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Investigation of effective connectivity alteration during hypnosis induction using direct directed transfer function

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Abstract— **Hypnosis therapy is a widely applied method for treating psychiatric disorders, pain relief, and sleep irregularity. Research findings have demonstrated that hypnosis therapy will be useful, mostly for high hypnotizable subjects. Another factor which makes hypnosis therapy efficient is the hypnotic depth. In this study, we were interested in relationship between hypnotic depth and its corresponding effective connectivity patterns. Furthermore, effective connectivity changes between different hypnotizable subjects was studied. Direct directed transfer function (dDTF) was used in order to estimate effective connectivity between EEG channels. Based on our result, in medium and high hypnotizable groups, as subjects reach to their final depth of hypnosis, effective connectivity patterns were significantly reduced in delta and theta frequency bands while for low hypnotizable group, reduction was only seen in delta band and effective connectivity among channels in theta, beta and gamma frequency bands remained unchanged.**

Keywords-component; EEG; Effective Connectivity; Direct Directed Transfer Function (dDTF); Hypnosis Induction; Hypnotic Depth

Introduction(Heading 1)

Hypnosis is defined as "A state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion"[1]. It has been proven that hypnosis therapy is useful under many conditions like pain relief[2], depression and sleep disorders[3]. furthermore, high hypnosis susceptible groups were shown to be treated more successfully compared to low hypnosis susceptible ones[4]. Most traditional methods to estimate hypnosis susceptibility is subjective. Also, given that the hypnosis process could be up to 45 minutes[5], subjects may be tired at the end of the procedure. Therefore, estimation of hypnosis susceptibility can be misleading. Hence, finding the level of susceptibility is critical for deciding whether the patients need hypnosis therapy or not.

Some authors[6]–[8] have been tried to classify hypnotizability of individuals using normal EEG or during early stages of hypnosis induction. Baghdadi et al[6] used phase synchronization to find pair channels in different frequency bands which could differentiate between different groups of hypnotizability. Chiarucci et al[7] combined recurrence quantification analysis and detrended fluctuation analysis to classify various hypnotizable groups using normal EEG. Elahi et al[8] used several features such as fractal dimension, auto regressive (AR) coefficients, and wavelet entropy and band power to estimate hypnosis susceptibility of subjects.

Effective connectivity is the influence of one neural exerts over another[9]. The other definition of effective connectivity is the flow of information between different neural sources within the brain[9]. Estimation of effective connectivity by data-driven methods such as directed transfer function (DTF), granger causality (GC) and partial directed coherence has been widely used by authors in classification of emotion induction by music[10], resting and working memory[11] and differences in effective connectivity pattern between drowsiness, mediation and awareness[12]. Although some authors have reported functional connectivity analysis of hypnosis state[13], but to our knowledge, there has not been effective connectivity report so far. In this study, we try to find different patterns of effective connectivity associated with hypnotic depth. Kaminski and Blinowska[14] claimed direct directed transfer function is robust to volume conduction and could apply to EEG channel without any further preprocessing (e.g. source localization, ICA decomposition, etc.). Hence, dDTF was chosen in order to estimate effective connectivity of EEG channels.

In this study, we use statistical testing to investigate changes of effective connectivity patterns during hypnosis induction. Moreover, distinguishability of different levels of hypnosis susceptibility by effective connectivity features is studied.

I. Data & Methods

A. Data & Subjects

EEG recorded from 32 healthy subjects using 10-20 standard system by Ali Motie Nasrabadi. The sampling frequency was 256 Hz. The recording performed between 4-8 PM and lasts

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for 45 minutes which the first 15 minutes were for hypnosis induction. All subjects were male, right-handed and had no physical activity before recording. The hypnotizability scores were obtained using Waterloo-Stanford Group Scale (WSGS)[5]. Based on WSGS, subjects with score 12-22 classify as low, 22-42 classify as medium and 42-60 classify as high hypnotizable. Between 32 subjects, 12 of them were high, 15 of them were medium and 5 five of them were low hypnotizable. Given that a person reaches the final depth of hypnosis during hypnosis induction, first 15 minutes of recording was used throughout this study

B. Methods

In this study, we used direct directed transfer function (dDTF) to estimate effective connectivity between channels. Direct directed transfer function is data-driven and based on multivariate autoregressive model, which estimates causal interaction (aka. flow of information) between channels. Because of the MVAR modeling of data, dDTF is very robust to noise and leads to promising result on non-linear EEG signals[15].

Let X(t) be the recorded EEG; An MVAR model can be expressed by[16]

$$X(t) = \sum_{i=1}^{p} A(i)X(t-i) + E(t) \quad (1)$$

Where p is model order and E(t) is random white noise. By taking Fourier transform from the equation (1) we obtain:

$$X(f) = A^{-1}(f)E(f) = H(f)E(f) \quad (2)$$

Where the H(f) denotes the transfer matrix of the system. The DTF score from channel j to i, showing flow of information is defined by[17]

$$\Theta(f)_{ij}^{2} = H_{ij}(f)^{2} \quad (3)$$

The normalized DTF is described as below[17]

$$DTF(f)^{2}_{j\rightarrow i} = \frac{|H_{ij}(f)|^{2}}{\sum_{m=1}^{k} |H_{im}(f)|^{2}} \quad (4)$$

Inversing the matrix A, leads to represent the cascade causal interaction between channels. Additionally, the way which DTF is normalized makes it hard to interpret the connectivity score between different frequencies. So, the modified version of DTF, called direct directed transfer function (dDTF) is introduced[18]:

$$dDTF(f)^{2}_{j\rightarrow i} = F^{2}_{ij}(f)C_{ij}^{2}(f) \quad (5)$$

Where

$$F^{2}_{ij}(f) = \frac{|H_{ij}(f)|^{2}}{\sum_{f}\sum_{m=1}^{k} |H_{im}(f)|^{2}} \quad (6)$$

$C_{ij}^{2}(f)$ is Partial coherence which is close to 1 when the relation between channels is direct. dDTF shows non-zero values only if there is a phase difference between channels. Since volume conduction does not make a phase difference between channels, dDTF is considered to be robust to volume conduction effect[14].

C. Data Processing

The first 15 minutes of EEG recording were chosen for processing. Data processing was performed by EEGLAB[19]. Since dDTF is said to be "robust to volume conduction effect"[14], it is commonly said that do not use ICA decomposition for eye artifact removal or other artifacts[14]. About 2 minutes after starting hypnosis induction, subjects were told to close their eyes. So, first 2 minutes of EEG signals were discarded. A band-pass 1-45 Hz filter were applied to EEG signals. All the EEG was visually observed and remaining noisy segment was removed. Data were divided into five segments (each segment was 2.5 minutes) Because of the non-stationary nature of EEG, it has been divided into 5-second segments with 50% overlap and then MVAR model was fitted to signal. MVAR model was fitted using Vieira-Morf algorithm[20], which seems to give a better model when the data points are not much. Model order was chosen using Schwartz Bayesian Criterion (SBC). All the model orders were found to be between 11 and 13. dDTF algorithms were applied to data using SIFT plugins[21]. dDTF were computed between 1-45 Hz. Connectivity matrix is 4-dimensional (channel*channel*frequency*time). Hence, all connectivity matrixes were integrated over time and then averaged over different frequency bands.

D. Statistical Testing

We hypothesize that at the end of hypnosis induction, subjects are at the final hypnotic depth. So, at the end of hypnosis induction, hypnotic depth is greater than the beginning of induction. In order to find the relation between hypnosis depth and effective connectivity patterns, paired sample t-test was carried out (pvalue < 0.01). Also, to obtain remarkable changes in effective connectivity between channels in different groups of hypnotizability, analysis of variance (ANOVA) was performed. Statistical significance was chosen at $\alpha = 0.05$. ANOVA only shows a difference between means of various groups. Hence, t-test was carried out to reveal the difference between different group pairs.

II. RESULTS

In the first step of this study, changes in effective connectivity patterns were investigated at the beginning and end of hypnosis induction. Paired sample t-test was used in order to find significant changes in different frequency bands. Significance level was considered to be 0.01. Figure1 shows the results of connectivity alterations during hypnosis induction. As can be seen in Fig.1 effective connectivity did not change at the subjects' final hypnosis depth compared to

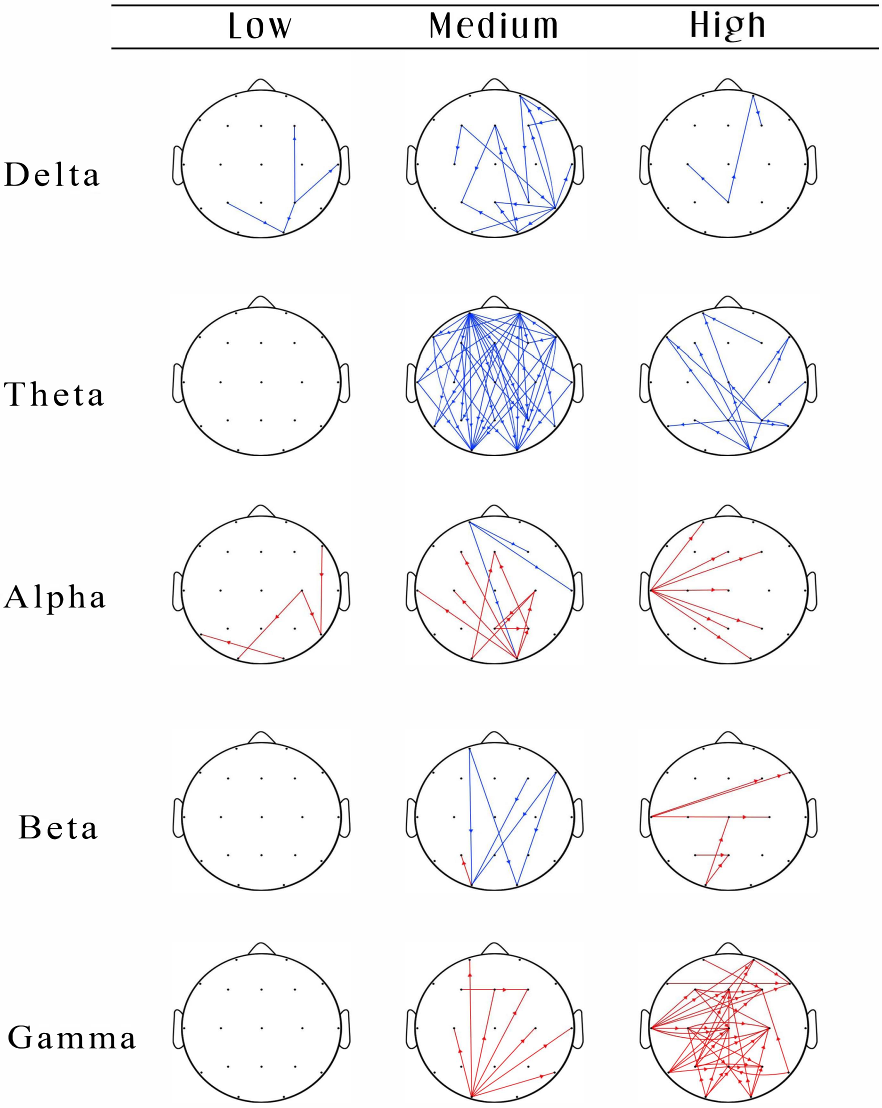

Figure 1 Effective connectivity changes at the end of hypnosis induction with respect to beginning of hypnosis induction. Only results with pvalue < 0.01 is reported. Red line indicates increase in connectivity score and blue line indicate decrease in connectivity. Head plot with no line represents there was no difference in effective connectivity

beginning of hypnosis procedure in theta, beta and gamma frequency bands. Also changes in effective connectivity scores in delta and alpha frequency bands were limited to a few channels in both cases. For medium hypnotizable group, reduction in effective connectivity values was seen in delta, theta and beta frequency bands, while an increase in dDTF scores was observed in alpha and gamma bands in which the changes were occurred from occipital to central and frontal channels. It can be observed in Fig.1 that in high hypnotizable subjects, effective connectivity patterns was lower at the end of hypnosis induction in low frequency bands, whereas in higher EEG frequency bands dDTF scores were higher remarkably.

In the second step of study, effective connectivity changes were investigated between different hypnotizable groups. ANOVA statistical testing were used to find any significant differences between hypnotizable subjects. Statistical significance was considered where pvalue < 0.05. Various frequency bands were examined in order to find significant connection between EEG channels. As finding the level of hypnotizability in the early stages of hypnosis induction was our concern, channels, which could distinguish between three hypnotizable groups or at least distinguish between high versus medium and low groups are listed in table1. In the beginning of hypnosis induction Information flow from O2 to P4 were found to be significant in all frequency bands. Moreover, we were interested in the connectivity scores

Table 1. Pair channels which could differentiate between high and medium versus low hypnotizable group

Source channel	Sink channel	Pvalue	Mean ± variance (low)	Mean ± variance (medium)	Mean +± variance (medium)	Frequency band
Pz	T7	0.0250	0.0164±0.0044	0.0184±0.0033	0.0216±0.0035	delta
O2	P4	0.0385	0.0150±0.0058	0.0235±0.0068	0.0259±0.0089	delta
O2	P4	0.0269	0.0102±0.0047	0.0205±0.0081	0.0210±0.0075	theta
O2	P4	0.0130	0.0038±0.0025	0.0098±0.0035	0.0066±0.0022	beta

between channels, which could distinguish between three hypnotizable groups or at least between low group and medium and high groups. As it can be seen in table1, there were not channels to satisfy our purpose in alpha frequency bands. In beta frequency band, statistical testing results show that information flow in the medium susceptible group was significantly greater than high and low hypnotizable groups. The most significant differences between the connectivity scores of channels were found in middle stages of hypnosis induction (7 to 12 minutes after beginning of hypnosis procedure) of hypnosis induction. In both delta and theta frequency band, 140 pair channels (out of 342) had remarkable different connectivity scores. In 4th segment of hypnosis induction outflow from channel F7 to other 18 channels was significantly greater than medium and high hypnotizable groups.

III. Disscussion

Paired sample t-test demonstrated that for high hypnotizable subjects, effective connectivity in delta and theta frequency bands reduced at the end of hypnosis induction. Instead, in alpha, beta and theta frequency bands, an increase was seen in effective connectivity between channels. Effective connectivity patterns for low hypnotizable subjects did not change is theta, beta and gamma frequency bands. In addition, differences in delta and alpha frequency bands were limited to only four pair channels in each case. The most significant changes in the effective connectivity scores were found in the theta frequency band for medium hypnotizable subjects where connections from frontal and prefrontal areas to occipital, temporal and parietal areas were reduced. Results also showed that as subjects reach to their final hypnosis depth, casual interaction in higher frequency bands increases. ANOVA statistical testing between different hypnotizable subjects showed that effective connectivity between channels in delta and theta frequency bands can distinguish between low, medium and high groups. Effective connectivity in the beta frequency band in medium hypnotizable subject was significantly higher than low and high hypnotizable subjects. Most differences between different groups of hypnotizability were found in third and fourth segment of hypnosis induction.

Baghdadi et al[6] showed that in high hypnotizable subjects, phase synchronization is less than medium and low ones. They found 22 channels in high hypnotizable subjects in delta band, which had less phase synchronization than medium and low susceptible subjects. Note that these channels were at the last three minutes of hypnosis induction while based on our finding, the most significant differences were seen in the middle stage of induction. Furthermore, effective connectivity patterns could distinguish between high and medium hypnosis susceptible versus low ones.

This study was performed at the sensor level. Based on these results, a simple and economic software system could design in order to give the physician useful and usable information about the hypnotizability of a patient. Physician could use effective connectivity between specified channels to find if the subjects have really reached to his final hypnotic depth or not. As it is reported that high hypnotizable subject would better respond to hypnosis treatment with respect to medium and low ones, physician could find hypnotizability of a subject at early stages of hypnosis induction. Other advantages of our finding are that the system could implement using a few channels, so the cost of maintenance and repairmen would dramatically decrease.

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