

# Physiological measurements of human binaural processing

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Many different electric and magnetic responses to sound can be recorded as the human brain processes binaural information: (1) A binaural interaction component can be measured by comparing binaural responses to the sum of separate monaural responses. (2) Locating sounds in a reverberant environment can be examined by evaluating echo suppression. (3) Binaural beats can evoke following responses. (4) Responses can be evoked by binaural stimuli that are unmasked by changes in the interaural phase of stimulus or noise. (5) Occasional changes in the spatial location of a repeating sound can evoke a mismatch negativity. (6) A change in the binaural characteristics of an ongoing stimulus – interaural timing, correlation or phase – evokes a large N1-P2 response that is later than the response to the onset of a sound. The concomitant disruption and reinstatement of the 40-Hz steady state response can measure temporal perception and integration. (7) Moving sounds evoke large cortical responses when the movement begins and when a moving object crosses the midline. All paradigms may become useful in objectively demonstrating normal or abnormal binaural function in patients who cannot respond reliably during behavioral testing.

## HUMAN AUDITORY EVOKED RESPONSES

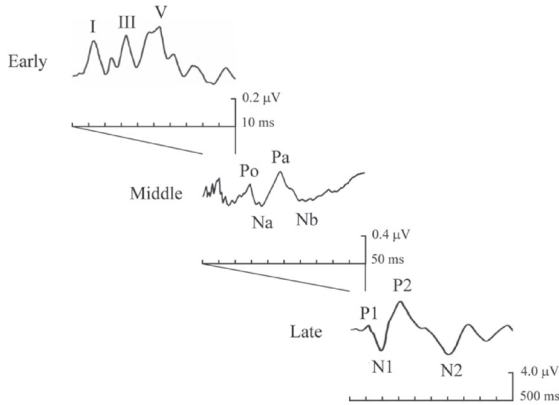
Many different responses can be recorded from the human ear and brain in response to sounds. These are generated at all levels of the auditory system from the cochlea to the cortex. When neurons respond to sound they generate electric and magnetic fields. If the neurons are organized in space and synchronized in time, the fields sum together and can be recorded at the scalp. Evoked responses demonstrate the function of these particular neurons. Many auditory processes occur without generating measurable responses – either because the neurons are not time-locked to the stimuli or because they are not spatially organized. Human physiology is less precise than animal physiology.

The evoked responses can be classified as those that respond to stimulus change – transient responses – and those that last throughout a stimulus – sustained responses. In response to a stimulus that changes repetitively one can record a following response. If the changes are periodic, this becomes a steady-state response. Each of these different types of response has been evaluated in relation to binaural processing.

The evoked responses are also categorized in terms of their latency. Early responses come from the cochlea and brainstem; middle-latency responses derive from the

activation of auditory cortex and late responses come from auditory and association cortices. The transient responses are shown in Fig. 1.

Recording electromagnetic responses from the human brain takes time. The stimuli have to be repeated and the responses averaged or analyzed in the frequency domain over prolonged periods before reliable measurements are obtained. Human physiology takes longer than psychophysics. Nevertheless the evoked responses can demonstrate the timing and nature of processes that occur before perceptual decisions are made. More importantly, they can be used to assess subjects who cannot respond reliably during behavioral testing.



**Fig. 1:** Early, middle and late transient evoked potentials.

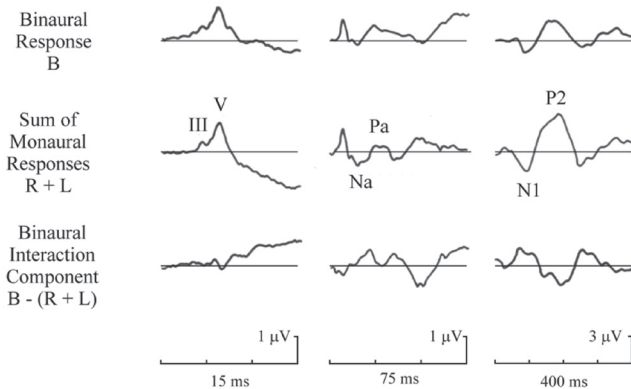
## BINAURAL INTERACTION COMPONENTS

A simple way to evaluate binaural processing in the human evoked response is to compare the response of a binaural stimulus to the response of a monaural stimulus. The difference between the sum of the responses to stimuli in the left (L) and right (R) ear and the response to the stimuli presented binaurally (B) gives a binaural interaction component (also known as the binaural difference). This was initially estimated for the auditory brainstem response by Dobie and Berlin (1979). The difference waveform shows a small complex of waves near the latency of wave V of the monaural auditory brainstem response, as illustrated in the left section of Fig. 2. Many further studies (e.g., Dobie and Norton, 1980; Levine, 1981) have confirmed the initial findings. Unfortunately, some investigators (e.g. Levine, 1981) subtract the binaural response from the sum of the monaural responses and get an interaction component of opposite polarity.

Exactly what the brainstem binaural interaction component represents remains unknown. Binaural responses might just have slightly faster latencies than monaural responses. However, the most common interpretation is that the brainstem binaural

difference waveform represents extra activity in the superior olive generated when a stimulus is identified as binaural. Lesions to the pons can disrupt the interaction component and interfere with binaural perception (Pratt *et al.*, 1998). Evaluation of the binaural interaction components when stimuli are presented at different interaural time differences give latencies that fit with physiological models of ipsilateral excitation and contralateral inhibition in the superior olive (Riedel and Kollmeier, 2006).

A major difficulty with the brainstem binaural interaction component is its small size. The usual monaural brainstem response is typically averaged over one to several thousand trials to provide a reasonable signal-to-noise ratio. Since the binaural difference is less than half the size of the monaural response, averaging would need to be at least four times more. Calculating the difference waveform further increases the noise levels in the waveforms and makes it necessary to average over even more trials.



**Fig. 2:** Binaural interaction components in human evoked potentials. The early responses were recorded from vertex to larynx at 21/s (average of 8000, filters 30-3000 Hz), the middle latency responses at 11/s (4000, 10-300Hz), and the late responses at 1/s (400, 1-30 Hz). The larynx reference explains the lack of any wave I in the ABR. The middle and late binaural interaction components are similar to an inverted monaural or binaural response.

The frequency-following response is a brainstem response that follows tones with frequencies of about 2000 Hz or less – the representation at the human scalp of the brainstem neurophonic. This response has not been extensively studied in relation to binaural processing, but it does show clear binaural interaction components (Krishnan and McDaniel, 1998). The frequency-based techniques used to identify these responses and their binaural differences may provide more robust measurements than the transient auditory brainstem response.

The middle latency and slow cortical responses show large binaural interaction components that are essentially an inverted representation of the monaural response (McPherson and Starr, 1993, 1995; Picton *et al.*, 1985). The cortex responds with a similar waveform to stimuli that are presented monaurally or binaurally, and the binaural response is only slightly larger than either monaural response. The algebra then gives the inverted response. Exactly why brain's binaural responses are similar to the monaural is not known. There could be some inhibition between the responses to each ear. The synaptic connections could respond as an OR-gate, giving the same response for either or both inputs. Most likely, the information coming to the auditory cortex from the brainstem is already tagged by its spatial location. Auditory objects from one or other side or from straight ahead are then treated equally.

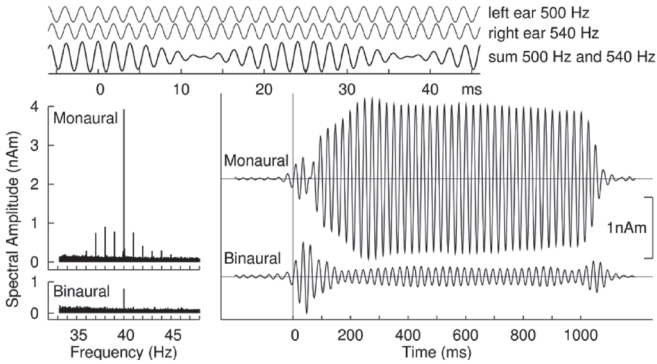
The 40 Hz steady-state responses probably represent a combination of brainstem and cortical responses (at least in the electrical recordings – the magnetic recordings may be predominantly cortical). Zaroor *et al.* (2003) and Picton *et al.* (1985), found that the binaural 40 Hz response was larger than either monaural response. The binaural interaction component was therefore only about 60% of the binaural response.

## **PRECEDENCE EFFECTS**

In a reverberant environment an auditory source produces echoes in addition to the initial binaural activation of the ears. The perceived location of the sound is dominated by the initial input. What is the physiological basis for the suppression of the echoes? Lieberthal and Pratt (1999) presented binaural clicks and followed these by an echo (from a different location). By subtracting the response to the click alone from the response to the click and echo, they obtained a response to the echo. The brainstem response to the echo was essentially normal but the middle-latency Pa response was suppressed. They therefore proposed that echo suppression occurs at the level of the auditory cortex where Pa is generated. The lack of any suppression of the brainstem response to an echo was confirmed by Damaschke *et al.* (2005).

## **BINAURAL BEATS**

A simple way to evaluate binaural interaction is to measure binaural beats. Tones of slightly different frequencies are presented to each ear and the response checked for the presence of a response at the beating frequency. These responses are best measured at a frequency of 40 Hz (Schwartz and Taylor, 2003) where the steady state response has its maximum amplitude. The responses are about one quarter the size of the response obtained if both stimuli were presented to the same ear (monaural beat). As shown in Figure 3, similar results were obtained with magnetic recordings, which indicated sources in or near the primary auditory cortex with slightly larger amplitude in the right hemisphere (Draganova *et al.*, 2008). Binaural beat responses can also be recorded at more rapid rates with a similar amplitude relation to the monaural beats (Picton, 2007). At slower rates the signal to noise ratio is very low and beats are difficult to recognize.



**Fig. 3:** Binaural beats recorded with magnetoencephalography. The upper part of the figure shows the superimposition of a 500 and a 540-Hz tone produces a 40-Hz beat. The lower part of the figure shows individual response spectra on the left and group averaged waveforms on the right. The response to binaural beats is much smaller than the response evoked by the sum of both tones presented to both ears (peripheral or monaural beat).

We have found (unpublished) that it is also possible to record small responses to what might be called envelope beats. If a binaural tone is amplitude modulated at different rates in the two ears, there is a steady-state response as the difference between the modulation frequencies. This is much smaller than the responses to the envelopes themselves.

## BINAURAL UNMASKING

### Binaural masking level difference

When binaural signals are presented in binaural noise, the threshold for detecting the signal is decreased if either the phase of the noise or the phase of the signal is inverted between the ears. In the usual coding,  $SoN\pi$  or  $\pi N0$  show significantly lower thresholds than  $SoNo$ . Early studies demonstrated that the N1-P2 waves of the late auditory evoked potential showed larger amplitudes and lower thresholds if the signal or the noise were inverted (Butler and Kruskens, 1972; Fowler and Mikami, 1992). Similar effects were obtained with magnetic recordings (Sasaki *et al.*, 2005).

Although the early and middle latency components of the evoked potential were affected by the changes in phase in these masking level difference paradigm, the changes in the evoked potentials did not relate well to the perceptual changes (e.g. Fowler and Mikami, 1995). Similar findings were obtained with the steady state responses (Galambos and Makeig, 1992; Wong and Stapells, 2004). These findings suggest that information about the phases of the stimulus and the noise are registered

in the brainstem and transmitted separately to cortex. Perceptual discrimination between signal and noise on the basis of their binaural features likely takes place in the cortex. These decisions are registered in the processes that generate the N1-P2 response.

### **Dichotic pitch**

If a narrow portion of the spectrum of diotic noise is given a clear interaural time difference, the subject hears a tone in the leading ear in addition to the central noise. The evoked potentials to this stimulus show an N1-P2 onset response and an additional late negative wave peaking near 240 ms (Johnson *et al.*, 2003). This late negative wave appears to represent the detection of an additional auditory object (the tone as well as the noise) and is likely related to the object-related negativity described by Alain *et al.* (2001).

## **RESPONSES TO A DEVIANT STIMULUS – THE MISMATCH NEGATIVITY**

The usual paradigm for evoking the mismatch negativity (MMN) presents a regular train of standard stimuli and occasionally changes the stimulus in some way. The response to the deviant stimulus contains a late negative wave that follows the usual N1 component either prolonging the duration of the N1 or adding a separate N2 peak. The MMN is usually evaluated by subtracting the response to the standard away from the response to the deviant. The MMN can be elicited by changes in any parameter of the stimulus (Näätänen *et al.*, 2007). The fact that the MMN can be recorded without the subject paying attention to the stimuli makes it useful as an objective indicator of discrimination. However, it is often very small in amplitude.

Paavalainen *et al.* (1989) demonstrated the MMN to a change in the location of sounds. The location-MMN increased in amplitude and decreased in peak latency as the difference in the perceived locations of the sounds increased (see also Deouell *et al.*, 2006; Schröger and Wolff, 1996). The MMN can be evoked by pinna-detected changes in the spatial spectral characteristics as well as interaural time and intensity differences (Röttger *et al.*, 2006). Damaschke *et al.* (2005) recorded MMNs in relation to the precedence effect. The MMN only occurred when the echo was perceptibly different. The precedence effect is not due to suppression at the level of brainstem but to cortical processing.

There is controversy about what the MMN represents. Näätänen *et al.* (2007) propose a cortical process that keeps a running memory of previous stimuli and automatically detects deviances from what this memory predicts. May and Tiitinen (2009) suggest that the MMN is related to selective adaptation of the N1 wave and reflects the response of cortical neurons that have not been rendered refractory by preceding stimuli.

The selective adaptation idea derives from Butler (1972), who showed that the N1-P2 amplitude of the late cortical evoked potentials increased when the stimulus was

alternated between two spatial locations compared to when it was presented always at the same location. He proposed that the neurons responding to the different spatial locations came from different but overlapping populations and that these could be selectively adapted. Those neurons not common to the two populations would be less refractory when the stimuli alternated – essentially they would be activated at one half the rate as when the stimulus was always the same.

Schröger and Wolff (1996) recognized that the deviant-standard difference waveform can represent the effects of selective adaptation as well as an additional MMN. They therefore used a control condition wherein the stimulus varied in location on every trial to remove the adaptation effect. Subtracting control response from the deviant response left only the late part of the location-MMN. In a similar experiment, Sonnadara *et al.* (2006) found no late MMN, perhaps because their subjects paid less attention to the stimuli.

## **RESPONSES TO CHANGES IN AN ONGOING STIMULUS**

When the location of a stimulus changes at the same time as the stimulus begins, it is difficult to disentangle the brain's response to the spatial aspects of the stimulus from its response to other characteristics (onset, intensity, frequency, etc.). An ongoing stimulus that changes only its spatial aspects allows us to record responses that are specific to binaural processing.

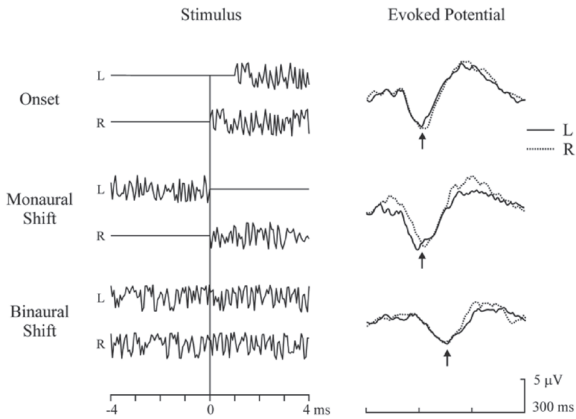
### **Interaural timing**

With a binaural noise stimulus, we can change the interaural timing without any audible change in either monaural stimulus. Halliday and Callaway (1978) recorded the first evoked potentials to an interaural time-shift – the response was similar in its morphology and scalp topography to the slow evoked N1-P2 potential to the onset of a sound. However, McEvoy *et al.* (1990, 1991) found that the response occurred 20-50 milliseconds later than the onset response and suggested that the brain required several tens of milliseconds to integrate binaural timing information. Figure 4 illustrates these findings. Jones *et al.*, (1990, also Jones, 1991) thought, however, that the response was more like a mismatch negativity in that it indicated a change from a remembered sound location more than the simple onset of a stimulus in a new location. Neither McEvoy *et al.* (1990) nor Jones *et al.* (1991) found early brainstem components of the evoked potential. Clearly the brainstem must detect the rapid change in interaural timing. However, since when the detection occurs may not be closely time-locked to the stimulus, it may not show up in the averaged response.

### **Interaural correlation**

Even more basic than changing the interaural timing of a stimulus is changing the interaural correlation. A stimulus that is completely uncorrelated between the ears will be perceived as diffusely located in space (a buzzing around the ears) whereas one that is exactly the same in the two ears will be very focal (a buzzing in the pineal).

Jones *et al.* (1990) recorded similar responses for the onset or offset of correlation. More recent work with both magnetic (Chait *et al.*, 2005, 2007; Soeta *et al.*, 2004) and electric (Lüddemann *et al.*, 2009) recordings has indicated that the response may differ depending on the starting correlation and the direction of change. Lüddemann *et al.* (2009) suggested that both the perception and the amplitude of the N1-P2 response followed a power function based on the ratio of the correlation change.



**Fig. 4:** Evoked potentials to a change in the interaural timing of a binaural noise (Binaural Shift) compared to the Onset of a lateralized noise and to the simple shifting of the noise from one ear to the other (Monaural Shift). The main negative wave (arrow) is significantly longer for the Binaural Shift. The continuous-line responses are to stimuli going to the left whereas the dotted-line responses are to stimuli going to the right (as illustrated in stimulus part of the figure).

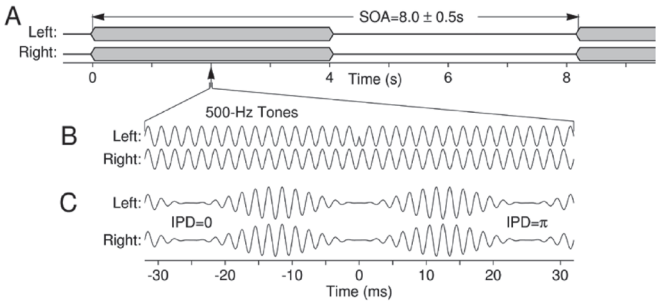
Dajani and Picton (2006) recorded steady state responses to binaural noise stimuli that alternated between uncorrelated and correlated. They found clear responses at slow rates of stimulus. These could be modelled using two processes – one with a time constant near 50 ms and a second with a time constant near 4 ms. These might represent a running correlation mechanism in the brainstem followed by a cortical integration of the information received from the brainstem. The largest response occurred at the second harmonic for stimuli with a fundamental near 4 Hz. This response could be used to estimate behavioral thresholds.

### Interaural phase

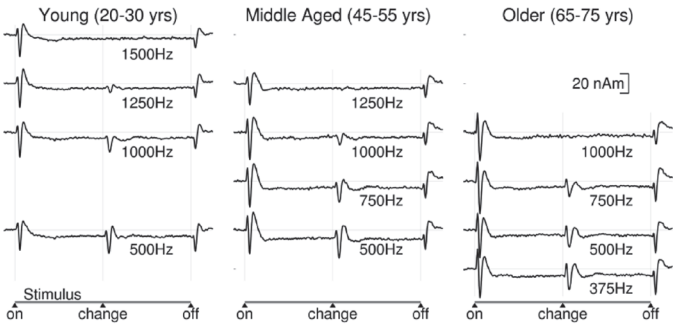
So far we have been considering changes in noise stimuli. The changes are not audible in the monaural stimulus and any response must therefore be mediated by binaural processing. Abruptly changing the timing (or phase) of a pure tone would generate an audible click and we would not be able to distinguish binaural processing from



click detection. Ross *et al.* (2007a,b) designed a stimulus that allows the phase to be changed without any audible transient. The stimulus is a tone amplitude-modulated at 40 Hz with a 100% depth of modulation. The change in phase occurs at the point in the modulation when the instantaneous amplitude is zero. Figure 5 shows the stimulus.



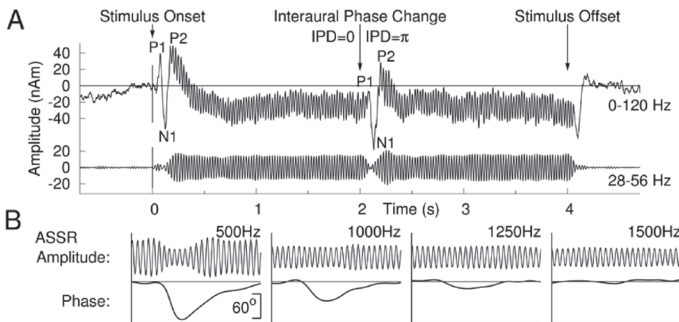
**Fig. 5:** Stimulus for eliciting responses to changes in the phase of an ongoing tone. A: Tone bursts of 4-s duration presented to left and right ear. B: A phase shift of 180° appears at 2 s in the left ear tone. C: The tones are 40-Hz amplitude modulated and the phase shift appears at a minimum of the modulation. Listeners perceive such stimuli at the center of the head for the first two seconds, then changing into a spacious sound at 2 s.



**Fig. 6:** Magnetic responses to changes in the phase of an ongoing tone for three age groups and various tone frequencies. The responses have been low-pass filtered at 24 Hz to remove the steady state response to the modulated sound. For low frequency stimuli all waveforms show an onset, change, and offset response. With increasing stimulus frequency, the amplitude of the change response becomes smaller and it is absent at 1000 Hz in the young group, 1250 Hz in the middle aged group, and at 1000 Hz in the group of older adults. In contrast, the onset and offset responses did not change with increasing frequency.

We have recorded the magnetic responses to this stimulus (using a phase change of  $\pi$  radians) in young, middle-aged and elderly subjects (Ross *et al.*, 2007a,b). The change in phase evoked a P1-N1-P2 response with a latency that was 10-40 ms later than for the response to sound onset. It could be recognized with carrier frequencies up to 1250 Hz in young subjects. In elderly subjects, it could only be recorded up to 750 Hz. Middle-aged subjects showed no recognizable response to phase changes for carrier frequencies higher than 1000 Hz. This indicates that our binaural timing abilities decline in mid-life. Figure 6 illustrates these findings.

The stimulus also has the advantage that it allows us to monitor the steady-state response evoked by the modulation of the tone. When the phase changes, the steady-state response rapidly decreases in amplitude and then slowly becomes reinstated. This change in the response can be used to estimate the threshold for recognizing the phase change with the same sensitivity as the N1-P2 response. Its advantage is that it can be recorded at faster rates. The N1-P2 gets smaller as the interval between stimuli decrease below 2 seconds but the change in the steady state response can be recorded at much faster rates. Figure 7 shows these changes.



**Fig. 7:** Auditory steady-state responses (ASSR) to changes in the phase of an ongoing tone. A: 40-Hz ASSR superimposed to the low frequency auditory evoked responses in the wide band filtered signal. The band pass filtered signal shows an amplitude decrement after the IPD phase change. B: ASSR amplitude and phase for carrier frequencies between 500 and 1500 Hz (young adults).

## MOVING SOUNDS

When a sound source moves in space there are changes in the interaural time and intensity differences, in the spectra of the sounds received at each ear (mediated by the pinnae and head shadow), in the perceived frequency of periodic components (Doppler effects) and in the overall intensity of the sound (sounds becoming louder as they come closer). These processes can all be modelled and very realistic auditory motion can now be provided through earphones. Xiang *et al.* (2005) recorded magnetic responses to moving sounds that moved from one side to the other. A clear N1-P2 occurred as the movement began and a later response occurred with a latency that

varied inversely with the speed of movement. This may have been related to the stimulus crossing the midline, changing its direction from ‘toward’ to ‘away from’ the subject.

## CONCLUSIONS AND CAVEATS

Many different paradigms that can be used to record evoked responses during human binaural processing. The evoked responses demonstrate activity within the brain that might be important in showing what happens prior to cortical decisions (for example, in the brainstem or thalamus). An important application of the evoked responses is to demonstrate binaural auditory functions in subjects who cannot cooperate reliably with behavioral testing. Infants are the most obvious subjects for such testing, but the sick and the elderly also often have difficulty discriminating complex stimuli. For such testing it is important that the signal to noise ratio allow clear recognition of the evoked responses within a reasonable time. In this regard, the N1-P2 onset response is best. This can be evoked by many different changes in an ongoing binaural stimulus. However, the morphology of this response changes dramatically with the age and the state of arousal of the subject. Infants and young children show a large P1 with no clear N1 wave, and in sleep the most prominent component is usually the N2 wave. Responses to binaural changes need to be further evaluated in infants and young children before they can be used to demonstrate normal or abnormal binaural processing in these subjects.

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