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Decomposition and Evaluation of activity in multiple Event-Related trials

K. Michalopoulos[1,2], M. Zervakis[1], N. Bourbakis[2], P. Giannakopoulos[3], M-P. Deiber[4,5]
[1]Department of Electronics and Computer Engineering, Technical University of Crete, Chania, 73100 Greece
[2]Wright State University –ATR Center, Dayton OH, 2AIIS Inc. Centreville OH and 3NIA, Baltimore, MD
[3]Division of General Psychiatry, Department of Psychiatry, University Hospitals of Geneva, Switzerland
[4]INSERM Unit 1039, Faculty of Medicine, La Tronche, France
[5]Clinical Neurophysiology and Neuroimaging Unit, Division of Neuropsychiatry, Department of Psychiatry, University Hospitals of Geneva, Switzerland

Abstract— **It is generally accepted that evoked and induced activations represent different aspects of cerebral functions during an Event Related Potentials (ERP) experiment. Independent Component Analysis (ICA) has been successfully applied to event related electroencephalography (EEG) to decompose it into a sum of spatially fixed and temporally independent components that can be attributed to underlying cortical activity. A major problem in the application of ICA is the stability of estimated independent components. In this paper we exploited the split-half approach to assess component stability. We used different measures quantifying both phase and energy aspects of the ERP, in order to distinguish evoked from induced oscillations. We applied these measures to the stable independent components derived from a dataset of progressive Mild Cognitive Impairment (PMCI) and elderly controls. We found reduced energy in the induced theta activity in PMCI subjects, in accordance with previous studies. In addition, PMCI subjects presented lower phase-locking values and diminished late alpha band energy in contrast to controls.**

Keywords- ICA; intertrial coherence measures; time-frequency content characterization;evoked and induced activity

I. INTRODUCTION

Event-related or event-locked activity induced by an external or internal stimulus involves both phase-locked and non phase-locked rhythmic oscillations. Event-related potentials (ERP) encompass the phase-locked (evoked) activity at different frequency bands. Recent studies have also revealed responses that are not phase-locked to the occurrence of event (induced), which vary with stimulus and can interact with the ERP. The origins of brain sources relate to multiple task conditions and many stimulus types that define topographically distinct brain functions, some operating independently and some being coupled[1].

In the above context it is quite important to provide efficient means of decomposing the multichannel EEG signal into meaningful components, through Independent Component Analysis (ICA). A major problem in application of ICA relates to the instability of derived components. Another difficulty refers to the matching and characterization of the components throughout multiple ERP trials. A variety of measures have been proposed to characterize the nature of the derived components [2, 3]. In this paper, we address these issues and describe a complete methodology for characterizing the content of a multi-trial ERP experiment. Different approaches have been proposed in order to estimate the stability of the ICA solution [4, 5]. In this study we are using a split-half approach introduced in [6], which allows the derivation of a subset of components representing stable, reliable sources. The content of each component is expressed in the Time-Frequency (TF) domain through the wavelet transform. Furthermore, using various measures of ERP activity as well as the recorder topography, we analyze the multi-trial content of the components and attempt to characterize the brain activations that they capture. The obtention of components representing stable and well characterized activations enables the extraction of quantitative features and their use as markers for assessment of pathological conditions.

We applied the proposed methodology on a dataset consisting of control subjects and patients with Progressive Mild Cognitive Impairment (PMCI), while they performed a visual memory test. The results indicated that the proposed component analysis and framework is able to depict the synchronized activations during a certain mental task, e.g., working memory. As such, it can efficiently reveal and quantify both group and individual differences in pathologic populations.

II. METHODS

A. Independent Component Analysis

ICA is increasingly used in the field of biomedical signal processing. It aims at separating multi-channel biomedical signals into their constituent underlying components. ICA has been successfully applied on continuous or event-related EEG to decompose it into a sum of spatially fixed and temporally independent components that can have different spatial distribution patterns, which in turn may be directly attributed to underlying cortical activity [7-9].

B. ICA stability

A major problem in the application of ICA is the stability of estimated independent components. Since the ICA techniques are stochastic in nature, their results may be somewhat different in different runs of the algorithm. In fact, many algorithms give different components when run multiple times, due to different initial conditions. A closely related issue is that the contrast function used in estimation may possess many local minima so that ICA may converge to different solutions. Another issue is the uncertainty in the nature of the

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EEG recorded data. ICA converges towards a solution that maximizes component independence, but there is no guarantee that the brain sources are completely independent. There are also effects of the finite sample size, inducing statistical errors in the estimation[6]. In order to address stability issues in independent components, we adopt the method described in [6] based on a concept similar to bootstrap, in which we essentially perform ICA analysis on a large number of possible subsets of the data [4]. Rather than using random permutation of the data, we perform the analysis twice on 50% of the data. One disadvantage of this approach is that it can be biased by the data split, as well as by the pairing of Independent Components (ICs). Nevertheless, the use of derived stable components for the characterization of the ERP content presents the advantage that the statistics produced by this analysis can be reproduced safely. On top of that, the number of reliable components is usually smaller than the number of total extracted independent components, so that the assessment of activity of stable components becomes faster and easier.

C. Time-Frequency transforms

EEG signal analysis provides the advantage of high time resolution and, as such, it can deduce information related to both local and widespread neuronal activations in short-time periods and their evolution time-course. While FFT reveals significant frequency information, there is no information concerning the temporal distribution of those frequencies. A a highly non-stationary signal with composing frequencies changing through time, EEG cannot be fully supported by the stationary nature of FFT.

Wavelet approaches decompose the signal into constituent time–frequency (TF) ranges of energy, based on the notion of scale applied on a set of basis functions. The application of wavelet transforms in TF analysis is guided by the tradeoff between frequency and time, since wavelets compute small scale (high-frequency) intervals with shorter time windows and large scale regions (low-frequency) with longer time windows. As a result, they resolve higher scale energy with high resolution in time but not in frequency. In this study we use wavelets to implement TF decompositions of EEG content using the complex Morlet wavelet functions[10].

III. Intertrial Synchronization Measures

The similarity or consistency of components across trials has been initially addressed in ERP studies either through the average signal across trials or the spectral energy (SE) of the inter-trial average. We define the consistency measures on the TF representation of a component in the wavelet domain [11].

A. Phase Intertrial Coherence

In order to quantify phase locked coherence along the trials, we use a variant of the inter-trial coherence (ITC) measure [11] which reflects the phase-locked consistency among trials and is derived from the analysis of individual trials TF maps at each specific channel/ component. It takes under consideration only the phase of the signal in each trial, so that any phase-locked activity of either large or small amplitude has the same effect. In order to engage the amplitude along with the phase of each trial, the phase inter-trial coherence (PIC) is defined as:

$$C_{PIC}[k,n] = \frac{|\sum_i X_i[k,n]|}{\sum_i |X_i[k,n]|} \leq 1 \quad (1)$$

where Xi[k,n] denotes the frequency coefficient at the i-th trial and the k-th frequency tick. Equality holds if and only if all trials involve the same signal with the same phase, but each trial contributes to the measure according to its amplitude. The PIC measure performs just scaling, preserving the structure of the cloud of coefficients (amplitude and phase), so that it measures uniformity on a mixed product term involving both the angle and amplitude of coefficients. Trials of little amplitude in a frequency band affect the ITC measure identically as trials with significant amplitude activity, but this is not true for PIC which is proportionally affected by the amplitude of phase-locked trials.

B. Phase-shift Intertrial coherence

For the quantification of event-related but not phase-locked activity, we can use a measure based on the energy of single-trial decompositions which highlights the frequency bands of increased energy in all trials. More specifically, the phase-shift intertrial coherence (PsIC) is defined as:

$$C_{PsIC}[k,n] = \frac{\sum_i |X_i[k,n]|^2}{\max_{k,n} \sum_i |X_i[k,n]|^2} \leq 1 \quad (2)$$

where equality implies the same magnitude of X[k,n], even with different shifts at each trial[11]. Complementary to PIC, the PsIC map reflects the non-phase-locked activity, which implies similar structure of the signal but without phasic coherence across trials. PsIC is a variation of the energy measure used in Event-Related Desynchronization/ Synchronization (ERD/ERS), using only the post-event energy.

C. Event-Related Synchronization and Desynchronization

ERD/ERS represent a mean decrease/ increase of event-related power relative to a baseline [12]. In our study, the baseline is computed per subject and corresponds to the average power over all trials, time instances and frequency points considered pre-stimulus. The reasoning behind this measure implies that there exist pre-stimulus brain sources that change their post-stimulus energy status due to event presentation. In the same line, the PsIC measure reflects persistent activity in all trials without baseline comparison; a frequency band active in all trials would have a PsIC close to 1. Thus, it can be used in conjunction with the ERD/ERS measure in order to evaluate event-related changes in ongoing oscillations.

IV. Methodology

Significant effort has been dedicated to the analysis of EEG channel signal content. Prominent approaches focus on specific frequency bands and examine the ERP (for evoked activity) and the ERD/ERS measures (for induced activity)[9, 13]. Furthermore, by subtracting the mean signal (ERP) from each single trial, the induced oscillations can be highlighted [13].

In our study we attempt to explore an alternative approach, which considers all involved activities simultaneously. We consider independent components instead of channels in order to decouple EEG signals, mixed due to volume conduction effects. Using the split-half approach, we derive a subset of the available components representing stable, reliable sources.

Then, we consider the TF activity maps to study the different types of activations involved in each component. These measures do not integrate activity over trials, but rather reflect the synchronization structure of activity over trials. Thus, they do preserve the nature of activity they are intended to quantify. Finally, we isolate regions of important activation in each measure and compute population statistics, to derive robust markers for population comparison and assessment of disease effects.

In sum, we use the split-half approach described in [6] to extract stable independent components of each subject. Next, we apply the inter-trial measures and evaluate the activations taking place. Finally, statistics are extracted from components with significant activity and group comparison is performed.

A. Selection of components and segmentation of significant TF regions.

Selecting individual components that capture interesting brain activity is not a trivial task. Using the measures of PIC and PsIC we initially compute their average values per band, which can be plotted and compared in a single diagram for all derived components. By comparing the overall power in this plot, we can identify those components that express significant activation lasting for a significant time interval, justified through the integration over time. Thus, for each component we obtain a global value of each measure, as a single average value for each band. Components presenting activity above a certain threshold are selected for further visual evaluation. For the detailed analysis of selected components, we then consider the two-dimensional TF maps of the three measures that reflect the component consistency (in energy and/or phase) along trials.

Using this selection method we are able to initially select interesting components that contain both phase and non phase-locked activity relevant to the task. We prefer to use a conservative threshold on the average measures, i.e. the upper quartile of all values, in order to capture components presenting partial phase-locked and non-phase locked activity, that otherwise would be discarded. Then each component is visually evaluated and characterized according to the values of the measures (taking under consideration topography, latency and frequency band of activation).

Visual inspection of the selected components confirms that the selected components present relevant activations. Finally, for each time-frequency map we compute the histogram of its values and use the upper quartile in order to derive a threshold for defining significant regions in the map. Then we calculate the center mass of the significant region in order to classify the central band and latency in which the activation occurs. Based on this threshold, we segment regions of interest in the measures and derive their mean time, frequency and spectral power. For each subject, we group the stable components that present significant activation in each measure (power of the mean signal, PIC, PsIC or ERD/S) according to the band in which the activation takes place.

B. Dataset Description

The dataset used was provided by the Clinical Neurophysiology and Neuroimaging Unit, University Hospitals of Geneva (Switzerland). All individuals in the control group were screened using extensive neuropsychological testing to confirm the absence of cognitive deficits [13]. The elderly controls group used in this study consists of 12 subjects. MCI cases were recruited in a large acute and intermediate care geriatric hospital. The same clinical and neuropsychological screening as for elderly controls was used [13]. Fifty five percent of the original MCI cases demonstrated significant cognitive decline after 1 year follow-up and constituted the progressive MCI group (mean age: 82.8 ± 5.4 years) [13]. The final PMCI group used is this study consisted of 14 subjects. Detailed description of the experimental conditions and data acquisition can be found in [14].

All trials from the detection task (0-back) were used in our analysis and for each trial, we analyzed a time portion starting 1000ms before visual stimulus presentation and lasting for 3000ms post-stimulus. The vertical line in the TF illustrations of Figure 1 indicates stimulus onset; the vertical axis spans frequencies from 1Hz to 14Hz in a logarithmic scale.

V. RESULTS

A. Control Subjects

Elderly control subjects show phase-locked activity in delta, theta and alpha bands in the period 200 to 300ms after the event. Theta and alpha phase-locked activity precedes the one in delta band for all components. In essence, delta band seems to spread in a larger temporal interval following the event. More specifically, alpha and theta phase-locked activity occurs at around 200-300ms, whereas delta evoked components peak at 330ms after the event. All phase-locked theta and delta components present a power increase compared to pre-stimulus baseline, which appears as an increase in the ERD/ERS measure. In many cases, delta and theta activations are coupled into a single component (Figures 1a and 1d). These results are compatible with other findings indicating power increase in theta and delta bands associated with attention and cognitive processing, respectively [15]. In addition, early evoked alpha activity was reported in other studies related to stimulus perception [16].

Theta band induced activity was observed 1200 ms after the event. Since the PsIC measure is normalized according to the maximum energy, which often appears with increased in delta band, we evaluated theta and alpha activity separately from delta. There was an increase in the power of the theta post-stimulus induced activity, as expressed in the ERD/ERS measure. An example can be viewed in Figure 1d. As induced theta we treat the components that do not present significant PIC measure in the same region where strong PsIC is identified. Theta induced response has been associated with working memory processes in many studies [16].

Alpha components generally display activity in the time period of 250 ms to 350 ms after the event. In fact, three types of alpha activity can be distinguished. a) Some alpha oscillatory activity synchronizes its phase right after the event and presents high phase locking coherence at 200 ms, just

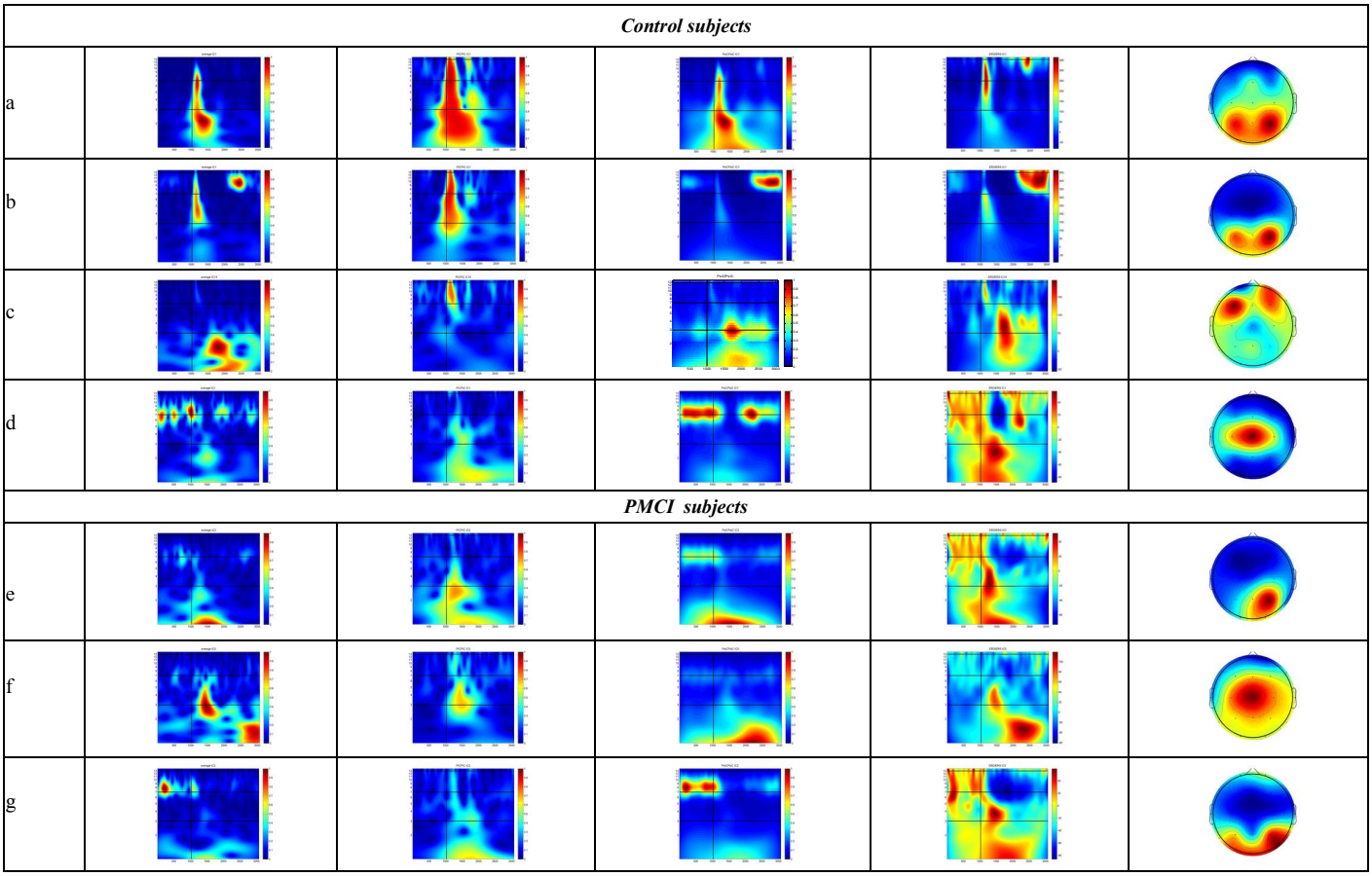

Figure 1: Rows a-d indicative maps of activity measures for Control subjects. Rows e-g indicative maps of activity measures for PMCI patients. First column displays the spectral energy of the mean signal. Second , third and fourth columns display PIC, PsIC and ERD/ERS measures, respectively. Last column presents the component topography based on the mixing vector of the corresponding IC. For PIC and PsIC measures legend is scaled from 0 to 1, while ERD/ERS legend represents percentage of increase with red shades and percentage of decrease with blue shades.

before power desynchronization. Example is shown in Figure 1a (early alpha component). The phase locking effect in alpha oscillatory activity does not necessarily display significant increase in power compared to pre-stimulus baseline. Phase locking without power increase appears in Figure 1b, revealing phase synchronization of ongoing oscillations after the event. Alternatively, the power increase in Figure 1c indicates a slightly different, additive nature of these components that contribute to an evoked part of ERP. b) Some pre-stimulus alpha oscillatory activity, showing power decrease after the event but no phase locking before or after the event, is present in control components as in Figure 1d. This kind of activity, which recovers after some time, forms the main contribution to the alpha desynchronization in the ERD effect. c) Finally, there exist additive non (or partially) phase-locked alpha activations after 1000 ms, such as in Figure 1a and 1b (late alpha activation), which also display an instantaneous power increase in the ERD/ERS measure.

Alpha desynchronization (ERD) is known to correlate with memory performance in normal subjects [17]. In addition, early alpha phase-locking has been reported to relate to attention and perception of the stimulus. Higher alpha phase locking seems to be related to good perception and memory performance in normal subjects [16]. Our findings support such reports, since control subjects present alpha phase-locked activity and strong alpha ERD after the event. Finally, late alpha induced oscillations were found in control subjects after the desynchronization effect. This late alpha induced activity can be seen in Figure 1a and Figure 1b and is associated with working memory activation as a response to the presented target [17].

In terms of spatial localization of the activations, components that present strong delta phase-locked activity exhibit posterior topography (Figure 1a and 1b). Theta phase-locked components present parietal and occipital topography as can be observed in Figure 1b. Theta induced activity displayed mainly frontal topography as in Figure 1c. Alpha early phase-locked activity (Figure 1a, 1b) appears with posterior distribution, whereas late additive activation shows frontal localization. Induced alpha oscillations contributing to alpha ERD displayed mainly a central topography (Figure 1d), similar to previous studies.

B. PMCI Subjects

Statistical results for this group are presented in Table 1b. Progressive MCI subjects display decreased phase locking in delta and theta bands. Activations follow the same pattern as in controls, with delta band presenting later evoked oscillations. Theta phase-locked activations occur at 200 ms post-stimulus and precede delta band activations that occur on average at 340 ms post-stimulus. Induced theta activity is significantly

Table 1a. Statistics for phase locked activity			
Band	***Controls PIC***	***PMCI PIC***	***P-Value: a=0.05***
Delta	time= 473 freq =3.4 PIC energy = 349 PIC values = 0.60	time = 339.5 freq =3.0 PIC energy = 303 PIC values = 0.51	No signif diff. p=0.0216(Control)
Theta	time = 236 freq =6 PIC energy = 510 PIC values = 0.72	time = 269 freq = 5.2 PIC energy = 490 PIC values = 0.55	No signif diff. p=0.004(Control)
Alpha	time = 296 freq =11.3 PIC energy = 205 PIC values = 0.65	time = 193 freq =10.55 PIC energy = 105 PIC values = 0.47	p =0.009(Control) p =0.031(Control)

Table 1b. Statistics for Phase-Shift activity			
Band	***Controls PsIC***	***PMCI PsIC***	***P-Value: a=0.05***
Delta	time= 629 freq = 3 PsIC energy = 550	time = 474 freq =3.2 PsIC energy = 529	No signif diff.
Theta	time = 1249 freq =6 PsIC energy = 810	time = 1266 freq = 4.2 PsIC energy = 470	P = 0.008(Control)
Early Alpha	time = 229.70 freq =12.12 PsIC energy = 322	time = 302 freq =9.8 PsIC energy = 307	No signif diff.
Late Alpha	time = 1036 Freq = 11.3 PsIC energy = 267	time = 1300 Freq = 10.5 PsIC energy = 185	p=0.032(Control)

reduced in PMCI as compared to control subjects. Delta and theta power is significantly lower in PMCI than in control subjects. This finding is in agreement with other studies that attribute theta as the main band related to memory functions. Reduced theta phase-locking and power in PMCI patients can be attributed to the alteration of memory functions due to MCI pathology[13].

A major difference between PMCI and control subjects is the absence of alpha phase-locked activations in most PMCI, resulting in reduced power and phase locking values as compared to controls. This is in line with studies that report lower peak of alpha power in PMCI and Alzheimer's disease (AD) patients. Furthermore, induced alpha activations (Figure 1e, 1f, 1g) formulate the ERD with little or no power reorganization after the event in contrast to controls. This results in significantly higher energy in late alpha regions of the PsIC plots (late alpha reactivity) in control subjects as compared to PMCI. This is in line with findings suggesting that higher frequencies are sensitive to mental decline, associating late alpha activity with memory processes [18]. Another important finding is that ERD of alpha induced oscillations lasts longer in PMCI compared to controls (about 300ms in total). This could be explained by the fact that the duration of alpha ERD response increases with increasing memory load. Memory deficits in PMCI subjects would result in greater memory load, resulting in increased duration of alpha ERD[19]. This is also in agreement with the literature, where enhanced ERD has been observed with increased memory load.

The topographical distribution of the different activations is similar in PMCI and controls. Theta phase-locked activations present mostly a posterior topography (Figure 1e, 1f), as delta phase-locked activity. Theta induced activity, expected in more frontal locations, is much weaker in PMCI than in controls and often appears together with induced delta activity at more central location (Figure 1f). PMCI alpha ERD activity is weaker than in controls with no late recovery, being shifted to more posterior location (Figure 1g).

VI. CONCLUSSIONS

During a memory task, different brain mechanisms are activated that allow recognizing and processing of the incoming information. We analyzed a 0-back, visual detection, working memory experiment performed by elderly control and PMCI subjects.

Phase-locked activity that can be attributed to stimulus perception and attention was detected in both groups. More specifically, phase-locked delta, theta and alpha activations were found in the period following stimulus presentation in both groups. They presented a parietal topography, being affected by the visual nature of the stimulus. This is in line with reports suggesting that the superposition of phase-locked activity in delta to alpha frequencies contribute to the generation of the average ERP[16]. Delta and theta phase-locked activations were accompanied by a power increase, reflected in the ERD/ERS measure in the specific bands, supporting their stimulus-related characteristics [15, 20].

As compared to controls, PMCI patients presented reduced phase-locking in theta/ delta bands without significant power differences. This can be attributed to the limited capacities of PMCI subjects to attention/ cognition, inducing response variations from trial to trial. Similarly, alpha band presented reduced phase-locking, accompanied by reduced energy. This could be related to deficits in stimulus processing, orientation and attention in PMCI, higher frequency bands tending to be more sensitive to mental decline[18].

Theta induced oscillations (as expressed by the PsIC measure with no PIC values) were found at around 1200 ms after the stimulus, and also presented power increase (ERS). PMCI subjects showed reduced theta induced power compared to controls, that could be attributed to the alteration of their attention and memory functions[13].

Induced alpha activity presented significant power decrease following the stimulus, expressed as ERD, which was found to

be significantly larger and of longer duration in PMCI patients. Alpha ERD is known to correlate with memory performance and mental activation. Increased alpha ERD in PMCI subjects suggests the use of increased cognitive resources for completing the task[19]. Increased ERD has been also reported in patients with dementia and AD in other studies[19]. Alpha induced oscillations presented a late ERS in control subjects which was reduced or completely absent in PMCI patients. Such late alpha induced activity is related to working memory maintenance for further tasks[17]. The lack of alpha power increase in PMCI patients could be related to memory deficits and can also be associated with the reduced energy of late induced theta, the later relating to reduced engagements of working memory[13].

Our results are in agreement with and extend a previous study on the same dataset [13], where the authors reported evoked theta activity at posterior locations while induced theta activity was located in frontal regions. Furthermore, induced theta emerged later than evoked theta activity. Global theta energy did not reveal any differentiation between the two groups because of the mixed evoked and induced activities. In contrast, a significant reduction of induced theta power was found. These findings are in agreement with our results, as we found no significant difference in the evoked theta energy between the two groups, but detected significant decrease in theta induced energy. The PsIC measure shows that induced delta lags in time the evoked theta activation, expressed by the PIC measure. Furthermore, the derived topography in our analysis agrees with that of [13] for both induced and evoked theta.

Our methodology enables the separation of evoked and induced activations that can be observed and evaluated in parallel, in terms of their activation content and topography. In addition to the study of theta activation as in[13], our approach enables the analysis of other bands, such as alpha, where we also detect evoked and induced activity of distinct nature and topography. Another advantage is that we make no assumptions about the generation and manifestation of the evoked activity. Removing the mean activity in a specific band, as in [13], makes use of the assumption that the evoked activation is generated in each trial at the same latency. Many studies suggest that phase-locked activations emerge with some jitter in latency from trial to trial and are affected by fatigue and level of attention[2]. This suggests that removing the mean activation in a certain frequency band leaves residual energy which cannot be anticipated beforehand.

We explored a recent method for evaluating the stability of the ICA components. Through the use of activation measures that summarize activity over trials in various ways, we were able to study simultaneously many frequency bands and types of activation (evoked or induced), with clear distinction of time, topography, and frequency signature. The proposed methodology forms an alternative technique that can be used to complement previous studies and derive new associations of brain activity.

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