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Cortical sources of awake scalp EEG in eating disorders

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Abstract

Objective: To investigate quantitative EEG (qEEG) in anorexia nervosa (AN) and bulimia nervosa (BN) in comparison with healthy controls.
Methods: Resting EEG was recorded in 30 healthy females (age: 27.1 ± 5.5), 16-AN females (age: 26.4 ± 9.5) and 12-BN females (age: 27.0 ± 6.3). Cortical EEG sources (delta, theta, alpha 1, alpha 2, beta 1, beta 2) were modeled by LORETA solutions. The statistical analysis was performed considering the factors Group, power Band, and region of interest (central, frontal, parietal, occipital, temporal, limbic).
Results: Alpha 1 sources in central, parietal, occipital and limbic areas showed a greater amplitude in Controls versus AN and BN groups. Alpha 2 sources in parietal, occipital and limbic areas showed a greater amplitude in Controls than in both AN and BN groups. Alpha 1 sources in temporal area showed a greater amplitude in Controls compared to both the BN and AN groups as well as in the BN group compared to AN group. Central alpha 1 source correlated significantly with BMI in patients.
Conclusions: These results support the hypothesis that eating disorders are related to altered mechanisms of cortical neural synchronization, especially in rolandic alpha rhythms.
Significance: To our knowledge this is the first study by LORETA able to detect modifications of cortical EEG activity in eating disorders.

Keywords: Anorexia nervosa; Bulimia nervosa; Electroencephalography; Low resolution brain electromagnetic tomography (LORETA)

1. Introduction

Brain cortical dysfunction has been shown in eating disorders by several tools, including visual (Crisp et al., 1968) and computerized (Grebb et al., 1984; Toth et al., 2004) Electroencephalography (EEG) analysis, evoked potentials (EPs) (Bradley et al., 1997), Single Photon Emission Tomography (SPET) (Naruo et al., 2001; Takano et al., 2001) and Positron Emission Tomography (PET) (Delvenne et al., 1995). In anorexia nervosa (AN), these studies have consistently shown that brain dysfunction can still be

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detected even with subjects having recovered metabolic and electrolyte balance. During weight recovery, cortical dysfunction tends to improve, but a body of evidence indicates that some changes can still be detected by appropriate analysis (Green et al., 1996; Kingston et al., 1996). Recently, electroencephalographic (EEG) studies have pointed to abnormal cortical responses (including resting EEG rhythms) in eating disorders, with a prevalence of right hemispheric dysfunction (Bradley et al., 1997; Grumwald et al., 2004; Silva et al., 2002) but these data wait for further confirmation.

Since eating disorders might be related to some distortion of body image (Fairburn and Harrison, 2003) one would expect that a careful topographical evaluation of the cortical rhythmicity might unveil abnormalities.

This working hypothesis was tested in the present study. To this aim, cortical sources of resting EEG rhythms were investigated in AN and bulimia nervosa (BN) as compared to matched healthy controls. Cortical EEG sources were computed by a popular method called "low resolution brain electromagnetic tomography" (LORETA) (Pascual-Marqui and Michel, 1994), which uses thousands of dipole sources within a 3D brain model co-registered into Talairach space (Talairach and Tournoux, 1988). LORETA is a functional imaging technique belonging to a family of procedures (Hernandez et al., 1994) in which the cortex can be modeled as a collection of volume elements (voxels) in the digitized Talairach atlas. LORETA accommodates neuroanatomical constraints and finds the linear inverse solutions that maximize only the synchronization of strength between neighboring neuronal populations (Pascual-Marqui et al., 2002). This roughly corresponds to the 3D distribution of electric neuronal activity that has the maximum similarity (i.e., the maximum synchronization) in terms of orientation and strength among neighboring neuronal populations. LORETA has been shown to be quite efficient when compared to other linear inverse algorithms like minimum norm solution, weighted minimum norm solution or weighted resolution optimization (Pascual-Marqui et al., 1999). Independent validation of LORETA solutions has been provided by recent studies (Phillips et al., 2002; Yao and He, 2001).

2. Methods

2.1. Subjects

The present report concerns a first set of consecutive AN and BN inpatients (Division of Eating Disorders, Department of Mental Health, Pietra Ligure, Savona, Italy) enrolled since the beginning of the study in July 2003 up to May 2004. In this specialized Unit for the treatment of eating disorders, AN and BN patients are usually admitted in the acute phase and undergo a re-feeding program together with psychotherapy and drug support, when necessary, according to the guidelines of the National Collaborating Centre of Mental Health (2004).

All patients underwent a complete diagnostic work-up according to current standards of the DSM IV-TR (American Psychiatric Association, 2000). They underwent general and neurological examination and routine blood and urine screening investigations.

There were 16 females with AN (age range: 16–45 years; mean: 26.94 ± 12.75). EEG was recorded between 5 and 47 days (mean: 22.06 ± 12.5) from hospital admission to avoid a gross effect from the acute starvation phase. Body Mass Index (BMI) ranged from 10.81 to 18.07 (mean: 14.7 ± 2.1) on the day of hospital admission and from 12.1 to 18.2 (mean: 15.7 ± 1.8) on the day of EEG recording. Mean years of education were 12.5 ± 3.2.

Patients with BN were 12 females (age range: 19–41 years; mean: 27.0 ± 6.3). EEG was recorded between 1 and 31 days (mean: 10.6 ± 12.1) from hospital admission. BMI ranged from 17.5 to 23.6 (mean: 20.0 ± 2.1) on the day of hospital admission and from 17.9 to 23.2 (mean: 20.0 ± 1.8) on the day of EEG recording. Mean years of education were 12.4 ± 2.4.

The following drugs were regularly administered to patients during the period of the study: oral benzodiazepines (AN patients number: 1, 2, 5, 6, 7, 8, 10, 12, 13, 14, 15, 16; BN patients number: 1, 4, 6, 8, 9, 10, 11, 12); Selective Serotonin Reuptake Inhibitors (AN patients number: 3, 7, 15, 16; BN patients number: 1, 4, 6, 9, 11); tricyclic antidepressant (AN patients number: 4,16; BN patients number: 7,10); other drugs with effects on CNS i.e. antiepileptic drug or antipsychotic agents (AN patient number 8; BN patients number: 4, 7, 8). Main physiological and clinical data of patients are reported in Table 1a and b.

Because all patients were already on treatment with regular oral doses of psychoactive drugs when admitted to the Hospital, the variable represented by duration of treatment was not considered. In fact, the precise timing of treatment start before admission could not be dated with accuracy in all patients.

The control group included 30 healthy young volunteers who were free of medication (Controls; age ranging from 18 to 42 years; mean: 27.1 ± 5.5) and were chosen from an EEG database of normal subjects with the only criteria to be females of the same age as patients. Mean years of education were 16.5 ± 2.3.

A written consent, according to the specification of the Helsinki declaration (1964-2002), had to be signed by all participants before undergoing EEG.

2.2. EEG methodology

2.2.1. Recordings

EEGs were recorded in resting subjects with eyes closed in a dimly-lit room. Subject's vigilance was constantly controlled to avoid drowsiness. During recordings, patients were asked to hold a small bell in their right hand and keep the button pressed in order to keep the bell from ringing. When drowsiness occurred muscle relaxation led the patient to depress the button which in turn caused the bell

Table 1
Main physiological and clinical data of patients with anorexia or bulimia nervosa

Subject no.	ED type	BMI	Age at onset of first AN episode (years)	Duration of current episode of illness (months)	Serum glucose (mg/dl)	Drugs
(a)						
1	AN-R	12.10	14	13	76	Benzodiazepines
2	AN-R	15.73	16	3	75	Benzodiazepines
3	AN-P	17.58	11	11	71	SSRIs
4	AN-R	16	16	18	64	Antipsychotics
5	AN-R	16.76	15	168	73	–
6	AN-R	16.4	20	17	73	Benzodiazepines
7	AN-R	15.2	24	3	69	Benzodizepines; SSRIs
8	AN-P	13.2	24	6	70	Antipsychotics
9	AN-R	14.25	20	60	70	–
10	AN-R	16.24	17	12	60	Benzodiazepines
11	AN-R	15.1	18	108	69	–
12	AN-P	12.7	26	10	73	Bezodiazepines
13	AN-R	16.47	24	20	61	Benzodiazepines
14	AN-P	17.9	17	6	72	Benzodiazepines
15	AN-P	17.4	20	4	65	Benzodiazepine; SSRIs
16	AN-P	18.2	28	72	70	Benzodizepines
(b)						
1	BN	21.36	18	1	67	SSRIs
2	BN	19.36	26	2	64	–
3	BN	19	28	1	80	–
4	BN	18.95	14	3	69	Antiepileptics
5	BN	17.89	21	2	68	Antipsychotics
6	BN	21.13	17	4	77	–
7	BN	17.90	15	3	87	Benzodiazepines
8	BN	22.29	15	2	79	Antiepileptics
9	BN	23.16	20	2	71	SSRIs
10	BN	19.3	25	1	79	Antipsychotics
11	BN	21.6	24	2	66	Benzodiazepines
12	BN	17.9	24	3	74	Benzodiazepines

BMI = Body Mass Index. AN-R = Anorexia restrictive type and AN-P = Anorexia purging. The ''duration of current episode of illness'' was expressed in months.

to ring. Moreover, the EEG technician visually checked the patient during the whole recording.

EEG was recorded with an average reference (0.3–70 Hz bandpass) from 19 electrodes positioned according to the International 10–20 System (i.e., Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2).

To monitor eye movements, electro-oculogram (0.3–70 Hz bandpass) was also collected. The two EOG electrodes were attached to the outer canthum and below the right eye.

All data were digitized in continuous recording mode (5 min of EEG; 256 Hz sampling rate).

The EEG data were analyzed and fragmented off-line in consecutive epochs of 2 s. On average, 103 epochs for each subject were examined. For standardization purposes, the preliminary analysis of all data was performed at the EEG laboratories of the Deptartment of Human Physiology and Pharmacology in Rome (University ''La Sapienza''). The EEG epochs with ocular, muscular and other types of artifact were first identified by a computerized automatic procedure and the ocular artifacts were then corrected by an autoregressive method (Moretti et al., 2003).

2.2.2. Visual analysis

In the case that transient abnormalities were identified by visual analysis, performed by two independent experimenters, these abnormalities were not selected for further automatic elaboration.

2.2.3. Spectral analysis

A digital FFT-based power spectrum analysis (Welch technique, Hanning windowing function, no phase shift) computed the power density of EEG rhythms with 0.5 Hz frequency resolution. The following standard band frequencies were studied: delta (2–4 Hz), theta (4.5–7.5 Hz), alpha 1 (8–10.5 Hz), alpha 2 (11.0–13.0 Hz), beta 1 (13.5–20.0 Hz), and beta 2 (20.5–30.0 Hz). This allowed a better comparison of the present results with previous literature but did not account for individual EEG markers such as the individual alpha and transition frequencies (Klimetsch, 1999). However, it should be underlined that the present definition of the alpha bands allowed the inclusion of the alpha frequency peaks of the large majority of the Controls, AN and BN subjects in the alpha 1 band (8–10.5 Hz). In fact, the mean alpha frequency peak was

10.1 (±1.1 SD) Hz in the Controls subjects, 10.3 (±1 SD) Hz in the AN subjects and 9.3 (±1.6 SD) Hz in the BN subjects. Moreover, in the evaluation of cortical sources of EEG rhythms, we accounted for the individual alpha frequency peak as a co-variate (Klimetsch, 1999).

Of note, we could not use narrow frequency bands for beta 1 (13-20 Hz) and beta 2 (20–30 Hz), because of the variability of the beta peaks in the power spectra. Therefore, the LORETA results for the beta bands could suffer from the sensitivity limitations of EEG spectral analyses for large bands (Szava et al., 1994).

2.2.4. Cortical source analysis of the EEG rhythms by LORETA

As aforementioned, the popular LORETA technique was used for the EEG source analysis as provided at http://www.unizh.ch/keyinst/NewLORETA/LORETA01.htm (Pascual-Marqui et al., 1994, 1999, 2002). LORETA computed 3-D linear solutions (LORETA solutions) for EEG inverse problem within a three-shell spherical head model including scalp, skull, and brain compartments. The brain compartment was restricted to the cortical gray matter/hippocampus of a head model co-registered to Talairach probability brain atlas and digitized at the Brain Imaging Center of the Montreal Neurologic Institute (Talairach and Tournoux, 1988). This compartment included 2.394 voxels (7 mm resolution), each voxel containing an equivalent current dipole.

The LORETA solutions consisted of voxel spectral density of estimated *z*-current density values able to predict EEG spectral data at scalp electrodes. These solutions are reference free, in that one obtains the same LORETA source distribution for EEG data referenced to any reference electrode including common average. To enhance the topographical results, a "spatial" normalization was obtained by normalizing the LORETA current density at each voxel with the LORETA power density averaged across all frequencies (0.5–45 Hz) and across all 2.394 voxels of the brain volume. After the normalization, the LORETA solutions lost the original physical dimension and were represented by an arbitrary unit scale. This procedure reduced inter-subject variability and was used in previous our EEG study (Babiloni et al., 2004). The general procedure fitted the LORETA solutions in a Gaussian distribution and reduced inter-subject variability (Nuwer, 1988; Leuchter et al., 1993).

Of note, other methods of normalization using the principal component analysis are effective for estimating the subjective global factor scale of the EEG data (Hernandez et al., 1994). These methods are not available yet in the LORETA package, so they were not used here. Solutions of the EEG inverse problem are underdetermined and ill-conditioned when the number of spatial samples (electrodes) is lower than that of the unknown samples (current density at each voxel). To account for that, the cortical LORETA solutions predicting scalp EEG spectral power density were regularized to estimate the distributed rather than the punctual EEG sources (Pascual-Marqui and Michel, 1994; Pascual-Marqui et al., 1999; Pascual-Marqui et al., 2002). In line with the low spatial resolution of the LORETA technique, we collapsed the LORETA solutions at frontal, central, temporal, parietal, occipital, and limbic regions of the brain model coded into Talairach space. The Brodmann areas listed in Table 2 formed each of these ROIs.

2.2.5. Statistical analysis of the LORETA solutions

Regional normalized LORETA solutions from the Controls, AN and BN subjects were used as dependent variables for ANOVA, using subjects' education and individual alpha frequency peak (IAF) (Klimetsch, 1999) as covariates. To test the working hypothesis, the ANOVA factors (levels) were Group (Controls, AN, BN; independent variable), Band (delta, theta, alpha 1, alpha 2, beta 1, beta 2), and ROI (central, frontal, parietal, occipital, temporal, limbic). Mauchly's test evaluated the sphericity assumption. Correction of the degrees of freedom was made with the Greenhouse-Geisser procedure. Duncan test was used for post-hoc comparisons ($p < 0.05$). On one hand, the planned Duncan post-hoc testing evaluated (i) the prediction of difference of the LORETA solutions in the Controls subjects compared to both AN and BN subjects. That prediction would be confirmed by the LORETA pattern Controls ≠ AN and BN (where AN = BN). On the other hand, the planned post-hoc testing evaluated (ii) the prediction of difference in magnitude of the LORETA solutions among the Controls, the AN, and the BN subjects. That prediction would be confirmed by the LORETA pattern Controls ≠ AN ≠ BN.

The LORETA solutions of the AN and the BN subjects in central and parietal areas, where body map is represented, were used for the evaluation of the correlation with Body Mass Index (BMI). The AN and the BN subjects were considered as a single group. To reduce the number of statistical runs, we considered only the central and parietal LORETA solutions showing statistically significant differences according to the LORETA pattern Controls ≠ AN ≠ BN or Controls ≠ AN and BN. The correlation was computed with Spearman test ($p < 0.05$).

3. Results

3.1. Visual EEG analysis

Six out of 28 patients (21.4%) (4 in the BN group and 2 in the AN group) showed either diffuse or bi-temporal

Table 2
Brodmann areas included in the cortical regions of interest (ROIs)

LORETA Brodmann areas included in the regions of interest (ROIs)	
Frontal	8, 9, 10, 11, 44, 45, 46, 47
Central	1, 2, 3, 4, 6
Parietal	5, 7, 30, 39, 40, 43
Temporal	20, 21, 22, 37, 38, 41, 42
Occipital	17, 18, 19
Limbic	31, 32, 33, 34, 35, 36

LORETA solutions were collapsed in frontal, central, parietal, temporal, occipital, and limbic ROIs; a.u. = arbitrary units.

transient EEG abnormalities, mainly consisting of fast spike-and-waves complexes, small sharp spikes and positive spikes, similar to previous reports (Crisp et al., 1968; Goor, 1954; Grebb et al., 1984; Struve, 1986).

3.2. Topography of the EEG cortical sources estimated by LORETA

Fig. 1 maps the grand average of the LORETA solutions (i.e., relative current density at cortical voxels) modeling the distributed EEG sources for delta, theta, alpha 1, alpha 2, beta 1, and beta 2 bands in the Controls, AN and BN groups. The Control group presented alpha 1 and alpha 2 sources with maximal values of the relative current density distributed in the parieto-occipital regions. Delta and theta sources had moderate relative current density values compared to the alpha sources. Finally, beta 1 and beta 2 sources were characterized by the lowest relative current density values. Compared to the Control group, both AN and BN groups showed a clear reduction of the relative current density of the alpha 1 and alpha 2 sources in central, limbic, temporal, occipital, and parietal areas. In addition, the reduction of alpha 1 sources in temporal area was stronger in the AN than the BN subjects.

3.3. Statistical analysis of the EEG cortical sources estimated by LORETA

Fig. 2 shows the mean regional LORETA solutions (distributed EEG sources) relative to a statistical ANOVA interaction (F (50,1375) = 2.31; MSe = 0.774; $p < 0.0001$) among the factors Group (Controls, AN, BN), Band (delta, theta, alpha 1, alpha 2, beta 1, beta 2), and ROI (central, frontal, parietal, occipital, temporal, limbic). In the figure, the LORETA solutions had the shape of EEG relative power spectra. Notably, profile and magnitude of these spectra in the Controls, AN and BN groups differed in the diverse cortical regions, thus supporting the idea that scalp EEG rhythms are generated by a distributed pattern of cortical sources. The planned Duncan post-hoc testing assessed: (i) the differences in the regional LORETA solutions in the Control group compared to both AN and BN groups (Controls ≠ AN and BN, where AN = BN), and (ii) the differences in the regional LORETA solutions among the three groups (Controls ≠ AN ≠ BN). According to point (i), the alpha 1 sources in central, parietal, occipital and limbic areas showed stronger amplitude in the Controls compared to AN ($p = 0.000006$) and BN ($p = 0.00004$) groups. Furthermore, the alpha 2 sources in parietal, occipital and limbic areas showed stronger

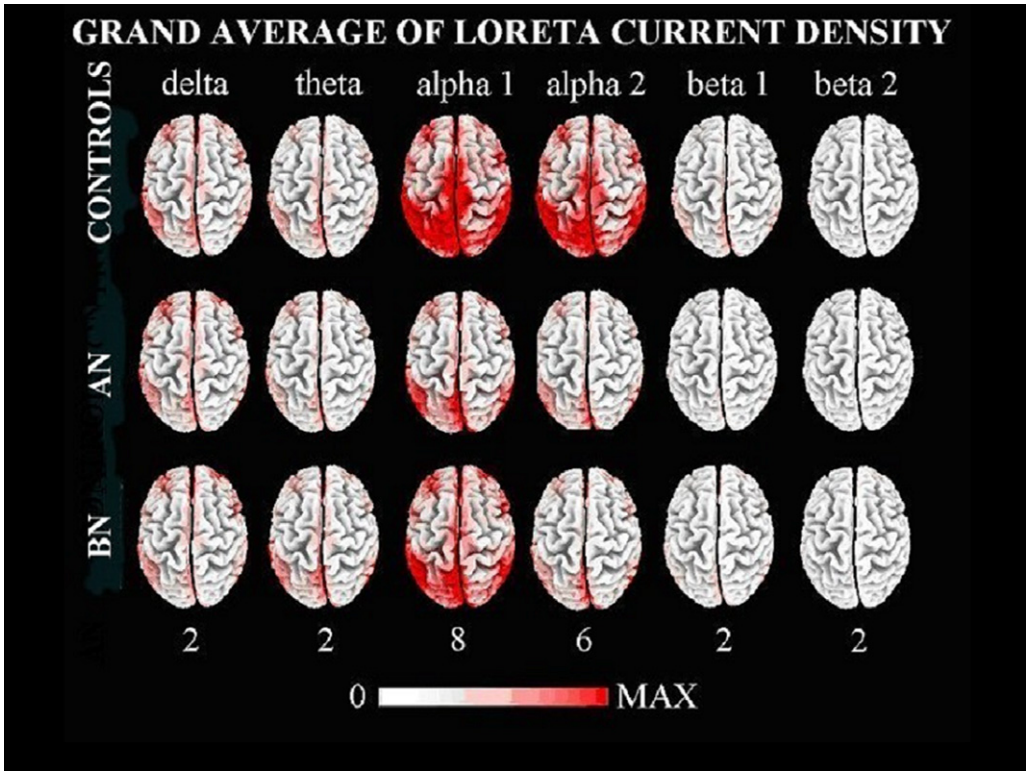

Fig. 1. Grand average of LORETA solutions (i.e., normalized relative current density at the cortical voxels) modeling the distributed EEG sources for delta, theta, alpha 1, alpha 2, beta 1, and beta 2 bands in Controls, AN and BN groups. The left side of the maps (top view) corresponds to the left hemisphere. Legend: LORETA, low resolution brain electromagnetic tomography. Color scale: all power estimates was scaled based on the averaged maximum value (i.e., alpha 1 power value of occipital region in Controls). The maximal value of power is reported under each column.

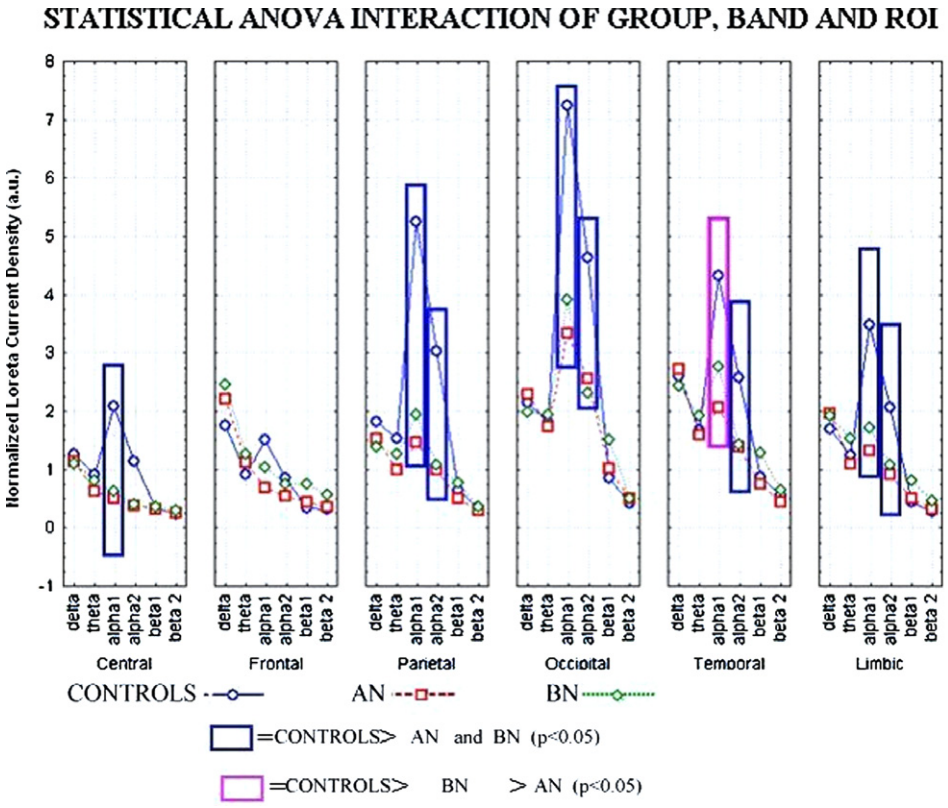

Fig. 2. Regional LORETA solutions (mean across subjects) relative to a statistical ANOVA interaction among the factors Group (Controls, AN, BN), Band (delta, theta, alpha 1, alpha 2, beta 1, beta 2), and ROI (central, frontal, parietal, occipital, temporal, limbic). This ANOVA design used the normalized relative current density values at ROI level as a dependent variable. Regional LORETA solutions modeled the EEG relative power spectra as revealed by a sort of "virtual" intracranial macro-electrodes "disposed" on the macrocortical regions of interest. Legend: the rectangles indicate the cortical regions and frequency bands in which LORETA solutions presented statistically significant different among Controls, AN and BN groups (Controls ≠ AN ≠ BN, $p < 0.05$, planned Duncan post-hoc testing) or statistically significant difference in Controls group compared to both AN and BN groups (Controls ≠ AN and BN where BN = AN). See Section 2 for further details.

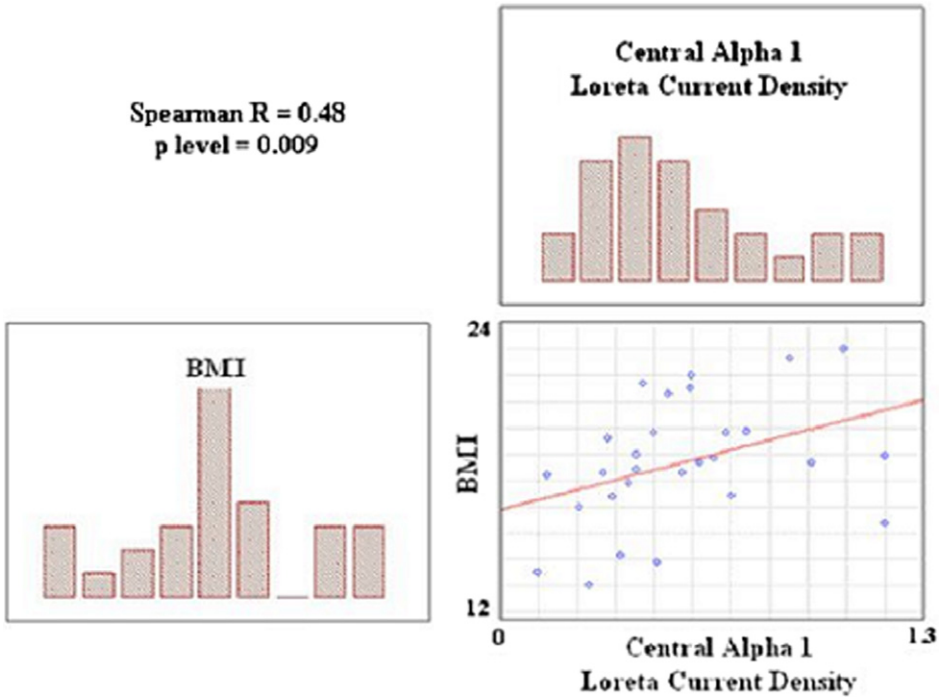

Fig. 3. Correlation (Spearman test) between the central alpha 1 LORETA current density and the body mass index (BMI) in all AN and BN subjects considered as a unique group.

amplitude in the Controls compared to AN ($p = 0.002$) and BN ($p = 0.001$) groups. According to point (ii), the alpha 1 sources in temporal area showed stronger amplitude in the Controls compared to the BN ($p = 0.000004$) and AN groups ($p = 0.000002$), and in the BN compared to AN group ($p = 0.04$).

The magnitude value of central alpha 1, central alpha 2 and parietal alpha 2 sources was used as an input for the statistical correlation with the BMI values in the AN and BN subjects as a unique group (Spearman test). Only the central alpha 1 source correlated significantly with BMI. Fig. 3 shows this significant positive correlation ($r = 0.48$, $p = 0.009$).

3.4. Control analyses

When EEG is employed for patients with eating disorder, the glucose level in blood should be checked, since EEG data are very sensitive to blood glucose level and these patients often vomit and/or fast. To address this issue, we tested whether the significant positive correlation between central alpha 1 source and BMI in AN and BN subjects considered as a single group depended on glycaemia levels. As a first control analysis, a partial correlation analysis (Pearson test; $p < 0.05$) tested whether such a correlation was due to glycaemia level. The results of the partial correlation analysis gave a statistically significant result ($p = 0.04$; $r = 0.39$), confirming the results of the main study. As a second control analysis, we evaluated the correlation between glycaemia and BMI as well as between glycaemia level and central alpha 1 source in AN and BN subjects considered as a single group (Spearman test; $p < 0.05$). Both correlations showed no statistically significant results ($p > 0.6$). These findings suggest that the correlation between alpha 1 source and BMI in our patients was not due to glycaemia level.

Our main analysis of the regional LORETA sources of EEG rhythms did not consider hemispherical effects, to reduce the complexity of the ANOVA design. However, one may argue that these effects could be an important feature of EEG dis-rythmicity in the patients with eating disorders. To address this issue, we performed an ANOVA analysis of regional LORETA solutions for each band (delta, theta, alpha 1, alpha 2, beta 1, beta 2). The ANOVAs had the factors (levels) Group (Controls, AN, BN; independent variable), Hemisphere (Left, Right) and ROI (central, frontal, parietal, occipital, temporal, limbic). These ANOVAs showed no statistical interaction including the factors Group and Hemisphere ($p > 0.1$), thus suggesting that there were no hemispheric differences in the regional LORETA solution among Controls, AN and BN.

4. Discussion

The main result of this study is that both AN and BN patients have sources of alpha 1 and alpha 2 lower in amplitude than healthy control women, especially in the posterior regions represented by the temporal, parietal and occipital lobes. Moreover, BN patients showed greater alpha 1 amplitude in the temporal region than AN patients.

Somewhat unexpectedly, no significant differences were found among groups in source amplitude of theta and delta bands. Transient and often focal EEG changes have been known for a long time in eating disorders (Crisp et al., 1968; Goor, 1954; Grebb et al., 1984; Hughes, 1996) and they have mainly been ascribed to electrolyte imbalance in the acute starvation phase. The absence of differences in delta and theta bands in the present LORETA elaboration could be explained by the elimination of epochs with transient slow changes from automatic elaboration. This elimination is required by definition before applying the FFT computation, entailing a stable EEG signal, but actually transient slow changes were found in some (21.4%) of patients.

Although the influence of electrolyte unbalance on cortical rhythms cannot be completely excluded, it should be underlined that AN patients underwent EEG 5–47 days (mean: 22) after hospital admission, and most of them after the 10th day. Moreover, no serum electrolyte unbalance was present on the day of EEG recording. Malnutrition may have caused neuronal loss and thus a power reduction of alpha 1–2 cortical sources. As a matter of fact, a severe proteic or caloric-proteic malnutrition may lead to neuronal death and/or synaptic dysfunction in adulthood. A reduction of both number and shape of dendritic spines has been reported (Bronzino et al., 1983; Fiala et al., 2002; Granados-Rojas et al., 2004; Lukoyanov and Andrade, 2000). In rats, proteic malnutrition has been shown to produce cortical and hippocampal electrical signal changes. Prenatal protein malnutrition has significantly slowed the development of theta frequency and produced higher values of power in the theta rhythm in awakening rats. Moreover, it delays the normal sleep/wake cycle by significantly reducing the REM sleep time between the 14th and the 18th day of age and increasing the time spent in aroused waking at both these ages (Bronzino et al., 1980; Engel, 1956).

Of note, the present power reduction of alpha sources in AN patients might reflect the activity of dominant oscillatory neural networks in the adult and resting awake brain, which are mainly modulated by thalamo-cortical and cortico-cortical interactions facilitating/inhibiting the transmission (Klimetsch, 1999), namely for arousing mechanisms (alpha 1) and sensorimotor information and the retrieval of semantic information from cortical storage (alpha 2).

A similar process might be suggested even in man. Kwashiorkor (a severe form of proteic malnutrition) causes changes in EEG rhythms (Engel, 1956), consisting of reduced alpha activity and more slow-wave activity in comparison to controls (Bartel et al., 1979). The suspected mechanism leading to EEG changes would start with malnutrition leading to a reduced nutrient supply to maintain

adequate brain trophism, particularly glucose (Thibault and Roberge, 1987). This in turn would produce neuronal and synaptic damage reflected by power reduction of the main rhythms, i.e., alpha rhythm. Therefore, even in eating disorders such a mechanism may play a role. In AN, glucose homeostasis is deranged since both fasting and diurnal hypoglycaemia have been reported (Munoz and Argente, 2002; Thibault and Roberge, 1987) and glucose cortical hypometabolism has been shown by a ^{18}FDG-PET study (Delvenne et al., 1995).This interpretation seems to be supported by the finding of alpha power reduction as a common final pathway of several diseases leading to synaptic dysfunction and neuronal loss. A reduction of cortical sources of alpha power has been reported in Mild Cognitive Impairment (MCI), Alzheimer's disease (AD) and Vascular Dementia (VaD), together with other EEG changes (Besthorn et al., 1997; Jelic et al., 1996; Moretti et al., 2004). A reduction of alpha power is an early marker of AD, which is characterized by an impairment of cortico-cortical connections. The predominance of white matter changes in VaD is the suggested mechanism to produce a slowing-down of the background rhythm (Moretti et al., 2004).

Since the majority of both AN and BN patients were treated with regular oral doses of psychoactive drugs, mainly benzodiazepines and Selective Serotonin Reuptake Inhibitors (SSRIs), the hypothesis that these drugs may have affected EEG results at least in part cannot be excluded.

These drugs could not be withdrawn before EEG recordings because of clinical and deontological reasons.

However, benzodiazepines mainly affect fast rather than slow and alpha frequencies (Blume, 2006; Bauer and Bauer, 2005; Van Cott and Brenner, 2003).

As far as the SSRIs (the second most used class of drugs in our patient series) are concerned, in an EEG study with LORETA elaboration, citalopram has been shown to induce an increase of fast alpha and beta power, especially in the right frontal–temporal region (Saletu et al., 2006).

According to this evidence, it seems unlikely that the psychotropic drugs used in our patients may have grossly affected the finding of alpha 1 reduction both in AN and BN groups.

In this study, a significant, discrete relationship between EEG data and BMI was only found for central alpha 1. This result agrees with the idea that the alteration of cortical rhythms is not spatially unselective in eating disorders when referenced to pathological aging (see aforementioned studies). Furthermore, this result is in keeping with other data failing to find a significant correlation between BMI and cognitive performances (Fowler et al., 2005), brain glucose metabolism (Delvenne et al., 1995) and hippocampal and amygdala volume (Giordano et al., 2001). A possible explanation is that a 'spot' BMI is not a very sensitive index of the damage caused by the eating behavioral changes, especially taking into account the impact of a long disease duration.

Therefore, it may be suggested that several acute relapses in the history of the patient (thus possibly not reflected by a spot BMI at the time of EEG recording) have produced not fully reversible changes even in the periods when the patient has recovered a correct nutritional status. The exclusion of severely malnourished patients from the present series might have emphasized this lack of correlation even more.

To this stage of research, the meaning of EEG changes in eating disorders remains uncertain. Another possible explanation is that the EEG changes are independent of eating behavior and that, on the contrary, they may reflect the underlying psychiatric disorder. In fact, eating disorders have been suggested to be part of the 'obsessive-compulsive' spectrum (Halmi et al., 2005; Serpell et al., 2002). In patients with obsessive-compulsive disorders (OCD), a reduction of alpha power has been reported together with other qEEG changes, especially in fronto-temporal regions (Karadag et al., 2003; Tot et al., 2002). According to this alternative hypothesis, EEG changes in eating disorders would not be caused by malnutrition but would rather be an epiphenomenon of a primary cortical dysfunction, similarly to what has been suggested in OCD.

This alternative hypothesis should be verified in fully recovered patients with a past history of eating disorders several years before. However, we think that this alternative explanation cannot take into account the fact that in our AN and BN subjects, we observed strict correlations between abnormal cortical alpha rhythms and BMI over central (body map) but not frontal regions, the former more specifically involved in OCD.

In conclusion, we tested the working hypothesis that EEG rhythms overlying cortical sensorimotor body maps are related to eating disorders such as AN and BN. Central and parietal alpha sources were used as an input for the statistical correlation with BMI values in the AN and BN subjects as a unique group. Only the central alpha 1 source correlated significantly with BMI. These results are in keeping with the working hypothesis that eating disorders such as AN and BN are related to abnormal mechanisms of neural synchronization (alpha frequencies) in the rolandic cortical areas including body map. Future studies should evaluate the relations between these mechanisms and behavioural distortion of body schema and image in AN and BN subjects.

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