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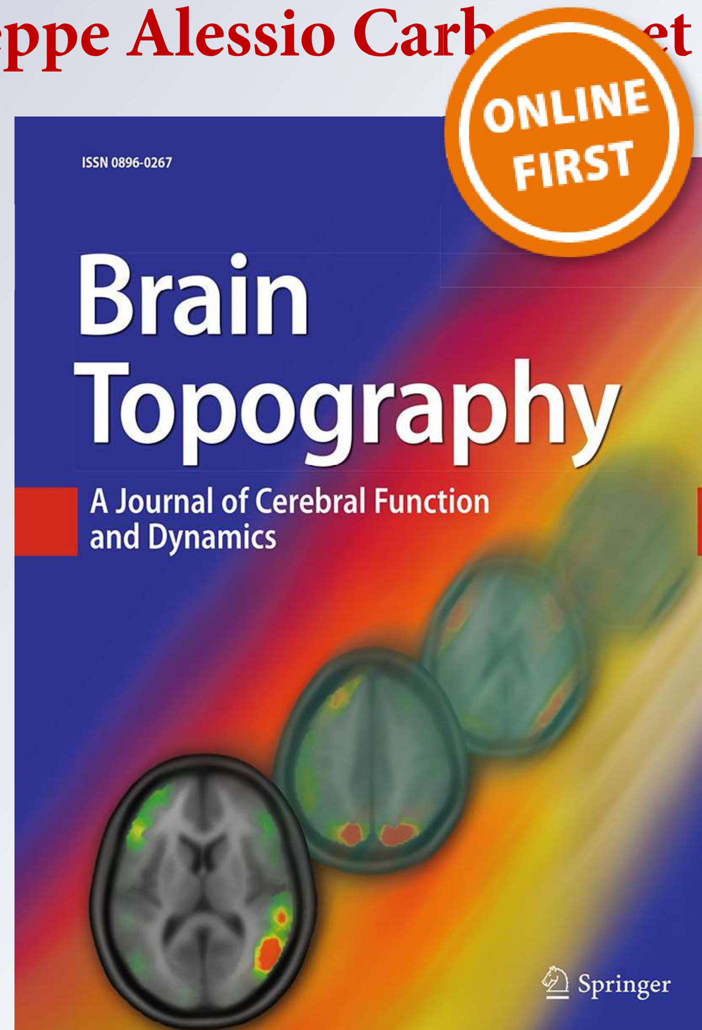

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ORIGINAL PAPER

Alpha/Theta Neurofeedback Increases Mentalization and Default Mode Network Connectivity in a Non-Clinical Sample

Claudio Imperatori[1] · Giacomo Della Marca[2] · Noemi Amoroso[1] · Giulia Maestoso[1] · Enrico Maria Valenti[1] · Chiara Massullo[1] · Giuseppe Alessio Carbone[1] · Anna Contardi[1] · Benedetto Farina[1]

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Abstract Several studies showed the effectiveness of alpha/theta (A/T) neurofeedback training in treating some psychiatric conditions. Despite the evidence of A/T effectiveness, the psychological and neurobiological bases of its effects is still unclear. The aim of the present study was to explore the usefulness of the A/T training in increasing mentalization in a non-clinical sample. The modifications of electroencephalographic (EEG) functional connectivity in Default Mode Network (DMN) associated with A/T training were also investigated. Forty-four subjects were enrolled in the study and randomly assigned to receive ten sessions of A/T training [neurofeedback group (NFG) = 22], or to act as controls [waiting list group (WLG) = 22]. All participants were administered the mentalization questionnaire (MZQ) and the Symptom Checklist-90-Revised (SCL-90-R). In the post training assessment, compared to WLG, NFG showed a significant increase of MZQ total scores (3.94 ± 0.73 vs. 3.53 ± 0.77; $F_{1;43} = 8.19$; $p = 0.007$; $d = 0.863$). Furthermore, A/T training was also associated with a significant increase of EEG functional connectivity in several DMN brain areas (e.g. Posterior Cingulate Cortex). Taken together our results support the usefulness of the A/T training in enhancing mentalization and DMN connectivity.

Keywords EEG-neurofeedback · Alpha/theta training · Mentalization · Default mode network · EEG functional connectivity · eLORETA

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Introduction

Neuromodulation techniques are increasingly investigated as potential therapeutics in clinical practise (Gevensleben et al. 2014). Contrary to 'exogenous' neuromodulation techniques (i.e., deep brain stimulation) electroencephalographic-based neurofeedback (EEG-NF) training is a method used to modulate cortical activity leading to "neuronal changes caused by the patient's activity" (Gevensleben et al. 2014, p. 20). It is based on operant conditioning "where through immediate feedback the participant learns to self-regulate their neurophysiology" (Gruzelier 2014, p. 143). Within EEG-NF training, alpha/theta (A/T) training has been one of the most widely studied in the last three decades (Egner et al. 2002). The aim of this training is to raise posterior theta (4.5–7.5 Hz) over alpha (8–12.5 Hz) amplitude with eyes closed, without falling asleep, in order to produce "a state of deep relaxation, resembling a meditative or quasi hypnagogic state" (Egner et al. 2002, p. 262).

Several studies showed the effectiveness of A/T training in treating some psychiatric conditions. This NF training was originally introduced in order to improve standard therapy approaches in substance-related and addictive disorders (Trudeau 2005). Peniston and Kulkosky (1989), in the first randomized and controlled study, reported that compared to a non-alcoholic control group and a traditionally treated alcoholic control group, patients receiving fifteen 30-min sessions of A/T NF showed significant modifications in resting EEG parameters (e.g., increased alpha rhythm amplitudes) as well as significant decrease in self-reported depressive symptoms. NF was also associated with a sustained prevention of relapse at 13 months follow-up (Peniston and Kulkosky 1989). Similar results were obtained in patients with history of chronic alcohol abuse and depression (Saxby and Peniston 1995).

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Peniston and Kulkosky (1991) also showed that compared to traditional medical treatment, thirty 30-min sessions of A/T training were related to a significant decrease in 13 scales of the Minnesota Multiphasic Personality Inventory (MMPI) (e.g., depression, psychastenia) as well as a sustained prevention of relapse in veterans with post-traumatic stress disorder.

More recently, A/T training has been consistently employed in the treatment of patients with substance use disorder (for a review see Sokhadze et al. 2008). For example, Scott et al. (2005) investigated the usefulness of NF (i.e., beta and sensorymotor training followed by A/T training) in a mixed substance abusing sample, and reported a decrease in 5 of the 10 MMPI scales (e.g., depression, social introversion) after A/T training. Moreover, Dehghani-Arani et al. (2010, 2013) showed the effectiveness of NF (i.e., sensorymotor training followed by A/T training) in reducing drug craving and psychopathology in opioid-dependent patients.

The usefulness of A/T training has been also widely investigated in non-clinical samples. For example, several studies showed the association between A/T NF and the enhancement of music and artistic performance (for a review see Gruzelier 2009, 2014). Furthermore, it has been reported (Raymond et al. 2005) that, compared to a control treatment (i.e., mock feedback), twenty 20-min sessions of real A/T NF were related to a significant increase of participants' moods (e.g., participants felt significantly more energetic and less depressed). Finally, it has been recently observed (Imperatori et al. 2017) that ten 27-min sessions of this training were associated with a significant decrease in self-reported food craving severity as well as a significant modifications in resting EEG parameters (e.g., increased alpha power in brain areas involved in food craving and food cue reactivity).

Despite the evidence of A/T effectiveness, the psychological and neurobiological bases of its effects is still unclear (Raymond et al. 2005). Different explanations have been proposed to account for A/T's mechanisms of action. It has been proposed (Boynton 2001; Dehghani-Arani et al. 2013; Gruzelier 2014; Imperatori et al. 2017) that the deep relaxation associated with A/T training enhances well-being, the ability to better tolerate stress as well as emotional self-awareness. It has also been proposed that the neurophysiological substrates of the A/T training could be represented by an increase of functional connectivity in cortical networks, especially between anterior and posterior areas (Gruzelier 2009).

All these features are closely related to the construct of mentalization, which can be theorized as the ability to understand inner mental states in oneself and others, including the ability to think about thoughts, emotions, wishes, desires, and needs (Fonagy and Bateman 2008; Fonagy et al. 2002). From a neurophysiological point of view, mentalization is considered to be associated with the dynamic activity of large neural networks (Ciaramidaro et al. 2007; Denny et al. 2012; Gaillard et al. 2009; Tononi and Koch 2008), especially the default mode network (DMN) (Lombardo et al. 2010; Mars et al. 2012), which reflect the neural activity of resting brain characterized by high degree of functional connectivity between regions (Knyazev 2013).

To the best of our knowledge, no studies have investigated the potential role of A/T training in increasing mentalization ability. Therefore, the main aim of the present study was to explore the usefulness of the A/T training in enhancing mentalization in a non-clinical population. Furthermore, we also investigated the modifications of EEG functional connectivity in DMN associated with A/T training. We hypothesized that: (i) A/T training would be associated with an increase of mentalization ability and (ii) A/T training would be associated with an increase of EEG DMN functional connectivity.

Materials and Methods

Participants

Participants were recruited from the European University of Rome through advertisements posted in the university. Participants contributed voluntarily and anonymously after providing informed consent. They did not receive payment or any other compensation (i.e., academic credit).

The enrollment lasted from January 2016 to July 2016. Inclusion criteria were: age between 18 and 40 years, both genders. Exclusion criteria were: history of medical, psychiatric and/or neurologic diseases; head trauma; assumption of Central Nervous System active drugs in the 2 weeks prior to assessment (pre and post assessment). A checklist with dichotomous items was used to assess inclusion criteria and exclusion criteria.

Fifty-nine respondents were assessed for eligibility. Forty-four individuals fulfilling the inclusion criteria were enrolled in the present study (10 men and 34 women, mean age: 22.73 ± 2.32 years).

After receiving information about the aims of the study (in order to avoid the participants' awareness of the experimenters' hypotheses, we did not reveal to the participants any hypotheses regarding the possible benefits of A/T training on mentalization), all subjects provided written consent to participate in the study that was performed according to the Helsinki declaration standards of 1975, as revised in 2008, and was approved by the European University's ethics review board.

Study Design and Procedures

Pre-treatment Phase (T0)

After giving written informed consent, all participants were administered the mentalization questionnaire (MZQ; Hausberg et al. 2012) and the Symptom Checklist-90-Revised (SCL-90-R; Derogatis 1977). All participants also completed a checklist assessing socio-demographic (e.g., age, educational attainment) and clinical data (e.g., tobacco and alcohol use in the last six months). After the psychological assessment, all participants underwent a resting state (RS) EEG recording.

Neurofeedback Training (NFT)

According with a randomized, controlled study design, participants were randomly assigned to receive neurofeedback training [neurofeedback group (NFG) = 22], or to act as controls [waiting list group (WLG) = 22], with the constraint that the groups would be matched regarding sex. WLG participants did not receive any kind of allowance.

Post-treatment Phase (T1)

At the end of NFT, all participants (i.e., NFG and WLG) were asked to complete again the MZQ and the SCL-90-R and to perform another RS EEG recording.

Questionnaires

The Mentalization Questionnaire (MZQ) is a 15-item self-report scale measuring mentalization, the ability to represent and understand inner mental states in oneself and others (Hausberg et al. 2012). Respondents are asked to rate each item (e.g., "Sometimes I only become aware of my feelings in retrospect", "Often I don't even know what is happening inside of me") on a 5-point Likert scale, from "I disagree" to "I agree". In the original validation study (Hausberg et al. 2012) a confirmatory factor analysis supported a four-factor solution: (i) Refusing self-reflection, which reflects "avoidance of thinking about inner states or a categorical rejection of one's own feelings combined with fear of being overwhelmed by them" (Hausberg et al. 2012, p. 5); (ii) Emotional awareness, assessing the lack of perceiving and differentiating one's own inner states; (iii) Psychic equivalence mode, which reflects the tendency to equate inner mental states and outer reality so that everything appears to be real; (iv) Regulation of affect, which investigates the inability to modulate emotions. Lower scores on the MZQ denote more difficulties in mentalization. In the present study, the Italian version of the scale was used (Innamorati et al. 2015) and the Cronbach's alpha in the present sample was 0.87 for the total score.

The SCL-90-R (Derogatis 1977) is a 90-item questionnaire on 5-point Likert scale (0–4) widely used to assess psychopathology. It consist in nine primary symptom dimensions: somatization, obsessive–compulsive symptoms, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. Furthermore, seven additional items assess disturbances in appetite and sleep. The SCL-90-R also provides a global severity index (GSI) which is designed to measure overall psychological distress. Higher scores indicate more psychological symptoms in each subscale as well as a higher degree of distress, higher intensity of symptoms, and more self-reported symptoms (Sarno et al. 2011). In the present study, a previously validated Italian version of the scale was used (Sarno et al. 2011) and the Cronbach's alpha in the present sample was 0.89 for the GSI.

EEG Recordings and Functional Connectivity Analysis

RS recordings were performed in the European University 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. Participants were asked to refrain from drinking alcohol and caffeine for 4–6 h immediately before their EEG recordings.

Micromed System Plus digital EEGraph (Micromed© S.p.A., Mogliano Veneto, TV, Italy) has been used to perform EEG recordings, which 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 ECG. The reference electrodes were placed on the linked mastoids. Impedances were kept below 5KΩ before starting the recording and checked again at the end of the experimental recording. 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. The following band-pass filters were used: HFF = 0.2 Hz; LFF = 128 Hz.

Artifact rejection (eye movements, blinks, muscular activations, or movement artifacts) was performed visually on the raw EEG, by posing a marker at the onset of the artifact signal and a further marker at the end of the artifact. The recordings were attended by trained technicians, and the simultaneous recording of EOG and ECG further improved the artifact recognition and removal.

Successively, the artifact segment (i.e., the EEG signal interval included between the two markers) was deleted. In this way, all the EEG intervals characterized by the presence of artifacts were excluded from the analysis. After artifact rejection, the remaining EEG intervals were exported into American Standard Code for Information Interchange (ASCII) files, and imported into the exact Low Resolution

Electric Tomography software (eLORETA). More details on the artifact rejection procedure have been described elsewhere (Imperatori et al. 2013, 2014). The minimum length of the artifact-free EEG recording included in the analysis was 180 s (even if not consecutive) for each participant.

In the present study the following frequency bands have been 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).

All EEG analysis were performed by means of the eLORETA, a validated tool for localizing the electric activity in the brain based on multichannel surface EEG recordings (Pascual-Marqui et al. 1994).

Lagged phase synchronization index, which has been widely used to investigate electrophysiological connectivity in both psychiatric and neurological diseases (Canuet et al. 2011, 2012), was chosen to compute connectivity analysis. The eLORETA software computes lagged phase synchronization "ρ", by the formula (Pascual-Marqui et al. 2011):

$$\varphi^2 \mathrm{x,y}(\omega) = \frac{\{\mathrm{Im}\ [f_{x,y}(\omega)]\}^2}{1 - \{\mathrm{Re}\ [f_{x,y}(\omega)]\}^2}$$

Details on eLORETA lagged phase synchronization formula have been described elsewhere (Pascual-Marqui 2007; Pascual-Marqui et al. 2011).

In order to evaluate the association between mentalization, psychopathology and connectivity in the DMN, 12 Regions of Interest (ROIs) were defined according to Thatcher et al. (2014). These procedure has been recently used to investigate DMN alterations in alexithymia (Imperatori et al. 2016). According to Canuet et al. (2011) the 'single nearest voxel' option (i.e., each ROI consisted of a single voxel, the closest to each seed) was chosen. The 12 cortical ROIs determined by eLORETA are listed in Table 1. The eLORETA calculated the lagged phase synchronization values between all these ROIs (total $12 \times 12 = 144$ connections). Furthermore, the eLORETA performed the source reconstruction algorithm (Pascual-Marqui et al. 1994, 1995).

Table 1 Cortical 12 regions of interest (ROIs) Adapted from Thatcher et al. (2014)

ROI	MNI coordinates			Anatomical regions	Brodmann areas
	x	*y*	*z*		
1	−30	40	25	Left frontal lobe	8–9–10
2	20	35	30	Right frontal lobe	8–9–10
3	−45	−15	−25	Left temporal lobe	21–28–36
4	55	−15	−20	Right temporal lobe	21–28–36
5	−5	−5	35	Left posterior cingulate cortex	23–24
6	5	−10	30	Right posterior cingulate cortex	23–24
7	−5	30	20	Left anterior cingulate cortex	32
8	5	30	20	Right anterior cingulate cortex	32
9	−5	−55	25	Left hippocampus	29–30–31
10	5	−50	25	Right hippocampus	29–30–31
11	−45	−50	40	Left parietal lobe	39–40
12	45	−50	35	Right parietal lobe	39–40

ROI region of interest

Neurofeedback Training

According with previous NF studies in non-clinical samples (Schmidt and Martin 2015; Vernon 2005) ten neurofeedback sessions were chosen (each session lasted 27 min) for the NFG. ProComp5 Infiniti hardware and Biograph Infiniti software (Thought Technology Ltd, Montreal, Canada) were used for the neurofeedback sessions.

According to a recent NF study (Imperatori et al. 2017), the basic principles of A/T training were explained to participants during the first session: they were instructed to close their eyes, relax as deeply as possible, without falling asleep, and listen to the sound being played to them. Two distinct tones were used for alpha and theta reinforcement: (i) a "babbling brook" sound was heard when participants' alpha was higher than theta, and (ii) an "ocean waves" sound was heard when participants' theta was higher than alpha. The aim of the training was to increase of theta over alpha, to reach the "crossover", defined as "point at which the alpha amplitude dropped below the level of theta" (Dehghani-Arani et al. 2013, p. 136).

EEG-NF was only in audio format. The frequency bands connected to feedback were: Theta (4.5–7.5 Hz), associated with the sound of ocean waves, Alpha (8–12.5 Hz), associated with the sound of a stream's flow, and Delta (0.5–4 Hz), linked with a bell sound and aimed at preventing slippage in the first sleep phase (Dehghani-Arani et al. 2013; Scott et al. 2005). Beta frequency band was also recorded, but it was not connected to feedback.

According to Burns (2015), in the present study NF was set to automatically adjusting the reward threshold for alpha and theta amplitudes in real time in order to: (i) maximize rewards to encourage training (ii) slowly increase the level of difficulty. The Biograph Infiniti software computes the reward threshold by the formula:

$$\frac{Theta - Alpha}{Theta + Alpha}$$

Each A/T session started with the subject sitting in a comfortable chair with his/her eyes closed. According to Egner et al. (2002) the active electrode was placed on Pz referred to joint mastoids. The impedances were kept below 5 kΩ. Then, a 2-min guided imagery script was presented to the subjects, in order to elicit relaxation. After that, the A/T training has begun. According with Dehghani-Arani et al. (2013) individuals reporting previous meditative practices were asked not to use them during the training, because the association between meditation and A/T crossover has been previously reported (Scott et al. 2005). At the end of each session, a set of exercises [i.e., autogenic training "taking back" procedure (Linden 2007)] have been performed by participants in order to facilitate the return to a state of alertness. Finally, they were given the opportunity to discuss about their experience.

Statistical Analysis

Two-way chi-squared and univariate ANalysis Of VAriance (ANOVAs) were used to analyze differences between groups at T0, respectively for dichotomous and dimensional measures. According with the recommendations for pre-post designs (Senn 2006), questionnaire data were analyzed using multivariate analyses of covariance (MANCOVAs) with group (NFG vs WLG) as a between-subject factor, value at T1 as dependent variables, and value at T0 as a covariate. Effect sizes were calculated with Cohen's d value, where values between 0.20 and 0.49, 0.50–0.79, and >0.80 were defined as small, medium, and large effects, respectively (Cohen 1988).

In order to assess NF learning in NFG, the theta/alpha ratio progression was calculated according with Raymond et al. (2005). Specifically, the mean theta/alpha ratios for all NFG participants were calculated for each of the twenty-seven 1-min time periods in all the sessions. These data were then pooled together across sessions and participants, and the Spearman's rank correlation index has been calculated between theta/alpha ratio and time (i.e., number of epochs since the start of the session). This procedure is considered a reliable method to assess NF learning (Gruzelier 2014). Spearman's rank correlation index has been also used in order to investigate the association between the magnitude of the theta/alpha ratio (i.e., mean theta/alpha ratio for each subjects across the entire NFT) and the value of MZQ and connectivity at the end of NF. All data were analyzed using SPSS software version 20.

EEG connectivity was performed with eLORETA software. The following comparisons were performed: (i) T0-NFG vs T0-WLG, (ii) T1-NFG vs T1-WLG; (iii) T1-NFG vs T0 NFG; (iv) T1-WLG vs T0-WLG. Comparisons were performed using the statistical non-parametric mapping (SnPM) methodology supplied by the LORETA software (Nichols and Holmes 2002), which is based on the Fisher's permutation test. In order to avoid family-wise type-I errors, correction of significance for multiple testing was computed for all comparisons for each frequency band, using the non-parametric randomization procedure (supplied by the eLORETA softweare). Technical details of this method have been described elsewhere (Nichols and Holmes 2002). For all comparisons, the eLORETA statistical package provides experimental values of T, and a two-level T-threshold for statistical significance; the T-thresholds are the values of T corresponding to a significance of $p<0.01$ and $p<0.05$ (Friston et al. 1991).

Results

Socio-demographic and clinical data for both NFG and WLG were reported in Table 2.

The two groups did not significantly differ in age, educational level, and in the other clinical variables. Visual evaluation of the EEG recordings (T0 and T1) showed no relevant modifications of the background rhythm frequency (e.g., focal abnormalities or evidence of drowsiness).

The average time analyzed for NFG and WLG patients was 231 ± 16 and 228 ± 19 s respectively.

Neurofeedback Learning

According to Raymond et al. (2005), the time progression of the mean theta/alpha ratios was calculated for all NFG participants. A Spearman's rank correlation showed that theta/alpha ratios significantly increased with time (Spearman's rho $=0.81$, $p<0.001$).

Table 2 Demographic and clinical data of participants

Variables	NFG (N = 22)	WLG (N = 22)	Test statistics	*p*
Age—$M \pm SD$	22.91 ± 2.51	22.55 ± 2.15	$F_{1;42} = 0.27$	0.608
Educational level[a]—$M \pm SD$	17.67 ± 1.29	17.91 ± 0.81	$F_{1;42} = 4.91$	0.487
Alcohol use in the last 6 months—N (%)	16 (51.6%)	15 (48.4%)	$\chi^2_1 = 0.11$	0.741
Tobacco use in the last 6 months—N (%)	14 (56.0%)	11 (44%)	$\chi^2_1 = 0.83$	0.361

NFG Neurofeedback group, *WLG* waiting list group, *T0* Pre-treatment phase, *T1* Post-treatment phase

[a]Years

Mentalization and General Psychopathology

Detailed descriptive and F-statistics are displayed in Table 3. In post-treatment phase, significant group main effect was observed for MZQ total score as well as for emotional awareness and affect regulation dimensions. Compared to WLG, NFG showed a significant increase of MZQ total score (3.94 ± 0.73 vs. 3.53 ± 0.77; $F_{1;\,43}=8.19$; $p=0.007$; $d=0.863$) as well as for emotional awareness (4.05 ± 0.85 vs. 3.50 ± 1.08; $F_{1;\,43}=5.43$; $p=0.025$; $d=0.703$) and affect regulation dimensions (3.97 ± 0.94 vs. 3.42 ± 0.80; $F_{1;\,43}=9.03$; $p=0.005$; $d=0.906$).

No significant group main effect was observed for the other MZQ dimensions. No significant group main effect was also observed for the GSI total score, although a statistical trend was detected (0.59 ± 0.35 vs. 0.51 ± 0.34; $F_{1;\,43}=3.00$; $p=0.092$; $d=0.522$).

EEG Functional Connectivity

In the between-groups comparison at T0, the thresholds for significance were T = ± 3.90 corresponding to $p<0.05$, and T = ± 4.01, corresponding to $p<0.01$. In this comparison, no significant modifications were observed between groups.

In the within-group comparison (T1 vs. T0), the thresholds for significance were T = ± 3.60 corresponding to $p<0.05$, and T = ± 4.27, corresponding to $p<0.01$. In this comparison, significant modifications were observed in the alpha frequency band in the NFG, but not in the WLG (Fig. 1). Compared to T0, NFG showed at T1 an increase of alpha connectivity between: (i) ROI 8 [Brodmann area (BA)32] and ROI 10 (BAs 29–30–31) (T = 3.63; $p<0.05$); (ii) ROI 8 (32) and ROI 9 (BAs 29–30–31) (T = 3.64; $p<0.05$); (iii) ROI 10 (BAs 29–30–31) and ROI 3 (BAs 21–28–36) (T = 3.69; $p<0.05$). No significant differences were observed in the other frequency bands.

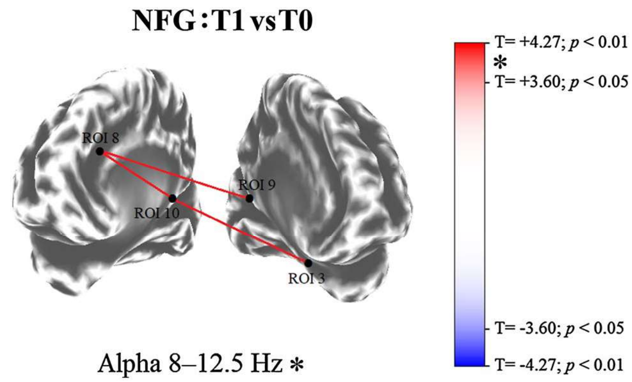

Fig. 1 Results of the eLORETA within comparison (T1 VS T0) of EEG functional connectivity in alpha frequency bands in NFG. Red lines indicate connections which presented an increase of EEG functional connectivity. Blue lines would indicate reduction of EEG functional connectivity (not present). Threshold values (T) for statistical significance (corresponding to $p<0.05$ and $p<0.01$) are reported in the right side of the figure. *NFG* Neurofeedback group, *T0* pre-treatment phase, *T1* post-treatment phase, *ROI* region of interest. (Color figure online)

In the between-groups comparison at T1, the thresholds for significance were T = ± 3.76 corresponding to $p<0.05$, and T = ± 4.29, corresponding to $p<0.01$. In this comparison, significant modifications were observed in the alpha and in the beta frequency band (Fig. 2). Compared to WLG, NFG showed an increase of alpha connectivity between ROI 10 (BAs 29–30–31) and ROI 12 (BAs 39–40) (T = 3.92; $p<0.05$). NFG also reported an increase of beta

Table 3 Pre–post means and group differences in treatment outcomes

Variable	Time	NFG (N = 22) *M* ± *SD*	WLG (N = 22) *M* ± *SD*	Test statistics	Cohen's *d*
MZQ	T0	3.54 ± 0.67	3.46 ± 0.79	$F_{T0}(1; 43)=0.15$; $p=0.703$	
	T1	3.94 ± 0.73	3.53 ± 0.77	$\mathbf{F_{T1}(1; 43)=8.19; p=0.007}$	**0.863**
Self-reflection	T0	3.80 ± 0.84	3.63 ± 0.78	$F_{T0}(1; 43)=0.49$; $p=0.489$	
	T1	4.17 ± 0.80	3.80 ± 0.96	$F_{T1}(1; 43)=3.09$; $p=0.087$	0.530
Emotional awareness	T0	3.57 ± 0.81	3.50 ± 1.02	$F_{T0}(1; 43)=0.06$; $p=0.814$	
	T1	4.05 ± 0.85	3.50 ± 1.08	$\mathbf{F_{T1}(1; 43)=5.43; p=0.025}$	**0.703**
Psychic equivalence	T0	3.25 ± 0.98	3.23 ± 0.95	$F_{T0}(1; 43)=0.01$; $p=0.938$	
	T1	3.59 ± 0.94	3.38 ± 0.98	$F_{T1}(1; 43)=2.34$; $p=0.132$	0.461
Affect regulation	T0	3.56 ± 0.81	3.48 ± 0.95	$F_{T0}(1; 43)=0.08$; $p=0.777$	
	T1	3.97 ± 0.94	3.42 ± 0.80	$\mathbf{F_{T1}(1; 43)=9.03; p=0.005}$	**0.906**
GSI	T0	0.69 ± 0.49	0.50 ± 0.33	$F_{T0}(1; 43)=2.26$; $p=0.140$	
	T1	0.59 ± 0.35	0.51 ± 0.34	$F_{T1}(1; 43)=3.00$; $p=0.092$	0.522

Mean and standard deviation for T1 are not adjusted for the covariates. Bold represents significant tests
T0 pre-treatment phase, *T1* post-treatment phase, *NFG* neurofeedback group, *WLG* waiting list Group, *MZQ* Mentalization Questionnaire, *GSI* global severity index

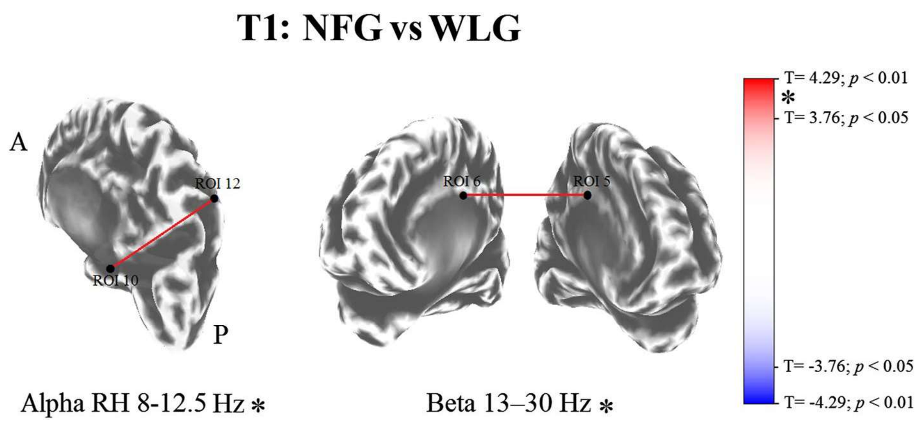

Fig. 2 Results of the eLORETA between comparison (NFG VS WLG) at T1 of EEG functional connectivity in alpha and beta frequency bands. Red lines indicate connections which presented an increase of EEG functional connectivity. Blue lines would indicate reduction of EEG functional connectivity (not present). Threshold values (T) for statistical significance (corresponding to $p < 0.05$ and $p < 0.01$) are reported in the right side of the figure. *NFG* Neurofeedback group, *WLG* Waiting List Group, *T1* Post-treatment phase, *ROI* region of interest, *A* anterior, *P* posterior, *RH* right hemisphere. (Color figure online)

connectivity between ROI 5 (BAs 23–24) and ROI 6 (BAs 23–24) (T = 3.90; $p < 0.05$). No significant differences were observed in the other frequency bands.

Theta/Alpha Ratio, Mentalization and EEG Functional Connectivity

The magnitude of the theta/alpha ratio during NF was positively associated with the increase of beta connectivity between ROI 5 and ROI 6 (Spearman's rho = 0.51, $p = 0.02$). No significant association was observed between theta/alpha ratio and the increase of alpha connectivity between ROI 10 and ROI 12 (Spearman's rho = −0.12, $p = 0.58$). No significant association was also reported between theta/alpha ratio and MZQ total score (Spearman's rho = 0.39, $p = 0.07$) as well as emotional awareness (Spearman's rho = 0.12, $p = 0.59$), affect regulation (Spearman's rho = 0.31, $p = 0.15$) and psychic equivalence mode dimensions (Spearman's rho = 0.29, $p = 0.19$) at the end of NFT. However, a positive correlation was observed between the magnitude of the theta/alpha ratio during NF and self-reflection MZQ dimension (Spearman's rho = 0.41, $p = 0.04$) at the end of NFT.

Discussion

The main aim of the present study was to investigate the usefulness of the A/T training in enhancing mentalization and DMN EEG connectivity in a non-clinical sample. In line with our hypothesis, our results showed that ten sessions of A/T NF are associated with an increase of MZQ total score (large effect sizes). We also detected an increase of emotional awareness and affect regulation dimensions of MZQ, but not in the refusing self-reflection and psychic equivalence mode dimensions, although a statistical trend was observed. This result may suggest a possible selective role of this NF training on emotional dimension of mentalization (Luyten and Fonagy 2015). However, in the absence of an a priori hypothesis about how A/T training may affect specific mentalization dimensions, this interpretation must be treated with caution and it might be useful in guiding future researches. Furthermore, contrary to previous studies (Arani et al. 2010; Dehghani-Arani et al. 2013; Fahrion et al. 1992; Peniston and Kulkosky 1991; Rostami and Dehghani-Arani 2015), no significant effect of A/T training was observed on psychopathological symptoms. As already hypothesized (Imperatori et al. 2017), this result is probably due to the non-clinical sample involved in the present study.

According to our hypothesis, the present results showed that ten sessions of A/T NF are also associated with an increase of DMN EEG connectivity. In the post treatment assessment, NFG, but not WLG, showed a significant increase of alpha connectivity between: (i) right anterior cingulate cortex (ACC) and bilaterally hippocampus and (ii) right hippocampus and left temporal lobe. Furthermore, in the post treatment assessment, compared to WLG, NFG showed an increase of alpha connectivity and beta connectivity respectively between right hippocampus and right parietal lobe and between right and left posterior cingulate cortex (PCC).

All these brain areas are supposed to be crucial in several aspects of mentalization, especially affective mentalizing (Takahashi et al. 2015). For example, functional connectivity between ACC and hippocampus and between hippocampus and temporal lobe has been associated to self-related processing during social emotions (Immordino-Yang and Singh 2013). Similarly, the PCC is considered a crucial node of the DMN (Leech et al. 2011), with critical relevance in processing information related to self, emotion (i.e., feeling of emotion and level of consciousness) and internal monitoring (Tsuchiya and Adolphs 2007).

It is interesting to note that, contrary to the hypothesis that A/T training would related to an increase of theta connectivity (Gruzelier 2009), we observed an increase of EEG connectivity in alpha and beta frequency bands. Indeed, although the aim of A/T training was the increase of theta power over alpha power, we did not observed an increase of EEG theta connectivity at post-treatment. This result may be due to several factors, such as the study design and methods. We have investigated the modifications of DMN EEG connectivity following A/T NF during RS condition. The increase of alpha and beta connectivity observed after NF are in accordance with several studies showing that the increase of EEG connectivity in these frequencies is positively related to DMN activity (for a review see Knyazev 2013). Furthermore, although EEG power spectra and coherence are two related neurophysiological measures, they supplies different information. Indeed, coherence analysis "supplies information on the degree of synchrony of brain activity at different locations for each frequency, independent of power" (Bowyer 2016, p. 5). Previous studies hypothesized that deep relaxation (i.e., hypnagogic experience) associated with A/T NF enhances well-being and emotional self-awareness (Boynton 2001; Gruzelier 2014). Therefore, we may speculate that the neuro-physiological pattern observed in our study after NF training (i.e., the increase of EEG connectivity in those frequencies strongly related with DMN activity), reflects the participants' tendency to be more aware of their introspective abilities, such as emotional self-awareness. However, we did not detected a positive correlation between the magnitude of the theta/alpha ratio during NF and MZQ post scores, although a statistical trend has been observed. The magnitude of the theta/alpha ratio was only associated with the increase of beta connectivity between right and left PCC and with self-reflection MZQ dimension at the end of NFT. These non-significant results may be due to the small sample size ($N = 22$). Moreover, a correlation between within-session theta/alpha ratio and changes in mentalization and functional connectivity after each session could further clarify the relationship among A/T training, mentalization and DMN.

Although our data are promising, there are some limitations in generalizing our results that must be considered. First, we have focused on non-clinical sample. The applicability and effectiveness in patients with mentalization deficit (e.g., borderline personality disorder) should be investigated by future studies. Secondly, we did not compare A/T training with a sham procedure to rule out the placebo effect. Third, we have not assessed the long term effect of A/T training on mentalization and DMN connectivity.

In conclusion, to the best of our knowledge, this is the first study which investigated the effectiveness of A/T training in enhancing mentalization and DMN connectivity in a non-clinical population. Taken together, our results showed that ten sessions of A/T NF are related with an increase of mentalization, suggesting that deep relaxation associated with this training may enhance mentalization ability possibly through an increase of DMN connectivity. Further studies are needed to confirm these preliminary results and to extend them in the clinical population.

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Compliance with Ethical Standards

Conflict of interest The authors have no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all patients for being included in the study.

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