DEBLURRING TECHNIQUES FOR THE STUDY OF CORTICAL NETWORKS OF HUMAN BRAIN IN A CLINICAL CONTEXT

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ABSTRACT

Objectives: EEG scalp potential distributions recorded in humans are affected by low spatial resolution and by the dependence on the electrical reference used. High resolution EEG technologies are available to drastically increase the spatial resolution of the raw EEG. Such technologies included the computation of surface Laplacian (SL) of the recorded potentials, as well as the use of realistic head models to estimate the cortical sources via linear inverse procedure (low resolution brain electromagnetic tomography, LORETA). However, these deblurring procedures are generally used in conjunction with EEG recordings with 64-128 scalp electrodes and with realistic head models obtained via sequential magnetic resonance images (MRIs) of the subjects. Such recording setup it is not often available in the clinical context, due to both the unavailability of these technologies and the scarce compliance of the patients with them. In this study we addressed the use of SL and LORETA deblurring techniques to analyze data from standard 10-20 system (19 electrodes) in a group of Alzheimer disease (AD) patients.

Methods: EEG data related to unilateral finger movements were gathered from 10 patients affected by AD. SL and LORETA techniques were applied for source estimation of EEG data. The use of MRIs for the construction of head models was avoided by using the quasi-realistic head model of Brain Imaging Neurology Institute of Montreal.

Results: It was observed a similar cortical activity estimated by the SL and LORETA techniques during identical time period of the acquired EEG data in the population examined

Conclusions: The results of present study suggest that both SL and LORETA approaches can be usefully applied in clinical context, by using quasi-realistic head modeling and standard 10-20 system as electrode montage (19 electrodes). These results represent a reciprocal cross-validation of the two mathematically independent techniques in a clinical environment.

I.

INTRODUCTION

It is well known that the EEG potential distributions recorded from the scalp in humans are affected by low spatial resolution and by the dependence on the electrical reference used. Nowadays, modern high resolution EEG technologies are available to drastically increase the spatial resolution of the raw EEG. Such technologies include the computation of surface Laplacian of the recorded potentials, as well as the use of realistic head models to estimate the cortical sources via linear inverse procedure. The deblurring techniques are generally used in conjunction with EEG recordings with 64-128 scalp electrodes and realistic head modeling as obtained via sequential magnetic resonance images (MRIs) of the subject's head [1]. However, EEG recordings cannot be performed with more than 19 electrodes (standard 10-20 system) in clinical a context. In addition, it is difficult to acquire and manage MRIs for all patients, in order to build realistic head models. This happens not only for the unavailability of the technical devices, but also for the emotional problems of some patients. For instance, Alzheimer Disease (AD) patients cannot be subjected to the long procedure of high-density electrodes montage (and relative lowering of electrode impedance). On the other hand, the use of spherical head models instead the realistic ones decreases the precision of the deblurring techniques. All these considerations were at the basis of our study, aimed at analyzing the performance of two techniques for EEG source estimation such as the surface Laplacian and low resolution brain electromagnetic tomography (LORETA) [2]. These techniques were applied to the EEG data of a group of AD patients and age-matched controls. EEG data were recorded from 19 scalp electrodes and a quasi-realistic head model was used instead of individual realistic head models. The quasi-realistic head model was realized at Brain Imaging Neurology Institute of Montreal as an average of 152 individual MRI data sets. The surface Laplacian and LORETA solutions were co-registered with that model. Surface Laplacian and LORETA solutions were also compared each other.

Convergent results obtained with SL and LORETA techniques suggest that such procedures can improve efficiently the spatial details ("deblurring") of the recorded EEG data also in a clinical context using standard

10-20 system (19 scalp electrodes) and a quasi-realistic head model. From a clinical point of view, the computation of SL and LORETA was able to model the sources of movement-related cortical EEG rhythms in mild to moderate AD patients, with respect to an age-matched group of healthy subjects. The results are consistent with the working hypothesis that AD is a brain disease that involves not only the cognitive systems but also neural networks contributing to sensorimotor functions.

METHODS

Subjects: The AD group consisted of 10 right-handed subjects with age of 79.4 ±SD 8.6 (7 females and 3 males). Only patients with mild to moderate AD were included in the study. The control group consisted of ten right-handed healthy subjects with age of 72.1 ±SD 9.1 (5 females and 5 males).

EEG recordings: The motor task consisted of brisk right middle finger extensions, which were triggered by a verbal instruction (i.e. "go") of the experimenter (8-12 s inter-movement intervals). Nineteen scalp electrodes were positioned according to international 10-20 system (Fp1, Fp2, F7, F43, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2). EEG data were recorded with 0.3-70 Hz bandpass and linked-earlobes reference. Electrooculogram (0.3-70 Hz bandpass) and surface rectified electromyographic activity of bilateral extensor digitorum muscles (1-70 Hz bandpass) were also collected. For each subject, recorded EEG data were related to about 100 movements.

Spatial deblurring or source estimation: Artifact-free EEG activity (from 4 s before to 4 s after the onset of electromyographic response, zerotime) was used as an input for EEG source estimation with SL and LORETA. EEG segments contaminated by blinking, eye movements, mirror movements, and/or other artifacts were rejected off-line. Artifact-free EEG activity was then considered for the SL estimate by spline function [1]. The single trial analysis was repeated on the SL data, to discard the single trials contaminated by computational artifacts. Percentage event-related desynchronization/synchronization (ERD/ERS) of alpha and beta EEG rhythms was computed by the well-known procedure of (Graz) Pfurtscheller's group. Amplitude gray scale maps of the alpha and beta ERD/ERS peaks were calculated on a 3-D "quasi-realistic" head model

by a spline interpolating function, which was constructed based on the quasi-realistic head model of Brain Imaging Neurologic Institute of Montreal.

LORETA is a well-known technique computing 3-D, discrete, linear solutions for the EEG inverse problem that have been previously tested with an extensive simulation study [2]. In brief, LORETA used a three-shell spherical head model, which was registered to the Talairach brain atlas [3] digitized from magnetic resonance images at Brain Imaging Neurologic Institute of Montreal. LORETA solution space was restricted to the cortical gray matter and hippocampus, as determined by the digitized Probability Brain Atlas. The discretization of the solution space was performed with 2,394 voxels (7 mm resolution), each containing an equivalent current dipole. LORETA solutions were represented as axial, sagittal, and coronal slices (17x20x25). These slices were identified based on their distance (mm) from the origin of a 3-D Talairach head coordinate system. In this system, the positive x-axis passed approximately through the right ear (medial-lateral direction), the positive y-axis through the forehead (anterior-posterior direction), and the positive z-axis (representing the superior-inferior direction) through the top of the head.

LORETA provided current density values in each voxel of the source space, from individual EEG power spectrum (digital filtering, narrow bandpass, no phase shift). The EEG bands of interest were alpha (8-12 Hz), beta 1 (13-18 Hz), and beta 2 (19-21 Hz) and the analysis periods were the movement ("movement") and post-movement ("post-movement") ones. "Rest" ranged from -4 to -3 sec, "movement" from zerotime to +1 sec, "post-movement" from +1 to +2 sec. Event-related LORETA solutions were computed based on the ratio between dipole power density values at "movement" (or "post-movement") and rest. Event-related LORETA solutions in AD vs. N subjects were compared by t-paired test, corrected for multiple comparisons.

In both techniques, individual alpha or beta frequencies showing maximal differences between the "rest" and other periods of interest were chosen for the ERD/ERS computations. This provided individual (i) "movement"/alpha reactivity band, (ii) "movement"/beta reactivity band, (iii) "post-movement "/beta reactivity band, for ERD/ERS computations.

Cross-validation between SL and linear inverse solutions. The comparisons between SL and linear inverse (mathematics at the basis of LORETA) solutions were accomplished by using also standard median-nerve

somatosensory evoked potentials (SEPs) and averaged movement-related potentials (MRPs) recorded in normal subjects. This because the neural sources of SEPs and MRPs are well known in literature by intra-cortical recordings.

RESULTS

Fig. 1 presents the results obtained by the two spatial deblurring/source estimation techniques on a common dataset of SEPs and MRPs recorded in one healthy subject. The SL distributions computed from SEPs and MRPs were projected radially onto the cortical reconstruction of a realistic head model, for a better comparison with those computed with the linear inverse technique. Each column in Fig. 1 presents the raw scalp potentials, the SL solution, and the linear inverse solution for components of MRPs and SEPs. In particular, the first column present the distributions for the pre-movement readiness potential (RP) component of MRPs, the second one for the on-going movement evoked potential (movement-related response 1, MRR1) and the third one for the negative component occurring after 30 msec of stimulus delivery for the SEPs (N30). It is well known that these components are generated in primary sensorimotor and supplementary motor cortical areas. It is interesting to note that the cortical potentials estimated with the two procedures are really similar, demonstrating the activation of the appropriate cortical areas. This result encouraged us to apply these deblurring tools to the EEG recordings in both normal and AD patients.

Application to normal and AD patients of SL computation

The topography of the alpha and beta ERD/ERS peak obtained with the SL technique is illustrated in the gray scale maps of Fig. 2. The "movement" alpha and beta ERD distribution of all groups was characterized by maximum response in the centroparietal areas of both sides (contralaterally preponderant). In addition, there was a marked "movement" beta ERD around scalp vertex in the control group with respect to the AD data. During the "post-movement", the topographical ERS difference between the two groups appeared to be more pronounced. The "post-movement" beta ERS distributions showed a strong preponderant response on

the contralateral central area in the control group. In contrast, AD group data showed a paradoxical emerging beta ERS maximum in the ipsilateral centroparietal area. Furthermore, the contralateral beta ERS maximum tended to be localized more anteriorly and to be distributed more largely in the AD than in the normal group.

Application to normal and AD patients of LORETA computations

Fig. 3 plots 3-D statistical maps of movement-related alpha and beta band power density changes computed by LORETA in AD patients vs. normal subjects. The maps were registered to Talairach space and digitized Probability Brain Atlas. For the "movement", statistical maps showed significantly lower desynchronization of alpha and beta oscillations (i.e. reduction of the spectral power density during the event compared to baseline period) in the AD than in the control subjects (dark gray region) within contralateral inferior frontal gyrus (alpha t=3.41, p<0.0016), bilateral superior frontal gyrus (beta 1 t=3.93, p<0.0005), and supplementary motor area/cingulate gyrus (beta 1 t=3.65, p<0.0009/beta 2 t=2.93, p<0.0045). In contrast, a lower desynchronization of alpha and beta oscillations in the normal group than in the AD one (light gray region) was computed but not showed here in contralateral (i.e. left), middle temporal gyrus (beta 2 t=4.23, p<0.0002), and parietal lobe (alpha t=2.14, p<0.02). For the "post-movement", not shown in the figure, statistical maps indicated a statistical trend for higher synchronization or "rebound" of alpha and beta oscillations in the AD than in the normal subjects within ipsilateral superior frontal gyrus (alpha t=1.97, p<0.0322). On the contrary, a statistical trend for higher synchronization of alpha and beta oscillations in the normals than AD subjects was observed in contralateral inferior parietal lobule (alpha t=2.40, p<0.0137).

DISCUSSION

Results of the present study suggest that the use of deblurring tools like SL and LORETA improved the spatial details of the raw recorded EEG scalp potential distributions. In addition, similar cortical distributions were retrieved by processing SEPs and MRPS with the two procedures. In precedence, the agreement between linear inverse estimation and SL techniques was also assessed by using data simulations within unrealistic

spherical head model [4]. Although in the present study a formal correlation coefficient between the two cortical distributions was not computed, it seemed reasonable from the observation of Fig.1 to assert a general agreement between the two EEG spatial deblurring/source estimation methods. The application of EEG spatial deblurring/source estimation tools in a clinical context produced interesting results. These results showed that the activation of contralateral rolandic cortex and motor performance are preserved in mild to moderate AD. Moreover, SL (Fig. 2) and LORETA (Fig.3) procedures demonstrated an abnormal recruitment of other functionally-related nonprimary frontal and ipsilateral sensorimotor areas in AD patients with respect to normal subjects. This would support the hypothesis that AD is a brain disease globally affecting also neuronal connectivity involved in the processing of sensorimotor information (despite no overt movement disorder).

CONCLUSION

The results of present study suggest that both SL and LORETA approaches can be usefully applied in clinical context, by using quasi-realistic head modeling and standard 10-20 system as electrode montage (19 electrodes). These results represent a reciprocal cross-validation of the two mathematically independent techniques in a clinical environment.

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FIGURE LEGENDS

Fig. 1. Cross validation between the cortical source estimation performed with the surface Laplacian (RL row), the linear inverse solution (SD row) from the scalp EEG data (P row). First column presents the distributions for the pre-movement readiness potential (RP) component of movement-related potentials (MRPs), the second one for the on-going movement evoked potentials (movement-related response 1, MRR1) and the third one for the negative component of median-nerve somatosensory evoked potentials occurring about 30 msec after stimulus delivery. Roughly the same information is conveyed by the two EEG spatial deblurring procedures.

Fig. 2 Three-dimensional maps of across-subjects alpha and beta event-related desynchronization/synchronization (ERD/ERS) peaks in Alzheimer disease (AD) and normal subjects. These ERD/ERS peaks were computed during the movement and post-movement periods. Gray scale: maximum ERD and ERS are coded in light and dark gray, respectively. Note that AD data showed a paradoxical ipsilateral preponderance of post-movement ERS distributions. Of note, ERD/ERS was computed by the well known procedure of (Graz) Pfurtscheller's group.

Fig. 3. Three-dimensional statistical maps of movement-related alpha and beta band power density changes computed by low resolution brain electromagnetic tomography (LORETA) in AD patients vs. normal age-matched subjects. Brain slices (axial, sagittal, coronal) illustrating LORETA solutions were identified based on their distance (mm) from the origin of Talairach head coordinate system. Statistical comparisons were performed with t test. T values were represented by a gray percent scale. Negative t values (dark gray) mean lower power density in AD than normal age-matched subjects and *viceversa* for positive t values (light gray).