 DOI:10.3217/978-3-85125-378-8-75

Detecting Brain Network Changes Induced by a Neurofeedback-based Training for Memory Function Rehabilitation After Stroke

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Abstract

The efficacy of rehabilitative interventions in stroke patients is routinely assessed by means of a neuropsychological test battery. Nowadays, more evidences indicate that the neuroplasticity which occurs after stroke can be better understood by investigating changes in brain networks. In this pilot study we applied advanced methodologies for effective connectivity estimation in combination with graph theory approach, to define EEG derived descriptors of brain networks underlying memory tasks. In particular, we proposed such descriptors to identify substrates of efficacy of a Brain-Computer Interface (BCI) controlled neurofeedback-based intervention to improve cognitive function after stroke. EEG data were collected from two stroke patients before and after a neurofeedback-based training for working memory deficits. We show that the estimated brain connectivity indices were sensitive to different training intervention outcomes, thus suggesting an effective support to the neuropsychological assessment in the evaluation of the changes induced by the BCI-based rehabilitative intervention.

1 Introduction

In the post-stroke subacute time frame, the estimated proportion of patients having cognitive impairment ranges from below 50% to over 90%. Currently, the diagnosis of cognitive impairments after stroke and their treatment efficacy relies upon a neuropsychological assessment battery. Nowadays, evidences form neuroimaging studies indicate that the neuroplasticity which occurs after stroke might be better understood by investigating changes in brain networks (Cramer et al., 2011).

In this study we proposed the application of advanced methodologies for effective connectivity estimation (Milde et al., 2010), combined with a graph theoretical approach (Astolfi et al., 2013) to extract indices describing the topology of the brain networks as derived from EEG signals. The aim was to seek for neurophysiological descriptors which could serve as a sensitive outcome measures and thus, support the neuropsychological assessment in evaluating the efficacy of a Brain-Computer Interface controlled neurofeedback training to promote recovery of memory function after stroke. As such the BCI-controlled neurofeedback training module has been implemented within the EU funded project CONTRAST (www.contrast-project.eu) which is currently deploying a Brain Neural Computer Interface based technology to provide cognitive training modules to improve cognitive rehabilitation outcomes in institutionalized and at home stroke patients.

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2 Material and Methods

2.1 Experimental Design

Two representative stroke patients (Patient A, female, 70 years old; right hemisphere stroke lesion and Patient B, male, 20 years old, left hemisphere stroke) were selected among those currently enrolled in a neurofeedback-based intervention protocol implemented in BCI close loop to target post-stroke memory disorders. According to the pilot study purpose, the selection of 2 "representative" patients was solely based on their response to the training experimental intervention. The adopted protocol consisted of 10 training sessions in which the patients were instructed to voluntarily increase their sensorymotor rhythm (SMRs; 12-15 Hz; Kober et al., 2014) amplitude over an established threshold. Each time the SMR amplitude exceeded the threshold for ≥ 250 ms, the participant was rewarded by gaining points. The threshold was automatically adapted after each run on the basis of all previous runs. Cz was used as feedback electrode; each training session lasted 25' (3 min baseline; 6 feedback runs, 3-min each). The acquisition and the real time feedback were implemented in Biotrace software for Nexus10 (Mind Media).

Before (PRE) and after (POST) the neurofeedback based intervention, EEG scalp signals were recorded (64 channels; Brain products, 200Hz sampling frequency) while patients were performing the Sternberg memory task. The Sternberg paradigm task consists of 3 phases Encoding, Storage and Retrieval during which a series of numbers have to be memorized, retained and retrieved within a short time interval (Sternberg, 1966). Patient's declarative memory and the visuo-spatial short-term memory deficits were assessed before and after the training by means of the Rey Auditory Verbal Learning Test (RAVLT) and the Corsi Block Tapping Test (CBTT), respectively.

2.2 Effective Connectivity and Graph Theory

Partial Direced Coherence

The Partial Directed Coherence (PDC) is a full multivariate spectral measure used to determine the directed influences between any given pair of signals in a multivariate data set (Baccalá and Sameshima, 2001). In this work we applied an adaptive formulation of PDC based on a time varying multivariate autoregressive (MVAR) model, whose coefficients are estimated by means of Kalman filter (Milde et al., 2010).

Graph Theory Approach

A graph is a mathematical object consisting in a set of nodes linked by connections which represent the existence of interactions between the nodes. The structure of a graph is described by means of an adjacency matrix G whose entries are $G_{ij} = 1$ if the link exists, otherwise $G_{ij} = 0$. We considered two indices to describe the properties of the EEG derived patterns of effective connectivity: i) <u>Degree</u>, consisting in the number of links connected directly to a node and ii) <u>Anterior Density</u> defined as the number of connections exchanged between the electrodes located in the anterior part of the scalp. The sensitivity/specificity of these 2 indices in accounting for brain network characteristics during memory tasks was already validated in a previous study on healthy age-matched volunteers (Astolfi et al.2013).

Connectivity Analysis

PRE and POST EEG data were pre-processed (1-45Hz band-pass filter) and analysed at single subject level. Time-varying effective connectivity networks (Milde et al., 2010) were estimated for each memory phase and frequency band (defined according to Individual Alpha frequency) and the corresponding salient properties were derived by means of graph theory approach (Sporns et al., 2004). PRE and POST comparisons were performed to capture, at single subject level, the differences in connectivity networks and in graph indexes associated to them. In particular, an independent sample t-test was applied for a significance level of 5% corrected by means of False Discovery Rate for preventing type I errors.

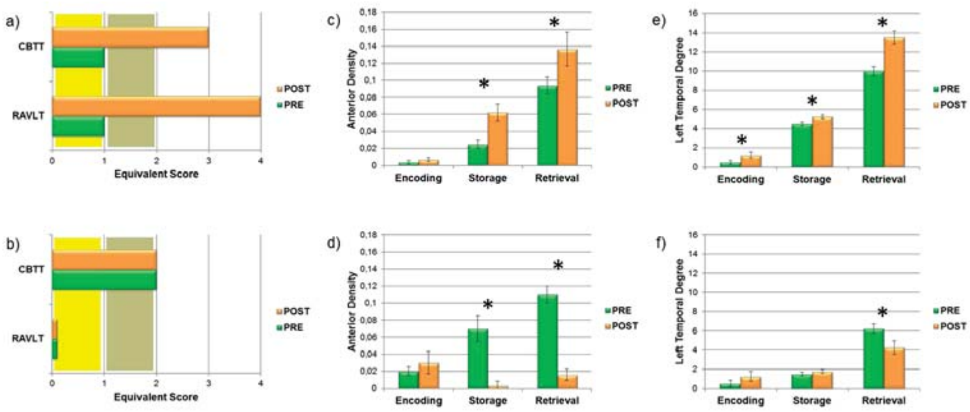

Figure 1: a-b) Bar diagrams reporting the equivalent scores achieved for RAVLT and CBTT tests administered to patient A (panel a) and B (panel b) before (PRE, green bars) and after (POST, orange bars) the SMR training. Equivalent scores below 2 (in yellow) highlight a pathological condition. c-f) Anterior Density and Left Temporal Degree indexes estimated in alpha band in PRE (green bars) and POST (orange bars) sessions relative to the two stroke patients A (panels c and e) and B (panels d and f). The symbol (*) denotes a significance difference between PRE and POST session scores (unpaired t-test; $p<0.05$).

3 Results

3.1 Patient A

The Patient A was able to learn the modulation of her SMR as indicated by the increase of SMR amplitude from 7.7 μV^2 to 8.4 μV^2 across the 10 training sessions.

Memory Assessment. As reported in Fig.1a, the neuropsychological tests revealed a significant improvement of the tested memory function after the neurofeedback-based training. Equivalent scores for both CBTT and RAVLT tests increased from 1 to 3 and 4 respectively, thus indicating a transition from a pathological (PRE) to a physiological (POST) condition.

Behavioral Data. Analysis of the behavioral performance obtained at the Sternberg task revealed an increase of correct answers and a significant decrease (df=68, t=2.16, p=0.034) of the reaction time after training (PRE-POST comparison, unpaired t-test).

EEG derived Brain Network. Analysis of the connectivity patterns revealed a significant POST training increase of Anterior Density index (Fig.1c) estimated in the alpha band only for Storage (df=198, t=2.87, p=0.0045) and Retrieval (df=198, t=3.97, p=0.0001) phases of the Sternberg task associated with an increase of Left Temporal Degree index (Fig.1e) in alpha band for all the three memory phases (Encoding (df=198, t=1.99, p=0.048), Storage (df=198, t=2.08, p=0.039) and Retrieval (df=198, t=3.05, p=0.0026)).

3.2 Patient B

The Patient B did not show changes in the amplitude of his SMR across the 10 training sessions. The amplitude value remained stable around 2.3 μV^2.

Memory Assessment. In this Patient (Fig.1b) we did not find significant changes in the memory functions as evaluated by means of neuropsychological assessment. Equivalent scores for both RAVLT and CBTT tests remained around 1 and 2 respectively, indicating a persistency of the pathological profile.

Behavioral Data. Similar negative outcome was found for the behavioral assessment. Data analysis revealed a decrease of the percentage of correct answers and no significant difference (df=68, t=0.76, p=0.46) in reaction time between PRE and POST sessions of Sternberg task (unpaired t-test).

EEG derived Brain Network. Connectivity pattern analysis revealed in Patient B an opposite profile of changes in the POST training analysis with resect to what observed in Patient A. In fact, a significant decrease in the Anterior Density index (Fig.1d) for Storage (df=198, t=3.07, p=0.0024) and Retrieval (df=198, t=2.11, p=0.036) phases and of Left Temporal Degree index (Fig.1f) for the Retrieval (df=198, t=2.01, p=0.046) memory phase both estimated in the alpha band, were observed.

4 Discussion and Conclusion

The preliminary findings obtained in this pilot study indicated that the estimated brain connectivity indices were sensitive to different response (outcome) to the BCI-controlled neurofeedback training. In particular, for both *representative* patients the changes observed in the Anterior Density index and the Left Temporal Degree indices between PRE and POST training assessment were in agreement with Sternberg behavioral changes (Sternberg, 1966; Astolfi et al., 2013) and even more interesting, with the outcome of neuropsychological tests of memory function.

Validation in a proper sampled study is currently in progress within the EU CONTRAST project. If these preliminary findings will be confirmed, estimation of the brain networks derived from a non-invasive, cost/effective EEG technique would provide a solid evidence for clinical application of such methodology to empower a quantitative outcome measurement of novel post-stroke rehabilitation strategy aiming at promoting cognitive functional improvement after stroke.

5 Acknowledgment

Research supported by the European ICT Program FP7-ICT-2009-4 Grant Agreement 287320 CONTRAST.

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