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Time dynamics of stimulus- and event-related gamma band activity: contrast-VEPs and the visual P300 in man

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Abstract

Objectives: To investigate the time dynamics and phase relationship with the stimulus of the onset/offset visual evoked potentials (VEPs), P300 and gamma band oscillatory responses to visual (contrast) stimulation. Gamma band oscillatory activity mediates in sensory and cognitive operations, with a role in stimulus-related cortical synchronization, but is reportedly reduced in the time window of the P300 response.

Methods: Ten healthy volunteers were studied. VEPs and P300 were obtained in a stimulus condition combining standard contrast stimulation and a visual odd-ball paradigm. Visual stimuli were gratings with a sinusoidal luminance profile (9.0° central retina; 1.3 cycles/ degree; 70% contrast) that were presented monocularly in onset/offset mode, with vertical orientation (frequent stimulus; 80%) or with a 15° rotation to the right (infrequent, target stimulus). The total signal activity (temporal spectral evolution), the activity phase-locked to the stimulus onset (rectified integrated average), and the 'locking index' (ratio of the activity phase-locked to the stimulus to the total signal activity) were computed over time and across frequencies on the signals recorded at occipital (visual responses) and central locations (P300).

Results: Oscillatory activity centered around $\sim 20.0-35.0$ Hz and phase-locked to the stimulus was recorded at occipital locations with time dynamics anticipating the conventional VEPs. Phase-locking was higher after frequent than in response to target stimuli and after the stimulus offset compared to onset, while the phase-locking of the VEP frequency components was higher after the stimulus onset. The low frequency components of the P300 recorded at Cz (below $\sim 8.0-10.0$ Hz) were almost totally phase-locked to the stimulus, while the gamma band activity at the P300 location did not vary over time in amplitude or phase-locking and was mostly non-locked to the target stimulus.

Conclusions: These observations add to the evidence of a role of the gamma band oscillatory responses (centered at $\sim 20.0-35.0$ Hz) in visual information processing and suggest that the increment in gamma band activity during cognitive operations also depends on task characteristics, vigilance or selective attention, and brain functional state. The visual P300 appears to reflect low frequency synchronization mechanisms. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Gamma band activity; Onset/offset visual evoked potentials; Visual P300; Oscillatory visual response; Contrast stimulation; Phase-locking to the stimulus; Healthy humans

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¹ Gamma activities are often also referred to as the '40 Hz' rhythm mostly due to early detection of an auditory response at this frequency (Galambos et al., 1981), but span a wider range of frequencies often overlapping the beta EEG activities (Jefferys et al., 1996; Singer, 1993; Sannita, 2000). The frequency range of gamma responses is usually indicated in the literature with descriptive purposes, without implications about the signal frequency organization, and may vary also depending on recording procedures, applied data processing methods, or experimental contingencies (animal vs. humans, cortex vs. scalp recordings, etc.). In particular, several methods of frequency analysis of short signal epochs may require a larger bandpass than the actual frequency organization of the signal.

1. Introduction

Oscillatory activity with a frequency above ~ 20.0 Hz ('gamma band' activity)¹ is spontaneously generated by neurons of laminar CNS structures due to physical properties of the cell (Llinás, 1988) and specifically occurs in coherent cortical patterns in response to sensory stimulation (see for reference: Bressler, 1990; Steriade et al., 1991, 1993; Basar and Bullock, 1992; Singer, 1993; Singer and Gray, 1995; Jefferys et al., 1996; Tallon-Baudry and Bertrand, 1999; Sannita, 1994, 2000). According to models and single/multi-unit experiments in visual cortex, stimulus-

related gamma oscillatory activity is selectively distributed with high temporal resolution, reflects the global properties of the stimulus, and mediates in cortical synchronization during early information processing by providing a spatiotemporal neural coding system. It is thought to contribute in the 'binding' of multiple visual features into a single percept (Eckhorn et al., 1988; Gray and Singer, 1989; Gray et al., 1989; Bressler, 1990; Engel et al., 1990, 1992; Kreiter and Singer, 1992; Frien et al., 1994; Gray and Viana di Prisco, 1997; Buzsaki et al., 1994; Keil et al., 1999). Synchronization in the gamma range occurs between adjacent cells responding to the same stimulus characteristics as well as across columns, visual areas or hemispheres (Engel et al., 1991; Gray et al., 1989, 1992; König and Schillen, 1991; Gray and Viana di Prisco, 1997). Consistent with long-range synchronization, transient contrast stimuli conventionally applied for electrophysiological vision testing (e.g. sinusoidal or square-wave gratings, checkerboards) (Deuschl and Eisen, 1999) evoke an oscillatory mass response with frequency centered around \sim 20.0–35.0 Hz that is recorded in man by macroelectrodes and reference-free magnetic methods. This oscillatory response anticipates in time the conventional visual evoked potentials (VEPs), from which it is separated with limited distortion by adequate filtering methods, and is tuned to the contrast function of the visual system (Sannita et al., 1995, 1999; Bandini et al., 1999; Tzelepi et al., 2000; Sannita, 2000; Narici et al., 2000; De Carli et al., 2001). Distributed gamma band oscillatory activity is also observed in contiguity with selective attention, focused arousal, multistable visual perception, visualmotor integration, associative learning, sensorimotor integration, short-term memory or induced visual illusions (Bouyer et al., 1981; Bressler, 1995; Joliot et al., 1994; Singer and Gray, 1995; Basar-Eroglu et al., 1996; Revuonso et al., 1997; Roelfsema et al., 1997; Tallon-Baudry et al., 1996; Rodriguez et al., 1999; Gruber et al., 1999; Miltner et al., 1999; Keil et al., 1999; Tallon-Baudry and Bertrand, 1999). According to prevailing hypotheses, the gamma oscillatory activities form a class of signals with common frequency characteristics but multiple functional correlates and have implications both in higher brain functions and in sensory processes (notably in the phase coding of neuronal activity) depending on the brain state and dedicated neuronal assemblies (Basar and Bullock, 1992; Singer, 1993; Jefferys et al., 1996; Schürmann et al., 1997; Tallon-Baudry and Bertrand, 1999; Sannita, 2000).

In this respect, time dynamics and phase correlation with the generating stimulus or event are important aspects of the gamma activity and conceivably depend on the contingent functional role. Gamma activity is mostly phase-locked to stimuli during early sensory processing (Karakas and Basar, 1998; Sannita et al., 1999; Sannita, 2000) and also occurs as a sustained response with longer latency (about 200–300 ms) and no definite phase correlation in response to complex visual input (e.g. Kaniszka figures) (Tallon et al., 1995; Tallon-Baudry et al., 1996, 1997b). Although occasionally questioned (Herrmann et al., 1999) and observed by electric but not by magnetic recording techniques (Tallon-Baudry et al., 1997a), the long-latency sustained gamma band response suggests complex operations. It also reflects the target processing and stimulus discrimination involved in the generation of a P300 (Herrmann et al., 1999). However, gamma band activity is reduced in man in the time window of the auditory, somatosensory or visual P300 (Fell et al., 1997; Bodis-Wollner et al., 1998; Tomberg and Desmedt, 1998) and this effect was partly attributed to changes in phase-locking with respect to the stimulus (Fell et al., 1997). The purpose of the present study was to investigate the time dynamics and phase relationship with the stimulus of the oscillatory (gamma band) and non-oscillatory components of the human visual P300. The stimulus condition was designed to obtained a visual P300 while evoking the conventional VEP and visual oscillatory responses to standard contrast stimulation.

2. Materials and methods

The subjects were 10 volunteers (age 31.3 ± 2.6 years, range 24–37 years) with no evidence or history of ocular, neurological or systemic diseases. In all cases visual acuity was better than 18/20 with optimal correction for the appropriate viewing distance and the standard VEPs and electroretinograms were within normal limits. Subjects were acquainted with the recording procedures, laboratory setting and staff. The ethical principles of the Declaration of Helsinki (1964) by the World Medical Association concerning human experimentation were followed.

Standard contrast stimuli for VEPs testing (International Guidelines; Deuschl and Eisen, 1999) were combined to evoke during the same stimulation/recording session both the conventional VEPs and a P300 response to a visual oddball paradigm. For this purpose, gratings with a sinusoidal luminance profile (central 9.0° of visual field at 75 cm viewing distance; spatial frequency, 1.3 cycles/degree; contrast level, 70%) were produced on a Tektronix 608 oscilloscope under the control of a digital display generator (VENUS mod. 1020, Neuroscientific Co.). Stimulus presentation was in onset/offset mode, with temporal wave modulation at 1 Hz and each stimulus 'on' and 'off' period lasting 500 ms. When the gratings were off, the screen had the same luminance as the mean luminance of the pattern. The frequent stimulus (80% of presentations) was oriented vertically, while the rare (target) stimulus (20% of presentations) was rotated 15° to the right. Each eye was tested separately, while the other eye was covered with a translucent patch to maintain light adaptation. Each experimental session consisted of 12 runs of 30 s (each run including 30 stimuli) with 2 min of rest between runs. Subjects were requested to avoid blinking and eye movements during the experimental sessions, to focus on rare stimuli, and to report the number of target stimuli at the end of each run. The eye movements were recorded by electrodes positioned on the lower eyelid and supraorbital areas. The position of the eyes was TVmonitored during data acquisition to control fixation.

The VEPs were recorded by Grass gold dermal electrodes conventionally positioned 5 cm laterally to the inion and 5% of the inion-to-nasion distance above the inion, with reference at Fpz (Deuschl and Eisen, 1999). The P300 was recorded at Cz, with reference on linked mastoids (Katayama and Polich, 1999). The ground electrode was on the forehead. Electrode impedance was in all recordings below 5 k Ω ; the amplification and bandpass (Physio-Amp) were 50,000 and 0.5–250.0 Hz, respectively. The digital



Fig. 1. (Top) Averaged P300 (at Cz) and VEPs and oscillatory responses (at the right occipital location) as recorded from a normal subject. The responses to frequent and rare stimuli are superimposed to show differences at Cz, but not in the occipital VEP and oscillatory visual responses. Stimulation was in onset/offset mode, with temporal wave modulation at 1.0 Hz; stimuli were gratings with a sinusoidal luminance profile and either vertical orientation (frequent stimulus) or 15° rotation to the right (target stimulus). The oscillatory responses were separated from the VEPs by high-pass filtering with a cut-off at 19.0 Hz (second order Bessel Filter attenuating 3 dB at 0.003 Hz). (Bottom) Individual variability of the VEPs (right occipital) and P300 (Cz) in sequential, repeated averaged responses from one subject.

system generating the stimuli (VENUS, Neuroscientific) also controlled the electrophysiological data acquisition, which started synchronously with the stimulus onset. For each subject and recording, the VEP and P300 responses at proper locations were sorted by dedicated software (Neuroscientific Corp.). The first 70 VEP and P300 responses free of artifacts were processed offline in order to identify the portions of activity phase-locked and nonphase-locked to the stimulus (see Salmelin and Hari, 1994; Narici et al., 1998; Sannita et al., 1999). For this purpose, the time-frequency structure of the signal was analyzed by means of a bank of digital filters, implemented through the fast Fourier transform. The 0-50.0 Hz frequency range was partitioned into 36 frequency intervals (with 15.0 Hz width), overlapping in 1.0 Hz steps and centered at frequencies from 8.0 to 43.0 Hz. The raw and squared values of the filtered signal were averaged. The portion of signal activity phaselocked to the stimulus (rectified integrated average, RIA) and the total signal activity irrespective of phase-locking to the stimulus (temporal spectral evolution, TSE) were estimated across frequencies and time in the 1 s window. For each frequency interval, the RIA and TSE estimates were computed as the post-stimulus temporal evolution of, respectively, the square root of the averaged signal power (RIA) and the square root of the raw signal power (TSE). The 'locking index' (LOI), i.e. the ratio of the phase-locked activity to the total (locked and unlocked) signal activity, was also computed in order to provide normalized estimates of phase-locked activity. The same procedure was applied to pre-selected frequency intervals (0.0-15.0 and 20.0-35.0 Hz). The method is detailed elsewhere (De Carli et al., 2001). The TSE and RIA estimates (after normalization to the maximum TSE or RIA value of each subject/recording) and the LOI were averaged across subjects and the standard error was computed. The TSE, RIA (not normalized) and LOI corresponding to the frequent and rare (target) stimulus conditions or to the responses to stimulus onset and offset were compared by paired t test, computed on each frequency/time estimate.

3. Results

3.1. VEP and oscillatory visual responses

The standard contrast stimuli applied in the study evoked in all subjects conventional pattern onset/offset VEP responses with no differences in waveform, latency or amplitude between stimulus conditions (target, non-target) or stimulated eyes (Fig. 1 and Table 1). The latencies of VEP waves N70 and P100 were significantly shorter after stimulus onset than after stimulus offset, while the latency of wave N145 was longer (P < 0.001, paired t test). Amplitudes did not differ.

At occipital locations, the time dynamics and correlation with the stimulus of the signal activities below ~ 15.0 Hz

Stimulation	Latencies			Amplitudes	
	N70	P100	N145	N70/P100	P100/N145
VEPs response to stimulus onset					
Right eye	71.5 (9.1)	107.1 (5.1)	169.4 (9.9)	5.5 (4.2)	9.7 (7.8)
Left eye	74.0 (10.1)	108.1 (6.6)	170.7 (7.9)	5.6 (6.3)	10.5 (9.7)
VEPs response to stimulus offset					
Right eye	88.3 (6.1)**	116.8 (6.5)**	149.2 (7.5)**	4.9 (3.5)	4.7 (4.2)
Left eye	89.5 (6.1)**	118.1 (8.4)**	160.3 (13.4)*	4.7 (3.1)	3.8 (2.7)
P300 response to target stimulus	Latency	Amplitude			
Right eye	399.4 (25.2)	3.4 (2.3)			
Left eye	426.0 (54.4)	3.3 (1.9)			

Table 1 Latency and amplitude values of the VEP (occipital locations; frequent stimuli) and P300 (central; target stimuli) responses^a

^a Values are given as the mean across subjects; standard deviation; statistical comparison (paired *t* test). The statistical difference between the VEP responses to stimulus onset and offset is indicated as *P < 0.05, **P < 0.001.

(representative of the VEPs) and above \sim 20.0 Hz (gamma band response) differed. The signal TSE amplitude (estimated irrespective of the phase relationship) increased in the frequency interval below ~ 15.0 Hz in two clusters concomitant to the VEP responses to stimulus onset and offset, whereas in the frequency range above ~ 20.0 Hz it was homogeneously distributed throughout the sampling window without changes temporally related to the onset/ offset responses. Bursts of activity phase-locked to the stimulus (RIA estimates) were detected in both the frequency intervals below ~ 15.0 Hz and above ~ 20.0 Hz (oscillatory gamma response), with the peaks at $\sim 20.0-35.0$ Hz anticipating in time those of the activity below ~ 15.0 Hz reflecting the VEPs. These time dynamics were consistent among subjects and were emphasized when the LOI was computed (Figs. 2 and 3). The activity at $\sim 20.0-35.0$ Hz accounted for a transient oscillatory response that could be separated from and preceded the onset/offset VEPs in averaged signals after high-pass filtering at ~ 20.0 Hz (Fig. 1). The amplitude of the \sim 20.0–35.0 Hz oscillatory response phase-locked to the stimulus offset (RIA, LOI) was larger after frequent stimuli compared to infrequent (target) stimuli, in the absence of significant differences in the TSE in the same frequency range and in the RIA, LOI and TSE estimates in lower frequency ranges (Fig. 4). No significant clustering of the fast frequency activity associated with the frequent stimuli was observed at a central location.

In addition to the differences in VEP latencies, the phaselocking of the responses to the stimulus onset and offset proved different. In the VEP frequency range below ~15.0 Hz, the phase-locked activity was significantly higher after stimulus onset than after offset for both target and frequent stimuli (LOI; frequent stimuli: t = 4.655, P < 0.002; target stimuli: t = 2.342, P < 0.05 (paired t test, two-tailed)). The phase-locked activity in the ~20.0– 35.0 Hz interval was higher after stimulus offset limited to the frequent (non-target) stimulation (t = -2.676, P < 0.02 (paired t test, two-tailed)) without significant onset/offset differences of the response to target stimuli (Figs. 2 and 5). No significant differences between the onset and offset responses were observed for the TSE estimate in any frequency interval.

3.2. P300

Under the experimental conditions of the study, the 15° rotation of a standard contrast stimulus for VEP testing (vertical sinusoidal gratings) qualified as an adequate target stimulus in a visual odd-ball paradigm yielding a P300 response. A P300 with adequate morphology, amplitude and latency was recorded in parallel to the conventional VEPs from all subjects, with limited individual variability (Table 1). At the frequency analysis (central electrode location), the signal below $\sim 8.0-10.0$ Hz was clustered in concomitance with the P300 response to target (rare) stimuli and was mostly phase-locked to the stimulus, as indicated by the comparable TSE, RIA and LOI estimates. The signal activity above ~ 15.0 Hz (and specifically in the ~ 20.0 -35.0 Hz range) was distributed throughout the entire P300 window, without significant time-related changes in amplitude (TSE) or phase correlation (RIA, LOI) with the stimulus onset or offset, and was mostly non-phase-locked to the target or frequent stimuli (Fig. 2).

4. Discussion

The results further suggest resonant phenomena with frequency centered at $\sim 20.0-35.0$ Hz, occurring during early visual processing and featuring an oscillatory component of the visual response with time dynamics anticipating the VEPs (Sannita et al., 1995, 1999; Bandini et al., 1999; Sannita, 2000; Tzelepi et al., 2000; Narici et al., 2000; De Carli et al., 2001). Phase-locking to the stimulus is a predominant characteristic of the visual oscillatory response to



Fig. 2. For the primary visual response to frequent stimuli (VEPs; left column) and the P300 (target stimuli; right column) are shown the averaged time/frequency distributions of (top) the total signal activity (temporal spectral evolution, TSE), (middle) the signal activity phase-locked to the stimulus (rectified integrated average, RIA), and (bottom) the ratio of the RIA to the TSE ('locking index', LOI). Note the clustering of the phase-locked and non-phase-locked activities below ~15.0 Hz and of the phase-locked activity at ~20.0–35.0 Hz in relation to the onset and offset responses at occipital locations (left). Only low frequency activity, mostly locked to the target stimulus (with minor detectable differences among TSE, RIA and LOI estimates), was observed in the time window of P300 (right). For all estimates, values are expressed as pseudocolors according to the scale reported on the left. Averages across subjects (n = 10) were performed after normalization of the TSE and RIA estimates. Right eye stimulation.

transient (pattern reversal; onset/offset) stimulation in humans (Sannita et al., 1999; Sannita, 2000). It conceivably reflects frequency-specific mechanisms of synchronization among cortical neurons responding with proper timing to coherent visual stimulation that are eventually emphasized by the stimulation modalities (Eckhorn et al., 1988; Gray and Singer, 1989; Gray et al., 1989; Engel et al., 1992; see Bressler, 1990; Singer, 1993; Buzsaki et al., 1994; Singer and Gray, 1995; Sannita, 2000 for references). This phase correlation, however, may be less salient for 'cognitive' operations and related electrophysiological events that do not need to depend on time as strictly. In agreement with this instance, no changes in the gamma activity amplitude or phase correlation with target stimuli were observed in the time window of the P300, whereas the low frequency activity representative of the P300 response (below $\sim 8.0-10.0$ Hz) proved to be remarkably phase-locked to the target stimulus.

These observations further indicate a specificity of the gamma band oscillatory visual response with respect to the sensory input, while adding to the evidence of low frequency synchronization in the generation of P300 (Basar-Eroglu et al., 1992, 2001; Schürmann et al., 1995; Yordanova and Kolev, 1997, 1998). Low frequency synchronization in the absence of changes in (or in concomitance with the depression of) local gamma band activity may result from the interaction of the cortical/subcortical structures involved in the generation of the P300, such as the limbic system, thalamus, corpus callosum, and distributed cortical areas (Okada et al., 1983; Johnson, 1993; Polich and Squire, 1993; Polich and Hoffman, 1998; Ji et al., 1999; Katayama and Polich, 1999; Frodl-Bauch et al., 1999; Buchner et al., 1999; Clark et al., 2000; Trinka et al., 2000). In support of this hypothesis are the reduced amplitude of gamma activity at the onset of the human P300 (Müller et al., 1996; Fell et al., 1997; Bodis-Wollner et al., 1998) and its increase in the cat hippocampus during a P300 paradigm (Basar-Eroglu and Basar, 1991; Basar and Bullock, 1992). Tomberg and Desmedt (1998) suggest the P300 to reflect time-related inhibition (eventually due to subcortical activation) of the neuronal functional assemblies involved in the processing of attended stimuli. According to the threshold regulation model (Elbert and Rockstroh, 1987), surface positive activation would compete with the pyramidal neurons generating gamma activity (Fell et al., 1997). The interaction between mechanisms generating the P300 and cortical gamma band activity remains to be investigated in detail. In this regard, the geometry of sources may be crucial in the understanding of these electrophysiological events, as suggested by the observation of gamma band responses to Kaniszka figures in electric but not in magnetic recordings (Tallon-Baudry et al., 1997a). A rostrocaudal phase shift of gamma activity was also observed and would suggest spatiotemporally organized processes involving large portions of cortex at different times, eventually with a focus on the activated sensory areas (Llinás and Ribary, 1992).

Early and late oscillatory gamma activities (respectively phase-locked or non-phase-locked to visual input depending on the involved sensory/cognitive processes) (Tallon-Baudry et al., 1996) were not found to coexist as expected under the experimental conditions of the study. Though in the same line of evidence as previous reports (Müller et al., 1996; Fell et al., 1997; Bodis-Wollner et al., 1998; Tomberg and Desmedt, 1998), the results appear in contrast with the (localized or widespread) enhancement of gamma band activity described in concomitance with cognitive operations. Besides differences in phase-locking possibly affect-



Fig. 3. Average across subjects of the LOI distribution over time in the frequency intervals reflecting the VEP or P300 responses and the oscillatory activity (0.0–15.0 and 20.0–35.0 Hz, respectively). (Top) Primary visual response at occipital locations (frequent stimulus). (Bottom) P300 response at Cz (target stimulus). Note the faster and transient increase after the stimulus of the ~20.0–35.0 Hz activity evoked at occipital locations and its reaching a peak earlier after the stimulus than the signal at 0.0–15.0 Hz. The increase of 0.0–15.0 Hz activity occurs at Cz in the absence of changes in the ~20.0–35.0 Hz activity.

ing the response amplitude (Fell et al., 1997), the experimental setup and characteristics of stimuli or performed task(s) may be critical in this regard. Specifically, most studies reporting increased gamma band activity applied multiple/complex stimuli and cognitive tasks requesting a higher level of attention and participation than the odd-ball visual paradigm needed to elicit a P300 response may require. Coherent moving bars (Müller et al., 1996), 'mooney' faces (Rodriguez et al., 1999), downward/upward triangles (Shibata et al., 1999), random-dot autostereograms (Revuonso et al., 1997), Kaniszka figures (Tallon et al., 1995; Tallon-Baudry et al., 1996, 1997a; Herrmann et al., 1999), face figures (Keil et al., 1999) and blobs (Tallon-Baudry et al., 1997b) are examples in this regard. The stimulus complexity allows for the investigation and control of distinct aspects of information processing. However, task complexity is known to emphasize and modulate in time and topography the amplitude of task-induced gamma activity, while leaving the early gamma activity related to sensory processing virtually unaffected (Marshall et al., 1996; Yordanova et al., 1997; Karakas and Basar, 1998; Gruber et al., 1999; Haig et al., 1999, 2000). A differential

generation of gamma activity depending on pre-attentive and attentive auditory stimulus conditions has been reported (Marshall et al., 1996). In the present study, visual stimuli with constant physical properties and known physiological implications were deliberately combined to obtain a P300 response in conditions of limited task complexity also allowing the recording (as a control test) of conventional VEPs. In these conditions, the P300 response to visual target stimuli may mostly reflect perceptual processing in concomitance with limited cognitive requirements to perform the task. Shifts in the brain functional state (e.g. increased vigilance, selective attention) may also contribute significantly in the enhancement of gamma band activity or phase-locking in brain structures that are not necessarily primarily involved in the generation of a visual P300 (Steriade et al., 1996; Tiitinen et al., 1993; Munk et al., 1996; Marshall et al., 1996; Karakas and Basar, 1998; Gruber et al., 1999;



Fig. 4. Comparison (paired *t* test) between the signal total (TSE) and phase-locked activities (LOI) recorded at occipital locations in response to target and non-target stimuli (primary visual response). Averages across subjects (n = 10) were performed after normalization of the TSE estimates. The amplitudes of phase-locked activities at ~20.0–35.0 Hz (oscillatory response) were higher in response to the frequent compared to the target stimuli, particularly in response to the stimulus offset. No differences were observed in the TSE estimates. Right eye stimulation.



Fig. 5. Comparison between the phase-locked activity (LOI) recorded in response to the stimulus onset and offset in the 1.0–15.0 and 20.0–35.0 Hz frequency intervals (frequent stimuli; occipital location). The time and frequency windows of these responses were set based on evidence shown in Figs. 2 and 3 and from matching estimates obtained in previous studies (Sannita et al., 1995, 1999). Note that the portion of signal activity phase-locked to the stimulus onset is larger than in response to the stimulus offset in the 1–15 Hz frequency interval (paired *t* test; *t* = 4.655, *P* < 0.002 (two-tailed)). The opposite was observed for the 20.0–35.0 Hz signal activity (paired *t* test; *t* = -2.676, *P* < 0.02 (two-tailed)).

Shibata et al., 1999; Spencer and Polich, 1999; Kolev et al., 2001).

The asymmetries of the VEPs (below ~ 15.0 Hz) and oscillatory (above ~ 20.0 Hz) responses, with higher phase-locking to the stimulus onset and offset, respectively, also require further investigation. These asymmetries help to rule out significant effects of luminance in the generation of gamma band response to contrast. Unlike the known differences between onset/offset VEPs (for references see Zemon et al., 1988; Regan, 1989), the stronger phase-locking of gamma oscillatory response to the stimulus offset went undetected in previous studies with symmetrical pattern-reversal stimulation (Sannita et al., 1995, 1999). The time dynamics of phase-locked gamma activity - and its reinforcement by the sequential timing of the onset/offset stimulation paradigm but not by the subjects' attending to target stimuli - add to the hypothesis of a time-related coding function of the oscillatory response to visual stimulation (Engel et al., 1992; Singer and Gray, 1995; Sannita, 2000) that appears unrelated, at least in part, to later visual or cognitive processes (Karakas and Basar, 1998). An additional pacing effect from the odd-ball task procedure eliciting a P300 is conceivable, as also suggested by the VEP differences in latency. It should be noted that the ON and OFF channels of the visual system process information in the retina and cortex differentially and with a degree of independence (Schiller, 1982, 1992). The asymmetries of the ON and OFF visual pathways can be revealed in man using contrast VEPs (Zemon et al., 1988), but the contributions of these subsystems to the (visual) gamma response are still to be explored. It appears a practicable hypothesis that the asymmetric gamma band locking to contrast onset and offset be related to the selective activation of these subsystems. At a more conservative level, these findings further

imply a functional separation between the contrast-evoked gamma band oscillatory activity and the VEPs.

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