Gamma band activity in an auditory oddball paradigm studied with the wavelet transform


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Abstract

Objectives: To examine the characteristics of evoked and induced gamma band oscillatory responses occurring during P300 development in an auditory oddball paradigm.

Methods: A time-frequency analysis method was applied to an auditory oddball paradigm in 7 healthy subjects. This method combines a multiresolution wavelet algorithm for signal extraction and the Gabor transform to represent the temporal evolution of the selected frequency components. Phase-locked or evoked activity and also non-phase-locked activity were computed for both standard and target stimuli.

Results: The gamma band frequency components differed between target and non-target stimuli processing. The study showed an early and mainly phase-locked oscillatory response appearing around 26±28 ms after both standard and target stimuli onset. This response showed a spectral peak around 44 Hz for both stimuli. A late oscillatory activity peaking at 37 Hz with a latency around 360 ms was observed appearing only for target stimuli. The latency of this late oscillatory activity had a high correlation (P = 0.002) to the latency of the P300 wave.

Conclusions: EEG signal analysis with wavelet transform allows the identification of an early oscillatory cortical response in the gamma frequency range, as well as a late P300-related response. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Event-related potentials; Gamma band response; Oscillatory brain potentials; P300 wave; Time-frequency analysis; Wavelet transform

1. Introduction

Event-related brain potentials (ERPs) are time-varying signals which reflect the summed time courses of underlying neural events during information processing in the brain. The processing mechanisms may operate on different time scales and may also be entirely or partly overlapping, so the reliable component isolation remains problematic.

The neuronal correlates of the detection of subjectively relevant information are commonly studied with oddball paradigms, in which occasional relevant (target) stimuli, which require a specific cognitive response, have to be detected in a train of frequent irrelevant (non-target) stimuli. An ERP component around 300 ms post-stimulus named P300, a large positive-going potential with a parieto-central distribution, is consistently elicited by rare attended stimuli in an oddball task. This brain potential is thought to reflect attentional resource allocation when working memory is engaged and despite its simplicity it has provided a great deal of information about the neural activity underlying fundamental cognitive operations (Picton, 1992; Polich, 1998). P300 waves have shown condition-specific shapes, latencies and scalp topographies (Johnson, 1989). These observations imply that P300 is not an unitary phenomenon but may have an heterogeneous and multicomponent structure (Molnar, 1994; Kasaï et al., 1999).

Event-related oscillations interwoven with resonances and natural frequencies may constitute the main framework for communication, information and signal processing in the brain (Basar et al., 1999b, 2000; Sannita, 2000). Oscillatory neuroelectric theory has recently attracted much interest, mainly focused on synchronous gamma activity in spatially distributed cells. Frequencies in the gamma range are believed to be involved in the synchronization of neural responses, cortical binding and/or selective coupling of cortical areas involved in the processing of sensory stimulation (Singer, 1993; Jefferys et al., 1996; Kowalik et al., 2000) with relevant psychophysiological correlates and functional significance. This high frequency activity occurs in the time domain in which fundamental aspects of cogni-
tion are also likely to take place (Basar Eroglu et al., 1996). According to this hypothesis, synchrony serves as a temporal code to bind the cells representing features of an object (Engel et al., 1992; Desmedt and Tomberg, 1995; Skinner et al., 2000).

In order to evaluate gamma activity over time, various methods have been employed. The first type of approach has been to apply various kinds of digital filters to the signal in either the time or the frequency domain (Press et al., 1992; Pfurtscheller, 1999). The second type of approach has involved various forms of time-frequency analysis (Sinkkonen et al., 1995) such as a moving window short time Fourier transform (Haig et al., 1999) and wavelet transforms (WTs) (Mallat, 1989; Press et al., 1992). The WT, an efficient time-frequency (time scale) decomposition method, has recently been proposed as a tool to examine the multi-component structure of ERPs (Bartnik et al., 1992; Schiff et al., 1994; Samar et al., 1995; Kolev et al., 1997) and has been successfully used in the study of cerebral oscillatory rhythms in visual (Tallon-Baudry et al., 1997, 1998; Herrmann et al., 1999; Quiroga and Schürmann, 1999) and auditory (Sutoh et al., 2000) research. The major advantage of the WT is its variable time resolution involving shorter effective time windows for higher frequencies reflecting fast and short duration processes and longer effective time windows for lower frequencies reflecting slow processes. The WT can therefore partition the ERP between several orthogonal independent frequency components with parallel time courses, thus respecting the overlapping component composition of ERPs (Bartnik et al., 1992; Schiff et al., 1994; Singer, 1999). These wavelet functions can be chosen such that they are well localized in time, which allows proper recognition of events shortly separated from each other in time or frequency domains.

In recent years, several groups have reported that coherent, distributed, and strongly phase-locked (evoked) early oscillatory gamma band responses to auditory stimuli could be detected using EEG and magnetoencephalography scalp recordings (Pantev et al., 1991; Ribary et al., 1991; Basar et al., 1999a). These responses have been described as different from steady-state responses (Jacobson, 1994). An early phase-locked response in the gamma band, appearing shortly after stimulus onset, has been found in both humans and cats (Basar Eroglu and Basar, 1991; Demiralp et al., 1996; Schürmann et al., 1997). Several cognitive paradigms have shown in the auditory system that this early response shows spectral peaks between 30 and 40 Hz, around 25 ms from stimulus onset, and lasts for about 100 ms (Tiiitinen et al., 1993a; Pantev, 1995; Karakas and Basar, 1998). This high frequency activity has been observed in association with cognitive processing including stimulus perception, consciousness and selective attention (Pantev et al., 1991; Krause et al., 1998). Moreover, Tiiitinen et al. (1993) found an enhanced auditory evoked gamma response in the case of attended versus unattended stimuli, and Makeig and Jung (1996) reported increased gamma activity in detected versus undetected auditory target stimuli, demonstrating that gamma oscillations may be major modulators of selective attention or could also reflect mechanisms of increased attention (Aoki et al., 1999).

Not only the early, but also the late responses in the P300 latency range have manifested sensitivity in the processing of attended auditory stimuli and have been shown to differ between rare target and frequent non-target stimulus processing in the frequency domain delta (0.5–4 Hz), theta (4–7 Hz) (Basar Eroglu et al., 1992; Yordanova and Kolev, 1998a), and alpha (7–13 Hz) (Yordanova and Kolev, 1998b; Kolev et al., 1999). Taken together, these previous results indicate that gamma band components need further elucidation, especially with respect to possible independent variations of amplitude, time and phase-locking during specific task conditions.

Given the advantages of the time scale analysis provided by the WT, the present study was undertaken to examine whether this method is suitable for the detection of phase-locked and non-phase-locked oscillatory activity in the gamma band during the occurrence of the P300 wave.

2. Method

2.1. Subjects

Seven healthy subjects (3 female, 4 male) with a mean age of 28.4 years (ranging from 23 to 31 years) participated in the experiment. The subjects were volunteers from the university staff, medical staff and from the surrounding community who disavowed any psychiatric history, neurological disorder or substance abuse. Written consent was obtained from all subjects prior to testing. The procedure was approved by the local ethics committee.

2.2. EEG recordings

EEG activity was recorded at the F3, Fz, F4, C3, Cz, C4, P3, Pz and P4 electrode sites of the 10–20 system using silver silver-chloride electrodes affixed with electrode paste and tape and referred to linked earlobes with a forehead ground. All interelectrode impedances were below 5 kΩ. Additional electrodes were placed at the outer canthus and supraorbitally to the left eye with a bipolar recording of the electrooculogram (EOG) acquired. The EEG was amplified and filtered with a bandpass of 0.3–100 Hz and 1024 ms sweeps synchronized to the auditory stimulus were digitized at 400 Hz per channel, including a 128 ms pre-stimulus baseline. Trials on which the EEG or EOG exceeded ±81.7 μV on any channel were rejected automatically. All experimental conditions were recorded with eyes open. The subjects were highly co-operative in all task conditions, which resulted in very few trials being rejected due to artefactual responses. Rest periods were provided between task conditions as appropriate.
2.3. Stimuli and procedure

During the signal recording all subjects were sitting comfortably in a sound- and light-attenuated room with eyes open. The data were collected using a standard auditory ‘oddball’ paradigm. Auditory stimuli were presented binaurally over headphones. A 1000 Hz standard tone (\(P = 0.75\)) and a 2000 Hz target tone (\(P = 0.25\)) were presented. The intensity of the stimuli was 90 dB SPL with 70 ms duration with a 10 ms rise/fall time and a fixed interstimulus interval of 0.7 s. The subjects were instructed to ignore standard tones and to count the number of target tones. Subjects were also instructed how to avoid eye movement and muscle artefact. The recording session was continued until 600 and 200 artefact-free epochs were acquired for the standard and target tones, respectively, requiring about 630 standard and 210 target stimuli.

2.4. Data analyses

All the off-line analysis was carried out on a PC by means of specific software developed in the Matlab\textsuperscript{8} programming environment.

2.4.1. Time-frequency transformation of the data

Processing each response separately, without averaging, implies that the interesting elicited components are several orders of magnitude smaller than other rhythmical activities in the EEG. To overcome this problem a joint time-frequency analysis method has been used (Cohen, 1989; Hlawatsch and Boudraux-Bartels, 1992). This method combines a multiresolution wavelet algorithm for signal extraction and the Gabor transform to represent the temporal evolution at different frequencies.

The wavelet transform (WT\(X\)) of a signal \(s(t)\) is defined as the convolution of this signal with scaled and translated versions of a specific function (\(\psi\)) called the ‘mother wavelet’ (Daubechies, 1994; Samar et al., 1995; Bertrand et al., 1994) (Fig. 1).

\[
\text{WT}_X(\tau, a) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} s(t) \psi(\frac{t - \tau}{a}) \, dt
\]

Special digital filters can be designed to implement this analysis. In practice, it is possible to use a recursion scheme involving only one low-pass filter and one high-pass filter, whose coefficients are directly set once the wavelet function is chosen. As shown in Fig. 2, the output of the high-pass filter is retained and the filtering is recursively applied to the output of the low-pass filter. As the frequency content is reduced in each iteration, the output signals can be down-sampled. In this way, the number of samples at the end of the process remains the same as in the original signal.

Although Morlet’s wavelet has been successfully used to extract oscillatory components (Tallon-Baudry et al., 1998), its wavelet coefficients are not independent of each other, thus giving a redundant and non-orthogonal decomposition of the signal to analyze (Bertrand et al., 1994). According to this, the Daubechies wavelet family was chosen for our analysis method. Gabor coefficients were used because they are linearly independent, providing a non-redundant decomposition of the signal. In this way the computation processing time was highly reduced, offering advantages compared to previously used analysis. The wavelet coefficients can be used to reconstruct the signal reversing the same recursive filtering process (Mallat, 1998). Setting some of the wavelet coefficients to zero, only selected components are extracted.

Once the desired components are extracted, a discrete Gabor expansion is used to represent the time-frequency distribution of the energy in the signal. The signal is expressed as a weighted sum of time-frequency shifted versions of an elementary function \(g(t)\).

\[
s(t) = \sum_{n=\infty}^{\infty} \sum_{k=\infty}^{\infty} G_{kf} g_{nk}(t), \quad \text{with} \quad g_{nk} = g(t - nT) e^{j2\pi kf t}
\]

where the Gabor coefficients \(G_{kf}\) are defined as

\[
G_{kf} = \int_{-\infty}^{\infty} s(t) e^{-\frac{j}{\pi} f^2 - 2\pi kf t} \, dt df
\]

Each coefficient \(G_{kf}\) can be interpreted as the energy present in the signal around time \(t\) for the components around frequency \(f\), and when displayed as a 2D coloured graph gives a complete picture of the temporal evolution at different frequencies.

The interest of the Gabor expansion comes from the fact that the basis functions \(g(t)\) can be designed so that they are optimally localized with respect to both time and frequency. In fact, as they are taken to be time-frequency shifted Gaussians, they provide the best possible localization.

2.4.2. Analysis of phase-locked activity

Oscillatory gamma activity associated with perceptual phenomena may appear with a certain jitter in latency from trial to trial. If all trials are averaged, all activity not coincident in phase tends to disappear. Therefore, the time-frequency representation of the average of all trials only represents an oscillatory response that is strongly phase-locked to the stimulus. This response is called an evoked response (Galambos, 1992). To measure this phase-locked activity, all sections in each group were averaged. A double transform as explained above was computed afterwards. First, the activity between 30 and 60 Hz was extracted by means of a discrete WT with a Daubechies function. The signal thus reconstructed was transformed into a time-frequency domain by means of a Gabor transform, and represented with a 2D graphical interface.

2.4.3. Analysis of both phase-locked and non-phase-locked activity

In contrast to evoked activity, responses which are observable in single sweeps but not in the averaged responses due
to a weak time-locking to the stimulus are called induced responses (Galambos, 1992). To evaluate both phase-locked and non-phase-locked activity, the same procedure (WT, reconstruction and Gabor transform) was applied to each individual section. All time-frequency transforms in each group were averaged afterwards, adding all the signal power in each frequency and thus eliminating the phase information of the signal. The result of this average was also represented in a 2D colour encoding time-frequency diagram. Individual power values for different frequency bands were obtained from the transform in order to quantify the changes in energy values along time.

These methods were applied to the ERPs elicited by standard and target stimuli, first for every subject and then for the grand average over all subjects. Responses to standard and target stimuli were processed separately. The times with maximum total gamma power were identified and the latency, peak frequency and duration of these response were measured. The duration for oscillatory activities has been measured for maximum oscillatory peak frequency in temporal evolution signal power plots such as those shown in Fig. 4. Note that the power of a limited frequency band cannot be measured without temporal spreading of the response, which gives rise to an apparent response before the stimulus onset, or higher in duration than those illustrated in the time-frequency representation of the power as shown in Fig. 3.

2.4.4. Statistical analysis

The non-parametric test of Wilcoxon for matched pairs
was used for the statistical analysis of frequency, latencies, duration and power values. Correlations between latencies of P300 and latencies of late phase-locked and non-phase-locked gamma band activities were tested with the Pearson correlation coefficients.

3. Results

All subjects performed well on the detection of the target stimuli, with a detection error lower than 3.3%.

The time-frequency representation of the power grand-averaged across subjects at electrode Cz for standard stimuli is shown in Fig. 3A. After the analysis with WT of the averaged evoked potential, an early phase-locked oscillatory response peaking at $44.25 \pm 1.89$ Hz (41–47 Hz), always ranging in the gamma band frequency, with a mean latency of $26.07 \pm 15.31$ ms with respect to the stimulus onset was observed, with a duration of $325.45 \pm 74.33$ ms, and power of around $0.18 \mu V^2$. The average of the WT of every single trial, representing all phase and non-phase-locked activity, showed an early oscillatory activity with a mean latency of $44.98 \pm 20.86$ ms with respect to the stimulus onset. The mean oscillatory frequency was $42.92 \pm 2.9$ Hz (39–46 Hz), the mean duration was $310.3 \pm 64.24$ ms, and the mean power was $2.67 \mu V^2$. No other oscillatory

Fig. 2. From level (L) to level of decomposition the output of the high-pass filter (HPF) is retained, and the filtering is recursively applied to the output of the low-pass filter (LPF).
activity in the gamma band was found along the studied time window.

Fig. 3B illustrates the time-frequency representation at electrode Cz of the power for target stimuli grand-averaged across all subjects. As can be seen in the time-frequency diagram of phase-locked activity, two main oscillatory responses in the gamma band were observed. The first activity, called early oscillatory response, was similar to that obtained for standard stimuli and appeared at $28.89 \pm 15.08$ ms with a mean oscillatory frequency of $43.94 \pm 2.45$ Hz, ranging from 41 to 48 Hz, with a mean duration of $331.29 \pm 80.39$ ms and a mean power of 0.12 $\mu$V$^2$. The second gamma band oscillatory activity, called late oscillatory response, was observed related to the P300 slow wave. This late phase-locked activity appeared at $359.09 \pm 58.6$ ms with a mean frequency of $37.26 \pm 1.38$ Hz, a mean duration of $334.07 \pm 62.67$ ms, and a mean power of around 0.04 $\mu$V$^2$. The analysis of the average of the WT of every single trial showed an early activity with a mean latency of $32.54 \pm 15.71$ ms, peaking at $43.97 \pm 1.63$ Hz, with a duration of $289.07 \pm 79.82$ ms and power of around 2.93 $\mu$V$^2$. Although not as clear as in previous analysis, a P300-related oscillatory response could also be extracted with an oscillatory response with a latency of $340.82 \pm 78.85$ ms, a frequency of $35.96 \pm 1.83$ Hz, a duration of $313.75 \pm 62.57$ ms, and mean power of 3.56 $\mu$V$^2$.

Temporal evolution of the signal power is shown for the 37 Hz frequency in order to quantify the changes in energy values with time (Fig. 4).

The mean latency of the P300 wave was $327 \pm 26.73$ ms. A significant positive correlation between latencies of P300 and latencies of P300-related phase-locked responses was revealed ($r = 0.927, P < 0.0026$). No correlation was found between latencies of P300 and P300-related non-time-locked responses ($r = 0.109, P = 0.816$).

The Wilcoxon matched-pairs test showed no differences between standard and target early activities extracted from the WT of the average over the single trials for frequencies ($Z = 0.253, P = 0.799$), latencies ($Z = 0.104, P = 0.916$), duration ($Z = 0.524, P = 0.6$) and power ($Z = 1.183$, $P = 0.24$).
A. Standard stimuli

![Graph showing signal power evolution for standard stimuli.]

B. Target stimuli

![Graph showing signal power evolution for target stimuli.]

Fig. 4. Temporal evolution of the signal power calculated for the 37 Hz frequency in the grand average across subjects. Time is presented on the x-axis and power is presented on the y-axis. (A) For standard stimuli, an early in time power enhancement at about 26 ms after stimulus onset can be observed. (B) For target stimuli, power enhancement can be obtained for two time windows: an early response around 28 ms similar to that obtained for standard stimuli, and a late in time power enhancement peaking at about 359 ms. The Wilcoxon matched-pairs test showed a significant difference between standard and target late oscillatory activity power while no differences were found for early power activity.

Our results showed that during auditory stimulus processing, clearly discernible gamma oscillation bursts were elicited in two time windows of the post-stimulus epoch. For both standard and target stimuli, an early gamma response was observed in the WT of the average over single trials and also after averaging the WT of every single trial. Therefore, this response was the representation of phase-locked and non-phase-locked oscillatory activity to stimulus onset. In line with earlier reports, this pronounced and well synchronized gamma burst was present around 25 ms after stimulus onset (Basar et al., 1987; Tiitinen et al., 1993, 1994; Pantev, 1995; Demiralp et al., 1996; Yordanova et al., 1997a,b; Karakas and Basar, 1998). As Marshall et al. (1996) pointed out, no other differences were observed for early responses between standards and targets. The early response was found to be mainly phase-locked. This strong synchronization with the stimulus is consistent with previously reported associations of gamma band EEG power with states of high arousal, alertness, and focused attention (Tiitinen et al., 1993; Jokeit and Makeig, 1994; Makeig and Jung, 1996; Krause et al., 1998).

Otherwise, no oscillatory responses were obtained in the analysis of the late time window for the standard stimuli. For target stimuli, our WT analysis showed a late high frequency activity around 359 ms that could be better extracted from the WT of the average over the single trials than after averaging the WT of the single trials. This behaviour evidenced a mainly phase-locked activity. The phase-locked component of this late response showed a high corre-
lation to the latency of the P300 wave, while the non-phase-locked component did not. The power of these late oscillatory activities showed a significant difference (Z = 2.366, P = 0.017) with standard oscillatory activity power in the late time window, providing direct support for the specific late oscillatory response that suggests that this late activity was not spurious.

In the last 20 years, oscillatory processes of neural assemblies have attracted much interest. Oscillations are not proposed to represent information themselves, but rather to provide a temporal structure for correlations in the neurons that do encode specific information. Such oscillations, and specially synchronous gamma band activities (30–70 Hz), have been suggested as a possible mechanism of feature linking in relation to the binding theory, in which synchronous EEG activity at about 40 Hz appears to be involved in binding sensory inputs into one unitary sensation that we perceive (Jefferys et al., 1996). It has also been suggested that perception in most or all modalities involves coherent rhythmic activity at gamma frequencies (Pantev et al., 1991; Basar et al., 1999b). Although it is impossible to assign a single function to a given type of oscillatory activity, some kind of relationship has been established. Like early responses, auditory late gamma band responses also correlate with attention to auditory targets (Marshall et al., 1996) and sensory-motor integration (Jokeit and Makeig, 1994).

Late gamma oscillatory activity during visual (Tallon-Baudry et al., 1997, 1998) and sensory-motor (Jokeit and Makeig, 1994) cognitive tasks has been described. Studies using auditory oddball paradigms have not shown such a clear late gamma activity. A late (250–400 ms) gamma response to target auditory stimuli (P300, 40 Hz component) has been recorded as an induced oscillation during auditory oddball (Haig et al., 2000) and omitted stimulus conditions in both humans and cats (Basar Eroğlu and Basar, 1991; Basar et al., 1992). Initial studies showed that these wave bursts had a variable latency and produced weak signals often masked by other activities, so enormous intrindividual and interindividual fluctuations were found (Basar et al., 1993). Recently, late gamma band activity has been shown to be weakly phase-locked with an enhanced phase-locking activity when motor task relevance was used (Yordanova et al., 1997a,b). Otherwise, a suppression of induced P300-related gamma activity has also been reported (Fell et al., 1997). These discrepancies could be due to different cognitive tasks or different analysis methods used. When motor tasks are required to notice target stimuli, activity in different frequency bands could overlap and enhance or diminish these responses. Motor response preparation and execution have to be shown to enhance the power of gamma band activity before movement and to substantially suppress it during movement (Pfurtscheller and Neuper, 1992; Pfurtscheller et al., 1993; Pfurtscheller, 1994). Anyway there is strong evidence of late gamma responses in oddball and omitted stimulus paradigms even when no motor response is required (Yordanova et al., 1997a).

Otherwise, gamma oscillations may occur in different and distant structures and can be found to be phase-locked, time-locked, or weak time-locked to the onset of experimental stimuli (Galambos, 1992; Tallon-Baudry et al., 1995; Pulvermüller et al., 1995). Besides frequency, the degree of synchrony and site of oscillations, other parameters, namely amplitude enhancement, delay and duration of oscillations, can influence the results of different studies. Moreover, these parameters continuously vary in accordance with their dynamic nature (Tallon-Baudry et al., 1996; Yordanova et al., 1997b). In this way, new mathematical approaches have to be used in the study of these task-related oscillatory responses. The combination of digital filtering, WT and the representation using the Gabor transform provides an easy-to-evaluate time-frequency representation with an adequate energy distribution of the signal. Therefore, the results obtained using this procedure are mathematically more precise than previous studies using Fourier-based methods. Few studies have been performed with WT so far. Wavelet analysis has been applied to delta, theta and alpha frequency ranges in auditory ERP responses by Demiralp et al. (1999a,b) and Kolev et al. (1997), revealing the presence of several functional components in the P300 latency range during an oddball condition, but they have not paid attention to frequencies of the gamma band. Our results show how the cortical processing of auditory presented standard and target stimuli differs and how EEG signal analysis with WT allows the identification in the gamma frequency range of an early oscillatory cortical response, as well as a clear late P300-related response. We suggest a relationship between late gamma responses and attentional processes although we can not discard that this high frequency activity may not correspond to the mental counting activity that subjects were required to perform during the detection of targets.

The P300-related gamma activity strongly indicates that event-related gamma oscillations are involved in higher brain functioning, although the precise mechanisms of this involvement are currently being studied. We assume that the analysis of oscillatory activity performed within the scope of WT can be developed into a most important tool to understand and to interrelate sensory and cognitive functions of the brain.

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