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Single subject EEG analysis based on topographic information

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Abstract. We propose and demonstrate a novel method for analyzing human EEG at a single-subject and single-trial level. We focus here on the analysis of data from an auditory object recognition experiment. The analysis is based on the topographic information that can be extracted in response to each stimulus. Temporally structured periods were statistically identified wherein a given topography predominated without any prior information about the temporal behavior and at single-subject level. Within these periods of stability, we were able to statistically identify the time periods over which responses to different object categories differed. In addition to providing novel methods for EEG analysis, these results show intriguing evidence that Event Related Potentials (ERPs) are reliably observable at a single-trial level when examined topographically.

Keywords: Electroencephalography, single trial, topography

1. Introduction

High temporal resolution scalp electroencephalography (EEG) is typically used to investigate responses to external stimuli by averaging peri-stimulus epochs at each electrode and across the entire montage. This procedure provides an estimation of the event-related potential (ERP), eliminating to a great extent the instrumental and physiological noise present at the single-trial level. The drawback of this approach is the inevitable loss of any non-phase-locked activities as well as smearing due to latency jitter across trials. Moreover, collapsing all the original information to an average response often prevents the performance of statistical analyses of effects at a single-subject level. This is particularly needed when studying individual patients with specific sensory-cognitive impairments.

Due to these and other limitations of canonical ERP analyses, increasing attention in the neuroscientific community has been devoted to the development of single-trial analysis methods. The majority of these approaches are based on modeling the brain processes underlying the amplitude modulations of the EEG signal. Among them, Independent Component Analysis has been proposed to disentangle contributions to the EEG that are spatially fixed but temporally independent [1]. The differentially Variable Component Analysis (dVCA) has been introduced in order to identify multiple evoked components using trial-to-trial variability [2]. Moreover, several other approaches have been proposed for filtering and de-noising the single electrical responses at specific electrodes [3][4][5].

In this paper, we propose an approach to contrast statistically two experimental conditions at a single-subject level using solely spatial features of the electric field and without taking into account any *a priori* temporal information [6]. We demonstrate the method on data previously analyzed at an ERP level including microstates analysis [7]. These previous results provide a comparison that can support the reliability of the present method.

2. Methodology

Subjects, stimuli, and task

Nine healthy subjects (six female), 21-34 years of age participated after providing written informed consent to the experimental procedures that were approved by the Ethics Committee of the University of Geneva. All subjects were right-handed. Auditory meaningful sounds of common objects

-500 ms in duration- were used for a target detection task [7]. On each block of trials, subjects were asked to discriminate target sounds via a button press. Targets (10% in each block) were living or man-made auditory objects alternating in each block of trials. Each block comprised 300 trials and each subject completed four blocks.

EEG acquisition and pre-processing

Continuous 64-channel EEG was acquired through Neuroscan Synamps, referenced to the nose, band-pass filtered 0.05-200 Hz, and digitized at 1000 Hz. Peri-stimulus epochs of continuous EEG (-100 to 500 ms) were obtained from each subject separately for each category of sound of object (living and man-made). DC correction and a 50 Hz notch filter were applied to each epoch. Trials with blinks or eye movements were rejected off-line, using a criterion of ±100 μV applied at all electrodes. Data from artifact electrodes from each subject and trial were interpolated using a 3-Dimensional spherical spline [8]. Data were finally recalculated against the average reference and down-sampled to a 62-channel montage. No baseline correction was applied.

In the following, we will consider two datasets: *dataset1* will refer to the trials involving presentation of sounds of living objects, and *dataset2* will refer to the trials involving presentation of sounds of man-made objects. In each of these two datasets the number of distracter and target trials is counterbalanced. Sixty EEG epochs in each dataset and for each subject is considered.

Single-trial analysis

We define a potential map as the vector of potential measurements at one time frame after the Global Field Power (GFP) at each time point [9] has normalized it. The algorithm is based on clustering maps with similar spatial features considering at once all the potential maps of both datasets. The estimation of the clusters is achieved using an expectation maximization algorithm for a mixture of Q (here Q=5) Gaussians [10][11]. We do not make any assumption about the temporal information conveyed by the maps because all the data are pooled together in the same N-dimensional space, where N is the number of electrodes.

The algorithm is initialized with a first estimation of the priors, the centers and the covariance matrix for each Gaussian. A k-means algorithm with 500 iterations is used to determine the centers [12]. The priors are computed from the proportion of examples belonging to each cluster. The covariance matrices are calculated as the sample covariance of the points associated with (i.e. closest to) the corresponding centers. A new estimate of priors, mean maps and their covariance was achieved by 500 iterations of the expectation-maximization algorithm.

The estimated model was used to label the data according to the higher conditional probability. The labeled data were then reorganized recovering their position in time and for each trial, considering the two datasets separately. This new representation of the evoked response can demonstrate whether there exist specific patterns for each condition at a single-trial level.

To statistically evaluate our results, first a one-way repeated measures ANOVA was performed on the conditional probabilities for each of the two datasets; next, a series of post-hoc paired t-tests was performed between pairs of conditional probabilities as a function of time. To account for temporal auto-correlation, we applied a criterion to both the ANOVA ($\alpha<0.05$) and t-tests ($\alpha<0.01$), such that an effect was only considered statistically robust if it was significant for at least 11 consecutive data points [4]. The series of post-hoc t-tests was subdivided in two groups of analysis. First, we contrasted the conditional probabilities related to different maps in the two datasets and extracted those temporal periods during which only one map was significantly higher than all the others (Fig 1, e2). Secondly – within those periods - we contrasted the conditional probabilities related to the same maps and across datasets. This second series of t-tests provides an estimate of the differences elicited by the two types of stimuli at a single-trial level (Fig1, e3).

3. Results

We here present the results for one subject of the group. Results show that the occurrence of each map is structured in time and consistent across trials (Fig1, a-b). Indeed, the mean conditional probabilities across trials (Fig1, c-d) shows that there was a higher posterior probability of a given map for specified post-stimulus onset periods, which was not evident before the stimulus onset. The one-way repeated measures ANOVA identified a main effect of map over several post-stimulus time intervals, as well as some short-lived periods during the pre-stimulus period (Fig1, e1).

From the post-hoc t-tests, we identified several periods over which only one map was significantly predominant (Fig1, e1-e2). Contrasting statistically the conditional probabilities for each map in the two conditions, we were able to identify several time periods of interest (Fig1, e.3); only one of those periods survived to the 11-samples temporal criterion and this was related to the occurrence of map four over the period 200-213 ms (Fig1, e.3).

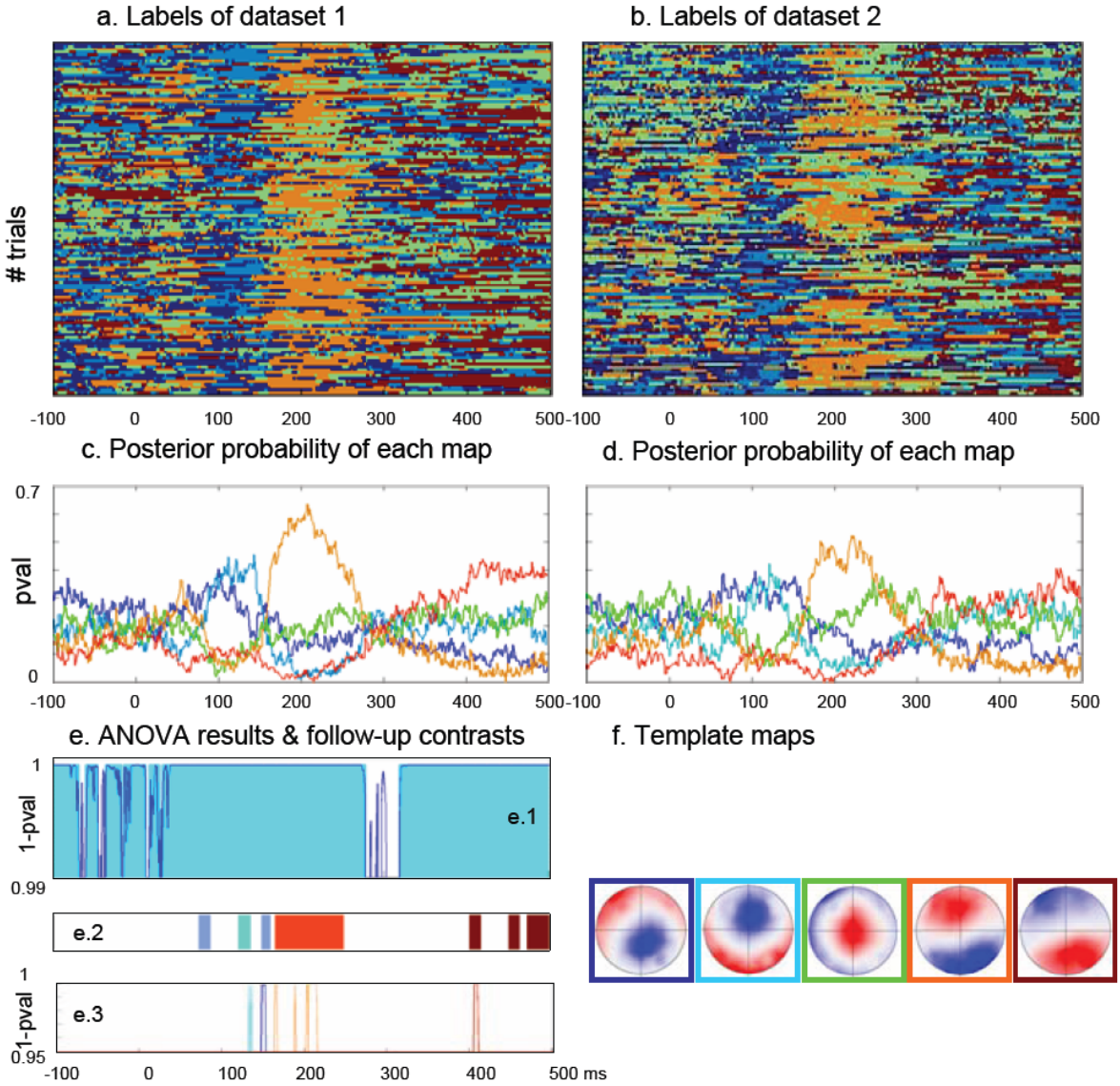

Fig1. *(a-b) Labels according to the highest conditional probability at each time frame and trial; (c-d) mean conditional probability of each map; (e) statistical analyses: e.1 light blue highlights period of significant difference bethween conditional probabilities for each map based on one way Anova; e.2 periods over which one map was predomint over the others based on t-test;e.3 t-test probability contrasting the same maps in the two conditions (restricted to the interval of where one map was dominant). (f) Mean maps for each cluster.*

4. Discussion

We proposed and demonstrated a novel approach to analyze ERPs at a single-subject level based solely on topographic information. The method allows for statistically identifying time periods over which two conditions differ most with minimal *a priori* constraints.

This novel approach offers ERP visualization [13] at a single-trial level with the same temporal resolution as the original EEG data. Other single-trial analysis methods, based on the EEG amplitude

modulation instead of topographies, require *ad hoc* filtering of the single waveforms [3][4][5] or strong hypotheses about the underlying brain activity (i.e. ICA) [1].

We implicitly demonstrated that by modeling the data's noise as a mixture of Gaussians we are able to provide an ERP representation that is consistent across trials and structured in time. This evidence is in agreement with our expectation that the topography of the electric field at the scalp exhibits temporal structure – i.e. microstates – that can last from tens to hundreds of milliseconds [14][15][16]. The result is particularly convincing because we did not take into account temporal information and therefore they can be interpreted as an inherent property of the data.

In order to demonstrate the method we applied the algorithm to a published data set, previously analyzed at a group-average ERP level [7]. The results obtained with the present method show several points of agreement with the previous analysis, supporting the reliability of this novel approach. Indeed, the difference found between the two conditions is within the same temporal period. The here derived template maps present evident similarities with the microstates estimated in the ERP analysis and are in general agreement with auditory evoked potential (AEP) components typically observed at ERP level [17].

One limitation of the presented methods is its necessity for *a priori* constraining the number of clusters. One solution to this could be to incrementally increase the number of clusters until a limit is reached at which one or more of the additional maps are only negligibly present in the representation, much like what has been proposed for dipole modeling.

Future directions include establishing whether this model can be informative about trial-specific activity (e.g. reaction time, accuracy, or other classifiers for the stimulus being encountered), and to investigate the relation between this approach and other single-trial representations, such as the one based on Independent Component Analysis. Another important direction is investigating inter-trial variability as a result of plasticity or learning effects, and also inter-individual differences. This is particularly needed when analyzing patients with specific sensory-cognitive impairments and their brain activity in comparison to healthy populations.

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