SEIZURE TRACKING AND DETECTION IN ICTAL EEG USING TIME-STRUCTURE BASED BLIND SOURCE SEPARATION METHODS AND PRIOR SPATIAL TOPOGRAPHICAL INFORMATION

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Abstract: Blind source separation (BSS) techniques are increasingly being used in biomedical signal processing applications involving the analysis of multichannel electroencephalogram (EEG) signals. These methods extract a set of underlying sources from the EEG, reflecting neurophysiological brain activity, artifacts and noise, and in some cases clinically relevant components relating to epileptic seizures. Tracking and detecting sources of interest fundamentally requires some *a priori* knowledge or assumptions regarding their spatial and/or temporal characteristics. This work presents and explores a spatial topographical approach to source tracking and detection in multichannel EEG based on prior knowledge of the sensor projections (scalp potential distributions) associated with the target sources, which can be estimated from a representative data segment using conventional BSS methods, e.g., using signal time-structure. Thus, for a given segment of EEG, the absence or presence of each target source can be determined on the basis of a comparison of its sensor projection with those of the underlying sources extracted from the segment using BSS. Applied to ictal EEG, this spatial topographical approach may play a useful role in tracking and detection seizure related epileptiform activity.

Introduction

The development of reliable methods for monitoring epileptiform multichannel electroencephalogram (EEG) signals and automated tracking and detection of seizure related activity poses a considerable biomedical signal processing challenge in clinical neurophysiology. Data-driven techniques for blind source separation (BSS) and independent component analysis (ICA), e.g. [1, 2] are increasingly used for signal processing and analysis of multichannel biomedical data [3]. Such methods exploit spatial, and temporal, spectral or statistical dependencies in the observed data in order to extract a set of so-called sources which reflect the underlying signal generating and mixing processes, including physiological sources of interest, as well as artifacts and noise. Applied to EEG, these methods can separate ocular artifacts from brain activity [4] and extract neurophysiologically meaningful sources reflecting epileptiform brain activity [5, 6].

Conventional methods for monitoring clinical (epileptiform) multichannel EEG generally involve morphological, spectral or time-frequency analysis on individual channels to determine features for detecting and classifying events such as seizures and spikes [7, 8], and do not take full account or advantage of the inherently spatio-temporal nature of the EEG signal. In some cases, localization of focal epileptiform activity within the brain volume is possible by means of a biophysical volume conductor model and assuming simple dipolar current sources, see e.g., [9], yet such (exclusively) spatial approaches can have difficulties in distinguishing sources with strong spatial and temporal correlations.

BSS methods not only estimate the waveforms of the underlying sources but also provide spatial topographical information in terms of the source sensor projections, which uniquely identify each source. In the case of EEG data, these sensor projections are analogous to the scalp potential distributions (topographies) associated with each source waveform. Approximate prior knowledge of target source sensor projections may be useful for tracking and detection, if the spatial source attributes and mixing process remain relatively stable.

This work presents an approach to source tracking and detection in multichannel data, which exploits prior knowledge of the target source sensor projections, and uses these for comparison with the sensor projections of sources extracted from the EEG by means of BSS based on time-structure. Specifically, the method is illustrated in conjunction with a potential application for seizure detection epileptiform EEG.

Materials and Methods

Blind Source Separation: Conventional BSS methods assume a generative data model where M time-varying signals $\mathbf{x}(t) = [x_1(t), \ldots, x_M(t)]^T$ are a linear mixture of N sources $\mathbf{s}(t) = [s_1(t), \ldots, s_N(t)]^T$ subject to sensor noise $\mathbf{n}(t) = [n_1(t), \ldots, n_M(t)]^T$ so that

$$\mathbf{x}(t) = \mathbf{A}\mathbf{s}(t) + \mathbf{n}(t), \qquad (1)$$

ISSN: 1727-1983

where $\mathbf{A}$ is a $M \times N$ matrix whose columns represent the source sensor projections. The source number, time-series and sensor projections are all unknown, and the aim is to determine N, $\mathbf{s}(t)$ and $\mathbf{A}$ from $\mathbf{x}(t)$ using a set of minimal and generic assumptions only.

Such assumptions usually require that $N \leq M$, that $\mathbf{s}(t)$ are zero-mean signals with unique time-structure, and that $\mathbf{A}$ is non-singular matrix with unit norm columns. The noise term $\mathbf{n}(t)$ is often modelled by a zero-mean, spatially and temporally white, multivariate (gaussian) random process, or conveniently neglected.

Provided that $N \leq M$, a model order estimate $\hat{N} \approx N$ can be obtained from an eigenvalue decomposition of the data cross-covariance matrix, in terms of the number of dominant eigenvalues, e.g. using variance thresholds. In this study, $\hat{N}$ reflects the number of eigenvalues whose proportional contribution to overall variance is at least 1%. Determination of source waveform estimates $\hat{\mathbf{s}}(t) \approx \mathbf{s}(t)$ essentially requires an estimate of the mixing matrix $\hat{\mathbf{A}} \approx \mathbf{A}$ and involves inversion of the model (1)

$$\hat{\mathbf{s}}(t) = \hat{\mathbf{A}}^{\dagger}\mathbf{x}(t) = \hat{\mathbf{A}}^{\dagger}\left[\mathbf{A}\mathbf{s}(t) + \mathbf{n}(t)\right], \qquad (2)$$

where the $\hat{N} \times M$ matrix $\hat{\mathbf{A}}^{\dagger} = (\hat{\mathbf{A}}^{T}\hat{\mathbf{A}})^{-1}\hat{\mathbf{A}}^{T}$ is the pseudo-inverse of the mixing matrix estimate $\hat{\mathbf{A}}$.

Finding the mixing matrix estimate $\hat{\mathbf{A}}$ in the context of time-structure based BSS methods involves a numerical optimization problem with the goal of minimizing the temporal (spectral) dependencies among the source waveforms, for example through joint approximate diagonalization of lagged cross-covariance matrices, e.g., [6, 10, 11]. In this study, for speed and stability, we used an orthogonally constrained version of joint-diagonalization algorithm in [12], applied to the temporal cross-covariances of the spatially whitened data.

Source Tracking using Spatial Information: The proposed spatial approach to source tracking requires that the sensor projections (scalp potential distributions) of the target sources are approximately known *a priori*. In the context of BSS based analysis approaches, it is straightforward to obtain such target topographies by means of manual selection from a set of sources extracted from a representative segment of EEG containing clear examples of the source activity of interest, e.g., epileptiform activity related to seizures. In the case of focal epileptic seizures, it may also be possible to approximate the relevant scalp voltage distributions using a dipole source model.

Subsequent tracking of the target source activity involves repeated application of BSS to shorter segments of novel data in a moving window fashion. Since BSS methods using signal time-structure involve computation of second order temporal statistics only, it is possible to used relatively short windows, depending on the sampling rate. Ultimately, the choice of window duration and the degree of overlap between windows will reflect a balance between temporal resolution, the time-frequency characteristics and non-stationarity of the target source activity, robustness of the temporal statistics and computational load. In the present context, the signals were sampled at 200 Hz and the target source activity is characterized by a dominant rhythmic component in the 4-6 Hz range; hence, moving windows of 4 seconds duration with a 2 second partial overlap were used.

Given an estimate of the mixing matrix for a particular window of EEG data, i.e. estimates of the scalp topographies of the underlying, active sources, one straightforward means of quantifying the degree of correspondence between these sources and the target source with reference to their spatial topographical properties is to compute the (absolute) correlations between the target and sample source sensor projections, i.e. the dot products, since these are all unit norm vectors. If the target source is active, then there ought to be a high correlation between its sensor projection and one of the columns of the mixing matrix. Thus, the activity of an (in principle) arbitrary number of target sources may be monitored by considering the maximum spatial correlation between each target topography and the mixing matrix columns in each window.

Detection of Target Source Activity: One way of determining the presence or absence of a given target source in a particular epoch would be to apply a set of threshold criteria to the maximum spatial correlation of its sensor projection with the mixing matrix columns, which might possibly take into account the values in neighbouring windows, especially when considering sustained source activity such as epileptic seizures. In the case of noisy data such as EEG, the detection criteria should accommodate the fact that, due to sampling and estimation errors, the maximum spatial correlations may never be quite perfect (i.e. 1.0) and are likely to be subject to small variations from one window to the next. Hence, one possible detection rule might be triggered if the maximal spatial correlation exceeds a fairly high threshold (e.g. 0.9) in the current window and remains above a slightly lower threshold value (e.g. 0.85) in the subsequent window(s). Similarly, if source activity was "detected" in the preceding window(s), successful detection in the current window may only require the correlation to exceed the lower threshold value.

Acquisition and Processing of Ictal EEG: The utility of the proposed spatial source tracking method for tracking epileptic seizure activity was tested on two segments of 25-channel ictal EEG, recorded from one patient in a long-term epilepsy monitoring unit on two separate occasions. The Ag/AgCl electrodes were arranged on the scalp in accordance with the international 10-20 system, and EEG signals were recorded with a sampling rate of 200 Hz referenced to channel Fpz. For subsequent analysis, the data segments were off-line re-referenced to an average reference, and the mean was removed from each channel.

ISSN: 1727-1983

The first data segment, shown in Figure 1(a), served as a reference and consisted of 200 seconds of EEG, heavily contaminated by ocular, muscle and movement artifacts, and showing prominent focal seizure related activity between about 160 and 190 seconds, most clearly visible on channel P9. The source waveforms and sensor projections (scalp potential distributions) extracted by means of joint-diagonalization of both instantaneous and lagged cross-covariance matrices ($\tau = 0, 1, \ldots, 200$) computed over 10 second non-overlapping windows for the entire segment (i.e. exploiting non-stationarity and spectral signal characteristics) are shown in Figure 1(b); these sources reflect ocular artifacts such as blinks (S1) and horizontal eye movements (S2), as well as a "seizure related" component (S4) characterized by strong 5 Hz rhythmic activity from about 160 seconds, which can also be seen in the spectrogram of Figure 1(c).

The second data segment, seen in Figure 2(a), was recorded from the same patient 7 days after the first segment. The EEG is again heavily contaminated with ocular, muscle and movement artifacts, but seizure activity is visible (P9) from about 100 to 140 seconds. The source waveforms and sensor projections (scalp potential distributions) extracted from this segment (using the same BSS method as for segment 1) are shown in Figure 2(b), and again reflect both ocular artifact sources (S1, S2) and a source showing "seizure related" activity (S3) comprising two burst of 4-6 Hz rhythmic activity at about 100 and 130 seconds, seen also the spectrogram of Figure 2(c).

Visual inspection alone clearly indicates that the sensor projections of the seizure related sources, S4 and S3, from the first and second EEG segments, respectively, are very similar, as are those of the ocular artifacts, S1 and S2. This seems to support the validity of the assumption that the spatial source attributes (i.e. location of the epileptogenic focus) and the mixing process (i.e. the electrode positions and impedances) are relatively stable, as this is prerequisite for the application of any spatial approach to source tracking and detection.

Application for Seizure Onset Analysis: The source tracking and detection approach was first applied to EEG segment 1 in order to validate that the presence of a known source can be successfully detected by monitoring and thresholding the maximum absolute correlations between the "true" source topography (S4) and the columns of the mixing matrices estimated, using joint-diagonalization of lagged cross-covariances ($\tau = 0, 1, \ldots, 200$), over short 4 second moving windows. The detection thresholds were chosen to maximize the number of hits during the 30 second period of strong 5 Hz activity, whilst also minimizing the number of false positives at other times. For cross-validation, the method was subsequently applied to EEG segment 2, using the same target topography, window parameters, source separation criteria and detection thresholds that were used in EEG segment 1.

Results

The spatial correlation measure and detection results for target source S4 in EEG segment 1 are shown in Figure 1(d), and illustrate that the maximum spatial correlation reaches and maintains the highest levels during the period from 160 to 190 seconds when the activity of the "seizure related" source S4 has a strong rhythmic component at 5 Hz, seen in Figure 1(c). The threshold values and detection criteria which take into account correlation values of neighbouring windows ensure that occurrence of epochs marked as "ictal events" is limited to the rhythmic part of the waveform, despite one brief supra-threshold deflection earlier on in the recording.

For the cross-validation case, the spatial correlation and detection results for tracking the target source S4 (from EEG segment 1) in EEG segment 2 are illustrated in Figure 2(d). Although overall values are slightly lower than for segment 1, the maximum spatial correlation again reaches and maintains the highest levels during rhythmic part of the (true) "seizure related" source S3 between 100 and 140 seconds, seen also Figure 1(c). Although all of the epochs marked as "ictal events" occur during this time, a short segment of activity towards the end of the seizure is missed. One plausible explanation for this lapse is that the complex temporal dynamics in that part of the waveform are projected onto two components during the spatial whitening, which the subsequent orthogonally constrained source is unable to recombine into one component. Nevertheless, the performance of the method is encouraging, and without false positives.

Discussion

The aim of this work was to introduce and illustrate a concept for a spatial approach to source tracking and detection in multichannel EEG, based on the maximum absolute correlation of a target source sensor projection with the sensor projections of the underlying sources found to be present in a short segment of data. One potential potential application of such a spatial approach to source tracking may be in clinical neurophysiology for the detection of epileptiform activity related to seizures and, in principle, inter-ictal spikes, when the spatial attributes of the epileptogenic focus (location) have been previously diagnosed, are stable and can be parameterized in terms of a source sensor projection, where the latter can be determined by means of conventional BSS methods applied to a representative segment of EEG data containing seizure activity. In the case of target sources which characteristically exhibit periods of sustained rhythmic activity, it seems appropriate and intuitive to use BSS methods based on signal time-structure.

A potential application of this spatial topographical source detection method was illustrated on two segments of 25-channel ictal EEG. In the first segment, the method could successfully detect a known seizure source (validation), and in the second segment, the method was able to

ISSN: 1727-1983

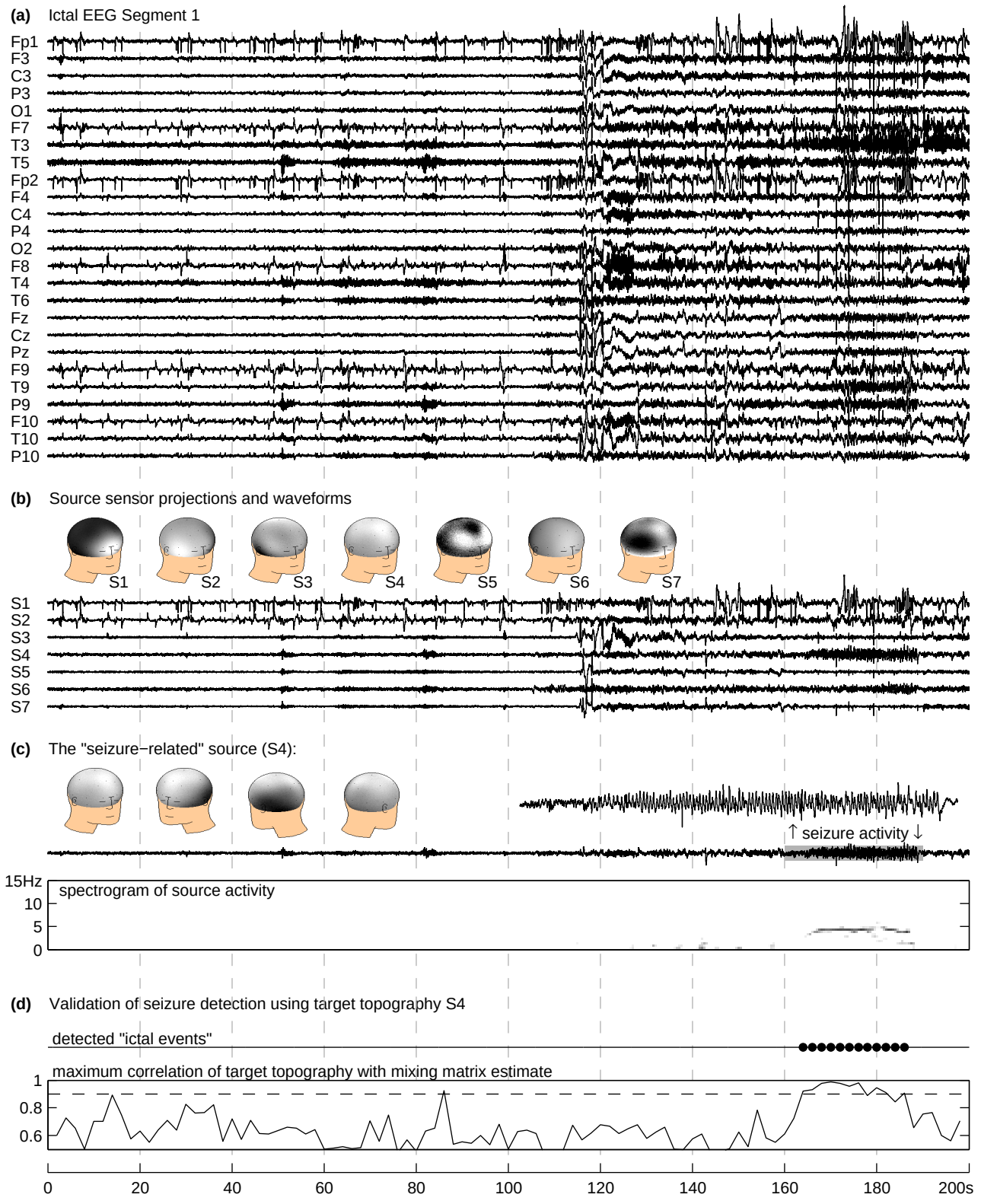

Figure 1: (a) 200 second segment of 25-channel ictal EEG with left temporal seizure onset after about 160 seconds. (b) Waveforms and sensor projections (scalp topographies) of the 7 strongest sources (from a total of 12), extracted by means of joint-diagonalization of both instantaneous and lagged cross-covariance matrices ($\tau = 0, 1, \ldots, 200$) computed over 10 second non-overlapping windows for the entire segment, thereby exploiting non-stationarity and spectral signal characteristics. These reflect ocular (S1, S2) artifacts as well as rhythmic seizure activity (S4). (c) A closer examination of the spatial and time-frequency properties of the "seizure related" source S4. (d) Validation of the seizure detection method using source S4 as the target, applied to 4 second windows with 2 seconds overlap. Detection involves thresholding the maximum correlation of the target topography with the columns of the mixing matrix estimated for each window.

ISSN: 1727-1983

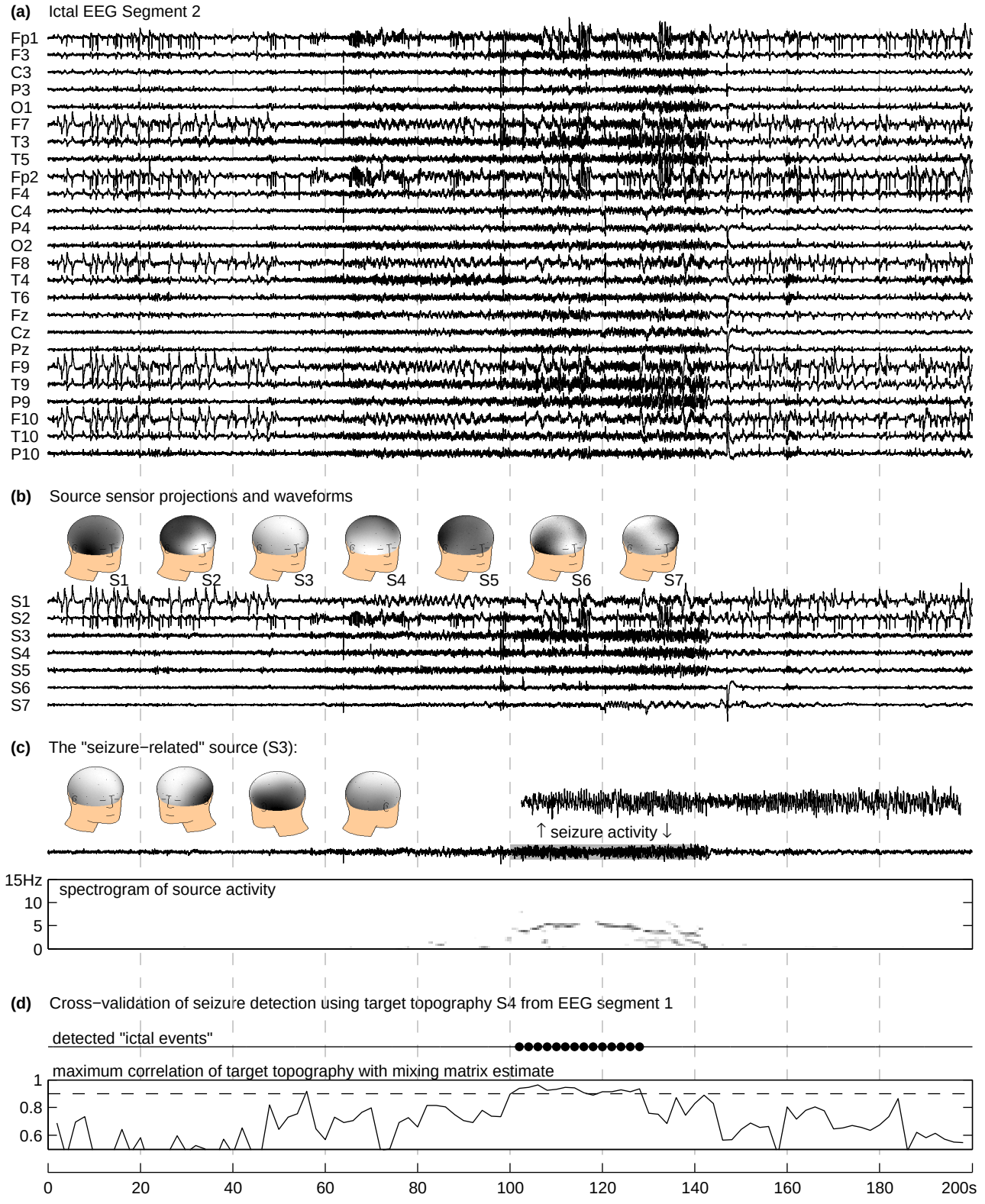

Figure 2: (a) 200 second segment of 25-channel ictal EEG (recorded 7 days after the previous segment) with seizure onset after about 100 seconds. (b) Waveforms and sensor projections (scalp topographies) of all 7 sources, extracted by means of joint-diagonalization of both instantaneous and lagged cross-covariance matrices ($\tau = 0, 1, \ldots, 200$) computed over 10 second non-overlapping windows for the entire segment, thereby exploiting non-stationarity and spectral signal characteristics. These reflect ocular (S1, S2) artifacts as well as rhythmic seizure activity (S3). (c) A closer examination of the spatial and time-frequency properties of the "seizure related" source S3. (d) Cross-validation of the seizure detection method using source S4 from the previous EEG segment as the target, and with application of the same tracking window parameters, detection measures and threshold criteria that were established before.

ISSN: 1727-1983

capture most of the activity associated with an unknown, but spatially similar, seizure related source. Since sources extracted by means of BSS methods are uniquely determined by their sensor projections, one advantage of this tracking approach is that the temporal characteristics of the target source waveforms need not be known explicitly, as is the case in other waveform-based seizure onset analysis approaches.

A potential disadvantage for this method is that in conjunction with BSS methods involving spatial whitening it is sometimes possible that complex source waveform dynamics may be projected onto several sources, which leads to a reduction in the spatial correlation of the relevant mixing matrix columns with the target topography and thereby fail to detect even relatively strong activity. One possible solution to the problem of such "split sources" would be to consider the spatial correlation of the target source with the entire source signal subspace, as proposed in [13], as a measure for detection. This alternative has a further advantage that determination of the source signal subspace, i.e. an orthonormal basis set spanning the same subspace as the columns of the mixing matrix, can be achieved using simpler and computationally more economical methods such as principal component analysis (PCA) and do not require the use of more advanced BSS methods during the tracking phase.

Whilst the detection results reported for the two segments of ictal EEG in this preliminary study serve to illustrate the concept of the method and show some promise, a more rigorous and extensive evaluation on data from several patients presenting with a wide range of seizures is required. Determining the reliability and accuracy of this and other spatial source tracking and detection methods forms a part of ongoing and future research efforts in our group.

Acknowledgment

This work was supported by United Kingdom EPSRC grant #GR/S13132/01.

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ISSN: 1727-1983