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Binaural interaction in the auditory brainstem response: A normative study

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HIGHLIGHTS

- The binaural interaction component is derived from the auditory brainstem response (ABR–BIC) elicited by two different stimuli, i.e. clicks and 500 Hz tone-bursts.
- The most reliable peaks in the click and 500 Hz TB ABR–BIC occur at a mean latency of respectively 6.06 ms and 9.47 ms.
- The ABR–BIC cannot be used for individual diagnosis since it is absent in an important portion of normal hearing subjects.

ABSTRACT

Objective: Binaural interaction can be investigated using auditory evoked potentials. A binaural interaction component can be derived from the auditory brainstem response (ABR–BIC) and is considered evidence for binaural interaction at the level of the brainstem. Although click ABR–BIC has been investigated thoroughly, data on 500 Hz tone-burst (TB) ABR–BICs are scarce. In this study, characteristics of click and 500 Hz TB ABR–BICs are described. Furthermore, reliability of both click and 500 Hz TB ABR–BIC are investigated.
Methods: Eighteen normal hearing young adults (eight women, ten men) were included. ABRs were recorded in response to clicks and 500 Hz TBs. ABR–BICs were derived by subtracting the binaural response from the sum of the monaural responses measured in opposite ears.
Results: Good inter-rater reliability is obtained for both click and 500 Hz TB ABR–BICs. The most reliable peak in click ABR–BIC occurs at a mean latency of 6.06 ms (SD 0.354 ms). Reliable 500 Hz TB ABR–BIC are obtained with a mean latency of 9.47 ms (SD 0.678 ms). Amplitudes are larger for 500 Hz TB ABR–BIC than for clicks.
Conclusion: The most reliable peak in click ABR–BIC occurs at the downslope of wave V. Five hundred Hertz TB ABR–BIC is characterized by a broad positivity occurring at the level of wave V.
Significance: The ABR–BIC is a useful technique to investigate binaural interaction in certain populations. Examples are bilateral hearing aid users, bilateral cochlear implant users and bimodal listeners. The latter refers to the combination of unilateral cochlear implantation and contralateral residual hearing. The majority of these patients have residual hearing in the low frequencies. The current study suggests that 500 Hz TB ABR–BIC may be a suitable technique to assess binaural interaction in this specific population of cochlear implant users.

1. Introduction

Binaural hearing refers to the ability of the auditory system to integrate sounds reaching both ears. It enables sound localization

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and improves speech perception in more adverse listening conditions. Binaural hearing has been investigated using psychoacoustic methods, as well as auditory evoked potentials. A binaural interaction component can be derived from the auditory brainstem response (ABR–BIC) by subtracting the response to binaural stimulation (B) from the sum of the monaural responses ($L + R$) (Wrege and Starr, 1981). In mathematical terms:

$$\text{ABR} - \text{BIC} = (L + R) - B$$

Noteworthy is that some authors apply the inverse formula: [$\text{ABR} - \text{BIC} = B - (L + R)$] (Dobie and Berlin, 1979; Dobie and Norton, 1980). These two derivation methods produce ABR–BICs that are opposite in polarity.

The presence of an ABR–BIC is considered to be evidence for binaural interaction at the level of the auditory brainstem. The concept is based on the law of linear superposition of electric fields. If the binaural response represented activity from two non-interacting pathways, the sum of the right and the left monaural responses would equal the binaural response. However, in normal hearing subjects, the ABR elicited by binaural stimulation differs from the sum of the monaural responses and consequently a difference wave is obtained (Dobie and Berlin, 1979).

There is a renewed interest in the ABR–BIC due to the growing amount of cochlear implant (CI) patients who might benefit from binaural cues. Bilateral input in CI-recipients can be provided by either (1) bilateral implantation or (2) bimodal stimulation. ABR–BICs have been successfully recorded in bilateral CI-users (Pelizzone et al., 1990; Gordon et al., 2007, 2008, 2012; He et al., 2010). Moreover, ABR–BICs have been used to assess binaural integration of acoustic and electric signals in bimodal listeners. The latter refers to the condition in which residual hearing is present in the non-implanted ear. Noh et al. (2007) recorded ABR–BICs in unilaterally implanted guinea pigs with normal hearing in the non-implanted ear. More recently, Battmer et al. (2011) succeeded in recording ABR–BICs in unilaterally implanted single-sided deaf adults. In both the studies by Noh et al. (2007) and Battmer et al. (2011) electrical stimulation was applied in the implanted ear, whereas the non-implanted ear was stimulated using clicks. Results from these studies suggest that binaural integration of electric and acoustic signals can occur at the level of the auditory brainstem.

In contrast to the subjects tested by Battmer et al. (2011), the majority of bimodal listeners have mainly residual hearing in the low frequencies. Therefore, clicks are insufficient to record ABR–BICs in this group of patients. Provided there is sufficient residual hearing in the non-implanted ear, 500 Hz tone-bursts (TBs) may be more feasible. Frequency-specific ABR, including 500 Hz TB ABR, has been shown reliable (Gorga et al., 1988). Note that morphology of click-evoked ABR differs from that of 500 Hz TB ABR. Responses to moderate-to-high intensity clicks show clearly defined vertex-positive peaks of which I, III and V are the most prominent. This is in contrast to 500 Hz TB ABR which primarily consists of wave V followed by a large negativity. This wave V is usually broad and has longer latencies than its click-evoked equivalent.

The differences between click and 500 Hz TB ABR are mainly explained by differences in neural synchronization. Clicks are broadband stimuli and thus excite a wide range of the cochlea. Nevertheless, click-evoked ABR is dominated by basal or high-frequency activity. As the traveling wave moves towards the apex, the velocity of the traveling wave front decreases. This results in less neural synchronization in apical parts of the cochlea. Furthermore, the onset of 500 Hz TB is shallower than the extremely abrupt onset of clicks. Both the disparate neural activity in low-frequency regions of the cochlea and the longer rise time of low-frequency TBs contribute to the poorer morphology observed in 500 Hz TB ABR. The longer wave V latency in 500 Hz TB ABR is mainly attributed to the longer travel time to reach the apical cochlear region.

Literature on 500 Hz TB ABR–BIC is very limited. Although the effects of stimulus frequency on the ABR–BIC have been investigated, 500 Hz TBs have hardly been used (Fowler and Leonards, 1985; Wilson et al., 1985; DeVries and Decker, 1988; Ito et al., 1988). To our knowledge, only Fowler and Horn (2012) described 500 Hz TB ABR–BICs in adults. Although the characteristics of the 500 Hz TB ABR–BIC were described, the reliability of the response was not investigated (Fowler and Horn, 2012).

In the present study, characteristics and reliability of both click ABR–BIC and 500 Hz TB ABR–BIC are investigated.

2. Materials and methods

2.1. Subjects

Eighteen young adults (eight women, ten men) aged 18–30 years (mean 23.9, standard deviation SD 3.42) volunteered in this study. None had a history of neurologic disorders. All participants were screened for normal hearing (i.e. $\leqslant$20 dB HL at octave frequencies from 250 to 8000 Hz) and normal middle ear function (i.e. no history of chronic ear disease, normal otoscopy and normal 226 Hz tympanometry). Interaural threshold asymmetries did not exceed 10 dB HL at more than two frequencies for octave frequencies between 250 Hz and 4000 Hz. Testing was carried out in a double-walled sound-proof room using a PC-based audiometer (Equinox 2.0, Interacoustics, Assens, Denmark) with TDH39 earphones calibrated according to the 6189 ISO standards. Subjects signed an informed consent before being enrolled in the study, which was approved by the institutional review board at Ghent University Hospital.

2.2. Procedure

ABRs were recorded using the commercially available Neurosoft Neuro-MEP system version 3 (Ivanovo, Russia). Ag/AgCl surface electrodes were used. The positive electrode was placed on the upper forehead (Fpz) and the negative electrode was placed at the midline in the nape of the neck (cervical 7). An electrode placed on the nasion served as ground. Impedances were less than 5 kΩ and inter-electrode impedances did not exceed 3 kΩ. Acoustic stimuli were delivered through TIP300 tubal insert phones. Two different acoustic stimuli were presented: (1) 0.1 ms alternating clicks and (2) 500 Hz alternating, Blackman-gated TBs with 2.5 cycles rise time, no plateau and 2.5 cycles fall time. Alternating polarity was used to reduce the stimulus artifact. Both stimuli were presented at 65 dB nHL. Potential contribution of acoustic cross-over and stapedial reflex – two potential artifacts according to Levine (1981) – were avoided by using moderate intensity levels and insert phones. A repetition rate of 15.1 Hz was used. For clicks, responses were averaged over a 20 ms interval (5 ms prestimulus and 15 ms poststimulus). Responses to 500 Hz TB stimuli were averaged over a 30 ms interval (5 ms prestimulus and 25 ms post-stimulus). Recordings were sampled with a sampling frequency of 40 kHz. All recordings were filtered online with a 30–3000 Hz band-pass filter. Artifact rejection was applied.

Before starting the test, all subjects were instructed to relax as much as possible. During the exam subjects were lying supine on a bed placed in a darkened room. The recordings could either start with click ABR or 500 Hz TB ABR. This was chosen randomly. ABRs were recorded in response to three stimulus conditions: right, left and binaural stimulation. For each condition at least three runs of 2000 sweeps were obtained. Hence, an average waveform of at least 6000 presentation was obtained for each stimulus condition.

2.3. Analysis of recordings

A derived waveform was obtained by subtracting the binaural ABR from the sum of both monaural ABRs. The subtraction paradigm, i.e. $(L + R) - B$, was performed online using the clinical software. Peaks in the ABR–BIC were defined as scalp-positive and reproducible deflections occurring in the downslope or the negative deflection following waves V, VI and/or VII of the ABR. Using a nomenclature introduced by Jiang (1996), these peaks are labeled DV, DVI and DVII respectively (Jiang, 1996).

Two independent observers judged whether the derived waveforms contained ABR–BIC peaks. Peaks were considered present if results of both observers corresponded in presence and latency. In the case of inter-observer disagreement, an objective criterion was applied. First, ABR–BIC recordings were digitally filtered using a Butterworth filter. Click ABR–BICs were filtered with a 100–1200 Hz bandpass filter, 500 Hz TB ABR–BICs with a 30–1000 Hz bandpass filter. Second, the variance of a 3.5–1.5 prestimulus interval was calculated. The variance ratio of a well-defined poststimulus period was then divided by the variance of the noise in the prestimulus interval (Arnold, 1985). Based on empirical data, the poststimulus period for DV, DVI and DVII in click ABR–BIC was respectively 5.50–7.00 ms, 7.50–9.00 ms and 9.50–11.00 ms. For the 500 Hz TB peak DV, the poststimulus period comprised a 7.50–11.50 ms interval. Whenever the variance ratio exceeded 1.4, a significant peak was found. This criterion was determined by means of the F-distribution. With a sampling frequency of 40 kHz, the 2 ms prestimulus interval consisted of 80 sample points. For the click-evoked ABR–BIC peaks, each poststimulus interval comprised 1.5 ms and thus consisted of 60 sample points. The $F(59, 79)$ statistic equals 1.49 for a significance level of 0.05. The same rationale was used for 500 Hz TB: $F(159, 79) = 1.36$ for $p < 0.05$. Therefore, an overall criterion of 1.4 was used to determine statistically significant peaks in the ABR–BIC. MATLAB version 8.0 (The Mathworks, Nantucket) was used for signal processing.

Peak latency and peak-to-peak amplitude of ABR waves V, VI and VII and the related ABR–BIC peaks are described. In the case of inter-observer agreement, the mean latency of both observations was used. When the objective criterion was applied and a significant peak was found, the latency difference between the ABR–BIC peak and its related ABR wave was calculated for each observer. The latency with the smallest latency difference was used for further analysis. Amplitudes were measured from the most positive point to the most negative point following it.

2.4. Statistical analysis

Latencies and amplitudes of waves V, VI and VII of the binaural response were compared to those of the $L + R$ response. Two-sided paired-sample t-tests were performed for this analysis, except for wave VII amplitude. The latter showed a serious departure from normality and therefore a two-sided Wilcoxon matched-paired signed-ranks test was performed.

Furthermore, inter-observer agreement for absence or presence of the ABR–BIC peaks was investigated. As each peak was judged by both observers, the data were not statistically independent and hence the conventional Chi Square test cannot be performed. Instead, a two-sample test for binomial proportions for paired data (McNemar test) was used. The degree of agreement is expressed by a κ-value. To interpret this value, criteria of Fleiss et al. (2003) were used. Excellent agreement was obtained when κ-values were between 1 and 0.75. Good to moderate agreement was found for values between 0.75 and 0.40. κ-values less than 0.40 were considered marginal to no agreement.

For all statistical analysis, a p-value less than 0.05 was considered significant.

3. Results

3.1. Click ABR–BIC

Table 1 lists the characteristics of all relevant ABR waves and their related ABR–BIC peaks. There was a significant difference in wave V latency for the $L + R$ response and the binaural response (two-sided paired t-test, $t(17) = 5.09$, $p < 0.001$), with the binaural responses having shorter latencies (mean 5.53 ms, SD 0.212) than the $L + R$ responses (mean 5.61 ms, SD 0.203). Wave VII amplitudes were significantly (two-sided signed-rank test, $p = 0.005$) smaller in the binaural condition (mean 0.29 μV, SD 0.167) compared to the $L + R$ condition (mean 0.38 μV, SD 0.135).

Fig. 1 shows an ABR–BIC in a subject. The most prominent peak, DV, is typically preceded by a negative deflection. Both observers indicated DVI, whereas DVII was considered absent. Noteworthy is the observation of a reproducible, positive peak prior to DV. Peaks occurring within a time-window between waves III and IV of the ABR, were found in nine subjects.

Prevalence of DV, DVI and DVII was assessed. The observers indicated DV in all derived waveforms. As shown in Fig. 2a, good inter-observer agreement for DV latencies was achieved in all but one subject. The objective test was performed, but did not result in a significant peak. It can be concluded that DV was present in 17 out of 18 subjects.

Fig. 2b illustrates that in nine traces DVI was indicated with similar latencies. In three waveforms DVI was considered absent. No significant difference between observers' judgment was found (McNemar, $p = 0.219$). However, a weak inter-observer agreement was obtained ($\kappa = 0.29$). From the objective analysis on six traces with contradictory results, one significant peak was identified. Thus, DVI was present in ten out of 18 traces.

Table 1
Characteristics of ABR and ABR–BIC in response to clicks.

		R			*L*			*L + R*			*B*			ABR–BIC		
		V	VI	VII	V	VI	VII	V	VI	VII	V	VI	VII	DV	DVI	DVII
n		18	15	15	18	15	15	18	15	16	18	15	16	17	10	6
Latency (ms)	Mean	5.58	7.13	9.25	5.67	7.19	9.33	5.61	7.12	9.28	5.53	7.09	9.28	6.06	7.95	9.80
	SD	0.205	0.197	0.328	0.184	0.321	0.411	0.203	0.254	0.360	0.212	0.249	0.257	0.354	0.482	0.474
	Min	5.27	6.77	8.78	5.35	6.69	8.55	5.27	6.69	8.68	5.21	6.72	8.78	5.58	7.18	9.29
	Max	5.93	7.49	9.87	5.98	7.75	10.10	5.93	7.57	9.98	5.90	7.49	9.68	6.90	9.00	10.40
Amplitude (μV)	Mean	0.60	0.39	0.23	0.49	0.33	0.20	1.06	0.69	0.38	1.04	0.75	0.29	0.28	0.24	0.26
	SD	0.194	0.144	0.09	0.152	0.117	0.075	0.329	0.232	0.135	0.301	0.234	0.167	0.098	0.072	0.128
	Min	0.31	0.20	0.08	0.19	0.11	0.11	0.45	0.30	0.24	0.52	0.38	0.09	0.13	0.13	0.10
	Max	1.00	0.63	0.41	0.69	0.51	0.33	1.69	1.00	0.68	1.58	1.13	0.58	0.48	0.36	0.40

ABR–BIC: binaural interaction component derived from the ABR, *B*: binaural ABR, *L*: left ABR, *L + R*: summed monaural ABRs, Max: maximum, Min: minimum, *R*: right ABR, SD: standard deviation.

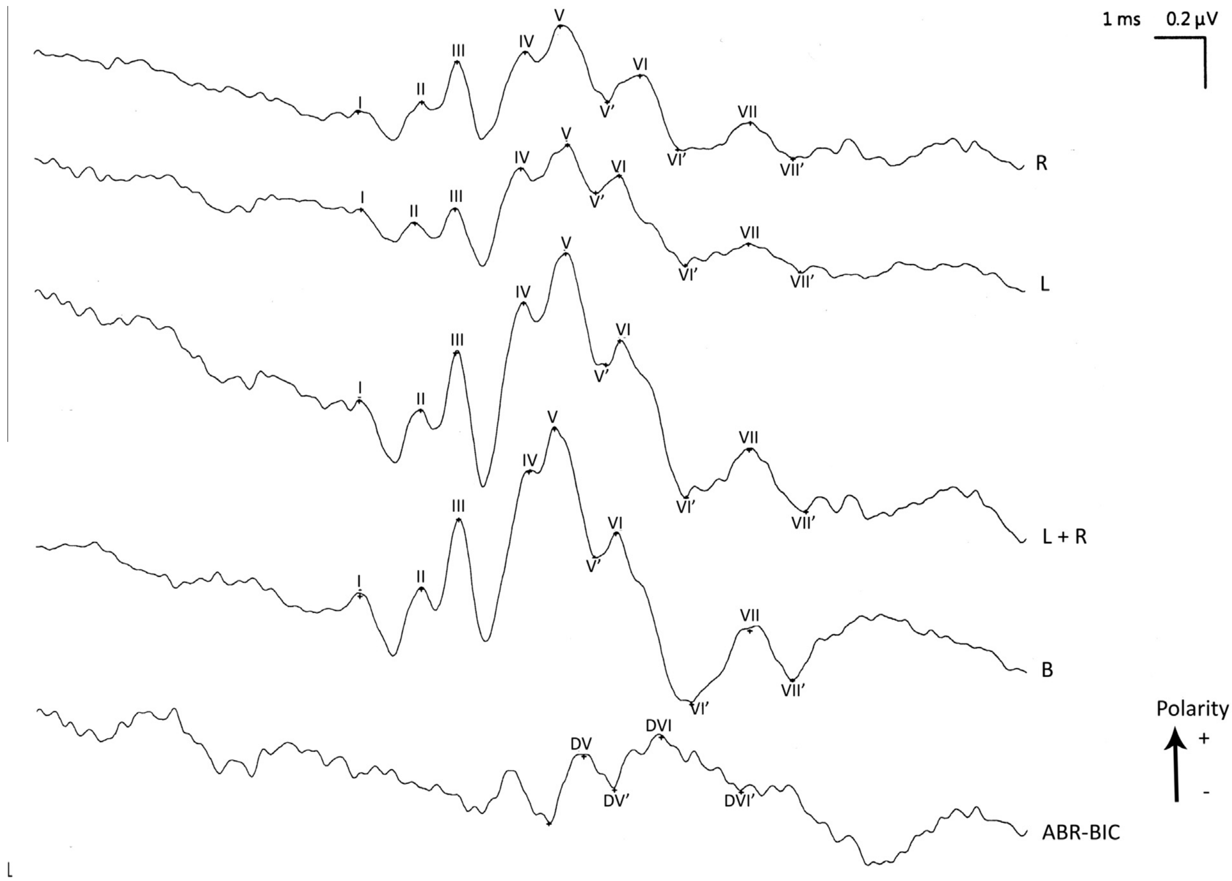

Fig. 1. Click ABR–BIC in a normal hearing adult. *L* is the ABR to left stimulation, *R* is the ABR to right stimulation and *B* is the ABR to binaural stimulation.

The observers considered DVII absent in nine traces, whereas six waveforms contained DVII. For one of these peaks an important latency difference of 2.34 ms was present (Fig. 2c). This peak was excluded when performing the McNemar test. The analysis showed no significant difference and good inter-observer agreement (McNemar, $p = 1.00$; $\kappa = 0.63$). Three out of four traces subjected to the objective test did not contain significant DVIIs. Overall, DVII was present in six out of the 18 derived waveforms.

3.2. 500 Hz TB ABR–BIC

Characteristics of wave V and peak DV in response to 500 Hz TB are summarized in Table 2. Latencies were borderline not statistically different ($t(17) = 2.08$, $p = 0.053$) between the binaural condition (mean 8.62 ms, SD 0.540) and the $L + R$ condition (mean 8.67 ms, SD 0.562). A significant effect of stimulus condition was found for wave V amplitudes ($t(17) = 9.63$, $p < 0.001$), with larger amplitudes in the $L + R$ response (mean 1.53, SD 0.370) compared to the binaural response (mean 1.19, SD 0.270).

Fig. 3 illustrates a 500 Hz TB ABR–BIC. Morphology differs from click ABR–BIC in several ways. First, no peaks other than DV can be demonstrated as 500 Hz TB ABR contains only wave V. Second, DV is broader for 500 Hz TB than for clicks. Third, 500 Hz TB DV is often rather a slope than a well-defined positive peak. Finally, it often occurs at the level of wave V rather than at its downslope.

Both observers considered DV present in 15 subjects and absent in one. Good inter-observer agreement was found (McNemar test; $p = 0.500$; $\kappa = 0.46$). As shown in Fig. 2d, observer II tended to indicate DV slightly later than observer I. The maximum inter-observer latency difference was 0.4 ms, which is clinically irrelevant as 500 Hz TB DV is rather broad. For the two traces with uncertain results, the objective test resulted in significant peaks. It can thus be concluded that 500 Hz TB DV was present in 17 of 18 subjects. It should be noted that 500 Hz TB DV was absent in another subject than the one with absent click DV.

4. Discussion

4.1. Click ABR–BIC

In the present study, characteristics of click ABR–BIC are described. Although click ABR–BIC is well-documented in literature, comparison between studies is difficult due to methodological differences. In addition, ABR–BIC nomenclature is highly arbitrary. Jiang (1996) attempted to standardize ABR–BIC nomenclature by labeling every peak in the ABR–BIC by a prefix 'D' followed by the Roman numeral of the related ABR wave. For instance, the peak occurring at the downslope of wave V is labeled 'DV'(Jiang, 1996). This nomenclature is recommended by the authors as it makes comparison of data more convenient. Comparing results is also hampered by the large inter-subject variability of ABR–BIC morphology. Numerous peaks have been described, but these are not consistently present in all normal hearing adults.

It can be stated that DV is the most consistent and most reliable peak in the ABR–BIC. DV was present in 17 out of 18 participating subjects and this is consistent with the literature (Dobie and Norton, 1980; Levine and Davis, 1991; Stollman et al., 1996; Brantberg et al., 1999). The excellent inter-observer agreement for DV confirms its reliability. In contrast, inter-rater agreement was lowest for DVI ($\kappa = 0.29$). There are two explanations for the poorer inter-observer agreement for DVI compared to DV. First, wave VI in the ABR is more variable than the ABR wave V. It is

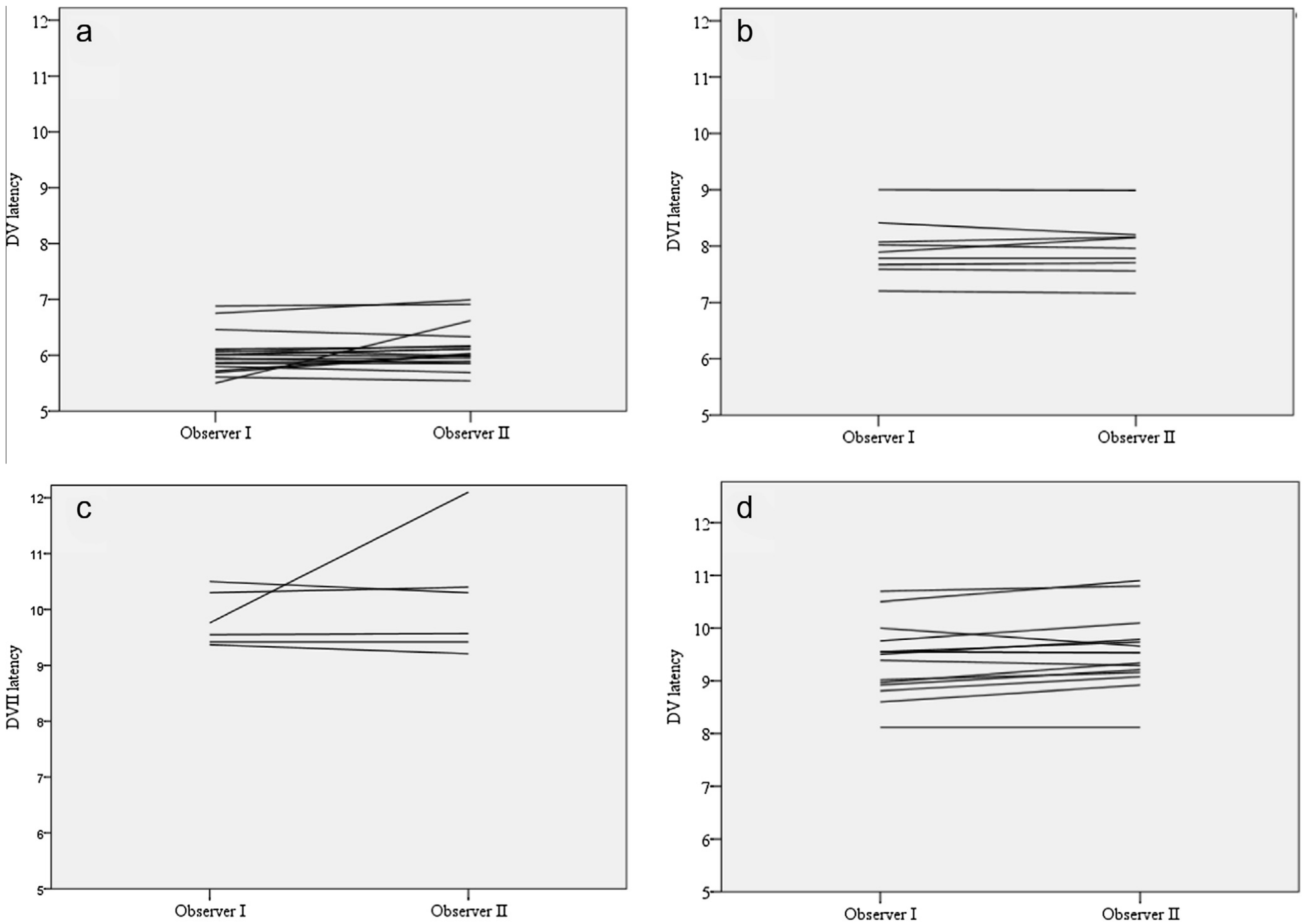

Fig. 2. Inter-observer latency difference in ms for DV (Fig. 2a), DVI (Fig. 2b) and DVII in response to clicks (Fig. 2c). Inter-observer latency difference in ms for DV in response to 500 Hz TB (Fig. 2d).

Table 2
Characteristics of ABR and ABR–BIC in response to 500 Hz tone-bursts.

		R	*L*	*L* + *R*	*B*	ABR–BIC
n		18	18	18	18	17
Latency (ms)	Mean	8.65	8.66	8.67	8.62	9.47
	SD	0.508	0.576	0.562	0.540	0.678
	Min	7.65	7.62	7.59	7.65	8.12
	Max	9.71	10.10	10.10	10.00	10.75
Amplitude (μV)	Mean	0.79	0.80	1.53	1.19	0.44
	SD	0.187	0.191	0.370	0.270	0.167
	Min	0.37	0.46	0.80	0.75	0.19
	Max	1.13	1.18	2.23	1.65	0.76

ABR–BIC: binaural interaction component derived from the ABR, *B*: binaural ABR, *L*: left ABR, *L* + *R*: summed monaural ABRs, Max: maximum, Min: minimum, *R*: right ABR, SD: standard deviation.

not present in all normal hearing subjects. Second, DVII can easily be mistaken for DVI. Using Jiang's nomenclature, peaks were named after the corresponding ABR wave. If a scalp-positive peak directly following DV occurs at the downslope of wave VII, the peak is labeled DVII. A peak following wave DV is, thus, not necessarily DVI. The latter may also explain the rather low presence of DVI in the current sample (i.e. ten out of 18 volunteers) compared to literature (Dobie and Norton, 1980; Ito et al., 1988). In literature, often only two ABR–BIC peaks are described. Peaks indicated as 'the second peak in the ABR–BIC' could have been DVI or DVII according to the nomenclature used in the present study. DVII shows good inter-observer agreement ($\kappa = 0.63$), but was only present in six participants. The low prevalence is explained by the variability of wave VII in the normal ABR.

Worth noting is that significant differences between the binaural and the *L* + *R* response were only found for waves V and VII. These waves correspond to the most reliable peaks in the ABR–BIC, respectively DV and DVII. The ABR wave V had significantly (two-sided paired *t*-test, $t(17) = 5.09$, $p < 0.001$) shorter latencies in the binaural condition (mean 5.53 ms, SD 0.212) compared to the *L* + *R* condition (mean 5.61 ms, SD 0.203). No significant wave V amplitude differences were found in the present study. These findings are consistent with the results of several earlier studies (Levine, 1981; Brantberg et al., 1999). However, an earlier report documents smaller amplitudes for the binaural condition compared to the *L* + *R* condition (McPherson and Starr, 1993). In a review by Fullerton et al., 1987, it was stated that the human DV – indicated as β in the original paper – mainly occurs because wave V occurs earlier for binaural stimulation than for monaural stimulation. In the same review, it was reported that the amplitude of wave V for binaural stimulation is 93% of the amplitude of the summed monaural waveform. These small differences in amplitude may not have been found in the current study due to the stimulus polarity, the current sample size and/or electrode placement. In contrast to wave V amplitudes, significantly smaller wave VII amplitudes were found for the binaurally evoked ABR compared to its monaural aggregate (two-sided signed-rank test, $p = 0.005$). These findings suggest that binaural interaction as measured by wave V of the click ABR is mainly caused by latency differences, whereas for wave VII this is mainly caused amplitude differences.

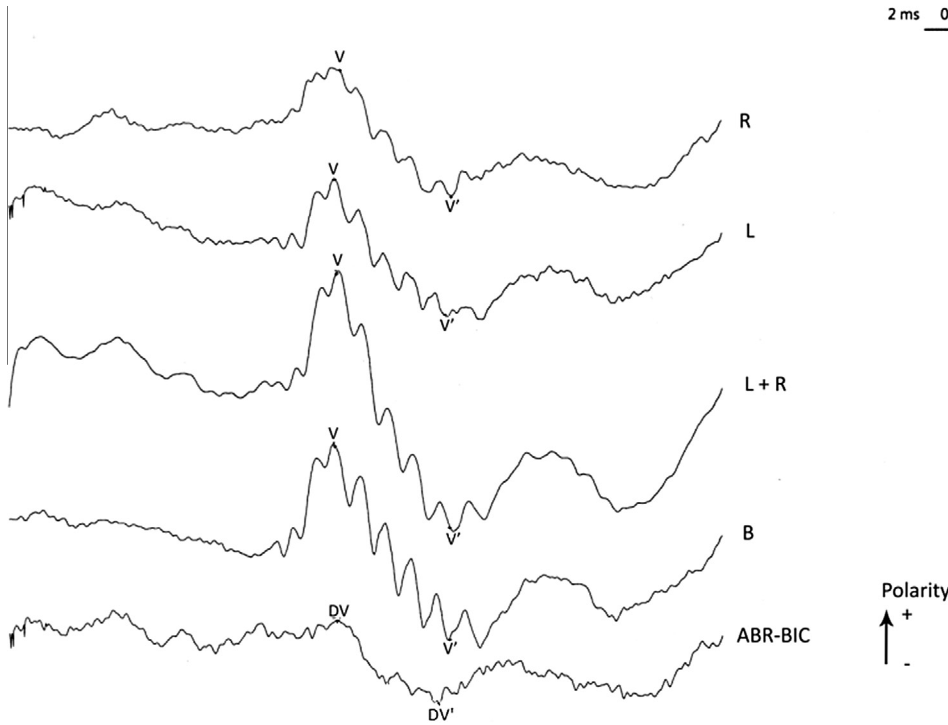

Fig. 3. 500 Hz TB ABR–BIC in a normal hearing adult. *L* is the ABR to left stimulation, *R* is the ABR to right stimulation and *B* is the ABR to binaural stimulation.

ABR–BIC peaks are characterized by their peak latencies and amplitudes. Peak latencies correspond to the results known from literature (Dobie and Norton, 1980; Wrege and Starr, 1981; Jiang, 1996). Comparison of peak amplitudes is more difficult due to methodological differences between studies. Different stimulus intensities, number of sweeps, filter settings and methods to measure amplitude have been used throughout different studies. Moreover, high inter-subject variability of ABR–BIC amplitudes is known.

In addition to the peaks DV, DVI and DVII, scalp-positive peaks are observed between waves III and IV. These early peaks have been described in literature. Wilson et al. (1985) identified ‘short-latency components’ at high intensity levels and for stimulus rates of 20 Hz and more. It was advocated that binaural interaction cannot contribute to these peaks as wave III originates from the ipsilateral cochlear nuclei. The occurrence of these ‘short latency components’ was attributed to the effect of the stapedial reflex. It was suggested that binaural stimulation is more likely to elicit a reflex than monaural stimulation at the same intensity. If the stimulation rate is fast enough, the reflex would persist to alter middle ear transmission. This can result in differences between the binaural ABR and the summed monaural waveform in the absence of binaural interaction (Wilson et al., 1985). In our opinion, it is very unlikely that early peaks are caused by the stapedial reflex. The argument by Wilson et al. (1985) does not take into account adaptation of the stapedial reflex. Moreover, early peaks were observed in our sample although moderate intensity levels and stimulation rates less than 20 Hz were used. A possible explanation for the early ABR–BIC peaks is found in the anatomy of the auditory brainstem. As projections from the cochlear nucleus to the medial nucleus of the trapezoid body (MNTB) cross the midline, fibers synapsing on the MNTB could contribute to the early peaks (Curio and Weigel, 1990). Furthermore, it is known that sources other than the cochlear nucleus also contribute to wave III. The argument that wave III is generated solely by neurons located in the cochlear nucleus is basically an oversimplification (MØller, 1985).

4.2. 500 Hz TB ABR–BIC

The second goal of this study was to describe 500 Hz TB ABR–BIC and to test its reliability. DV in response to 500 Hz TB appears as a rather broad downslope occurring at the level of wave V. Our findings suggest that this peak mainly results from amplitude differences between the binaural response and the $L + R$ response ($t(17) = 9.63$, $p < 0.001$). Amplitudes in the summed response (mean 1.53, SD 0.370) were larger than those in the binaural response (mean 1.19, SD 0.270). Noteworthy is the observation of a borderline non-significant trend ($t(17) = 2.08$, $p = 0.053$) of longer latencies in the $L + R$ condition (mean 8.67 ms, SD 0.56) compared to the binaural condition (mean 8.62 ms, SD 0.54).

Fairly good inter-observer agreement was found ($\kappa = 0.46$) and DV was absent in only one volunteer. However, some waveforms were rather noisy. In such traces, the authors would recommend to use more than three replications of each 2000 sweeps. As expected, DV latencies were longer for 500 Hz TB than for clicks. A mean latency of 9.47 ms (SD 0.678) was found. This is longer than the mean latency found in the study by Fowler and Horn (2012), who found mean latencies of 8.08 ms (SD 0.32 ms). Various factors may have contributed to this difference. As previously mentioned, 500 Hz TB DV is a rather broad peak. Latencies are therefore more variable for 500 Hz TB DV than for click DV. Other factors, such as differences in band pass filtering, stimulus rise time and stimulus intensity, may also have led to the slightly different outcome.

A mean DV amplitude of 0.44 µV (SD 0.167 µV) is reported. DV amplitudes are thus larger in response to 500 Hz TB than those in response to clicks. Although 500 Hz TB have hardly been investigated, a trend of increasing amplitude with decreasing stimulus frequency is documented in literature (Fowler and Leonards, 1985; Wilson et al., 1985; DeVries and Decker, 1988; Ito et al., 1988). To our knowledge, only Fowler and Horn (2012) described 500 Hz ABR–BIC in adults. The response to 500 Hz TB was compared with 4 kHz TB ABR–BIC and also in this study amplitudes were largest for the lowest frequency. This is remarkable since ABRs in response to low-frequency TBs are less clear than high-frequency or click-evoked ABRs. The reason for the larger amplitudes in 500 Hz TB ABR–BIC compared to its click-evoked equivalent is still unclear. Ito et al. (1988) attributed this to auditory nuclei being involved in the binaural processing of low versus high frequencies, respectively the medial superior olive (MSO) and the lateral superior olive (LSO). According to Caird and Klinke (1983), the LSO mainly encodes transient interaural time differences (ITD) and interaural level differences (ILD). Cells in the MSO, on the other hand, are particularly sensitive to continuous ITDs. Since clicks are transient stimuli containing mainly high-frequency energy, the processing of these stimuli would take place in the LSO. Five-hundred Hertz TB might elicit more phase-locking to the fine-structure of the stimulus and consequently the MSO might be more involved. Larger DV amplitudes for 500 Hz TB suggest that more neural resources are involved than when binaural interaction is investigated using clicks. In a recent study by Kulesza (2007) the number of neurons in human MSO and LSO were estimated. It was found that the MSO contains approximately 15.500 neurons and the LSO about 5.600 neurons. It is thus possible that more neurons are involved in the binaural processing of 500 Hz TB compared to clicks. Worth mentioning is that most research on MSO and LSO is based on animal models. Possible differences between species can be present and further research is needed to support this hypothesis.

4.3. Clinical relevance and future directions

As stated earlier, ABR–BICs were present in 17 out of 18 normal hearing subjects. This was found for click as well as 500 Hz TB ABR–BIC. ABR–BIC are absent in a portion of normal hearing subjects. Furthermore, the low signal-to-noise ratio (SNR) of some of the responses makes interpretation challenging. Therefore, ABR–BIC cannot be used for individual diagnoses. Another disadvantage of the technique is the rather long test time. Due to the low SNR, it requires relatively long average times to obtain the ABR–BIC.

Although the clinical use of the ABR–BIC is questionable, it is a very useful technique to investigate clinically relevant question on binaural interaction in certain populations. A better understanding of binaural processing in different populations will enable clinicians to provide more insightful counseling. For instance, ABR–BICs have been shown present in bilateral CI-users and this has been an argument for bilateral implantation (Pelizzone et al., 1990; Gordon et al., 2007, 2008, 2012; He et al., 2010). A critical period for binaural interaction in children with bilateral CI has been reported (Gordon et al., 2007, 2008). This has been an argument for simultaneous bilateral cochlear implantation. Furthermore, it has been suggested to use this technique to match interaural electrodes in bilateral CI-users. In literature, the ABR–BIC has been used to investigate binaural interaction in at least two populations other than CI-users. First, maturation of the binaural system has been investigated using this technique (Cone-Wesson et al., 1997). Second, it has been used to investigate central auditory processing disorders (Gopal and Pierel, 1999; Delb et al., 2003).

A new region of interest is binaural interaction in bimodal CI-users. New developments in CI-technology and its surgery have extended CI-candidacy to include patient with some low-frequency residual hearing in the ipsi- and/or contralateral ear. Psychoacoustic evidence shows that at least some of these patients benefit from binaural cues. There is however a great inter-subject variability in outcome and mechanisms underlying this variability are still unclear. The ABR–BIC might give more insight in binaural interaction in this growing population of CI-users.

5. Conclusions

DV is the most reliable peak in click ABR–BIC and occurs at a latency of 6.06 ms (SD 0.654 ms). Reliable 500 Hz TB ABR–BICs are recorded with mean DV latency of 9.47 ms (SD 0.678 ms). DV amplitudes for 500 Hz TB are on average larger than DV amplitudes for clicks.

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