed Transfer Function (DTF), Partial Directed Coherence (PDC) and their modifications [12].

Partial directed coherence (PDC) represents directed linear connection between two time series as occurring simultaneously with a set of other time series in a frequency domain. PDC's can disclose crucial aspects of functional connectivity in neuroscience due to the central role played by neural rhythms (α , β , γ , etc.) that are of paramount physiologic relevance [13].

Functional connectivity estimates the interaction between neural structures directly from the neuroelectric data [14]. PDC is based on the multiple time-series ‘directed coherence’ (DC) [15] and determines Granger Causality [11] in multichannel data when more pairs than the ones of time series are simultaneously analyzed. Other generalization of DC was introduced for multiple time series [16] (see [17], [18] for a comparison). However, PDC can distinguish cascade connection from direct connection because it is based on the notion of partial coherence. For example, where node 1 connects to 2 and node 2 connects to node 3, but nodes 1 and 3 not directly connect which PDC didn't show the connection between nodes 1 and 3, but some other methods suffer from this [19].

Several studies show that memory process is in low-frequency band [20], [21]. According to the ability of PDC one can estimate memory-related connectivity in measurement signals.

Already, directed coupling of macaque V4 during visual short-term memory estimated by Generalized Partial Directed Coherence (GPDC) by using multivariate autoregressive (MVAR) models [21, p. 4]. In this study, we investigate effective connectivity in recognition memory task by the use of GPDC method.

I. METHODS

A. Data input

In this study, we use the data associated with the twelve subjects from University of Colorado students who participated in the Combined Pharmacological and Electrophysiological study [1]. All subjects were right-handed, native English speakers and weighed in 83 kg who do tasks in two conditions (injecting saline or midazolam with double-blind). Stimuli words were 480 low-frequency English that were classified randomly into four 120-word sets which emerged equally in each condition (old/new and midazolam/saline). Each word was displayed in the center of a computer monitor for 4 s, with an inter-word interval of 1 s. During the recognition memory task, scalp voltages were collected with a 128-channel high-input impedance amplifier. Amplified analog voltages (0.1–100 Hz band-pass) were digitized at 250 Hz.

B. Data processing

The data processed by EEGLAB toolbox [22]. in first step data epochs are extracted from 100 ms before to 1,000 ms after stimulation. Baseline removed, then abnormal trials are rejected by rejecting extreme values. During a trial, if the data (at the selected electrodes) exceed 110 μV , the trial is marked as abnormal values and is rejected; also the values under -110 μV are rejected. Linear drift may exist in some electrodes. To detect such drifts, we fit data to the function in order to estimate slope in trial and then by R-squared limit set to 0.3, if the slope exceeds a 70 microvolt over the whole epoch we reject the trial. we compute the probability of each trial. Trials having out of 5 times standard deviations of the mean probability distribution are marked as artifact and rejected. The probability measure is applied both to single electrodes and to the collection of all electrodes. One can use kurtosis statistical measure to reject artifacts when discontinuity occurs in trial or other artifact that data epochs have very 'peaky' activity. Where kurtosis value was high positive, it is an abnormally 'peaky' distribution, while a high negative kurtosis value shows abnormally flat activity distribution. If single and all channel thresholds were exceeded 5 times standard deviations from mean kurtosis value, we could reject those.

Independent Component Analysis (ICA) is a useful tool for source separating and then classifying brain and non-brain activity to reject artifacts from measured data, but it largely depends on users. For compassing this issue, we use a completely automatic algorithm (ADJUST). It separates brain's independent components from artifact by using spatial and temporal features. Features are selected to capture blinks, eye movements, and generic discontinuities. Validation of ADJUST's classification on a totally different EEG dataset indicates that the result largely matches a manual one by experts (95.2%) [23].

The PDC and GPDC work with phase difference between signals; only when there is a phase difference between signals they have non-zero value. Volume conduction affects the magnitude of electrode and has a zero phase propagation, therefore volume conduction doesn't generate phase difference between channels. So in theory, PDC results should not be affected from volume conduction. In practice, it has some influence e.g., increasing the noise level, however, this influence is not critical [24]. We select four channels (24, 124, 52, 92 as shown in figure 1) from data as suggested in [1], [4], [5], fit AMVAR model and compute connectivity as will be explained at below.

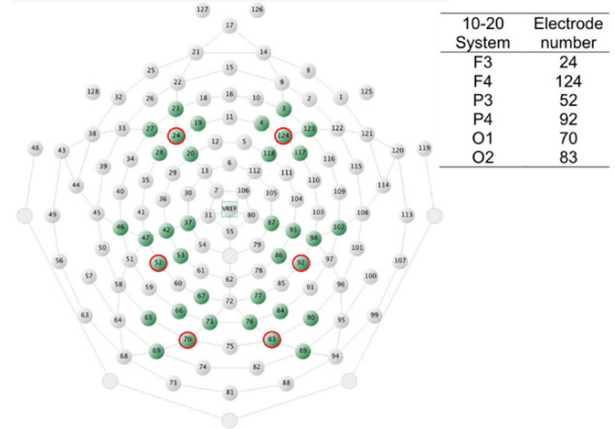


Figure 1. Coregistration between Geodesic Sensor Net and 10-20 system

C. Generalized Partial Directed Coherence

Partial Directed Coherence is a linear quantifier connected with the multivariate relationship between simultaneously observed time series in frequency domain for applying in functional connectivity inference in neuroscience. GPDC stands for the re-definition of PDC that would improve PDC's estimations under scenarios involving severely unbalanced and predictive modelling errors (additive Gaussian noise). The GPDC is more robust against the scale of time series [25]. If one assumes that $x(n)$ is a matrix of simultaneously observed time series as follows:

$$x(n) = [x_1(n) \dots x_N(n)]^T \quad (1)$$

It can be modeled by a Multivariate Autoregressive Model defined as:

$$x(n) = \sum_{k=1}^p A_k x(n-k) + w(n) \quad (2)$$

Where p is model order, A_k is the matrix of coefficients a_{ij} (k) implying how much sample of j^{th} time series affects i^{th} time series at lag k , $w(n)$ is also given as below:

$$w(n) = [w_1(n) \dots w_N(n)]^T$$

$w(n)$ is the vector of model's additive Gaussian noise with zero mean and with covariance matrix Σ_w . The PDC is defined as:

$$\pi_{ij}(f) = \frac{\bar{A}_{ij}(f)}{\sqrt{\sum_{k=1}^N \bar{A}_{kj}(f) \bar{A}^*_{kj}(f)}} \quad (3)$$

Where f is the normalized frequency in the interval $[-.5, .5]$ where:

$$A^{-1}_{ij}(f) = \delta_{ij} - \sum_{k=1}^p a_{ij}(k) e^{-2\pi f k}, \text{ for } \delta_{ij} = 1 \text{ whenever } i=j \text{ and } \delta_{ij} = 0, \text{ otherwise } j = \sqrt{-1} \quad [21].$$

In [25], Baccala et al. demonstrated a numerical issue in PDC with some examples. As one of the time series is scaled, PDC fails to estimate, too. This essentially leads to the use of weighing functions and generalized definition of PDC. To solve the numerical problem, they defined a new partial directed coherence estimator as:

$$\pi_{ij}(f) = \frac{\frac{1}{\delta_i} \bar{A}_{ij}(f)}{\sqrt{\sum_{k=1}^N \frac{1}{\delta_k} \bar{A}_{kj}(f) \bar{A}^*_{kj}(f)}} \quad (4)$$

Whence it follows as:

$$\left| \pi_{ij}^{(w)}(f) \right|^2 \leq 1. \quad (5)$$

And

$$\sum_{i=1}^N \left| \pi_{ij}^{(w)}(f) \right|^2 = 1 \quad (6)$$

Note that the new definition (4) preserves the normalizations (5, 6) that is also held for the PDC original definition (3) (see [19]).

L. Astolfi et al. applied this method to Predefined patterns of cortical connectivity and simulated it, where high-resolution EEG Data were recorded during the well-known stop paradigm and results therefore indicated that this method correctly estimates the simulated connectivity patterns under reasonable conditions [17].

A segmentation-based AMVAR [26] uses windowing techniques. First, it extracts parts of multichannel dataset by sliding window of length W , and fits VAR[p] model to this data (as seen in figure 2).

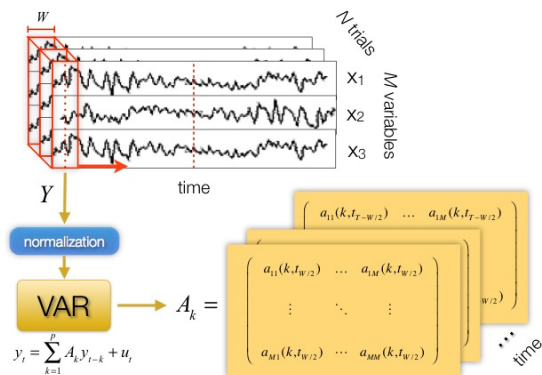


Figure 2. Schematic of sliding-window AMVAR modeling. W is the window length, T is the length of each trial in samples, N is the number of trials.

Estimation of windows' optimal length is a key choice in this method in order to have well temporal smoothing, local stationarity, sufficient amount of data in each window, process dynamics and neurophysiology. Short windows can improve the local stationarity of the data [26]. We use AIC, FPE, SBC and HQ criteria to select optimal order for MVAR model.

To validate our fitted model, we have to check the whiteness of the residuals, percent consistency, and model stability for each (or a random subset) of our windows. Residual whiteness tests include portmanteau and autocorrelation tests to be correlated in the residuals of the model. Here, we benefit Ljung-Box, Box-Pierce, and Li-McLeod multivariate portmanteau tests and a simple autocorrelation function test.

A. Statistical Analysis

We compared channels' connectivity between saline state and midazolam one of the 12 subjects by the use of a paired-sample t-test. Significant connection was determined by using P value of 0.05.

II. EXPERIMENTAL RESULTS

After preprocessing, data were fitted to time varying adaptive multivariate autoregressive (TV-AMVAR) model and then models were validated; then we estimated the connectivity of GPDC time frequency. For visualization of the difference between saline and midazolam conditions, we subtracted PDC measure in midazolam and saline (PDC_{mid} – PDC_{sal} in case number 8) pixel by pixel in time frequency domain as shown in figure 3, where the x axis is time and y axis is frequency. The difference in connectivity was coded by color in the interval $[-0.25, 0.25]$, blue code -0.25 and red code 0.25 . Direction of connectivity is from columns to rows.

Figure 3 shows the case study. For group analysis, we took GPDC measure in rectangle of time frequency (frequency: 8-13 Hz and time: 500-700 ms for figure 4) and then averaged measures in this box, subsequently we accomplished t-test on this point across 12 subjects and significant difference between midazolam and saline condition was reported.

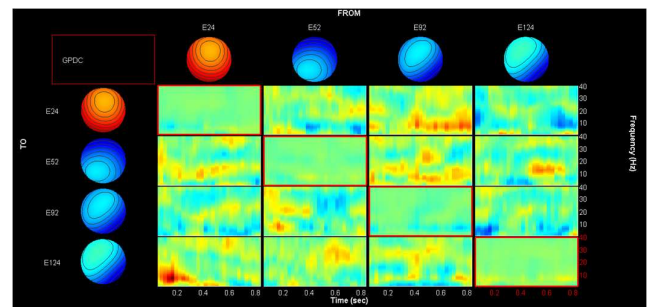


Figure 3. visualization of differenced time-frequency GPDC connectivity between saline and midazolam condition. The x axis show time and y axis is frequency and difference connectivity $[-0.25, 0.25]$ coded by color [Blue Red]. Connectivity is from Columns to Row.

Figure 4 shows solely the significant connection difference between saline and midazolam for channel 24 (left, anterior, superior (LAS)) and channel 124 (right, anterior, superior

(RAS)) regions; additionally, it illustrates for parietal channel 52 (left, posterior, superior (LPS)) and right, channel 92 (posterior, superior (RPS)) regions for the time between 500-700 ms in alpha frequency band. Color of arrows shows the significant connection in which midazolam>saline or midazolam<saline.

T-test with alpha 0.05 indicates that in 500-700 ms, 4 connections are significant (connection RPS to LPS, RPS to RAS, RAS to LPS and self RPS connection). Connections from RPS to LPS and to RAS and from RAS to LPS in midazolam are stronger than saline and self RPS connectivity in saline is stronger, as well.

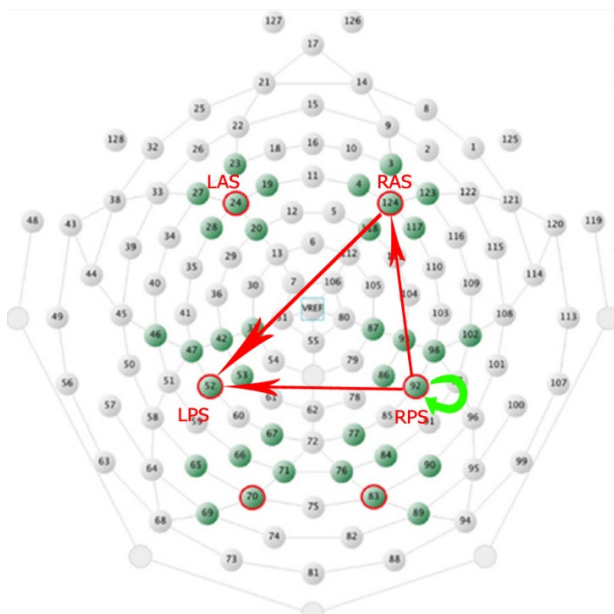


Figure 4 show significant connection between midazolam and saline for channel 24 (left, anterior, superior (LAS)), 52 (left, posterior, superior (LPS)), 92 (posterior, superior (RPS)) and 124 (right, anterior, superior (RAS)) for time between 500-700 ms. Red arrows show connection that in midazolam is stronger than saline and Green arrow show connection that in saline are stronger than midazolam.

I. DISCUSSION AND CONCLUSION

Evidence present that EEG oscillations in ~400 and ~600 ms [1] and alpha/theta bands relate to memory process [20], [21, p. 4] We investigate memory process between brain region connection in this rectangle of time frequency segment across twelve cases and significant results were reported.

Several studies by the use of functional magnetic response suggest that parietal and prefrontal cortex related to recollection [4], [5] whereas, medial temporal related to familiarity [6]. Other researchers from ERP data suggested that ~400 ms related to familiarity while ~600 ms related to recollection and they viewed more difference between ERP's peak in LPS at 600 ms [1]. In figure 4, self-connection of RPS in saline is stronger than midazolam that confirms the involvement of parietal regions in recollection.

Midazolam affects recollection, but not familiarity. Under control conditions (saline), accuracy of subjects was correlated

with the recollection-related, but not the familiarity-related ERP component which suggests that recollection dominance in driving memory. The opposite pattern observed under midazolam administration suggests that when recollection fails, subjects may leverage familiarity to compensate [1]. Figure 4 shows stronger connectivity in midazolam condition and also suggests that these information flows relate to familiarity in order to compensate recollection.

Grand-averaged ERPs are more different in LPS at 600 ms than other regions and times [1]. Connectivity in figure 4 shows information flow to LPS.

Recollection is a continuous rather than a discrete memory process [2]. Strong connectivity in midazolam may be an evidence for continuity.

In this study, we investigated familiarity- and recollection-related connection by comparing midazolam/saline condition. In the future research we will investigate the underlying neurophysiological cause of these connections and the source of these activations.

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