REVIEW ARTICLE

Binaural interaction component in auditory evoked potentials: characteristics and potential applications in audiology

Roya Nicknejad, Farzaneh Zamiri Abdollahi[*]

Department of Audiology, School of Rehabilitation, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Background and Aim: Since the first report of recording the binaural interaction component (BIC) in 1970, many studies have been conducted on BIC but none of them make its way to clinical application yet. The present paper aims at reviewing the characteristics and potential applications of BIC in audiology.

Recent Findings: BIC may be a potentially sensitive objective tool in identifying subjects with auditory processing disorders and monitoring auditory training effects. It can also help effective electrode insertion in bilateral cochlear implantation. Besides, BIC has shed light on the binaural processing maturation in infants. BIC recoding faces some difficulties as it is sensitive to noise and presentation rate, and has low amplitude, especially in brainstem level. These issues might contribute to its limited clinical applications.

Conclusion: Although BIC has not been introduced as an objective tool for testing binaural processing, it has the potential to be a reliable test. Furthermore, BIC may be used in situations where no behavioral test can be conducted. Such circumstances are during cochlear implantation or testing uncooperative pre-school children for auditory processing or the lack of standard behavioral tests for them. Further research on BIC is highly recommended before it can gain any clinical application.

Keywords: Binaural interaction; cochlear implant; spatial processing; auditory processing

Introduction

The binaural interaction component (BIC) in electrophysiological potentials may serve as an objective tool for the evaluation of binaural processing, especially in young children [1-3]. Accordingly, if there is a significant relationship between BIC and behavioral binaural processing tests, then BIC can be a good test for diagnosing disorders of binaural processing such as spatial processing disorder at a young age, even in pre-schoolers. Testing auditory processing in pre-schoolers is highly challenging partly due to lack of standard behavioral tests with age-appropriate norms and partly due to confounding factors such as lack of attention and cooperation [1-4]. Early diagnosis of auditory processing disorder (APD) has always been in the focus of researchers. Diagnosing APD before school age can provide early auditory training and preventing academic failure and its consequent

[*] **Corresponding author:** Department of Audiology, School of Rehabilitation, Tehran University of Medical Sciences, Piche-Shemiran, Enghelab Ave., Tehran, 1148965141, Iran. Tel: 009821-77530636, E-mail: audiology_zamiri@yahoo.com

emotional or social adverse effects on the children [5-7]. In addition, BIC has other interesting applications in audiology, such as monitoring symmetric electrode placement during cochlear implant surgery or evaluation of maturation/ development of binaural processing in children [8,9]. Kelly-Ballweber and Dobie (1984) were pessimistic that BIC could find a useful application in clinical settings. They showed that many subjects with even mild high-frequency loss lacked any recordable BIC. They suggested that scientists might find a way to decrease the inherent variability of the response and its' low signal to noise ratio (SNR) before BIC can gain any clinical attention. Since then, electrophysiologic devices have changed a lot, many studies investigated BIC, and exciting results have yielded [10]. The present paper aimed at reviewing the most critical characteristics of BIC and its' potential applications in audiology (clinical and research field).

Binaural interaction component in auditory evoked potentials from early to late responses

What is binaural interaction in electrophysiological responses?
BIC is calculated by subtracting actual binaural electrophysiological response from the sum of the monaural responses of the two ears [8,11,12]. Jewett (1970) was the first scientist who detected this subtractive potential at the level of the auditory brainstem response (ABR) in cats [13]. After his work, other scientists got interested in the BIC and investigated the responses at the level of middle and late latency. In general, most studies on BIC have been conducted on the ABR BIC.

Binaural interaction in auditory brainstem response and its' origin
The most stable wave in ABR BIC is the β wave, which occurs at the level of wave V. However, BIC is mostly a multi-peak component. ABR BIC components are α, β, γ, and δ. These components are also called DP1, DN1, DP2, and DP3. DN1 is equivalent to β which is the major component of BIC [8].

According to Brantberg et al., the latency difference of wave V in actual binaural response and the sum of monaural responses is the reason why BIC appears after subtraction [14]. Others believe that the amplitude difference of wave V between these two recordings is the main reason. In general, BIC has a highly variable amplitude, and the remaining noise in the recording contributes to this variability. Other factors affecting this variability comprise transducer, earphone placement, electrode placement, electrode impedance, etc. [15]. This inherent variability plays an important part in the clinical application of BIC.

At the level of ABR, binaural wave V is smaller than sum of the monaural responses. Therefore, an inhibition process may be the primary mechanism of the BIC [16,17].

Furst showed that ABR BIC is related to directional hearing [2,18]. Animal studies, especially on rats, show that ABR BIC is produced secondary to binaural processing at the level of superior olivary complex (SOC). Even in cases that we see multiple BICs in ABR at the level of wave V and VI or a wide wave from wave V to VI, the BICs are produced by binaural processing in SOC [19]. The reason might be the sluggish binaural processing that lasts for a while [20,21]. Studies on rats and guinea pigs showed that BIC would appear after the destruction of the lateral lemniscus (LL) or inferior colliculus (IC). On the other hand, BIC is sensitive to the integrity of the SOC or medial nucleus of the trapezoid body [22,23]. In general, two mechanisms have been proposed for the production of ABR BIC. The first mechanism is that binaural stimulation reduces the firing of contralateral inhibitory and ipsilateral excitatory neurons of SOC. The second mechanism states that monaural stimulation saturates contralateral and ipsilateral excitatory neurons. Therefore, the binaural response would not be twice larger than monaural responses [3]. The inhibitory mechanism theory is stronger.

SOC has two main nuclei: medial superior olive (MSO) and lateral superior olive (LSO). MSO is sensitive to the interaural time difference (ITD),

and LSO is sensitive to interaural intensity difference (IID) [4]. The size of the head is an important factor affecting ITDs and IIDs, and consequently, MSO and LSO function. Animals with small heads such as gerbils have small ITDs. On the other hand, in species with big heads such as humans, ITDs are larger [24]. The maximum possible ITD for humans is on the order of 1 ms [25,26]. So based on ecologic needs, MSO in humans must include neurons that can detect ITDs up to approximately 1 ms.

MSO receives excitatory inputs from the cochlear nucleus of both sides of the brainstem, but LSO receives excitatory inputs from one side and inhibitory inputs from the other side. MSO is the underlying nucleus for ABR BIC. Recordings from single neurons of MSO show that these neurons respond strongly to binaural stimuli, and their binaural response is larger than the summation of the monaural responses (facilitation) [27]. The question is how this nucleus can have inhibitory output or contribute to inhibitory BIC. Brand et al. showed inhibitory neurotransmitters (NTMs) in MSO (Glycinergic in mammals and GABAergic in birds). Removing these inhibitory NTMs adversely affects MSO function [28].

Jeffress proposed the place theory of localization. He mentioned that stimuli from the two ears travel in pathways with different distances along the axons to reach neurons in MSO. Therefore, the length of ipsilateral and contralateral pathways are different for neurons in MSO. So each neuron has the most sensitivity or maximum response to a specific ITD (characteristic ITD). In general, different neurons can detect different ITDs [29]. However, this hypothesis has some critical concerns. Different axon lengths can be seen in birds but not in mammals [30,31]. MSO neurons have a particular shape. The place of the cell body, input dendrites, and output axon can produce different types of input-output patterns that can potentially act the same as different axon lengths that were mentioned in the Jeffress model. Besides, different types of inhibitory inputs exist on the neurons' cell body that can delay neural conduction differentially [32].

Based on the Jeffress model and by considering maximum possible ITD in humans, BIC can be traced up only to ecologic ITDs. Wrege and Starr showed that ABR BIC could be seen at ITD of 0.1 µs, and the BIC is traced up to ITD of 500 µs and the latency of BIC changes systematically with ITD (larger ITDs, more BIC latency). They showed that BIC is not seen at ITDs over 800 µs [33], which is compatible with the Jeffress model. However, many studies have shown that BIC can be detected in ITDs as large as 2 ms (which is not ecologically possible in humans) [8]. The next question is why there are neurons for detecting such large ITDs. To answer this question, the precedence effect (PE) was proposed. In real life, there are latent echoes of the primary sound source that must be detected and deleted. These echoes do not affect localization, and localization is always based on the first wave front. PE is attributed to a higher-order function from IC to the auditory cortex, but MSO might be a preliminary step for this higher order function [34,35].

The amplitude of ABR BIC is larger in animals compared to humans. The reason might be related to animals' smaller heads, the closer place of recording electrodes to the wave origin, recording during anesthesia, and low muscle noise [36,37]. The test-retest variability of ABR BIC in animals is smaller than humans [8,15]. ABR BIC is highly sensitive to presentation rate and may disappear even with a slight increase in rate [8].

ABR can be recorded by speech stimuli such as /da/. In speech ABR (sABR), a transient response (onset response including wave V and A; offset response including wave O) and a frequency following response (FFR) (D, E, F) are recorded [38]. Huan et al. showed that BIC-V, BIC-A, BIC-D, BIC-E, BIC-F, and BIC-O were detected in 80%, 40%, 70%, 70%, 55%, and 50% of the normal subjects. So, BIC is also present at sABR, but it is not detected in all subjects [39]. Besides, sABR shows different results in females and males and probably binaural sABR, and consequently, BIC in sABR show the same trend [40]. More research in this field is highly recommended.

Binaural interaction component in middle latency and late latency response

Several BICs are seen in middle latency response (MLR) (20 to 40 ms) [41] and late latency response (LLR) (63 to 150 ms) [42,43]. BIC in these responses is larger than ABR. This condition may indicate that binaural processing is major in thalamocortical and cortical levels, and happens much more than the pontine level [41]. At the level of MLR and LLR, some components show a larger binaural response than the sum of the monaural responses. In these cases, an underlying facilitation mechanism might be involved. According to studies, these components belong to non-specific auditory pathways and nuclei, such as medial and dorsal nuclei of the medial geniculate body (MGB). Recordings from the temporal lobe indicate that specific auditory areas show inhibitory patterns, but areas with multisensory processing show facilitatory patterns [44,45].

MLR/LLR BICs are sensitive to the presentation rate and can disappear even with a small increase in the rate. BIC LLR has a strong relation to behavioral binaural fusion. When a subject perceives a single image of binaural stimulation, BIC LLR appears. However, if a subject perceives two separate sounds in his head (each from one ear), BIC decreases significantly or even disappears [11,31,46].

When ITD is applied to the binaural stimuli, the perceived location of the stimulus changes in response to ITD. It has been shown that the latency of BIC LLR changes systematically with ITD, and the latency correlates well with the perceived location of the sound source. This event happens even without attention to the perceived location of the sound source and may involve the echoic memory (automatic memory) [47-49].

There is a BIC at the 40 Hz response, too. This condition indicates that at least some rate resistant neurons at the thalamocortical level have binaural input and show an inhibitory mechanism for BIC production, as well. Unlike other BICs, 40-Hz BIC is rate-resistant [46].

Effects of presentation rate on binaural interaction components

Generally, binaural response and BIC are more sensitive to presentation rate than monaural evoked potentials. However, 40-Hz BIC is an exception to this fact [8,46]. Binaural inhibitory pathways seem to be more sensitive to presentation rate (maybe metabolic vulnerability), and cannot tolerate high presentation rate. Metabolic characteristics of inhibitory binaural processing pathways might differ from excitatory ones. With increasing the stimulus rate from 10 to 100/s, the latency of BICs in ABR increases and their amplitude decreases. The most stable component is β wave and other components disappear faster than β [46,50,51].

The rate of stimulation must be considered in performing BIC in auditory evoked responses. Testing with a slower presentation rate takes a longer time but ensures recording all possible components and makes it possible to interpret latency and amplitude of components.

Maturation of binaural interaction components

Human neonates can discriminate sound locations. Localization skill continues to develop remarkably in the first couple of years and undergoes sophisticated changes even through school-age [52]. About 50% of neonates show ABR BIC at birth, and only 10% of these neonates show systematic change of BIC latency with ITD. Generally, this fact indicates that localization circuits are present at birth but neonates cannot use them yet. As infants go through the developmental process (such as myelination) and experience different listening situations (synaptic changes), maturation of the circuits happen [53].

BIC cannot be seen in some neonates. These subjects often have well-formed monaural ABR with normal age-related latencies, but they do not show binaural wave V or BIC. This event indicates that monaural and binaural auditory processing pathways undergo differential maturation and development process. In general, binaural processing pathways have longer maturation process than monaural pathways [54,55].

ABR BIC in infants has inherent variability: some infants have β (related to wave V), some δ

(related to wave VI), some both components, and remaining no BIC at all. Besides, in some neonates with BIC, binaural components disappear with increasing ITD, but in others, BIC can be traced to ITDs as large as 1 ms. Does ITD as large as 1 ms occur in neonates?

The embryo lives in a liquid environment (uterus) in which the sound travels 4 times faster than air. Also, the fetus's head is small. Therefore, the largest possible ITD for human embryo is 125 µs. immediately after birth, the neonate is exposed to the air environment, so the sound speed changes dramatically. This change increases ITD to 500 µs. At birth, the neonates' head size is 60% of the adult size. In time and during development, the head size increases, and in an adult, ITD reaches 750 µs to 1 ms. This process shows that all hardwire pathways exist since birth (and even before that), and they only need to be re-calibrated based on infants' functional needs, head size growth, and experience [53]. At the level of MLR, infants show BIC (especially in the latency of Na) but with smaller amplitudes than adults. The state of arousal might affect the results because infants are usually tested during sleep [54].

The potential application of binaural interaction components in the clinical and research field

Binaural interaction component and auditory processing disorder

Subjective binaural processing tests such as localization tests can be easily affected by non-auditory factors, including attention, arousal, and general subjects' cooperation. So objective evaluations of binaural processing are desirable, and BIC in auditory evoked potentials might be an interesting tool [1,2]. It seems that BIC has 76% sensitivity in identifying APD [2].

The most consistent finding is that ABR BIC is smaller in subjects with APD [56]. Gopal and Pierel used BIC of ABR in 9 children at risk for APD and 9 normal peers. They reported that the amplitude of the BIC of ABR reduced significantly compared to the control group. They concluded that BIC of ABR could be potentially an objective response for determining children

with APD [57]. Delb et al. also introduced BIC as an objective test for diagnosing APD. They studied 17 children at risk for APD and 25 normal peers. The absence of ABR BIC was defined as the presence of APD. They found that BIC has a sensitivity and specificity of 76% for identifying children with APD [2]. Abdollahi et al. showed that BIC MLR has lower amplitude and longer latency in children with APD than healthy age-matched children. They suggested that BIC MLR could be recorded and analyzed easier than BIC ABR because of its generally larger amplitude [1]. In addition, BIC may be an objective tool to monitor the effects of auditory training in children with APD. It actually shows good agreement with behavioral auditory processing tests. Lotfi et al. showed that MLR BIC agrees well with the speech in noise/competition tests. They reported that with spatial auditory training, BIC MLR, and speech perception in noise/competition in children with suspected APD improve significantly [56].

Binaural interaction component and cochlear implant

With electric stimulation, auditory evoked potentials are the same as acoustic stimulation, but generally, they have larger amplitudes and shorter latencies. ABR BIC with electric stimulation is larger than acoustic stimulation because there is more synchrony among activated auditory fibers. Transient acoustic stimuli produce synchrony only in mid- and high-frequency fibers. Also, electric stimulation bypasses the cochlear transmission and produces BICs with shorter latencies [58-60].

In general, LLR BICs are present in subjects with the bilateral cochlear implant (CI), but they show high inter-subject variability in morphology, amplitude, and ITD sensitivity. Cortical BIC is dependent on interaural electrode spacing. Besides, if there is a significant delay (more than 2 years) between the first and second CI in sequential cochlear implantation, BIC will be different from healthy subjects or those received their second device earlier [9,61].

In bilateral CI, when electrodes are placed

symmetrically in both ears, there are larger BICs at the level of all auditory evoked potentials. This condition might indicate more natural binaural processing and better-fused sound perception. Therefore, it is feasible that surgeons use BIC as a tool to monitor electrode placement in bilateral CI to achieve a better outcome for their patients [59].

Besides, there are subjects with bimodal CI. These subjects have CI in one ear and a hearing aid in the other one. They benefit from binaural cues, as well. Investigating binaural interaction in these subjects seems beneficial and can guide the clinician to select cases who need binaural auditory rehabilitation and monitor their progress in time. There are studies on single-sided deaf animals and humans with unilateral CI. In these cases, ABR BIC (electric-click acoustic stimulation) has been recorded successfully. However, most patients with bimodal CI have a residual hearing at low frequencies; therefore, a 500-Hz tone burst seems a more suitable stimulus than click for recording ABR BIC [62]. However, more research is recommended in this field.

Binaural interaction component and specific language impairment
Specific language impairment (SLI) is a persistent language disorder without any neurologic, sensory, or cognitive involvement. Probably the auditory system could be involved in SLI. Binaural interaction is one of the most important central auditory processing, which has vital effects on understanding target signals in the presence of noise. Some studies have been conducted on BIC ABR in patients with SLI. Clarke and Adams showed that in children with SLI in the age range of 7 to 12 years, ABR BIC had lower amplitude than healthy peers, and BIC was only present in the latency range of wave VI. Gopal and Pierel also showed that BIC was less prominent in patients with SLI. This finding can indicate a disorder in binaural interaction processing in the brainstem, probably secondary to less synchrony of binaural neural activity [57]. Based on these findings, patients with SLI may have difficulty in auditory localization and

speech understanding in noise [57,63]. However, more research is recommended in this field.

Conclusion
Binaural interaction component (BIC) has low amplitude, especially at the level of ABR, and its' recording takes time because of recording three evoked potential responses (monaural responses for each ear and a binaural response) on one session. Besides, monaural responses must be added off-line, and binaural response must be subtracted from the sum of monaural responses. Not all clinical electrophysiologic devices have this capability. However, BIC can provide information that otherwise can be missed.

Although BIC has not introduced as an objective tool for testing binaural processing, it has an inherent potential to be a reliable test besides behavioral tests, showing auditory processing status and maturation. Furthermore, BIC may have a potentially fruitful application in situations where behavioral tests cannot be conducted. Such circumstances include during cochlear implantation surgery or in uncooperative pre-school children in auditory processing tests or lack of any standard behavioral tests for them. Further research on BIC is highly recommended before it can gain any clinical use.

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