Presbycusis and auditory brainstem responses: a review

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1. Introduction

Age–related hearing loss (ARHL) or presbycusis is a complex phenomenon consisting of elevation of the hearing levels as well as changes in the auditory processing. Although many adults retain good hearing as they age, hearing loss associated with ageing is common among elderly persons. There are a number of pathophysiological processes underlying age–related changes to functional components. Presbycusis is especially caused by cochlear degeneration, most pronounced in the basal cochlear coil. Causes include physiological ageing processes as well as endogenous or exogenous causes. The common form of hardness of hearing seen in old age is not due to physiological age–related changes, but rather to a complex sensorineural pattern of injury. In the industrial countries, two main exogenous causes are exposure to loud noise and obesity[2].

Some of the changes that occur in the aging auditory system may significantly influence the interpretation of the auditory brainstem responses (ABRs) in comparison with the ABRs of younger adults.

2. Presbycusis

Presbycusis is used to describe hearing loss as a result of degenerative changes of aging. According to Caspary et al.[3] presbycusis is a complex disorder that results in a slow deterioration in auditory function.

Presbycusis can be classified into four categories: 1) Sensory i.e. loss of hair cells; 2) Neural i.e. loss of nerve fibers and neural elements; 3) Metabolic or strial i.e. loss of blood supply to the cochlea; 4) Cochlear conductive.

Anatomical studies have shown a loss of neurons and neuroglia, accumulation of intracellular lipofuscin, changes in myelin and loss in brain weight with aging. Regardless of the cause of ARHL, to those investigating the effects of aging on the central auditory nervous system, this sensory deficit makes it difficult to separate out the effects of the aging brain from that of an aging cochlea[4].

Physiological changes in the peripheral auditory system reported in the aged include a reduction in the amplitude of the compound action potential, decrease in the magnitude of the endolymphatic potential and a threshold shift[5]. Similar physiological measures recorded from the central...
auditory nervous system also show age related changes, such as ABR threshold elevation and decrease in ABR peak amplitudes[6]. These later manifestations of aging are likely to be reflections of peripheral hearing loss.

3. Aging and threshold elevation

A major difficulty in studying the effects of aging on the ABR is the interaction of age with threshold elevation. Some workers have attempted to minimize the effects of threshold elevation by comparing young and older participants with hearing impairment but with similar thresholds or by comparing older, hearing impaired participants with young participants tested in the presence of a masker that elevates the young participant’s thresholds to levels that are equivalent to those of the older participants with hearing loss[7]. In contrast, it was postulated that choosing participants with normal threshold compared with young participants results in data that are not representative of the older population[8]. Some investigators suggest that understanding the effects of age itself requires that sensitivity of the aged system be normal, not normal for age matched control participants, but normal compared with a young control participant[9]. Therefore, it is critical to understand the role of threshold elevation on age–related changes in presbycusis, in order to determine what changes are truly age related.

4. Characteristics of ABR

The ABR represents the synchronized activity of the auditory nerve and brainstem. Although there is fairly uniform agreement that fiber tracts generate potentials that can be recorded with scalp electrodes, there is not as yet strong evidence that neurons within auditory nuclei elicit responses in a synchronized fashion so that they can be recorded with far field electrodes.

The ABR consists of a series of waveforms occurring approximately 1–7 ms, following a moderate level transient stimulus. The most common terminology to describe the waveforms is to refer to them relative to their absolute latencies following a moderate level transient stimulus. Usually seven vertex–positive waves, called brain stem auditory evoked potentials (BAEPs), are described in the first 10 ms[10]. It has been used in the last few years as a method of objective audiometry and in examining patients with lesions located in the brain stem. Among different laboratories varying stimulus and recording techniques are used, partly due to the purpose of examination, for example when BAEP recording is used as audiometry, repeated examinations with varying stimulus intensities are necessary[11].

Typically five to seven waves are recorded from the human scalp, with the most prominent being waves I, III and V. There are variations to this nomenclature scheme, and latencies of the responses will vary with the stimulus parameters. ABR is a valuable tool in the standard clinical test battery in both audiology and neurology as well as an important experimental technique in understanding the auditory brainstem. It is used for estimating the auditory sensitivity and to examine neural processing at the suprathreshold level in the central auditory system. A list of applications of ABR include estimation of auditory thresholds in difficult–to–test patients as well as in laboratory animals, site of lesion studies as in acoustic neuromas, examination of neural transmission as in neurological diseases, study of changes that occur in auditory brainstem independently of changes that occur in the cochlea (such as in auditory neuropathy and possibly in presbycusis). However, at times, the ABR must be viewed with caution because changes may occur at both peripheral and central regions of the auditory system that may influence the interpretation of results of an ABR examination.

5. Presbycusis and ABR thresholds

Thresholds measured behaviorally and electrophysiologically in young individuals are highly correlated. ABR stimuli are typically 1–2 ms in duration, and stimuli used to elicit behavioral responses are approximately 200–2 000 ms in duration. ABR and behavioral thresholds vary depending on stimulus frequency, typically ranging from several decibels at high frequencies to as much as 15–20 decibels at lower frequencies. Stapells et al[12] reported in 1990 that the average difference between ABRs elicited with tone pips in notched noise and behavioral thresholds ranged from 2.5 dB at 4 kHz to 16.7 dB at 15 kHz in participants with normal hearing. Approximately 91% of ABR and behavioral thresholds were within 20 decibels of each other. In participants with sensorineural hearing loss, differences between ABR and behavioral thresholds were smaller, ranging from 1 to 7 dB, presumably due, at least in part, to the lack of temporal integration in sensorineural hearing loss. Similarly, mean differences between ABR and behavioral thresholds of approximately 1.4 dB to 5.2 dB were reported for persons with sensorineural hearing loss by Munnerly et al[13]. Noorhassim et al[14] conducted a study in 1996 to find out the relationship between pure tone audiometry (PTA) results and the ABR wave abnormalities. The PTA and the ABR from 22 patients with diagnosed noise–induced permanent hearing loss were studied. It was concluded that there was a relationship between severity of noise induced hearing loss indicated by PTA and the pattern of ABR wave abnormalities among workers with noise induced hearing loss (Figure 1).

The hearing abilities of a group of 30 elderly (67–93 years of age) subjects were compared with those of a group of 30 young (19–27 years of age) normal hearing volunteers with the aim of characterizing the changes in the peripheral and central parts of the auditory system. In elderly subjects
the pure-tone thresholds were typically represented by a gradually sloping curve with a significantly greater decline in men than in women at frequencies of 3 kHz and 4 kHz. The results support the view that presbycusis represents a combination of deteriorated function of the auditory periphery with deteriorated function of the central auditory system[15].

Changes in hearing thresholds over a 10–year period in a large population of older adults (2 130) ranging in age from 48 years to 92 years were documented. Pure-tone thresholds at frequencies from 0.5 kHz to 8 kHz were evaluated at a baseline examination 2.5, 5 and 10 years later. For younger age groups (50–69 years of age), threshold changes were generally greatest for higher frequencies. In older age groups (70–89 years of age), threshold changes were generally greatest for lower frequencies due to a ceiling effect at higher frequencies. Other than age and gender, the best baseline examination predictors of 10-year thresholds at a specific audiometric frequency were the baseline threshold at that frequency followed by the baseline threshold for the next higher test frequency[16].

The expected co–relation between behavioral and ABR thresholds is not observed in presbycusis. Even when temporal integration effects between behavioral and ABR thresholds were accounted for, older participants have unexpectedly elevated ABR thresholds. It is reported that difference between behavioral and ABR thresholds was much larger in older individuals than in young participants. The differences between ABR and behavioral thresholds were approximately 12 dB, 7.5 dB and 8 dB for 1 kHz, 2 kHz and 4 kHz, respectively in young (17–37 years old) human participants. In contrast, older participants (65–74 years old) had ABR–behavioral threshold differences of 17.5, 18 and 21 dB at the three frequencies, respectively. Thus older participants had approximately 5.5 dB to 13 dB larger differences between ABR and behavioral thresholds than did young participants.

Age related differences in ABR and behavioral thresholds are probably based on a reduction in the number of spiral ganglion fibers in older participant and reduced synchrony among elements contributing to the generation of ABR.

Thus the clinical importance of such findings is that, an ABR may overestimate the behavioral sensitivity of an older individual, even when a correction factor based on simple temporal integration is incorporated.

6. Age–related changes in ABR

There are several differences in the ABR of newborns and adults[17]. The BAEP response is generally smaller. Wave I is often double peaked. There is little if any wave II. A prominent negative wave follows wave I. The negative wave after wave III is less prominent. The amplitude ratio of wave V to wave I is much lower.

A rarefaction click usually evokes an earlier wave I than a condensation click[17].

The change in latency with increasing stimulation rate is more marked in premature than in term infants[18]. The threshold for detecting BAEP decreases by about 10 dB in the first three months of life and by a further 5 dB by the end of first year[19].

The BAEP can be recorded in normal newborn down to at least 30 dB nHL provided the infant is asleep, averaging sufficient and acoustic noise in the surroundings is low[20].

Threshold higher than 30 dB nHL indicates some disorder of the auditory pathway. A recognizable BAEP can be recorded in premature infants as early as 3 weeks gestational age[20]. In premature infants, higher intensity and slower rate of stimulation are usually needed to record a BAEP response. The amplitude of BAEP, especially wave V is smaller than in full term neonates. The latencies of all components of the response decrease with increasing conceptional age.

V in the newborn, since wave I is double peaked, the latency norms involving this component differ from that of an adult. Wave V shows greater change than wave I. From
The latency of wave I decreases by 0.3 ms whereas the latency of wave II decreases by 0.3 ms to 0.6 ms[19]. The BAEP matures to adult pattern over a period from birth to the age of 18–24 months[21]. Different components of BAEP mature differently. Wave I reaches the adult values by 3–6 months, whereas wave III and V by the second year.

The amplitude of waves I and in response to binaural stimuli shows a marked increase after 6 months and the amplitude of wave V does not reach the adult value until about 5 years. In general, the amplitude norms in neonates are nearly half of those in adults[1].

7. Presbycusis and ABR amplitudes

The ABR amplitudes have been studied in both males and females. It is generally agreed upon that females show larger amplitude of ABR waves compared with males[1,10,17,22].

Most if not all studies on the effects of aging on ABR amplitudes in humans demonstrate a reduction in amplitude as a function of age[1,10,22].

The amplitude of ABR is a direct function of the number of neurons and the synchrony of neurons contributing to the response, as well as the value of the endocochlear potential (EP).

This would suggest that age-related changes in ABR amplitudes are a combination of a reduction in the number of neurons available to respond to a given signal, a reduction in the synchronized activity of neurons responding to a given signal and/or a reduction in the EP.

There has been a partial neglect in the study of BAEP amplitude, not induced by the lack of amplitude modification in pathology but by the fact that these modifications were frequently so marked that they were visually evident by comparison with the persistent components of the response BAEP amplitudes have a large standard deviation[29].

Theoretically the well-known difficulties in audition of presbycusis, particularly in the high frequency domain (4–8 kHz) to which the click stimuli belong would suggest a great diminution of amplitude at this age[24].

Mogens Kjaer[10] performed a study on the recognizability of the BAEP components in normal subjects aged 10–69 years of either sex. All subjects younger than 50 years had hearing thresholds at 20 decibels HL or better as determined by audiometry. The hearing threshold of subjects older than that age did not exceed 40 decibel HL at 4 000 c/sec and 50 decibels at 8 000 c/sec. Measurement of the amplitude of wave I was made from the positive peak to the subsequent negative trough, for the following waves from the preceding negative notch to the following positive peak.

Latencies were measured from the start of the triggering pulse to the peak and estimated to the nearest 0.05 ms. An increase in stimulus intensity was followed by an increase in the amplitude of the components. In normal subjects aged 10–69 years, a decrease in amplitudes was found with increasing age. Men older than 50 years had longer latencies than younger men. Women had shorter latencies and higher amplitudes compared with men.

Jerger et al[25] reported in 1980 that adults over 60 years had reduced ABR amplitudes relative to young subjects, correlated to hearing loss than age. They examined the ABR waveforms as a function of chronological age in 182 male and 137 female subjects. Hearing sensitivity was within normal limits in 98 subjects. The remaining 221 subjects had varying degree of sensorineural hearing loss. It was found that in subjects with normal hearing, latency increased about 0.2 ms over the age range from 25 years to 55 years. In the same group, wave V amplitude was decreased by 10%. In subjects with sensorineural hearing loss, the latency increase was smaller, but the amplitude decrease was equivalent.

BAEP amplitudes were considered unreliable for clinical investigation by Helfer[26]. For audiometric purposes auditory threshold determinations according to the occurrence of wave V were preferred to amplitude measurements. Age was revealed as a very important factor in BAEP variability. By canceling age variation the standard deviation of amplitude values can be reduced to less than 20% of the mean. In previous calculations standard deviation reached 30%–40% of the mean amplitude of the response, when smaller, they were always related to restricted age groups of subjects. There are amplitude differences depending upon the modality of stimulation (rarefaction, condensation) which have to be solved. Their separate utilization is probably superior because alternated rarefaction and condensation clicks may induce alteration in morphology of the response due to differences in latency.

Boettcher[1] studied the age-dependent amplitude variation of the BAEPs. Their goal was to analyze BAEP amplitudes to disclose the sources of their unusually high variability. Factors like age, gender, temperature and hearing level may influence amplitude to the same extent (or more) as latency. They analyzed the evolution of BAEP component amplitudes in ages between 1 and 70 years. Normative amplitude values of BAEPs were given for normally hearing subjects at 1, 10, 30, 50 and 70 years of age, with an intragroup age variation of only 6 months. Under these circumstances amplitude standard deviations decreased to less than 20% of the mean values. In contrast with the reduced evolution of latency with age, BAEP amplitude (for component I–V) undergoes a greater oscillation during ontogeny.

With the exception of wave I, it increases markedly from 1 year to 10 years of age and decreased thereafter constantly up to 50 years, with a mean rate of 10 nV yearly. The decrease slowed down between 50 years and 70 years. The amplitude differences between the subgroups are highly significant statistically (P < 0.01). They also calculated amplitude ratios between waves I and V at different ages. A subunitary ratio was found at one year of age. It was noted that this ratio increases progressively up to 2.6 at the age of 70 years. This
ratio is also dependent on the stimulation intensity, being slightly higher at the lower intensity (60 decibels HL). Hence it was concluded that BAEP amplitude is also a controlled parameter. The use of standard amplitude values of the IV – V complex proved superior to the amplitude ratio between components V and I.

This ratio depends strongly on age, being smaller in the young than in the aged. A reduction in amplitude of wave V to half the amplitude of wave I does not have the same significance at various ages between 1 and 70 years. The problem of true physiological amplitude modifications of responses in the auditory pathways with age remains to be solved experimentally by direct recording from various relay nuclei[1].

Boettcher[1] recorded BAEPs in 154 normo acoustic subjects with no history of neurological or otological pathology (72 were males and 82 were females). In all the subjects neurological examination was normal as well as the hearing capacity was evaluated by tonal audiometry. Homolateral and ipsilateral recording was done but only ipsilateral traces were used for latency and amplitude measurement. Latency and amplitude values of the seven waves and interpeak latencies I–III, I–II, II–III, III–V, I–V and II–V were measured. Superimposition of traces and contralateral recordings were used in doubtful cases. It was found that amplitude decreases with increasing age, this phenomenon is more evident for the first two components, even though it is statistically significant also for wave V.

There is abundant evidence that the number of SG neurons is reduced in presbycusis, resulting in decreased amplitudes. Direct measures of synchrony across neurons contributing to the ABR are difficult, but an indirect measure has been used, namely changes in responses across stimulus presentation rates. Thus ABR amplitudes are reduced in aging, to a large degree independently of threshold elevation.

8. Presbycusis and ABR latencies

In the case of high frequency loss, peak of basilar membrane motion may occur at a point of hair cell loss. Thus hair cells located apically to the peak of membrane motion respond to the signal, resulting in an increase in response latency. Furthermore primary degeneration of the spiral ganglion cells may alter the probability of a response in the central auditory neuron because of the reduction in the number of auditory nerve fibers that innervate the neuron in question. Changes in the interpeak interval (IPI – the time difference between two wave peaks) reflect changes in neural conduction time in the auditory pathway and are used diagnostically in case of acoustic neuromas and demyelinating diseases. They have been studied in detail in presbycusis to identify possible changes in the auditory brainstem that may occur independently of changes in the auditory periphery.

Most studies state that absolute latencies of ABR waves tend to increase in older adults[22,23,25,27].

Rowe [23] in 1978 studied ABRs under three combinations of intensity and rate of click stimulation in 25 young (mean age 25.1 years, range 17–33 years) and 25 old (mean age 61.7 years, range 51–74 years) adult subjects. The response showed a great intra and inter subject variability. Waves I, III and V are constant and reproducible markers of the response while waves II, IV, VI and VII are variable and frequently asymmetrical or absent. Wave peak latencies increase with an increase in stimulation rate, a decrease in stimulus intensity and an increase in age. Interpeak conduction times, except those involving wave II, are unaffected by a change in the stimulus intensity. Wave I–III time increases with an increase in stimulus rate and an increase in age while wave III–V time is not affected by any change in stimulus parameters or age. He concluded that the wave amplitude is not a reliable measure of normality.

In contrast with studies suggesting that age has a direct effect on ABR latencies and IPIs, other studies suggest that threshold elevation is more of a factor. Boettcher[1] did not find latency abnormalities in older adults with normal hearing.

Jerger et al[25] examined amplitude and latency of the ABR waveforms as a function of chronological age between 10 years to 79 years in 182 males and 132 female subjects. They...
concluded that sex difference in ABR amplitude and latency cannot be accounted for by subtle differences in high-frequency hearing sensitivity in the normal group. In subjects with normal hearing, latency increased about 0.2 ms over the age range of 25 to 55 years. In the same group, wave V amplitude decreased about 10%. In subjects with sensorineural hearing loss, the latency increase was smaller, but the amplitude decrease was equivalent. Wave V latency was about 0.2 msec shorter and wave V amplitude was about 25% larger in female subjects. Figure 2 and 3 show mean ABR latency (wave V) and amplitude respectively as a function of age in both the normal and sensorineural groups.

Hence the age effect on ABR was not unexpected. Anatomic and physiological changes in the peripheral and central auditory system have long reflected such changes. Almost similar findings were reported by Boettcher[1].

Boettcher[1] recorded ABR in young (19–32 years old) and older (63–79 years old) women. The older participants had slightly poorer hearing (by 17 dB) at 4 kHz than the young participants. Absolute latencies were prolonged for the older group, with no differences in the IPIs. The results suggest that the changes in latency were a result of threshold elevation and that no sign of central pathology was present.

Otto et al[27] in 1982 compared the ABR latencies in young and older participants with similar degree of high-frequency hearing loss. No difference was found between groups. 30 elderly subjects and young subjects with comparable sensorineural hearing loss and 30 normally hearing subjects were evaluated by them to examine the interaction of advanced age and high-frequency hearing loss on the ABR responses (Figure 4). Hearing loss plus age account for greater deterioration of ABR waveforms than hearing loss alone. Age of elderly subjects ranged from 60 years to 80 years with a mean age of 68 years. Young hearing impaired subjects ranged from 17 to 45 years of age with a mean age of 30.6 years. Young normally hearing subjects ranged from 18 to 31 years of age with a mean age of 25.4 years. They concluded that when advanced age and high-frequency hearing loss interact, high-frequency hearing loss generally is the greater factor in morphologic and latency changes. It was indicated that the hearing impairment in the aged is probably due not only to changes in the end organ but also to brainstem changes. Although other authors have reported similar conclusions and tried to clarify the degree and nature of the central changes, these are still unclear. Some researchers have stated that presbycusis is mainly due to brainstem impairment, however Jerger and Hall claimed that age has only a slight effect on ABR and Allison et al[22] reported uncertainty in the matter.

In many studies on presbycusis, hearing levels of young and older participants are not always closely matched, making it difficult to determine if purported aging effects may simply be a result of threshold difference between groups. Stimuli are often presented at high sensation levels (SLs) to overcome differences in hearing levels between young and older groups[22] but such techniques can lead to misinterpretation of results. In others, only certain frequencies have been matched between groups. Allison et al[22] in 1983 studied ABR recordings in subjects,
Electrophysiological measurements, exploring the upper portion of the central auditory nervous system, are probably not the tool to detect the origin of the slowing of the association processes in the CNS and the poor speech discrimination that is often noted in presbycusis.

The ABR responses in a group of 74 subjects (60–80 years) affected by presbycusis were evaluated for the presence of retrocochlear involvement by Boettcher[1]. The comparison of results from subjects with presbycusis with those from normally hearing elderly subjects and young subjects affected by cochlear sloping hearing loss, revealed that the latency response of ABR observed in presbycusis is mainly correlated to the audiometric shape of the hearing loss and not to age per se.

The latency values of ABR waves and IPL values show a statistically significant difference between the aged normal acoustic and presbyacusic subjects concerning waves III and V and V – I IPL. In contrast, no significant differences exist between presbycusis and young cochlear hearing loss subjects concerning the transmission time (I–III and I–V). Hence the results supported the hypothesis that the increased latency of ABR waves observed in the aged is more linked to the shape of hearing loss than to age itself[1].

Oku et al[29] in 1997 compared the ABR and electrocochleography in young and older participants (50–89 years old). Older participants had normal pure tone averages (PTAs) at 0.5–2 kHz, but their thresholds ranged from 35 to 72 dB HL at 4–8 kHz. The latencies of waves I, III and V showed a progressive delay in older participants, but again because of increased high–frequency thresholds in older participants, it is difficult to rule out an effect of threshold elevation on the latency effects.

In a study done to characterize age–related changes in brainstem auditory evoked response at different click rates from neonates to adults brain auditory evoked response (BAER) was studied in 165 normal neonates and children of various ages and 29 young adults. BAER wave latencies and inter–peak intervals increased linearly with increasing click rate at all ages. The younger was the age, the greater were ABR click rate–dependent changes, BAER is affected by stimulus rate more in younger children than in the older. Adult–like rate dependent changes are reached at 1–2 years for wave I latency and I–III interval, and 3–4 years for wave III and V latencies and I–V and III–V intervals[30].

IPLs may also increase in aging humans, although not all studies have shown evidence for age related increases in IPLs[27].

Age–related changes in auditory evoked potentials are complex and complicated by the confounding effects of gender; concomitant high–frequency hearing sensitivity loss; and in the case of event–related responses, the nature of the task used to elicit the v response. There is a tendency for amplitude to decline and latency to increase, but these
trends are not always clear—cut. There is also a tendency for activation patterns to move forward from parietal to frontal areas as age increases. The dichotic listening tool has revealed age—related changes in interaural and interhemispheric asymmetries. These asymmetries seem to be related to loss in the efficiency of interhemispheric transfer via the corpus callosum [31].

Conflict of interest statement

We declare that we have no conflict of interest.

References