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Aberrant EEG functional connectivity and EEG power spectra in resting state post-traumatic stress disorder: A sLORETA study

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ABSTRACT

The aim of the present study was to explore the modifications of EEG power spectra and EEG connectivity of resting state (RS) condition in patients with post-traumatic stress disorder (PTSD). Seventeen patients and seventeen healthy subjects matched for age and gender were enrolled. EEG was recorded during 5 min of RS. EEG analysis was conducted by means of the standardized Low Resolution Electric Tomography software (sLORETA). In power spectra analysis PTSD patients showed a widespread increase of theta activity (4.5–7.5 Hz) in parietal lobes (Brodmann Area, BA 7, 4, 5, 40) and in frontal lobes (BA 6). In the connectivity analysis PTSD patients also showed increase of alpha connectivity (8–12.5 Hz) between the cortical areas explored by Pz-P4 electrode. Our results could reflect the alteration of memory systems and emotional processing consistently altered in PTSD patients.

1. Introduction

Post-traumatic stress disorder (PTSD) is a severe and disabling psychiatric condition characterized by three cluster symptoms which may develop after the exposure to one or more traumatic events: persistent trauma re-living, cognitive and behavioural avoidance and hyperarousal symptoms (APA, 2000; Klimesch, Sauseng, & Hanslmayr, 2007).

The neurobiology of PTSD is characterized by alterations concerning different brain areas (e.g. limbic system, prefrontal cortex) and different neurotransmitter systems (e.g. catecholamine) (for a review see Pitman et al., 2012). Furthermore, recent studies (Bluhm et al., 2009; Cook, Ciorciari, Varker, & Devilly, 2009; Lanius et al., 2010; Lee, Yoon, Kim, Jin, & Chung, 2014; Sripada, King, Garfinkel, et al., 2012; Sripada, King, Welsh, et al., 2012; Yin et al., 2011) documented in PTSD patients and in subjects with a history of trauma alterations in the functional integration between brain areas, a neurophysiological index called "functional connectivity". This measure refers to the temporal synchrony or association between signals of two or more spatially separated regions (Fingelkurts & Kahkonen, 2005; Schoffelen & Gross, 2009).

Using fMRI, Sripada and coworkers reported an increase of functional connectivity in the amygdala (Sripada, King, Garfinkel, et al., 2012a) and the hippocampus (Sripada, King, Welsh, et al., 2012b) of PTSD patients; this could reflect the dominance of threat-sensitive circuitry in PTSD, even in resting-state conditions (Sripada, King, Welsh, et al., 2012b). Abnormal functional connectivity in hippocampal network was also observed by Chen and Etkin (2013) who detected this alteration in PTSD patients when compared to Generalized Anxiety Disorder individuals.

Although fMRI is widely used to investigate brain functional connectivity, EEG is suitable to assess instantaneous and lagged synchronization across a wider frequency range, because EEG time-series data directly relate to dynamic postsynaptic activity in the cerebral cortex with a higher temporal resolution (Canuet et al., 2011). Conversely, MR-based methods cannot asses fast-frequency synchronized neuronal activity (Razavi et al., 2013). Finally, the EEG offers a potentially valuable "*source of information for researchers and clinicians, since it assesses real-time electrical activity in the brain and is overall a less costly, time-consuming, and complex procedure*" (Todder et al., 2012, p. 49). On the other hand, EEG suffers the problem of volume conduction or common sources, which gives rise to spurious correlations between time series recorded from nearby

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electrode (Stam, Nolte, & Daffertshofer, 2007). This problem can be solved by using specific algorithms for the identification of signal sources and for the evaluation of functional connectivity (Pascual-Marqui, Michel, & Lehmann, 1994).

Up to now, only few studies have investigated functional connectivity in PTSD using EEG. Cook et al. (2009) reported that, when compared to control subjects, adults with childhood trauma had significantly higher EEG coherence in the alpha and beta frequency bands over the left temporo-parietal areas and in the right central and temporal areas, respectively. Sponheim et al. (2011), in a sample of soldiers with mild traumatic brain injury, detected that PTSD patients had higher frontal functional connectivity, especially in low frequency bands (delta, theta, alpha, beta1), than those without PTSD.

Moreover, in a recent network analysis study, Lee et al. (2014) observed that, compared to control subjects, PTSD patients had lower strength and efficacy connections between frontal and central areas, particularly in beta and gamma frequency bands.

As concerns EEG power spectra in PTSD few studies are available. Begic, Hotujac, and Jokic-Begic (2001) reported that un-medicated PTSD, compared to healthy subjects, showed an increase of theta power over the central brain regions, and an increase of beta activity over the frontal, central, and occipital brain regions. The increase of beta power was also replicated by the same authors (Jokic-Begic & Begic, 2003) comparing veterans with PTSD and veterans without PTSD. Todder et al. (2012) also observed that compared to control subjects, PTSD individuals have lower activity on the "low" theta band (4–5 Hz), mainly over the right temporal lobe and on the "high" theta band (6–7 Hz), over both the right and left frontal lobes.

The aim of the present study was to explore the modifications of EEG functional connectivity and scalp EEG power spectra in PTSD patients during resting state (RS) condition. The integration of these parameters contributes to the understanding of EEG correlates of mental disorders (Ford, Goethe, & Dekker, 1986). In order to detect modifications of EEG frequencies, especially their topographic distribution, we used the standardized Low Resolution brain Electric Tomography software (sLORETA), a validated method for localizing the electric activity in the brain based on multichannel surface EEG recordings (Pascual-Marqui et al., 1994). sLORETA has the benefit of superior time resolution of EEG measurements of milliseconds, which is 3-fold better than that of fMRI, with spatial resolution of approximately 7 mm, which is similar to that of fMRI (Grech et al., 2008; Stern et al., 2009). Furthermore, sLORETA benefits from an excellent localization agreement with different multimodal imaging technique (Dumpelmann, Ball, & Schulze-Bonhage, 2012; Pizzagalli et al., 2004; Vitacco, Brandeis, Pascual-Marqui, & Martin, 2002), also when standard 19-electrodes EEG montage was used (Cannon, Kerson, & Hampshire, 2011; Ridder, Vanneste, Kovacs, Sunaert, & Dom, 2011; Horacek et al., 2007; Muller et al., 2005). Finally, comparing with similar technique (i.e. LORETA), sLORETA gives the best performance both in terms of localization error and ghost sources (Grech, et al., 2008).

2. Materials and methods

2.1. Participants

Seventeen un-medicated patients with PTSD (seven men and ten women, aged 22–57 years mean age: 38.12 ± 10.42) who referred to a specialized trauma centre for treatment of trauma-related psychological disorders were enrolled. All patients received a complete psychiatric interview performed by a trained psychiatrist (BF), and were diagnosed according to the DSM-IV TR criteria (APA, 2000). No psychiatric comorbidities with Axis I and II DSM-IV disorders were observed. In order to exclude any neurological complications all participants also received a complete neurological examination performed by a trained neurologist (GDM). When head injury was suspected a neuroradiological evaluation (brain CT or MRI) was performed.

Table 1
Demographic data and the traumatic events of PTSD patients.

	Age	Sex	Traumatic event
1	55	M	Gun aggression
2	22	M	Family murdered
3	24	F	Rape
4	36	M	Car accident
5	42	F	Car accident
6	28	F	Rape
7	29	M	Fire victim
8	48	F	Physical aggression
9	33	F	Rape
10	42	F	Car accident
11	47	F	Gun aggression
12	25	M	Fire victim
13	43	M	Gun aggression
14	38	F	Rape
15	42	F	Physical aggression
16	37	M	Car accident
16	57	F	Physical aggression

Note: PTSD, post-traumatic stress disorder.

The demographic data and the traumatic events of PTSD patients enrolled in the study are listed in Table 1. A control group of healthy subjects (with no Axis I and II DSM-IV diagnosis) matched for age and gender was also included (seven men and ten women, aged 20–58 years mean age: 37.94 ± 10.32). Exclusion criteria were: left handedness; history of medical, neurologic diseases; psychiatric comorbidity; head trauma; assumption of Central Nervous System active drugs in the 3 weeks before the study; presence of EEG abnormalities at the baseline recording.

The research was approved by a human experimentation ethics committee. After receiving information about the aims of the study, all participants gave their written consent.

2.2. EEG recordings

RS recordings were performed in an EEG Lab, with each subject sitting in a comfortable armchair, with his/her eyes closed, in a quiet, semi-darkened silent room for 5 min.

EEG was recorded by means of a Micromed System Plus digital EEGraph (Micromed© S.p.A., Mogliano Veneto, TV, Italy). EEG montage included 19 standard scalp leads positioned according to the 10–20 system (recording sites: Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2), EOG and EKG. The reference electrodes were placed on the linked mastoids. Impedances were kept below 5 KΩ before starting the recording and checked again at the end of the experimental recording. In particular, impedances of the mastoids reference electrodes were checked to be identical. Sampling frequency was 256 Hz; A/D conversion was made at 16 bit; pre-amplifiers amplitude range was ±3200 μV and low-frequency pre-filters were set at 0.15 Hz.

Artefact rejection (eye movements, blinks, muscular activations, or movement artefacts) was performed on the raw EEG trace, by positioning a marker at the onset of the artefact signal and a further marker at the end of the artefact. Successively, the artefact segment (that is, the EEG signal interval included between the two markers) was deleted. In this way, all the EEG intervals characterized by the presence of artefacts were excluded from the analysis.

After artefact rejection, the remaining EEG intervals were exported into American Standard Code for Information Interchange (ASCII) files, and imported into the sLORETA software. At least 120 s of EEG artefact-free recording (not necessarily consecutive) were analyzed for each subject. The average time analyzed was 193 ± 21 s and 198 ± 18 s respectively for PTSD and control group. All EEG analysis was performed by means of the sLORETA software (Pascual-Marqui et al., 1994).

2.3. Frequency analysis

EEG frequency analysis was performed by means of a Fast Fourier Transform algorithm, with a 2 s interval on the EEG signal, in all scalp locations. The following frequency bands were considered: delta (0.5–4 Hz); theta (4.5–7.5 Hz); alpha (8–12.5 Hz); beta (13–30 Hz); gamma (30.5–60 Hz). For frequency analysis, monopolar EEG traces (each electrode referred to joint mastoids) were used. Topographic sources of EEG activities were determined using the sLORETA software. The sLORETA software computes the current distribution throughout the brain volume. In order to find a solution for the three-dimensional distribution of the EEG signal, the sLORETA method assumes that neighbouring neurons are simultaneously and synchronously activated. This assumption rests on evidence from single cell recordings in the brain that shows strong synchronization of adjacent neurons (Kreiter & Singer, 1992; Murphy, Blatter, Wier, & Baraban, 1992). The computational task is to select the smoothest three-dimensional current distribution, a common procedure in signal processing (Grave de Peralta-Menendez and Gonzalez-Andino, 1998; Grave de Peralta Menendez, Gonzalez Andino, Morand, Michel, & Landis, 2000. The