Experimental Brain Research (2019) 237:1931–1945
https://doi.org/10.1007/s00221-019-05562-7

RESEARCH ARTICLE

Event-related potentials to single-cycle binaural beats and diotic amplitude modulation of a tone

Pekcan Ungan[1] · **Suha Yagcioglu**[2] · **Ece Ayik**[3]

Received: 8 December 2018 / Accepted: 16 May 2019 / Published online: 20 May 2019

Abstract

When two tones with slightly different frequencies are dichotically presented, binaural beats (BBs) are experienced. BBs resulting from the cycling change in interaural phase difference elicit electroencephalographic responses. Because they repeat at short periods, allowing poor recovery of the cortical responses, these steady-state responses have small amplitudes, and their various wave components intermingle and might mask each other. Using single-cycle BBs separated by relatively long inter-onset intervals would be a solution, but introducing a transient interaural frequency shift requires response subtraction which may not be acceptable for non-additive brain responses. The proposed stimulation method employs transient and monaurally subthreshold frequency shifts in opposite directions in the two ears to produce single-cycle BBs of a 250 Hz tone. These shifts are perceived as distinct BBs when presented dichotically, but remain subthreshold when presented monotically. Therefore, no frequency-shift response is elicited, and the specific BB response is obtained with no need for waveform subtraction. We recorded from 19 normal hearing participants the event-related potentials (ERPs) to single-cycle BBs and also to temporary diotic amplitude modulation (AM) with matched perceptual salience. The ERPs to single-cycle BBs presented at 2 s inter-onset intervals had N1-P2 responses with up to seven times larger amplitudes than the conventional steady-state BB responses in the literature. Significant differences were found between the scalp potential distributions of the N1 responses to BB and AM stimuli, suggesting that the cortical sites, where envelope-based level processing and temporal fine structure-based spatial processing of the stimulus take place, are not totally overlapped.

Keywords Auditory evoked potential · Binaural hearing · Interaural time difference · Temporal fine structure · Envelope · Auditory cortex

Introduction

Acoustic interference of two tones with frequencies close to each other results in a sound whose intensity waxes and wanes at a rate that is equal to the difference of the two frequencies. This physical phenomenon, which is perceived like amplitude modulated sound as shown in Fig. 1 (upper panel), is called "acoustic beats". When the same tones are delivered dichotically to the ears the listener also perceives a sort of modulation in the sound. In this latter phenomenon, which has been known for about a century (Rayleigh 1907; Stewart 1917) and called "binaural beats" (BBs), the perceived modulation is not due to interference of the tones in the air but is due to binaural interaction of the cochlear neural codes in the brain. Besides several non-invasive brain stimulation methods such as transcranial electric stimulation or pulsed transcranial ultrasound stimulation (for a review, Polania et al. 2018), BB stimulation appears to be an

Some preliminary findings of this work were presented in 12th National Neuroscience Congress, Istanbul, May 28–31, 2014.

This work was funded by Turkish Scientific and Technological Research Council, Ankara (Project: 114S492) and supported by Koc University School of Medicine, Istanbul, and also by Science Academy, Istanbul, Turkey.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00221-019-05562-7) contains supplementary material, which is available to authorized users.

✉ Pekcan Ungan
pekungan@gmail.com

Extended author information available on the last page of the article

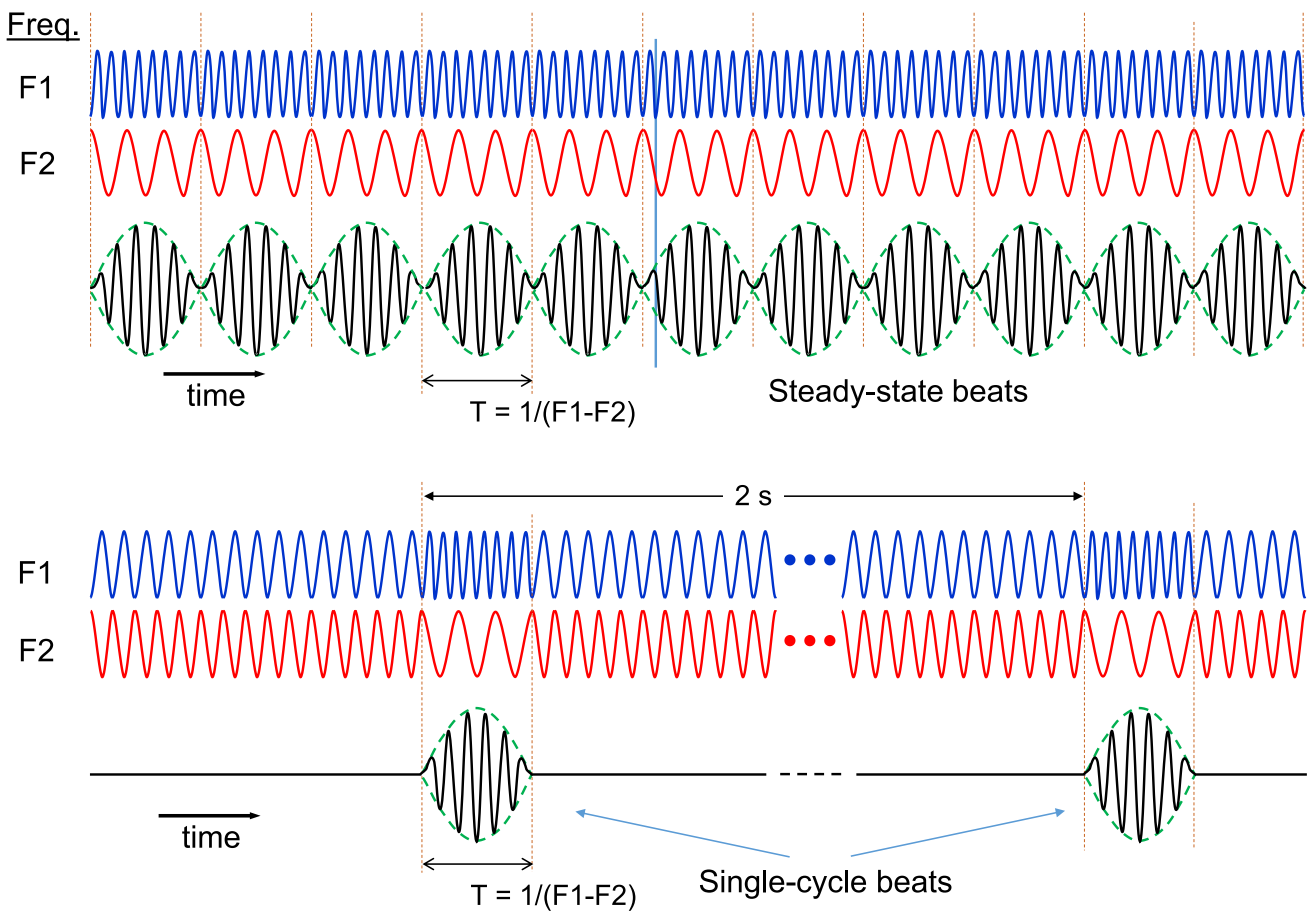

Fig. 1 Upper panel: Recurrent steady-state beats which result from acoustical interference of two tones with slightly different frequencies, repeating with a period corresponding to the reciprocal of the difference frequency. Lower panel: single-cycle acoustical beats which result from temporarily induced frequency differences between two tones. Because frequency shifts are exaggerated for illustrative reasons, time scales of the tone waveforms and beat envelope may not match

upcoming alternative technique that could be used to induce EEG phase synchronization in the brain and to study or modify cognitive brain function (Gao et al. 2014; Ioannou et al. 2015; Becher et al. 2015; Beauchene et al. 2016; Hommel et al. 2016; Chaieb et al. 2015; Garcia-Argibay et al. 2018; Derner et al. 2018). Further basic studies are thus necessary to have a better understanding of the acoustical and neurophysiological aspects of this phenomenon and to search for the optimal conditions that could improve its perceptual salience, thus increasing its effectiveness as a non-invasive stimulus modulating the brain's electrical activity (EEG).

BBs are perceived due to binaural neural interaction that results from the time difference between the tones in the left and right ears. As the difference between the frequencies of the tones in the two ears decreases below 2 Hz, BBs start to be perceived as an intracranial sound moving from one ear to the other (von Bekesy 1960; Grantham and Wightman 1978) rather than a modulation in some feature of the sound (Perrott and Musicant 1977). Observations of this sort show that the phenomenon called BBs is closely related to the sound lateralization function of the central auditory system.

Conventionally, beats are steady-state in nature as illustrated in the upper panel of Fig. 1. However, if the initially equal frequencies of two tones are temporarily shifted in opposite directions, beats will occur only for the duration of the shift as illustrated in the lower panel. If the temporary shift duration is made equal to the reciprocal of the induced frequency difference, only a single beat will occur. Because the phase difference between the tones makes a 360° of change during this period, which corresponds to a complete beat cycle, such a discrete beat will be called a "single-cycle beat". Single-cycle acoustical beats produced once every 2 s in this way are illustrated in Fig. 1 (lower panel).

When the brain is stimulated by any sensory or cognitive event and the changes it causes in the electroencephalogram (EEG) are recorded, a series of successive positive and negative waves peaking at different post-stimulus times (latencies) are observed. Such waveforms, called event-related potentials (ERPs), are considered the transient responses of the brain (mainly of its cortex) to the stimulating events. If the stimulus is a perceivable auditory event, the ERP has a typical response complex called N1-P2 around 100–200 ms following the stimulus onset. The vertex-negative N1 deflection of this response complex, which is recorded with maximal amplitudes at the fronto-central scalp electrodes (Vaughan and Ritter 1970; Picton et al. 1974), is the most studied and typical long-latency auditory ERP component and has been shown to reflect stimulus features such as its intensity, origin, duration, and timing (Näätänen and Picton 1987). Though categorized as "exogenous" due to its strong dependence on the physical characteristics of the stimulus, its amplitude was observed to increase with increasing attention (Hillyard et al. 1973; Knight et al. 1981; Ritter et al. 1988). It has been shown by numerous EEG/MEG and lesion studies that the cortical source of the auditory N1 response is on planum temporalis superior (e.g., Papanicolaou et al. 1990; Scherg et al. 1989; Knight et al. 1988). The EEG responses evoked by BBs, which are also auditory events, have been shown to be cortical in origin (Pratt et al. 2010), although early stages of the binaural interaction underlying this auditory event takes place in the brainstem (Wernick and Starr 1968; Ungan and Yagcioglu 2002).

Although binaural beats were known for almost a century as a psychoacoustic phenomenon, the first study in which they were investigated by means of electrophysiological methods was published by Oster (1973). The basic studies on the brain's responses to BBs are much fewer than those on other types of auditory evoked potentials. In almost all of them steady-state responses (SSRs), which are elicited in the brain due to the recurrent nature of the conventional BBs, have been recorded and described (Schwarz and Taylor 2005; Karino et al. 2006; Draganova et al. 2008; Pratt et al. 2009, 2010). However, mainly because of the poor recovery of cortical responses to recurrent beats, steady-state BB responses usually have small amplitudes. In case some response components could slightly recover despite rather short intervals between successive stimuli, the transient response to one stimulus would overlap with responses to succeeding stimuli (Picton et al. 2003), and they might even mask each other as in the model of Bohorquez and Özdamar (2008). Furthermore, in the SSRs, the responses evoked by each of the recurrent beats intermingle, making their identification, physiological interpretation and source analysis extremely difficult, especially when the beats recur at relatively high rates. Therefore, in the present study the evoked responses to single-cycle BBs like those explained in Methods and illustrated in Fig. 2 (lower panel), rather than those to steady-state BBs, were recorded and analyzed. Considering the results of the studies which report that the perceptual salience of BBs are highest for tones at low frequencies such as 250 or 400 Hz (Licklider et al. 1950; Perrott and Nelson 1969; Pratt et al. 2009), the base frequency of the tone for BB stimulation was chosen as 250 Hz.

An important issue encountered when single-cycle evoked potentials are used to study the dynamics of the binaural neural mechanism underlying the phenomenon of BBs is that the BB stimulus employed would also excite the monaural mechanisms. To produce a single-cycle BB, it is necessary to create a temporary interaural frequency difference; i.e., a temporary frequency shift must be made in the base tone in at least one of the ears. This change may evoke extra monaural FM (frequency modulation) responses which superimpose on the BB-response to be recorded. One may try to resolve this issue by recording in a control experiment the monaural FM response and subtracting this FM response from the compound response obtained by shifts in interaural frequency, as was attempted in the work of Özdamar et al. (2011). Actually, waveform subtraction is a widely used method in ERP studies to single out a functionally specific response component as in the examples of extracting the mismatch negativity (MMN), P300, or binaural interaction component (BIC). However, this method is based on the assumption that the brain responses are linearly additive. Such an assumption might be made if the events eliciting these responses are processed in totally different neural structures and when the neural codes representing these events do not undergo an interaction. This is not the case, however, for cortical long-latency ERP components which probably have partially overlapping and interacting cortical sources as revealed, for instance, by the refractoriness of the evoked potentials due to intra- or inter-modality interactions. Therefore, it should be desirable that a single-cycle BB stimulus does not evoke any FM response to avoid response waveform subtraction. The FM response is exogenous and its amplitude is highly sensitive to the amount of change in frequency (Dimitrijevic et al. 2008; Pratt et al. 2009). Like every sensory modality or sub-modality, tone frequency also has a change threshold (just noticeable difference) which is a fraction of the base frequency according to Weber's law. Therefore, there must be a change threshold for the base frequency selected for tone-BBs; and, if a frequency shift below this threshold is adequate for creating easily perceivable BBs, it should be possible to use these BBs as specific BB stimuli without any FM-effect. Such a specific BB stimulus would relieve the burden of the waveform subtraction in the process of obtaining the ERPs to single-cycle BBs (Özdamar et al. 2011) and provide a means for recording directly the specific responses to BBs without the confounding effect of an FM response. Actually, a preliminary study had been conducted in this laboratory (Ungan et al. 2014) to see if it was possible to produce single-cycle BBs in a 250 Hz-tone by shifting its frequency dichotically in opposite directions by about 1.5 Hz, which was well below the frequency change threshold determined to be 3 Hz by conducting a

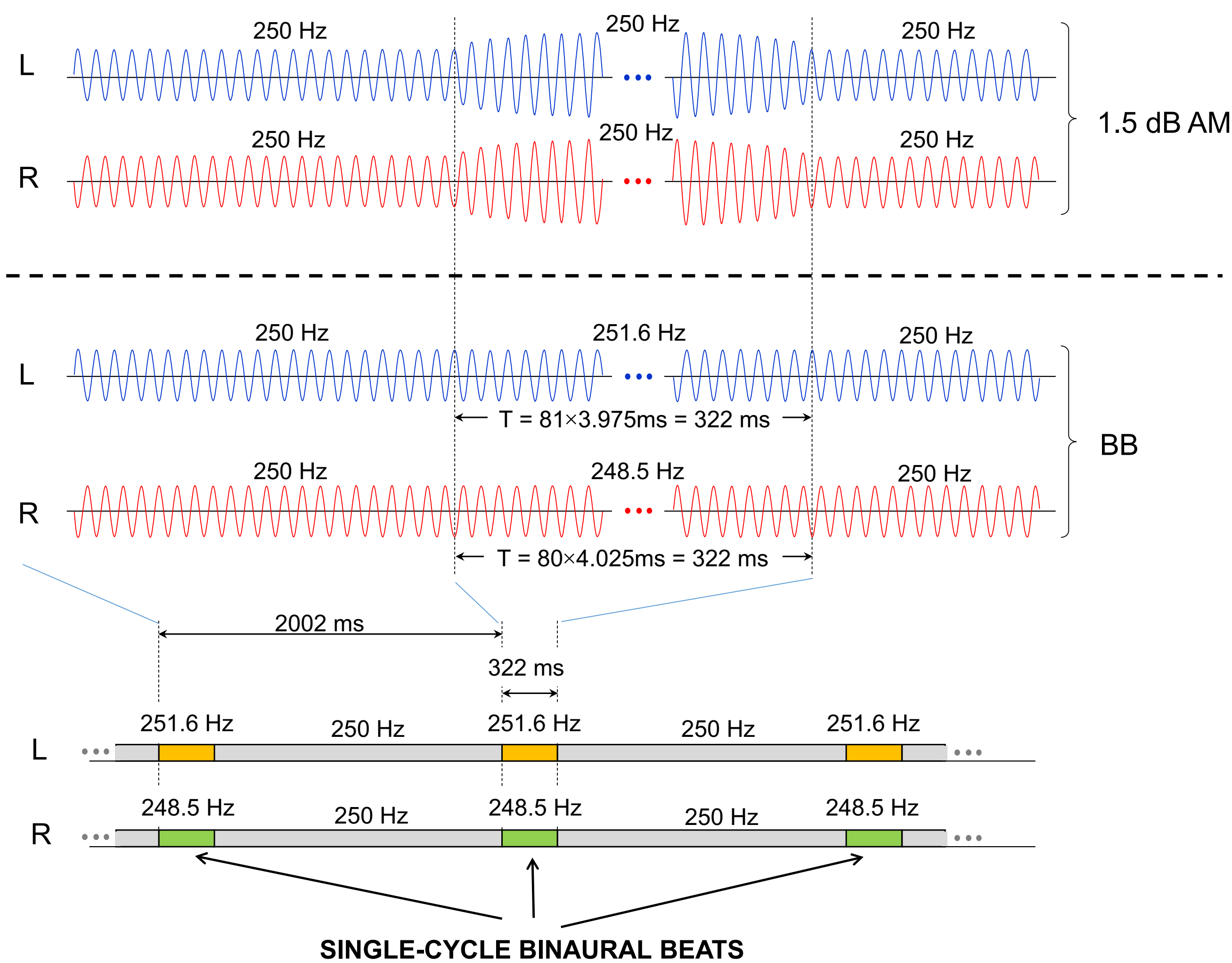

Fig. 2 Parameters and timing of the single-cycle binaural beats (BBs) used in recording the ERPs to BBs of a dichotic 250 Hz tone (lower panel) and to temporary half-cycle sine wave amplitude modulation (AM) of the same tone (upper panel)

psychophysical threshold test using an up–down staircase procedure (Levitt 1971). The results of this study (see Fig. 3), which were repeated by Mihajloski et al. (2014) for 2.5 Hz shifts in 250 and 400 Hz, showed that it was possible to directly record the single-cycle BB responses by relieving the need for subtraction of FM-responses, which would have been necessary when single-cycle BBs were created by monaurally detectable frequency shifts. In fact, this was a similar way to the one followed in an earlier study of our group (Ungan et al. 1989) where the ERPs elicited selectively by a change in the interaural time difference (ITD) of dichotically presented click trains were successfully recorded by making monaurally subthreshold shifts in the timing of clicks; thus without any confound from possible monaural responses to the change in inter-click interval.

In the classical psychophysical study of Rutschmann and Rubinstein (1965), BBs were investigated by comparing them with amplitude modulated tones. Inspired from this approach, the ERPs to diotic amplitude modulation (AM) of the same tone matched in perceptual salience with the BB stimulus were also recorded in the present study. The cortical responses of the binaural mechanisms processing the temporal fine structure (TFS) and achieving the lateralization of the incident sound were compared with those of the monaural mechanisms processing the level changes in the envelope of the sound. N1 deflection of the N1-P2 complex, which is the most typical auditory cortical transient response component, is given special emphasis in this comparison, and its amplitude, latency, and scalp potential maps were evaluated.

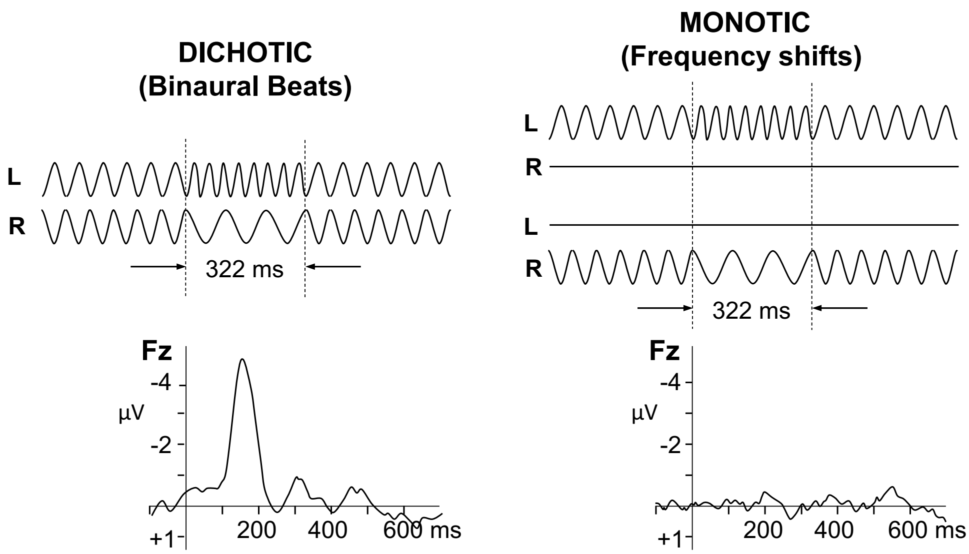

Fig. 3 The results of the preliminary control experiments demonstrating that the frequency shifts were perceived as BBs and evoked a robust N1 response when delivered dichotically to the ears in opposite directions, and that the same shifts failed to evoke any significant EEG response when they were presented monotically (grand averages, $N=10$). The waveforms of the stimuli delivered to the left (L) and right (R) ears are schematically illustrated above the ERPs. The control ERP recording given at the right panel is the average of the responses to monotic left and monotic right stimuli illustrated above the ERP (From Ungan et al. 2014)

Materials and methods

Participants

Nineteen normal hearing volunteers (13 males) between 22 and 26 years of age (mean 24) participated in the experiments and were paid for their time. Informed consent was obtained from all participants included in the study. Initially, five of the participants were given an audiological test and their hearing thresholds were determined to be between 12 and 28 dB SPL at 250 Hz. Their mean threshold was 22 dB SPL at 250 Hz and this level was referred as 0 dB nHL to express the sound intensities of stimuli in dB nHL. All of the participants who took part in the experiments were tested to have thresholds not higher than 6 dB nHL at 250 Hz and be able to perceive readily the 3-Hz steady-state BBs when 250-Hz and 253-Hz tones were delivered to their left and right ears. Procedures of the study were approved by the Ethics Committee of Koc University, Istanbul.

Stimulation

Single-cycle BBs and diotic AMs of a base tone at 250 Hz were used as stimuli. They were presented to the participants with an inter-onset interval of 2002 ms in separate experimental blocks each including either 128 BBs or 128 AM stimuli. These two types of ca. 256 s long stereophonic stimulus sequences, which are explained below in detail and schematically illustrated in Fig. 2, were designed and synthesized with a sampling rate of 40 kHz using Praat software (Boersma and Weenink 2013), and played under MATLAB. A USB sound card (MUSE Mini DAC) and audiological insert earphones (Etymotic, EARTONE-3A) were used to deliver the sound stimuli to the ears. The intensity of the tone stimulus at 250 Hz base frequency was set to 70 dB nHL, corresponding to 93 dB SPL. The SPL equivalent of the 70 dB nHL base intensity was determined by measuring the peak value of the sinusoidal voltage driving the earphone and converting the rms value of this voltage to dB SPL. This conversion was based on the technical data provided by the manufacturer of the earphone; i.e., for a 50 Ohm-earphone, a driving voltage of 200 mV(rms) produces 102.5 dB SPL in a HA-2 coupler. Although 93 dB SPL is a relatively high sound intensity, it should not have caused any cross-talk between ears owing to the high interaural attenuation of the earphone given as 90 dB at 250 Hz. Even if the lowest interaural attenuation reported for the insert earphone by Munro and Agnew (1999) is considered, 72-dB attenuation would still mean a subthreshold intensity in the opposite ear. This is because the intensity of the sound delivered is already 70 dB nHL.

Single-cycle BBs

The parameters of the single-cycle BBs were the same as those tested in our preliminary study (Ungan et al. 2014) to create a BB percept and elicit an ERP when presented dichotically, but to remain subthreshold and elicit no notable long-latency response when presented monotically. The design of the BB stimuli employed in the present study is illustrated in the lower panel of Fig. 2. The 4-ms period of the 250-Hz base tone covered with a good temporal resolution the physiologically relevant ITD range, which is known to be around 690 µs (Moore and Moore 1971). Consequently, when the frequency-shifted versions of this tone were presented dichotically, for about one-third of the BB cycle the ITD remained within the physiological range which extends from -0.7 to $+0.7$ ms corresponding to the leftmost and rightmost lateral positions.

The sampling rate of the sound card was 40 kHz, allowing a minimal change of 0.025 ms in the 4-ms period of a 250-Hz tone. The tone frequency was increased by 1.6 Hz ($\cong 1000$ ms/3.975 ms $- 250$) in one ear and decreased by 1.5 Hz ($\cong 250 - 1000$ ms/4.025 ms) in the other to create a binaural frequency difference of ca 3.1 Hz. These shifts were well below (almost half of) the monaural frequency change detection threshold that was estimated in our above-mentioned preliminary study as 3 Hz for a 250-Hz tone. This value is very close to the monaural FM detection threshold reported by Grose and Mamo (2012a) as ca 2.8 Hz for young subjects, and it is well below 2% of 250 Hz, which is reported by Dimitrijevic et al. (2008) as the frequency change for which a just detectable evoked potential can be recorded. This 3.1 Hz binaural frequency difference corresponded to a 322-ms BB cycle, which included 80 periods of the slower tone (80×4.025 ms) and 81 periods of the faster tone (81×3.975 ms). Because single-cycle BBs were to be used rather than steady-state BBs, the tone frequency was counter-shifted temporarily in the two ears only for a duration of 322 ms, corresponding to a single BB cycle. Frequency shifts were repeated with an inter-onset interval of 2002 ms and, in between the single BB cycles, the 250-Hz base tones were presented in counterphase to the two ears. Therefore, in recording ERPs to BBs the inter-onset interval included a 1680-ms long base tone in both ears and a 322-ms long BB cycle. To avoid any auditory transient due to a possible discontinuity, the onset and offset times of the frequency shifts were made to coincide with the peaks of the sinusoidal sound waveform where its differential was zero. At the start of a BB cycle the tones in the two ears were in counterphase; interaural phase difference linearly changed with time throughout the cycle and returned to 180° when the cycle ended. Therefore, during a BB cycle of 322 ms the ITD for the dichotic tones started from 2 ms (i.e., beyond physiological sound lateralization range), then decreased to 1-ms lead for the left ear, then pass through zero, then increased to 1 ms-lead again but for the right ear, and finally retuned to 2 ms. Initial interaural phase was selected as 180° to maintain continuity of the ITD change throughout its physiological range. Otherwise (i.e., for a beat starting with zero interaural phase), the sound image at the center would have moved first towards the right ear, then gone beyond the physiological range, then entered again into physiological range from the left side, and finally returned to the center. Therefore, within a beat cycle starting with zero interaural phase, the physiological ITD range would have been visited at two different times, and this would have caused some complexity in the response elicited, as described in the supplementary figure (Fig. S1). Actually, when the participants listened to the BBs, they described the percept as an auditory event like a brief change in loudness, but not as a moving sound. For them to experience a clear moving sound sensation, the interaural frequency difference had to be decreased to 1 Hz, thus increasing the beat cycle to at least 1 s. When steady-state versions of the same BBs were presented to the participants they described their experience in the same way. Despite these observations, which are in line with those reported in the literature (von Bekesy 1960; Perrott and Musicant 1977; Grantham and Wightman 1978), we consider the BBs used in the present study as auditory spatial stimuli, because the stimulus is basically a shift in interaural phase. We, therefore, take into account the time course of the interaural phase with regards to the physiological ITD range for sound lateralization.

Diotic amplitude modulation (AM) stimuli

A smooth and brief amplitude modulation to be used for AM stimulation was realized by multiplying a 250 Hz sinusoidal signal with a factor of $[1 + (10^{(A/20)} - 1)\sin(\pi t/T)]$, where t is time, T is the duration of temporary modulation, and A is the ratio of amplitude increase in dB. T was chosen as 322 ms, which was equal to the BB cycle. This type of an AM with half-cycle sine wave envelope was preferred rather than an acoustical beat, which could be obtained simply by mixing the two tones that were dichotically presented to produce the BBs, because the latter was reported to be perceived more strongly than the BB (Ross et al. 2014; Groen 1964; Grose et al. 2012). Taking into account the well-known effect of stimulus intensity on the amplitude and latency of brain responses, the depth of modulation was so adjusted that the perceptual strength of the AM stimuli would roughly match to that of the BB stimuli to maintain a fair comparison between their responses. For this adjustment, the BB stimulus and four AM stimuli with $A = 1$ dB, 1.5 dB, 2 dB, and 2.5 dB were presented in a psychophysical test to six participants and they were asked to select the AM stimulus which was most closely matched with the BB stimulus with regards to their perceptual salience. Because five of the participants matched the 1.5-dB AM with the BB stimulus (one matched the 2-dB AM), the 1.5-dB AM tone was selected to be the stimulus for recording the ERPs to AM. Sound waveforms used in recording the ERPs to temporary AM of diotic 250-Hz tones are illustrated in Fig. 2 (upper panel).

Recording and analysis of ERPs

EEG recording with 32 channels was made by means of an electrode cap (EasyCap GmbH, Etterschlag, Germany) connected to a 40-channel computerized recorder (Mega Electronics-NeurOne, Kuopio, Finland). The two electrodes slightly behind and slightly in front of the Fz electrode (FCz and AFz electrodes) were used for referencing and grounding, respectively). In addition to the 31 scalp electrodes located according to 10/20 system, an additional electrode was attached to the nose-tip for offline re-referencing. Two of the extra channels of the system were used to record the stimulus signals from the left and right sound channels simultaneously with EEG to align accurately the onset times of the BB and AM events for offline averaging of the ERP epochs. Therefore, an unusually wide filter bandwidth of 0.16–2500 Hz and a very high sampling rate of 10 kHz were used.

During experiments participants sat on a reclining chair in an electrically and acoustically shielded chamber and they were instructed to minimize eye blinks and facial movements. A participant took part in an ERP recording session of around 1 h during which they were presented with four blocks of 128 BB stimuli and four blocks of 128 AM stimuli. These blocks with BB and AM stimuli were separated by 1–2 min for rest and they followed an alternating order starting with either stimulus type randomly. Participants were instructed not to pay attention to stimuli, and read a printed or electronic material of their choice during recording.

The raw EEG data were 1–30 Hz band-pass filtered and re-referenced to nose (Ns) offline. BB and AM event triggers for temporal alignment of the ERP epochs to be averaged were added offline. This was achieved by finding and counting the successive peaks of the recorded stimulus tone, starting from its onset. Before this processing, possible noise on the recorded stimulus signal was eliminated by 250-Hz band-pass filtering to improve the temporal accuracy of the Matlab's "findpeaks" function. The EEG was then epoched according to the BB and AM onset times determined from the sound waveforms recorded simultaneously with EEG and, using ± 100 μV artifact rejection in all EEG channels, 800 ms single ERP epochs (including a 100 ms pre-stimulus part) were averaged for each stimulus type. The average ERPs and their grand average waveforms were computed. Because the peak amplitudes and latencies of the auditory ERP components may vary over electrodes (Scherg et al. 1989; Näätänen and Picton 1987) and the electrode at which a particular deflection reaches a maximal amplitude may display a notable intra-subject variability, global field power (GFP) curves (Lehmann and Skrandies 1980) were also computed for reference-free assessment of the peak latency and magnitude of a response component. Peak latency of the N1 deflection in ERPs, which is the most characteristic auditory ERP component, was measured as the post-stimulus time of the GFP maximum closest to the maximum negative deflection at electrode Fz within the time range of 100–200 ms.

Grand average ERP waveforms recorded from all electrodes were plotted topographically. Because the polarity-reversed positive potentials of an auditory N1 response recorded from posterior scalp electrodes are correlated with the typical frontally tilted orientations of the bilateral N1 dipoles (Ungan et al. 1992) that were shown to be generated in their respective supratemporal cortices (Scherg et al. 1989), the area covered by a group of six temporo-parieto-occipital electrodes (O1, O2, P7, P8, TP9, and TP10) was defined as a region of interest (ROI). Average of the N1 potentials measured from these six electrodes within the ± 10 ms latency range around their peaks were calculated for the ERPs of each participant to BB and AM stimuli. These averaged ROI-potentials were divided by their respective N1-GFP values to normalize them against the effect of a possible dipole strength difference on the recorded potentials. The normalized values obtained for BB- and AM-evoked N1 responses were compared statistically to see if there was a significant difference between them, indicating a difference between the frontal tilt angles of the N1 dipoles elicited by the two stimuli.

The scalp potential maps of the N1 deflection in the grand average ERPs of the participants to single-cycle BBs and temporary AM of the tone were plotted. They were color-coded according to the mean of the values for ± 10 ms around the N1 peak latency. All steps of the above mentioned offline EEG and ERP processing were carried out using MATLAB and ERPLAB toolbox (Lopez-Calderon and Luck 2014).

Results

The ERPs of 19 participants to single-cycle BBs which were recorded from the fronto-central electrode (Fz) and re-referenced to nose are presented in Fig. 4 together with their grand average. A fronto-central electrode is selected, because it is the scalp site where the most typical auditory cortical responses are generally recorded with maximal amplitudes. The time window is confined between − 100 and 500 ms because the ERPs did not display any significant deflection later than this post-stimulus time. In all these individual ERPs the N1-P2 complex is quite robust with an amplitude between 1.9 and 7.2 μV (4.3 ± 1.8 μV). Grand average ERP to BBs of the 250-Hz tone and the grand average ERP to the 1.5-dB AM of the same tone, all recorded from 31 scalp electrodes and re-referenced to nose, are topographically presented in Fig. 5. In line with the typical characteristics of long-latency auditory evoked potentials

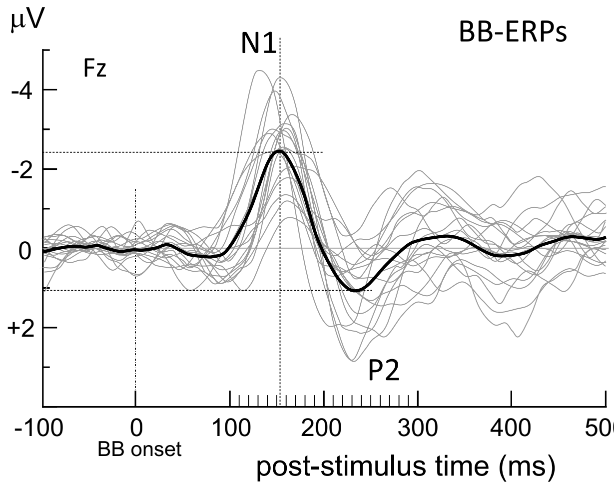

Fig. 4 Superimposed individual ERPs of 19 participants to BBs of a dichotic 250-Hz tone (thin lines), together with their grand averages (heavy line). Recorded from the midline-frontal electrode and re-referenced to nose. 100 ms pre-stimulus correction applied

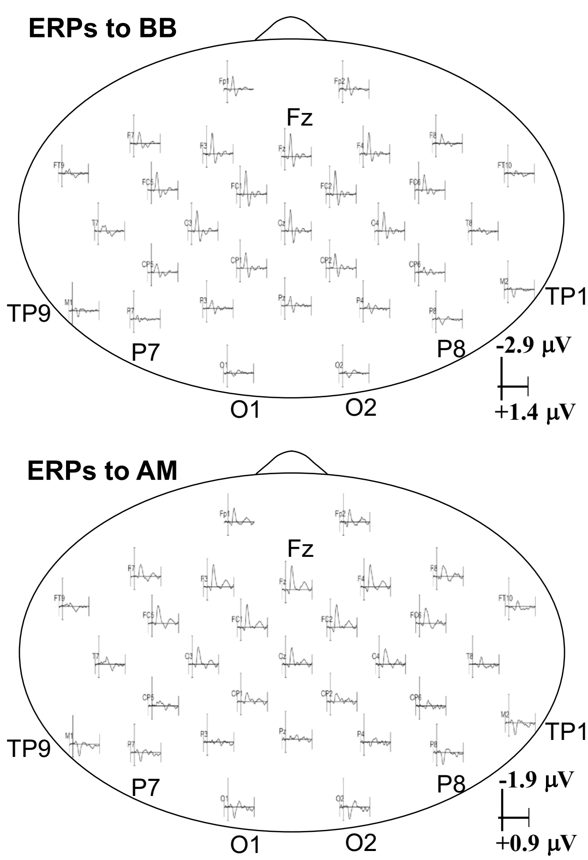

Fig. 5 Topographical plots of the grand average ERPs recorded from 19 participants to single-cycle BBs of a 250 Hz tone (upper panel) and to 1.5 dB amplitude modulation (AM) of the same tone (lower panel). Recorded from 31 scalp electrodes and re-referenced to nose. The horizontal scale bar shows the peri-stimulus time between − 100 and 700 ms

(Näätänen and Picton 1987), the ERPs to both types of stimuli are dominated with an N1-P2 complex that is recorded with maximal amplitudes from fronto-central electrodes and display a polarity inversion at mastoids and occipital sites. The P2 component of this response complex can hardly be noted in the ERPs to AM stimuli. The P1, which is another typical auditory response component to be observed in an earlier latency range of 40–70 ms, could be recorded only in a few of the participants and, therefore, is rather obscured in grand average ERPs. It is for this reason that the N1 response which is the most typical component of auditory ERPs is given special emphasis in the present study.

It is seen in Fig. 5, where the topographical plots of the grand average ERPs are presented, that the N1 wave is recorded with positive polarity from the electrodes of the ROI according to the typical behavior of auditory evoked potentials known as "polarity reversal across the Sylvian fissure". In that scalp area, the polarity-reversed N1 component of the AM-ERPs appears to have notably large amplitudes, whereas that of the BB-ERPs can hardly be noted.

Grand average ERPs to BBs and 1.5-dB AM of a 250-Hz tone, which were recorded from the midline-frontal electrode (Fz) and re-referenced to nose, are presented together in Fig. 6 (upper panel) for a comparison between their waveforms. In all the individual ERPs the N1 component was quite robust whereas the P2 component was not that prominent in the BB responses of some participants, and it was not even present in the AM responses of individuals except a single participant with an insignificant P2 deflection. Consequently, the P2 amplitude in the grand average BB-ERP appears to be smaller than the N1 amplitude, and the P2 component is almost absent in the grand average AM-ERP. The mean ± SD values of the N1 amplitude across individual ERPs to BB and AM stimuli were 3.0 ± 1.1 μV and 2.5 ± 1.1 μV, respectively. The N1 amplitudes in the grand average BB- and AM-ERPs are slightly below these mean values, probably because the N1 latencies had an inter-subject variability with a standard deviation around ± 16 ms around their mean values of 154 ms and 173 ms, respectively. Robustness of the N1 responses to both types of stimuli and absence of the P2 component in the ERP to AM stimuli are apparent also in their respective GFP curves presented in Fig. 6 (lower panel).

Scalp potential maps of the N1 components in the two grand average ERPs seen in Fig. 6 are given in Fig. 7 (lower panel). In line with the topographical differences seen in Fig. 5 between positivities of the BB- and AM-elicited N1 waves in the ROI, somewhat different distributions over these regions are noted between the N1 scalp potential maps of the BB and AM events (compare the upper maps in the lower panel). This dissimilarity was observed to be quite evident in most of the participants as in the case shown in the upper panel, whereas in some

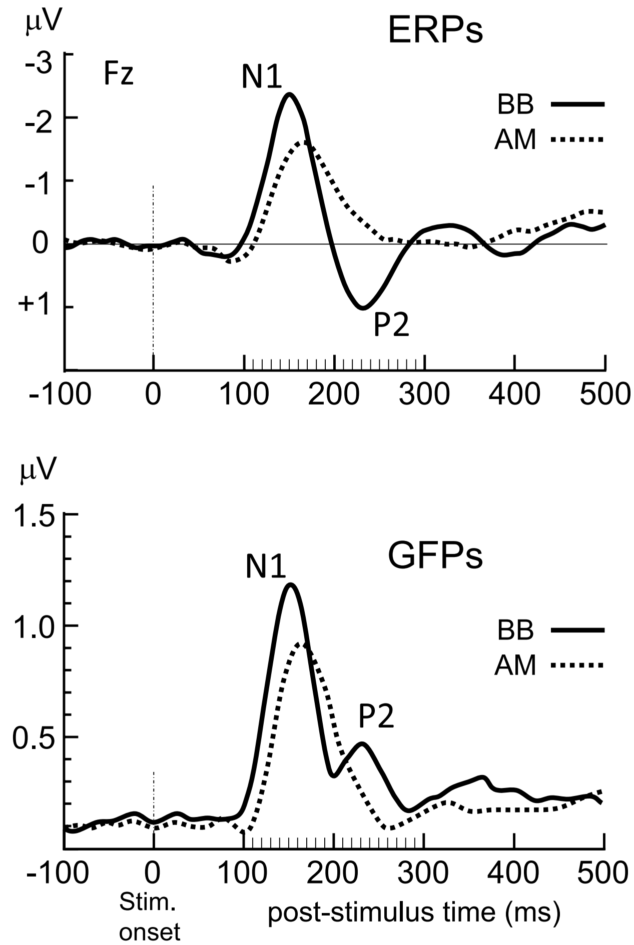

Fig. 6 Upper panel: Grand average waveforms of the ERPs of 19 participants to single-cycle BBs of a dichotic 250 Hz tone and to 1.5 dB AM of a diotic 250 Hz tone, recorded from the midline-frontal electrode (Fz) and re-referenced to nose. 100 ms pre-stimulus correction was applied to grand averages. Lower panel: GFP curves of the grand average ERPs seen in the upper panel

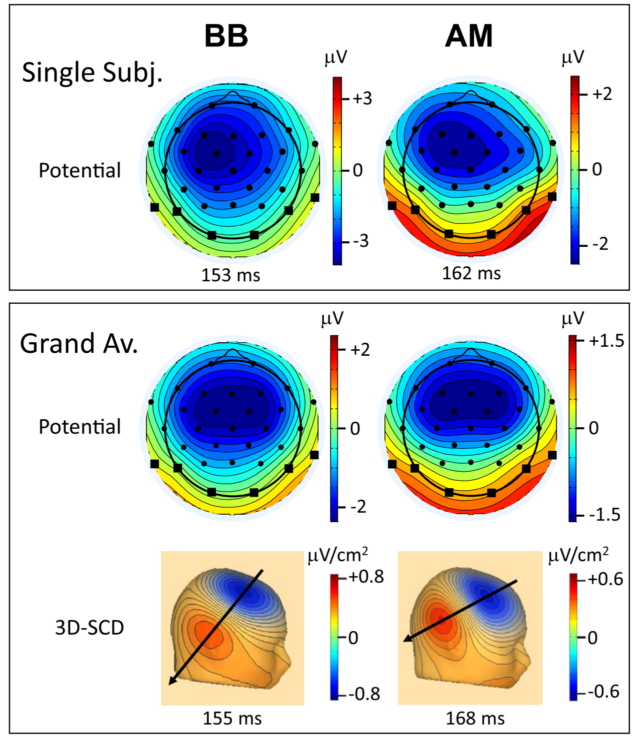

Fig. 7 Upper panel: 2D-scalp surface potential maps of the N1 deflection in ERPs of a typical participant to single-cycle BB and AM stimuli. Lower panel: 2D-scalp surface potential and right view 3D-current density (Laplacian) maps of the N1 deflection (upper and lower maps, respectively) in the grand average ERPs given in Fig. 5. Color-coded scalp maps were plotted for the mean values over a ±10 ms interval around the N1 latency given below each map. Temporo-parieto-occipital electrodes denoted by filled squares define the ROI that was considered to compare the scalp topographies of the N1 responses to BB and AM stimuli

others it was not that pronounced. This apparent spatial dissimilarity was supported by the result of the paired *t* test comparing the two GFP-normalized N1 amplitudes measured for BB and AM stimuli in the ROI that was defined to include the electrodes marked by filled squares in the figure. The 0.53 μV mean difference between these two ROI-potentials proved to be significant [$t(18) = 2.31$, $p = 0.033$; $d = 0.62$]. Normality of the difference data was verified by a Kolmogorov–Smirnov test ($D = 0.15818$; $p = 0.6715$). This significant difference between scalp potential distributions in the specified ROI is reflected in the respective 3D-scalp current density (Laplacian) maps given in Fig. 7 (lower panel) as an angular difference between the lines connecting the scalp sites of maximal current density corresponding to the superficial source and sink.

Discussion

The first of the two main findings of the present study is that the subthreshold temporary frequency shifts, which were demonstrated in our preliminary experiments on ten participants to elicit no significant EEG response when they were presented monotically (see Fig. 3), can create single-cycle BBs and do evoke robust N1-P2 responses when they are delivered dichotically to the ears in opposite directions (see Fig. 4). Actually, it would have been better if the preliminary monaural control experiments were repeated with the whole group of participants of the present study. However, the participants had to sit vigilantly in a small chamber already for eight recording blocks lasting ca. 60 min. Inclusion of extra four monaural control blocks would have added around 30 min to this time. Therefore, we had to maintain a balance between a possible inaccuracy due to differences among participants' monaural FM thresholds and a possible negative effect of lengthy experimental sessions on signal-to-noise ratio (SNR) of the ERPs as well as on the quality of the collected data due to violation of the time-invariance assumption in evoked potential approach.

The second main finding of the present study is that the transient single-cycle BB responses recorded are much larger in amplitude than the conventional steady-state responses to BBs found in the literature with comparable cohorts of subjects and stimulus parameters. In Pratt et al. 2009, for example, the peak-to-peak amplitude of the grand average ($N=18$; 18–24 years of age) responses to 3-Hz steady-state BBs of a 250-Hz base tone with 70 dB nHL is around 1 μV, which is about four times smaller than the grand average ($N=19$) amplitude of the single-cycle BB responses in the present study.

The BB phenomenon was described originally for continuous pure tones with slightly different frequencies (Rayleigh 1907; Licklider et al. 1950). BBs that are created according to this definition are steady-state because they are constantly repeated with a period which is equal to the reciprocal of the frequency difference between the tones in the two ears. For instance, the period of steady-state BBs created with the parameters used in the present study would be 322 ms. Because the recovery times of auditory ERP components are rather long, stimuli presented with such a short inter-stimulus interval can only evoke very low-amplitude responses. If this fact is considered together with the negative effect of the slow BB onset on the response amplitude, it becomes evident why periodic responses to steady-state BBs with stimulus parameters similar to those used in the present study can only be recorded with very small amplitudes.

Because no SNR data are explicitly reported in the above mentioned study of Pratt et al. (2009) with similar stimulus and processing parameters, a precise comparison between the SNR levels of the steady-state responses in their studies and the single-cycle BB responses in the present study cannot be made. However, using the fluctuations in the 100-ms pre-stimulus region of the tracings to estimate the level of the EEG noise in the responses, a rough estimate of the SNR can be obtained. In the mentioned study, the peak-to-peak amplitude of the fluctuations in the pre-stimulus region and that of the BB responses in the post-stimulus region can be read to be around 0.5 μV and 1 μV, respectively; roughly indicating a SNR of about 2. In the present study, on the other hand, these pre-stimulus and post-stimulus values are 0.2 μV and 4 μV, respectively, indicating a SNR of about 20. If the closeness of the number of peri-stimulus epochs averaged in the two studies ("400 epochs/subject" times 18 subjects versus "512 epochs/subject" times 19 subjects) are considered in addition to the similarity of the stimulus parameters, this comparison indicates that not only the amplitude of the BB responses but also their SNR levels are higher when transient single-cycle BB stimulation is used rather than steady-state BB stimulation. This conclusion is valid, of course, for the responses to BBs with parameters similar to those used in the present study. The case may be totally different with other cycle lengths or beat rates (e.g., 40 Hz), considering the results of the studies indicating different temporal and/or spatial response characteristics and different hemispheric dominance patterns for different BB rates (Ross et al. 2014; Jirakittayakorn and Wongsawat 2015).

Steady-state BB responses may sometimes be so tiny that their presence can only be detected by spectral analysis of the averaged EEG signal (Karino et al. 2006; Grose and Mamo 2012b). There are even studies which report that presentation of 1-min binaural beats of alpha and beta fails to elicit any clear evidence of a change in the EEG when it is searched using spectral analysis techniques (Vernon et al. 2014). Even recorded, steady-state BB responses are in the form of roughly sinusoidal undulations (Pratt et al. 2009, 2010; Hink et al. 1980; Schwarz and Taylor 2005). Therefore, identification and measurement of the N1-P2 complex, which has been repeatedly shown to be a typical long-latency response component originated in the auditory cortex (e.g., Scherg et al. 1989; Papanicolaou et al. 1990; Ungan et al. 2001) is not possible with steady-state BB responses. Furthermore, due to its transient character, single-cycle BB stimulation allows one to measure the latencies of the ERP components elicited, which provide information about the hierarchical level of their electrical sources in the brain. The magnetoencephalographic study by Ross et al. (2007), in which the authors recorded the cortical N1-P2 response to intermittent IPD (interaural phase difference) alterations, may also be cited here. The stimuli used in that study, however, were abrupt changes in the interaural phase of an amplitude modulated tone from 0° to 180°, and not BBs in which IPD or ITD changes gradually in a period corresponding to the frequency difference between dichotically presented tones.

It has long been known that the BB may lead to different percepts such as a single auditory image moving from ear to ear and back, or a tone with periodic loudness fluctuations, or a fast beating bitonal experience (roughness), as the beat rate increases (Licklider et al. 1950). To investigate the neural representations underlying these different perceptions, Ross et al. (2014) studied the neuromagnetic cortical responses to BBs across beat rates between 3 and 60 Hz. The authors report that the time courses of the magnetic responses to 3-Hz BBs have opposite polarities in the left and right auditory cortices and, therefore, the right and left hemispheric dipoles in their topographic map show opposite orientations. Consequently, the dipolar potential patterns from left and right auditory responses overlap with opposite polarity and would partially cancel each other in frontal central areas. In fact, this may be the reason why in the EEG recordings of the BB responses the amplitudes are very small. In the same study, for steady-state 3-Hz BBs, the latency estimated from the maxima of cross-correlation between the stimulus beat and the response is reported to be around 70 ms. This latency is much shorter than the N1 latency measured for the single-cycle BB response in the present study, and rather corresponds to that of the middle-latency responses of the thalamus and primary auditory cortex to transient auditory stimuli. The authors also report that the beat transfer function shows notably different auditory cortical hemispheric dominance patterns depending on the beat rate, which is in contrast to the well-known contralateral dominance of the N1 (Näätänen and Picton 1987). These findings suggest that the cortical responses to single-cycle and steady-state BBs have different neural origins. A detailed comparison of the characteristics and intracranial origins of the transient and steady-state auditory responses can be found in a review by Stapells (2010).

Of the three typical response components of auditory ERPs, namely P1, N1 and P2, the latter two were quite prominent in the ERPs to BB stimuli. On the other hand, the P1 was either not distinct or totally absent. This may be explained by the fact that the amplitude of this deflection largely depends on the sharpness of the stimulus onset; i.e., its rise time (Kodera et al. 1979). The BB stimuli used in the present study were not in the form of an abrupt change in interaural time or phase; they were rather slow changes in these interaural parameters with a relatively long cycle period of 322 ms. The AM stimulus had also the same slowness. Therefore, these auditory stimuli did not have an adequately steep onset like a click sound or tone-pip, or an abrupt shift in sound frequency, which are known to be optimum for eliciting a prominent P1 response. Another explanation for the absence of a notable P1 may be based on the above mentioned finding of Ross et al. (2014) indicating overlapped potential fields of the left and right hemispheric dipoles with opposite orientations in frontal central areas. This explanation seems likely if one considers the coincidence between the 70-ms latency of the 3-Hz BB response in the mentioned study and the typical latency of the ERP-P1, which is also around 70 ms.

In normal hearing subjects the auditory threshold decreases with increasing stimulus duration (Hughes 1946), and this observation indicates an integration of the auditory signal over time. The findings of Loveless et al. (1996), provide data about the time course of this integration. They report an increased N1 amplitude to the second stimulus of a pair of short tone-bursts, when the distance between the stimuli was shorter than 300 ms, indicating a long temporal integration process revealing itself as a short-term facilitation. Ross et al. (2002) also examine the time course of the developing steady-state magnetic responses of the brain to AM sounds, and report that the phase stabilization and amplitude development characteristics of the SSR relate to the timing of temporal integration. Based on several EEG and MEG studies (e.g., Näätänen 1992; Yabe et al. 1997) the long temporal integration window in audition is assumed to be around 200 ms, and sound sequences falling within this window of integration seem to be coded holistically as unitary events (Loveless et al. 1996). Considering this window length, even a single beat cycle of 320 s in the present study is long enough for full integration of the auditory event processed. For BBs with relatively higher rates such as 40 Hz, however, the event may not be completely integrated by the auditory system and encoded as a BB, because a single beat cycle will be much shorter than the window of auditory integration.

The event eliciting the N1 response in the present study is a change in some feature of an ongoing sound, and it is a well-known fact that the amplitude and latency of this response are affected by the magnitude and/or rate of the change; or, more accurately, the perceptual strength or salience of the change (Picton et al. 1974; Gutschalk et al. 2005). This was, in fact, the reason why we conducted the psychophysical tests to maintain an equivalence between the employed BB- and AM-stimuli regarding their perceptual salience in an attempt to roughly balance the amplitudes of their cortical responses. According to the results of these tests, the amplitude increase in AM-stimulus that matched with the employed BB-stimulus was found to be 1.5 dB. In an attempt to verify the results of this psychophysical test with relevant data in the literature, we were able to find three studies in which perceptual matching of BBs and AM tones was investigated. In one of them (Rutschmann and Rubinstein 1965), the median AM depth that was matched with the binaural beats was reported to be about − 13.5 dB, which corresponds to a peak-to-dip fluctuation of 3.8 dB. However, the maximum sound intensity used in that study (30 dB SL, which may roughly correspond to 40 dB SPL) is much lower than the intensity level used in the present study (90 dB SPL), although the beat rates and tone frequencies used in the two studies are similar. In the second study, Grose et al. (2012) measured the matching AM depth as − 21.2 dB, which corresponds to a peak-to-dip fluctuation of 1.51 dB. This value is almost equal to the intensity increase in the AM stimulus in the present study. However, although the beat rates were also comparable (4 Hz vs. 3.1 Hz), the 500-Hz base frequency of the tone used in that study was not. Furthermore, the sound intensity used in that study (65 dB SPL) was significantly lower than the intensity level used in the present study. In the third study (Groen 1964), which was a summary report, the peak-to-dip fluctuation of the AM that matched in salience with BBs was given as 2 dB for a beat rate of about 3 Hz and a sound level of about 60 dB SPL. However, stimulus details are largely missing in this short report. Since both the frequency and intensity of the beating tone are reported in the first two of these studies as important factors affecting the saliences of the BBs and AM tones, it is not possible to make an accurate comparison between the above mentioned matching data and the result of the matching test performed in the present study. Moreover, the BBs and AM stimuli in the mentioned studies were steady in nature and not transient or discrete like in the present one. Because of the discrepancies between the stimulus parameters in the above reviewed studies and those in the present study, we failed to verify, by referring to the literature, that our BB and AM stimuli were matched for their salience. However, the reason why we tried to match the two stimuli for their salience was just to obtain their responses with comparable N1 amplitudes; and this seems to be realized with a small difference between them.

The reason why we preferred a relatively high SPL for the base tone was because of the fact that the cortical response amplitudes increase with increased sound intensity. To obtain the BB-responses with as high a signal-to-noise ratio as possible, we, therefore, chose the highest SPL not causing discomfort of the participants or a risk of interaural crosstalk. As it was already pointed out in Methods, the relatively high sound intensity (93 dB SPL) employed should not have caused any cross-talk between ears owing to the high interaural attenuation of the earphone at 250 Hz. However, the acoustic reflex that would be caused by such a high-intensity sound through stiffening of the tympanic membrane as a result of contraction of the stapedius muscle (Møller 2000) might have affected the responses and impaired the assumed equivalence of stimulation levels across participants. One excuse against the severity of the issue would be that, in our preliminary experiments, we observed monotonously increasing BB-response amplitudes even when the sound level was increased to such high levels, indicating that this effect may not be strong enough to cause saturation of the BB-responses. Another excuse would be related to the well-known decay of acoustic reflex (Wilson et al. 1984), which may have caused at least a partial return-to-baseline throughout a long ERP recording session lasting several minutes. Still another excuse may be based on the fact that the acoustic reflex should similarly affect both responses (i.e., BB- and AM-responses) that are recorded from the same participants and compared with each other.

While in the ERPs to AM stimuli the P2 component of the N1-P2 complex was notable in only one of the participants and it does not appear, therefore, in the grand average ERP and its GFP curve, this positive wave proves to be a prominent deflection in the BB-evoked ERPs in the whole group. There are studies showing that this positive wave may be related with cognitive processes such as selective attention (Hillyard et al. 1973), stimulus change and feature detection (Näätänen 1990; Luck and Hillyard 1995), short-term memory (Golob and Starr 2000), modulation of attention (Novak et al. 1992) and stimulus classification (Garcia-Larrea et al. 1992), and that its amplitude is enhanced by learning and attention (Crowley and Colrain 2004). However, because in the present study the participants were not given any task concerning the above mentioned cognitive functions during recording of both types of ERPs, this amplitude discrepancy between their P2 components cannot be connected to such effects. It might suggest processing of the two auditory events by different neural mechanisms having different number of units.

It was reported in Pratt et al. (2010) that the scalp-recorded cortical responses to steady-state acoustic and binaural beats originated in the temporal lobe regions and both were lateralized to the left hemisphere. The conclusion was that the perceptions of binaural beats involve cortical activity that is not different than acoustic beats in distribution, indicating similar cortical processing. Based on the results of their magnetoencephalographic study, Draganova et al. (2008) also concluded that the initial responses to "central" (i.e., binaural) and "peripheral" (i.e., acoustic) beats are projected along the afferent auditory pathway and activated common cortical sources, although these two types of beats interact at different levels of the auditory system. In the present study, however, a notable topographical difference between the BB- and AM-evoked ERPs (see Fig. 5) was supported by a significant difference between the ROI scalp distributions of their N1 potentials, suggesting different dipole orientations of this most characteristic cortical response component. Because the ERP recordings with the two stimuli were carried out in a single session and according to a randomized block design, such a scalp topographical dissimilarity between the N1 responses elicited by the two stimuli cannot be attributed to different electrode cap placements in two cases. It should, therefore, indicate a significant difference between the frontal tilt angles of the N1 dipole orientations in two stimulation cases. This fact is indeed reflected in the 3D-scalp current density maps in the lower panel of Fig. 7, where a notable difference is apparent between the orientations of the lines connecting the respective superficial sources and sinks in the right sagittal view. Considering the fact that the orientation of cortical current dipoles should be radial to the surface of the cortex in which they sit and that the auditory N1 originates from transverse gyri on the supratemporal plane, it is conceivable that even two dipole sources on the same gyrus may have considerably different frontal orientations if there is some antero-posterior distance between them. Therefore, a difference between the frontal tilt angles of the two N1 dipoles may indicate a spatial difference between their cortical sources; though this difference may not be large.

It should be noted that a finer spatial resolution than provided by 31-channel EEG recording may be necessary to accurately localize and differentiate between the cortical sites where binaural beats and other auditory phenomena such as a simple change in sound level are processed. This spatial segregation in the auditory cortex may correspond to a functional distinction. The percept of BB is due to a complete cycle of change in the phase difference between the tones in the two ears. Therefore, the N1 response elicited in the cortex by this auditory event is associated with central spatial processing based on the TFS of the sound (i.e., the carrier). The diotic AM stimulus used in the present study, on the other hand, is a gradual change in the level of the tone in both ears simultaneously. Therefore, the N1 response elicited in the cortex by the AM stimulus should be associated with central level processing based on the gross structure of the sound (i.e., its envelope). This dissimilarity is also indicated by Ross (2018) based on the observations that the N1 responses to ITD changes decline steeply for frequencies beyond 1000 Hz whereas the onset N1 display only small variations across frequencies. In a recent study based on a model, which consists of two paths for auditory modulation detection using interaural phase (TFS) and monaural envelope cues, the simulations are shown to be consistent with the idea that both of the TFS processing and envelope processing decline with normal aging and sensorineural hearing loss (Ewert et al. 2018). However, it would be interesting to investigate, by means of an ERP study, if these two processing paths are differently affected by age-related neurocognitive disorders.

Conclusion

The main achievements and findings of the present study are as follows:

1. Using a modified form of the single-cycle BB stimulation suggested by Özdamar et al. (2011) instead of the classical steady-state BBs, it became possible to record the transient responses of the binaural cortical mechanisms processing this phenomenon.
2. By this way we were able to identify and analyze the auditory cortical ERP components which would have intermingled and masked each other when recorded using steady-state BB stimulation.
3. Owing to the significantly increased inter-stimulus interval in the single-cycle BB stimulation technique, the cortical responses, which could appear only with minimal amplitudes due to their rather poor recovery in the case of steady-state BB stimulation, could be recorded with average N1-P2 amplitudes of about four times as large.
4. By keeping the amount of monaural frequency shifts for BB stimuli below the FM perception threshold, it became possible to avoid the confound of monaural FM responses which would have been elicited otherwise. By this way, we were able to record the specific BB responses directly; i.e., with no need for subtraction of the monaural FM responses from the recorded ERP.
5. In addition to the methodological achievements above, the significant differences observed between the scalp potential distributions of the N1 responses to BB and AM stimuli suggested that partially different cortical sites may be responsible for processing these two stimuli involving, respectively, the TFS of a tone and its gross envelope. This result is in contrast with the literature reporting no difference between the cortical sources of the responses to binaural and acoustic BBs probably because of the inherently low magnitudes and composite nature of the responses obtained using steady-state BB stimulation in those studies.

Compliance with ethical standards

Conflict of interest The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be regarded as a potential conflict of interest.

Ethical approval Procedures of the study were approved by the Ethics Committee of Koc University, Istanbul.

References

Beauchene C, Abaid N, Moran R et al (2016) The effect of binaural beats on visuospatial working memory and cortical connectivity. PLoS One 11:e0166630

Becher AK, Höhne M, Axmacher N et al (2015) Intracranial electroencephalography power and phase synchronization changes during monaural and binaural beat stimulation. Eur J Neurosci 41:254–263

Boersma P, Weenink D (2013) Praat: doing phonetics by computer. [Computer program, Version 5.3.56]. http://www.praat.org. Accessed 15 Nov 2013

Bohorquez J, Özdamar Ö (2008) Generation of the 40-Hz auditory steady-state response (ASSR) explained using convolution. Clin Neurophysiol 119:2598–2607

Chaieb L, Wilpert EC, Reber TP et al (2015) Auditory beat stimulation and its effects on cognition and mood states. Front Psychiatry 6:70

Crowley KE, Colrain IM (2004) A review of the evidence for P2 being an independent component process: age, sleep and modality. Clin Neurophysiol 115:732–744

Derner M, Chaieb L et al (2018) Modulation of item and source memory by auditory beat stimulation: a pilot study with intracranial EEG. Front Hum Neurosci 12:500

Dimitrijevic A, Michalewiski HJ, Zeng F-G et al (2008) Frequency changes in a continuous tone: auditory cortical potentials. Clin Neurophysiol 119:2111–2124

Draganova R, Ross R, Wollbrink A et al (2008) Cortical steady-state responses to central and peripheral auditory beats. Cereb Cortex 18:1193–1200

Ewert SD, Paraouty N, Lorenzi C (2018) A two-path model of auditory modulation detection using temporal fine-structure and envelope cues. Eur J Neurosci. https://doi.org/10.1111/ejn.13846

Gao X, Cao H, Ming D et al (2014) Analysis of EEG activity in response to binaural beats with different frequencies. Int J Psychophysiol 94:399–406

Garcia-Argibay M, Santed MA, Reales JM (2018) Efficacy of binaural auditory beats in cognition, anxiety, and pain perception: a meta-analysis. Psychol Res. https://doi.org/10.1007/s00426-018-1066-8

Garcia-Larrea L, Lukaszewicz AC, Mauguiere F (1992) Revisiting the oddball paradigm. Non-target vs. neutral stimuli and the evaluation of ERP attentional effects. Neuropsychologia 30:723–741

Golob EJ, Starr A (2000) Age-related qualitative differences in auditory cortical responses during short-term memory. Clin Neurophysiol 111:2234–2244

Grantham DW, Wightman FL (1978) Detectability of varying interaural temporal differences. J Acoust Soc Am 63:511–523

Groen JJ (1964) Super- and subliminal binaural beats. Acta Otolaryngol 57:224–230

Grose JH, Mamo SK (2012a) Frequency modulation detection as a measure of temporal processing: age-related monaural and binaural effects. Hear Res 294:49–54

Grose JH, Mamo SK (2012b) Electrophysiological measurement of binaural beats: effects of primary tone frequency and observer age. Ear Hear 33:187–194

Grose JH, Buss E, Hall JW (2012) Binaural beat salience. Hear Res 285:40–45

Gutschalk A, Micheyl C, Melcher JR et al (2005) Neuromagnetic correlates of streaming in human auditory cortex. J Neurosci 25:5382–5388

Hillyard SA, Hink RF, Schwent VL et al (1973) Electrical signs of selective attention in the human brain. Science 182:177–180

Hink RF, Kodera K, Yamada O et al (1980) Binaural interaction of a beating frequency-following response. Audiology 19:36–43

Hommel B, Sellaro R, Fischer R et al (2016) High-frequency binaural beats increase cognitive flexibility: evidence from dual-task crosstalk. Front Psychol 7:1287

Hughes J (1946) The thresholds of audition for short periods of stimulation. Proc R Soc Lond B133:486–490

Ioannou CI, Pereda E, Lindsen JP et al (2015) Electrical brain responses to an auditory illusion and the impact of musical expertise. PLoS One 10:e0129486

Jirakittayakorn N, Wongsawat Y (2015) The brain responses to different frequencies of binaural beat sounds on QEEG at cortical level. Conf Proc IEEE Eng Med Biol Soc. 2015:4687–4691. https://doi.org/10.1109/EMBC.2015.7319440

Karino S, Yumato M, Itoh K et al (2006) Neuromagnetic responses to binaural beat in human cerebral cortex. J Neurophysiol 96:1927–1933

Knight RT, Hillyard SA, Woods DL et al (1981) The effects of frontal cortex lesions on event-related potentials during auditory selective attention. Electroenceph Clin Neurophysiol 52:571–582

Knight RT, Scabini D, Woods DL et al (1988) The effects of lesions of superior temporal gyrus and inferior parietal lobe on temporal and vertex components of the human AEP. Electroenceph Clin Neurophysiol 70:499–508

Kodera K, Hink RF, Yamada O et al (1979) Effects of rise time on simultaneously recorded auditory-evoked potentials from the early, middle and late ranges. Audiology 18:395–402

Lehmann D, Skrandies W (1980) Reference-free identification of components of checkerboard-evoked multichannel potential fields. Electroenceph Clin Neurophysiol 48:609–621

Levitt H (1971) Transformed up–down methods in psychoacoustics. J Acoust Soc Am 49:467–477

Licklider JCR, Webster JC, Hedlun JM (1950) On the frequency limits of binaural beats. J Acoust Soc Am 22:468–473

Lopez-Calderon J, Luck SJ (2014) ERPLAB: an open-source toolbox for the analysis of event-related potentials. Front Hum Neurosci 8:213

Loveless N, Levänen S, Jousmäki V, Sams M, Hari R (1996) Temporal integration in auditory sensory memory: neuromagnetic evidence. Electroenceph Clin Neurophysiol 100:220–228

Luck SJ, Hillyard SA (1995) The role of attention in feature detection and conjunction discrimination: an electrophysiological analysis. Int J Neurosci 80:281–297

Mihajloski T, Bohorquez J, Özdamar Ö (2014) Effects of single cycle binaural beat duration on auditory evoked potentials. Conf Proc IEEE Eng Med Biol Soc 2014:4587–4590

Møller A (2000) Hearing: its physiology and pathophysiology. Academic Press, New York, pp 181–200

Moore JK, Moore RY (1971) A comparative study of the superior olivary complex in the primate brain. Folia Primatol 16:35–51

Munro KJ, Agnew N (1999) A comparison of inter-aural attenuation with the etymotic ER-3A insert earphone and the telephonics TDH-39 supra-aural earphone. Br J Audiol 33:259–262

Näätänen R (1990) The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function. Behav Brain Sci 13:201–233

Näätänen R (1992) Attention and brain function. Erlbaum, Hillsdale

Näätänen R, Picton T (1987) The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure. Psychophysiology 24:375–425

Novak G, Ritter W, Vaughan HG Jr (1992) Mismatch detection and the latency of temporal judgements. Psychophysiology 29:398–411

Oster G (1973) Auditory beats in the brain. Sci Am 229:94–102

Özdamar Ö, Bohorquez J, Mihajloski T et al (2011) Auditory evoked responses to binaural beat illusion: stimulus generation and the derivation of the binaural interaction component (BIC). Conf Proc IEEE Eng Med Biol Soc 2011:830–833

Papanicolaou A, Baumann S, Rogers R et al (1990) Localization of auditory response sources using magnetoencephalography and magnetic resonance imaging. Arch Neurol 47:33–37

Perrott DR, Musicant AD (1977) Rotating tones and binaural beats. J Acoust Soc Am 61:1288–1292

Perrott DR, Nelson MA (1969) Limits for the detection of binaural beats. J Acoust Soc Am 46:1477–1481

Picton TW, Hillyard SA, Krausz HI et al (1974) Human auditory evoked potentials: I. Evaluation of components. Electroenceph Clin Neurophysiol 36:179–190

Picton TW, John M, Dimitrijevic A, Purcell D (2003) Human auditory steady-state responses. Int J Audiol 42:177–219

Polanía R, Nitsche MA, Ruff CC (2018) Studying and modifying brain function with noninvasive brain stimulation. Nat Neurosci 21:174–187

Pratt H, Starr A, Michalewski HJ et al (2009) Cortical evoked potentials to an auditory illusion: binaural beats. Clin Neurophysiol 120:1514–1524

Pratt H, Starr A, Michalewski HJ et al (2010) A comparison of auditory evoked potentials to acoustic beats and to binaural beats. Hear Res 262:34–44

Rayleigh L (1907) On our perception of sound direction. Phil Mag 13:214–232

Ritter W, Simson R, Vaughan H (1988) Effects of the amount of stimulus information processed on negative event-related potentials. Electroenceph Clin Neurophysiol 69:244–258

Ross B (2018) Auditory cortex responses to interaural time differences in the envelope of low-frequency sound, recorded with MEG in young and older listeners. Hear Res 370:22–39

Ross B, Picton TW, Pantev C (2002) Temporal integration in the human auditory cortex as represented by the development of the steady-state magnetic field. Hear Res 165:68–84

Ross B, Tremblay KL, Picton TW (2007) Physiological detection of interaural phase differences. J Acoust Soc Am 121:1017–1027

Ross B, Miyazaki T, Thompson J et al (2014) Human cortical responses to slow and fast binaural beats reveal multiple mechanisms of binaural hearing. J Neurophysiol 112:1871–1884
Rutschmann J, Rubinstein L (1965) Binaural beats and binaural amplitude modulated tones: successive comparison of loudness fluctuations. J Acoust Soc Am 38:759–768
Scherg M, Vajsar J, Picton TW (1989) A source analysis of the late human auditory evoked potentials. J Cogn Neurosci 1:336–355
Schwarz DWF, Taylor P (2005) Human auditory steady state responses to binaural and monaural beats. Clin Neurophysiol 116:658–668
Stapells DR (2010) Frequency-specific ABR and ASSR threshold assessment in young infants. In: Seewald RC, Bamford J (eds) A sound foundation through early amplification: an international conference, Chapter 4. Phonak, Stafa
Stewart GW (1917) Binaural beats. Phys Rev 9:502–508
Ungan P, Yagcioglu S (2002) Origin of the binaural interaction component in wave P4 of the short-latency auditory evoked potentials in the cat: evaluation of serial depth recordings from the brainstem. Hear Res 167:81–101
Ungan P, Sahinoglu B, Utkucal R (1989) Human laterality reversal auditory evoked potentials. Electroenceph Clin Neurophysiol 73:306–321
Ungan P, Erar H, Öztürk N et al (1992) Human long-latency potentials evoked by monaural interruptions of a binaural click train: connection to sound lateralization based on interaural intensity differences. Audiology 31:318–333
Ungan P, Yagcioglu S, Göksoy C (2001) Differences between the N1 waves of the responses to interaural time and intensity disparities: scalp topography and dipole sources. Clin Neurophysiol 112:485–498
Ungan P, Özdamar Ö, Yagcioglu S (2014) Long-latency binaural beat responses to subthreshold frequency shifts. 12th National Neuroscience Congress, Istanbul, May 28–31, 2014
Vaughan HG Jr, Ritter W (1970) The sources of auditory evoked responses recorded from the human scalp. Electroenceph Clin Neurophysiol 28:360–367
Vernon D, Peryer G, Louch J et al (2014) Tracking EEG changes in response to alpha and beta binaural beats. Int J Psychophysiol 93:134–139
von Bekesy G (1960) Experiments in hearing. McGraw-Hill, New York
Wernick JS, Starr A (1968) Binaural interaction in the superior olivary complex of the cat: an analysis of field potentials evoked by binaural-beat stimuli. J Neurophysiol 31:428–441
Wilson RH, Sahnks JE, Lilly DJ (1984) Acoustic reflex adaptation. In: Silman S (ed) The acoustic reflex: basic principles and clinical applications. Academic Press, New York, pp 329–387
Yabe H, Tervaniemi M, Reinikainen K, Näätänen R (1997) Temporal window of integration revealed by MMN to sound omission. NeuroReport 8:1971–1974

Affiliations

Pekcan Ungan[1] · Suha Yagcioglu[2] · Ece Ayik[3]

Suha Yagcioglu
yagcioglu.s@gmail.com

Ece Ayik
eceayik@gmail.com

1 Department of Biophysics, School of Medicine, Koc University, Istanbul, Turkey

2 Department of Biophysics, Faculty of Medicine, Hacettepe University, Ankara, Turkey

3 Graduate School of Science and Engineering, Koc University, Istanbul, Turkey