Auditory Evoked Gamma Band Potential in Normal Subjects

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Abstract

The gamma band response (GBR) is a predominantly exogenous, sinusoidal evoked response that occurs usually between 20 and 130 msec following stimulus onset. This response is believed to represent the synchronization of neuronal assemblies that serve auditory feature integration. The objective of the present investigation was to describe the characteristics of the scalp-recorded auditory evoked gamma band potential (aeGBP) recorded from normal young adult subjects. Results showed the aeGBP to consist of up to four oscillations and were best recorded at the frontal-central midline. The aeGBP was present 80 percent to 100 percent of the time, appeared as onset responses, and was recorded at the shortest latency over the contralateral anterior temporal scalp.

Key Words: Auditory evoked potentials, gamma band response (GBR)

Abbreviations: aeGBP = auditory evoked gamma band potential; gamma band response recorded using conventional electrical recording methods; aeGBR = auditory evoked gamma band response; ECD = equivalent current dipole; GBF = gamma band field, gamma band response recording with magnetoencephalographic recording methods; GBR = gamma band response; ISI = interstimulus interval; MEG = magnetoencephalography; MLR = middle latency response; SSR = steady-state response

A series of wavelets can be recorded from the skull following the onset of a click or tone burst. These evoked responses are predominantly exogenous in nature such that their latencies and amplitudes are dependent upon the physical characteristics of the evoking stimulus (e.g., sound frequency, intensity, and onset properties). The positive polarity evoked potential waveform occurring at or about 50 msec represents either the last wavelet of the middle latency response (MLR) (Pb) or the first wavelet of the long latency response (P50 or P1). The negative and positive going waves following Pb have peak latencies of approximately 100 msec and 175 msec, respectively, and are referred to as N1 and P2. When submitted to spectral analysis, these latter waveforms show most of their energy to be concentrated in the frequency range below 20 Hz (Pantev et al, 1991). The conventional stimulating paradigm that is used to elicit these responses entails the use of a tone burst with relatively slow onset (e.g., 10–15 msec rise/fall). Additionally, an interstimulus interval (ISI) of 500 msec to 1000 msec is used commonly to record N1 and P2, despite the knowledge that the response amplitude can be improved markedly by extending the ISI up to 8 to 16 seconds (Nelson and Lassman, 1968; Rothman et al, 1970; Hari et al, 1982).

Recently, investigators, including Basar et al (1987) and Makeig (1990), have described high-frequency wavelets that are superimposed upon the auditory middle latency and long latency responses. These oscillations have a period of approximately 25 msec and a spectral peak frequency of between 30 and 40 Hz and have been termed gamma band responses (GBR; Pantev et al, 1991).

The auditory evoked magnetically (e.g., Pantev et al, 1991, 1993; Pantev, 1995) and electrically recorded (e.g., Basar et al, 1987; Makeig, 1990) GBRs may be referred to as auditory evoked gamma band fields (aeGBFs) and auditory evoked gamma band potentials (aeGBPs),...
It is important to note that, unlike the 40-Hz steady-state response (SSR) (Galampos et al., 1981), the aeGBR is best elicited by transient toneburst stimulation with long ISI (>2 seconds).

The precise functional significance of the GBR is unclear but it has been theorized that this electrical event may serve to synchronize groups of neurons. These functionally coherent “neuronal assemblies” would serve to make it possible for a fixed number of neurons in the cerebral cortex to analyze and interpret an infinite number of stimulus combinations. These assemblies may be local (e.g., in adjacent cortical columns or adjacent cortical regions) and result in highly synchronized events that result in short latency GBRs (e.g., 20- to 130-msec latency range) that can be signal averaged (i.e., referred to as “evoked” GBR). Alternately, the GBR may be generated by remotely coupled neuronal assemblies (i.e., sources distributed throughout the cortex) or in the same cortical area by neurons with different receptive fields. These responses generally are not well synchronized and result in longer latency electrical events that do not signal average well (i.e., “induced” GBR). It is believed that these latter longer latency connections are called into play to help fuse or bind together characteristics of auditory signals (e.g., frequency spectrum, intensity, duration, velocity of frequency and intensity change, character of sound) into a single unitary perception (e.g., the sound associated with a dog bark; Pantev et al., 1991; Singer, 1993a, b). The establishment of neuronal assemblies and their permanence are probably influenced by the experience on the part of the listener to the same aggregate auditory event. It should be noted that these views are somewhat controversial. Evoked oscillations in the GB range have been recorded from stimulation of visual and olfactory sensory systems in animals (e.g., olfaction: Adrian, 1942; Freeman, 1975, 1979; vision: Gray and Singer, 1989; Gray et al., 1989, 1992; Engel et al., 1991a, b, c; Jagadeesh et al., 1992; Konig et al., 1995). It is noteworthy that both high- (Curio et al., 1994; Eisen et al., 1984) and low-frequency oscillations (Joutsiniemi, 1988) have been observed superimposed upon the cortical somatosensory evoked potentials and have been attributed to oscillatory thalamic discharges.

To date, magnetoencephalographic (MEG) investigations of the characteristics of the human aeGBR have shown that the GBR is present in as few as 33 percent of normal subjects (Christo Pantev, personal communication, 1994). This may be due to (1) the small magnitude of the GBR in comparison to background activity, (2) small trial-to-trial phase differences in the GBR leading to phase cancellation of the signal-averaged response, or (3) the orientation of the generator(s) of the GBR that are unfavorable to MEG recording devices (e.g., gyral sources generating radial fields). Previous research has demonstrated that the source location of generators underlying the GBR are spatially separate from those underlying P, the 40-Hz SSR, and N in the supratemporal auditory complex (Pantev et al., 1991, 1993). Unlike N, which appears as a stationary field, the GBR appears as a moving dipole (possibly reflecting sequential activation of adjacent cortical columns), arcing 1 cm or greater in an anterior-posterior trajectory over the time period from 20 to 130 msec (Pantev et al., 1991). Also, the GBR decreases in magnitude as a function of decreased ISI, but to a lesser extent than N (Makeig, 1990; Pantev et al., 1993).

Recent evidence suggests that the generator system responsible for the GBR is not tonotopically organized as are the generators of both P and N (Bertrand and Pantev, 1994). Finally, the GBR may be modulated by attention; therefore, it may not be entirely exogenous (Tiitinen et al., 1993).

Although much is understood about the aeGB field, less is known about the auditory evoked gamma band potential (aeGBP). The present investigation was conducted to determine (1) the characteristics of the aeGBP (wave-shape, recordability, general scalp topography) and (2) whether the aeGBP represents an onset response or a sustained response.

**METHODS**

**Subjects**

Subjects were 12 normal hearing, neurologically intact, young adults (9 female; mean age = 28.60 years, SD = 5.68 years). Normal hearing sensitivity was defined as pure-tone thresholds better than 15 dB HL for octave frequencies 250 to 4000 Hz.

**Procedures**

Stimuli were two types: (1) a 1000-Hz tone burst and (2) a white noise burst. Stimuli were 500 msec in duration with a 15-msec rise/fall time and were alternated in polarity. Five subjects received both stimuli. The auditory signals were presented through an ER-3A insert earphone delivery system to the right ear only,
at 60 dB nHL, at a mean ISI of 2 seconds (varying pseudorandomly between 1.5 seconds and 2.5 seconds). This stimulus delivery system imposed a 0.9-msec delay in the presentation of a stimulus to the ear canal. A total of 700 stimuli were presented in a single trial, and there were two trials for 10 subjects (representing two trials each of the 1000-Hz tone) and four trials for five subjects (representing two trials each of the 1000-Hz and noiseburst stimuli). The order of the trials for subjects receiving two stimuli were counterbalanced across the subject sample. Typically, 1½ to 4 hours were required for data collection from a single subject.

Recordings were made with each subject seated in a comfortable reclining chair. An attempt was made to ensure vigilance by presenting subjects with a subtitled movie during data acquisition. Additionally, viewing the movie encouraged subjects to maintain their gaze in a fixed area (decreasing random vertical and horizontal eye movements). Silver-silver chloride disk electrodes were placed at Fz, Cz, Pz, C3, C4, T3, and T4 (noninverting inputs). Further, electrodes were placed at the lateral canthus and below the left eye to record electrooculographic activity. The inverting input was a silver-silver chloride ear clip electrode placed at A0. A ground electrode was placed at FPz. The electrodes were applied using conventional surface electrode preparation techniques. Absolute electrode impedances were always less than 3000 Ω and interelectrode impedances less than 2000 Ω.

The bioelectrical activity was amplified and filtered (1–70 Hz) with a neurophysiologic amplifier (Neuroscan Synamp). The signals were digitized (A/D = 400 Hz) and signal averaged with a commercially available signal averaging system (Neuroscan Scan, Herndon, VA). The averaging epoch was 1000 msec (200-msec pre-stimulus period and 800-msec post-stimulus period). Data were stored as continuous EEG along with stimulus trigger pulses. The data were epoched and signal averaged offline. Samples contaminated with excessive electrooculographic interference (>±85 μV) were automatically rejected. The data were then digitally bandpass filtered 24 to 48 Hz (second order g-zero-phase shift, Butterworth filter, 12 dB/octave slope) to resolve the GB potentials.

RESULTS

General Characteristics

Following either toneburst or noiseburst stimulation, the N1 and P2 components could be observed in every subject. The spectral content of these long latency auditory evoked cortical components is less than 30 Hz (with peak energy at 10 Hz). The aeGBP evoked by tone or noise bursts prior to offline digital filtering often could be appreciated as small notches superimposed prior to and during the development of the N1 response; this is illustrated in Figure 1. Following offline digital filtering, in most subjects, the aeGBP could be observed as a series of up to four low-amplitude oscillations, with amplitudes exceeding that of the prestimulus period. The response was recorded with the largest amplitude at the Fz and Cz electrode sites, as shown in Figure 2. Statistical analyses were accomplished from data obtained at the Fz electrode location. It is clear in Figure 2 that oscillations in the GB range occur in the prestimulus period (i.e., the EEG contained low-level GB activity). However, these oscillations did not replicate on repeated trials (as did the aeGBP) and generally were less than 0.1 μV in amplitude, whereas the most repeatable wavelets of the aeGBP usually exceeded 0.2 μV. That is, for a response to be identified as an aeGBP, it had to exceed 0.2 μV and be reproducible on a subsequent trial. The reproducibility of the aeGBP for two subjects is shown in Figure 3.

Figure 1 Top: Broadband filtered (1–70 Hz) long latency AEPs obtained from a single subject in this investigation. The arrowheads represent locations of “notching” on the waveforms from which the aeGBP will be derived following digital bandpass filtering. Bottom: The same data as shown in top tracing but subjected to offline, digital bandpass filtering 24 to 48 Hz (see text for details). The aeGBP may be observed as three oscillations in the first 160 msec of the tracing. Note that N1 and P2 occur at stimulus onset and offset but that the aeGBP is present only for stimulus onset.
In general, the GBR to toneburst stimulation was present in 10 of 12 subjects (83% of sample). Examples obtained from five subjects are shown in Figure 4. The response consisted of a series of positive and negative going oscillations with each phase separated by approximately 10 msec. These oscillations began as early as 21 msec and continued for as long as 160 msec post-stimulus onset. The peak voltage of the aeGBP (i.e., the component with the largest amplitude) was, on average, 15 times smaller than the peak amplitude of the slow cortical N1 potential.

Noiseburst Stimulation

The aeGBP to noiseburst stimulation was present in five of five subjects (100% of subsample). Examples obtained from the five subjects are shown in Figure 5. Like the response to toneburst stimulation, the aeGBP to noiseburst stimulation consisted of a series of positive and negative going oscillations separated by approximately 10 msec, beginning as early as 23 msec and continuing as long as 173 msec post-stimulus onset. Generally, the aeGBP to noiseburst stimulation was larger in amplitude and more consistently present than that to toneburst stimulation. The peak aeGBP (i.e., the oscillation with the largest amplitude) was, on
average, 9.4 times smaller than the peak amplitude of \( N_1 \).

**Ipsilateral/Contralateral Effects**

Grand averaged aeGBPs from electrodes T3 and T4 to toneburst stimuli presented to the right ear are shown in Figure 6. Oscillations with identifiable peaks at 66 msec (positive) and 84 msec (negative) could be recorded at the T3 (contralateral) and T4 (ipsilateral) electrode sites in 50 percent to 80 percent of the subjects. Equivalent oscillations with identifiable peaks at 71 msec (positive) and 90 msec (negative) could be recorded at the T4 (ipsilateral) electrode site. A phase shift (time delay) in the responses recorded at the T4 electrode site can be observed in Figure 6B. This time delay ranged from 5 to 6 msec, and these latency differences were statistically significant \( (P_{66} \text{ vs } P_{71}: t = 2.84, df = 5, p = 0.04; N_{84} \text{ vs } N_{90}: t = 3.87, df = 4, p = 0.02) \).

**Onset Properties vs Sustained Properties**

The aeGBP occurred in response to stimulus onset for all 10 subjects. No subject demonstrated an aeGBP that occurred for the duration of the 500-msec stimuli, nor did any subject demonstrate an aeGBP that occurred at the onset of the stimulus (see Fig. 1 for an example). These findings suggest that the aeGBP represents an onset response and not a sustained response.

![Figure 5 A: Broadband filtered long latency AEPs from five subjects to noiseburst stimulation; B: the same data subjected to offline digital filtering 24 to 48 Hz.](image)

![Figure 6 A: Grand averaged long latency AEPs recorded from left (dashed line) and right (solid line) anterior temporal electrode sites (T3 and T4, respectively) to toneburst stimulation. Notice that both N1 and P2 latencies are noticeably shorter when recorded over the contralateral (left) anterior temporal area; B: the same data bandpass filtered 24 to 48 Hz to reveal the aeGBPs from the same electrode locations. Notice that there is a noticeable difference in the phase of the aeGBP recorded from the two sites. The aeGBP occurs, on the whole, earlier recorded from the T3 electrode site following presentation of stimuli to the right ear.](image)
DISCUSSION

Spontaneous brain rhythms are normally classified into the delta (>0.0 Hz–3.5 Hz), theta (>3.5 Hz–7.5 Hz), alpha (>7.5 Hz–12.5 Hz), and beta bands (>12.5 Hz–30 Hz). However, there has been described higher frequency EEG activity that is apparent during cognitive processing (Spydel et al., 1979; Sheer, 1989). These brain waves fall into the >30-Hz to 60-Hz range and are referred to as GB activity. It is noteworthy that the amplitude of these spontaneous EEG rhythms varies inversely with frequency; therefore, GB activity is not readily visible in the raw EEG record. Stimulus evoked GBRs have been described in the visual (40–80 Hz, Freeman, 1975, 1979; 100–110 Hz, Sannita, 1994), somesthetic (45–55 Hz, Kaukoranta and Reinikainen, 1985), olfactory (20–80 Hz, Bressler and Freeman, 1980), and, more recently, auditory (30–40 Hz) modalities (Basar et al., 1987; Makeig, 1990, Fig. 2). Finally, MEG recordings have suggested that the equivalent current dipole (ECD) locations of the MLR and SSR overlap, but the ECD location of the aGGR is distinctly different from that of the MLR and SSR (Pantev et al., 1993). These findings support the contention that the SSR is, in part, a frequency-modulated MLR (i.e., they at least share common neural generators), but that the generator source of the GBR is spatially separate and distinct. Additionally, the best stimulating paradigms for these responses are quite different. For example, the SSR is frequency driven (e.g., 40-Hz stimulus presentation rate). That is, the presence of the SSR is dependent upon the presentation of stimuli at the frequency of auditory system resonance (c. 40 Hz). Alternately, the GBR generator system has an extremely long absolute refractory period and, therefore, is effectively “invisible” when scalp recording techniques are used and when ISI of less than 2 seconds are employed (i.e., the signal-to-noise ratio becomes so adverse that the GBR cannot be observed at the scalp surface; see Makeig, 1990, Fig. 2). Finally, MEG recordings have demonstrated that the generator source (or sources) of the MLR and SSR appears stationary when activated, whereas the generator source of the GBR moves in a posterior arcing trajectory over a period of 20 to 130 msec (Pantev et al., 1991). The apparent “movement” of this ECD may represent the sequential activation of adjacent cortical columns or, possibly, the activation of two fixed dipoles, offset slightly in time, and located at the two ends of the observed arc (see Moran et al. [1993] for a discussion of this phenomenon specific to N). The net effect of
these observations is that the MLR and SSR differ from the GBR in several important ways.

First reports of the aeGBP occurred in 1987. In the seminal investigation, Basar et al (1987) demonstrated that the probability that an evoked GBR would occur varied inversely as a function of the magnitude of spontaneous GB activity prior to stimulus onset. Specifically, the larger the magnitude of the prestimulus GB activity, the lower the probability that the evoked GBR would occur. Interestingly, the investigators demonstrated, through selective averaging of single epochs, that the Pa and Pb of the MLR were absent when the GBR was absent. This finding suggested a common generation system for the MLR and GBR (not borne out by results of MEG studies to date). Basar-Eroglu and Basar (1991) employed near-field recordings in the hippocampus and evaluated the relationship between the aeGBP and P_{300} in cats. The investigators observed “packets” (i.e., bursts) of 40-Hz activity occurring 270 to 300 msec following onset of the omitted stimulus. This GB activity was poorly phase-locked initially. The GB activity, however, became strongly phase-locked at the end of the recording. The investigators implied that learning on the part of the subjects accompanied participation in the “oddball” paradigm, and this may have resulted in better synchronized GB activity at the end of the experiment. The investigators commented that it is their view that the 40-Hz response is a building block of brain responsiveness and is correlated with multimodal sensory and cognitive function. Pantev et al (1991) recorded the aeGBF using MEG recording techniques. Further, they demonstrated that the source location of the evoked GBR was spatially separate from M_{100} (N_{1}) and M_{300} (P_{2}) and (as noted above) acted as a moving dipole over a 1-cm area. In a later investigation, Pantev et al (1993) demonstrated that the SSR and MLR show overlapping ECD locations but that the ECD locations for the aeGBR and N_{1} were different. Additionally, they showed that the effects of stimulus habituation differed between N_{1} and the aeGBF. Finally, most recently, Pantev (1995) has reported his observations of induced GBRs during cognitive processing. The authors presented monosyllabic words (“moon”) and nonwords (“noom”) to subjects. The investigators observed an attenuation of induced GB activity following presentation of nonwords. The author explained that GB suppression occurred as a function of an unsuccessful lexical search. Pantev et al (1991) have suggested that the auditory induced GBR (as has been suggested about the visual evoked GBR) may serve to synchronize and bind together subregions of auditory cortex to “…combine separately represented auditory features into unitary auditory perception—for example, the pitch of complex tones.”

The present investigation was conducted to describe more fully the characteristics of the aeGBP in normal subjects (e.g., its waveshape, latency characteristics, recordability, and general scalp topography). The aeGBP is an onset response that appears in broad filtered data as a “notching” on middle and long latency AEPs when long ISI (>2 seconds) are used in data acquisition. Long ISI are required to improve the signal-to-noise ratio to the point where the aeGBP can be extracted from the noise floor in scalp recordings. This concept is illustrated in Figure 7. This aeGBP was obtained from a patient undergoing Phase II monitoring for intractable epilepsy. The recordings were obtained from an 8-contact, subdural electrode strip (PMT, Minneapolis, MN) during functional

![Figure 7](near-field-recorded-aeGBP.png)

Figure 7 Near field recorded aeGBP from one of eight contacts on a subdural electrode strip from a patient undergoing cortical mapping for intractable epilepsy. Top: Pre- (high-amplitude waveform) and post- (low-amplitude waveform) digital filtering (see text for details). Bottom: Superimposition of two aeGBPs obtained from the same electrode site on repeated trials.
mapping of the auditory cortex. This recording was obtained following only 200 repetitions of a 1000-Hz tone burst presented at a 1-second ISI (as opposed to a 2-second ISI) at 60 dB nHL. Despite the more rapid stimulus repetition rate and decreased number of signal averages (both of which serve to worsen the signal-to-noise ratio) than that used in the present study, the aeGBP was present clearly both before and following digital bandpass filtering. It is our feeling that the GBP was present with the more rapid stimulus rate in this instance because the generator source was closer to the recording electrode at the brain surface and, accordingly, the signal-to-noise ratio was improved compared to scalp recording techniques.

The aeGBP was recorded in 80 percent and 100 percent of our normal hearing neurologically intact subjects to toneburst and noiseburst stimuli, respectively. It should be noted that our more recent experience (i.e., a new sample of 15 subjects) shows the aeGBP to be present approximately 50 percent of the time. Generally, the onset and offset latency of the aeGBP was predictable, more so for the noiseburst stimulus. It may be speculated that the consistency of the response to the noise burst may have occurred as a function of the increased bandwidth of the stimulus (compared with the pure tone) and the recruitment of a larger number of neurons into the evoked response. Additionally, there was a clear phase lag at the ipsilateral temporal electrode site (T4) for the most prominent oscillations of the auditory evoked GBR. It is interesting that this latency difference occurred as early as 66 msec to 71 msec (i.e., slightly later than P50 but earlier than N1). This finding is consistent with previous reports that N1 latency is 5 to 10 msec earlier recorded over the contralateral temporal lobe using either electrical and neuromagnetic recording techniques (Elberling et al., 1981, 1982; Pantev et al., 1986; Hari and Mäkelä, 1988; Joutsiniemi, 1988; Jacobson et al., 1992). These findings demonstrate the superiority of the contralateral auditory pathway.

In conclusion, the aeGBP is an onset response with a predominant power spectrum of 30 to 40 Hz. Our results suggest that the aeGBP may be recorded with long ISI and a sufficient number of signal-averaged responses (700 or more). The aeGBP is recorded largest over F3 and C3. Finally, it has been hypothesized that the aeGBP may be the auditory correlate of the visual evoked gamma band potential. The neuronal assemblies underlying both evoked and induced GBRs, which are theorized to be influenced by experience, may underlie auditory feature linking and auditory perception.

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REFERENCES


