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Supra-threshold auditory brainstem response amplitudes in humans: Test-retest reliability, electrode montage and noise exposure

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ABSTRACT

The auditory brainstem response (ABR) is a sub-cortical evoked potential in which a series of well-defined waves occur in the first 10 ms after the onset of an auditory stimulus. Wave V of the ABR, particularly wave V latency, has been shown to be remarkably stable over time in individual listeners. However, little attention has been paid to the reliability of wave I, which reflects auditory nerve activity. This ABR component has attracted interest recently, as wave I amplitude has been identified as a possible non-invasive measure of noise-induced cochlear synaptopathy. The current study aimed to determine whether ABR wave I amplitude has sufficient test-retest reliability to detect impaired auditory nerve function in an otherwise normal-hearing listener. Thirty normal-hearing females were tested, divided equally into low- and high-noise exposure groups. The stimulus was an 80 dB nHL click. ABR recordings were made from the ipsilateral mastoid and from the ear canal (using a tiptrode). Although there was some variability *between* listeners, wave I amplitude had high test-retest reliability, with an intraclass correlation coefficient (ICC) comparable to that for wave V amplitude. There were slight gains in reliability for wave I amplitude when recording from the ear canal (ICC of 0.88) compared to the mastoid (ICC of 0.85). The summating potential (SP) and ratio of SP to wave I were also quantified and found to be much less reliable than measures of wave I and V amplitude. Finally, we found no significant differences in the amplitude of any wave components between low- and high-noise exposure groups. We conclude that, if the other sources of between-subject variability can be controlled, wave I amplitude is sufficiently reliable to accurately characterize individual differences in auditory nerve function.

1. Introduction

The auditory brainstem response (ABR) is a well-established diagnostic tool widely used in the clinic to assess auditory function (see Hall, 1992, for an overview). The ABR is evoked by transient stimuli, typically clicks or tone bursts, and consists of a series of waves, with wave I reflecting auditory nerve function, and wave V resulting from generators in the rostral brainstem. The threshold and latency of wave V are the most common clinical metrics of the response. However, wave I has also proved valuable, particularly in research studies, as a more direct measure of peripheral auditory function (Schaette and McAlpine, 2011; Santos et al., 2017).

Wave I amplitude has attracted considerable interest recently, following the demonstration of noise-induced cochlear synaptopathy in the mouse model by Kujawa and Liberman (2009). In the base of the cochlea, up to 50% of synapses between inner hair cells and auditory nerve fibers were destroyed after a 2-h exposure to 100 dB SPL noise (8–16 kHz). Post-exposure measures of absolute auditory sensitivity were unaffected, but histological analyses confirmed the dramatic loss of cochlear synapses. Post-exposure ABR measures showed unaffected responses close to threshold. However, at medium-to-high sound intensities there was a permanent reduction in the amplitude of wave I of the ABR (by 60% at 32 kHz and ~30% at 12 kHz), reflecting decreased auditory nerve activity.

These results suggest that wave I of the ABR might have

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potential as a non-invasive measure of cochlear synaptopathy in human listeners. However, the evidence for noise-induced synaptopathy in humans, based on ABR results, is somewhat inconsistent. Recent work from our laboratory has found no evidence that greater lifetime noise exposure, which we assume to be a proxy for greater synaptopathy, is associated with a reduction in ABR amplitude for normal hearing listeners (Prendergast et al., 2017) or listeners with tinnitus (Guest et al., 2017). An absence of a relation between noise exposure and ABR wave I amplitude has also recently been reported by a number of other laboratories using different normal-hearing cohorts (Spankovich et al., 2017; Grinn et al., 2017; Fullbright et al., 2017). Liberman et al. (2016) also reported no significant reduction in wave I amplitude with increasing noise exposure, but did find a significantly increased ratio between the summating potential (SP; reflecting hair cell function) and action potential (AP; equivalent to wave I of the ABR, reflecting auditory nerve function). Bramhall et al. (2017) reported that some groups of firearm users exhibited reduced ABR wave I amplitudes consistent with cochlear synaptopathy and Grose et al. (2017) found a reduced wave I/V ratio in noise-exposed listeners relative to controls. There remain many unanswered questions regarding how these studies can best be reconciled and the extent to which high-frequency hearing loss, gender, and homogeneity of noise exposure can account for the differing evidence for this phenomenon in humans. One additional concern, despite the clear changes in ABR wave I in the animal model of synaptopathy, is whether the ABR is the best tool for identifying these neural changes in the human listener.

If the early waves of the ABR are to have utility as a diagnostic measure in individual listeners, they must be reliable, with low measurement error. As ABR wave I amplitude tends to be lower than wave V amplitude, the response may be more difficult to measure reliably (Mehraei et al., 2016). However, there is little available evidence that addresses this issue directly. Much work on the test-retest reliability of the ABR focuses on the latency of wave V because of its clinical relevance. Edwards et al. (1982) provided an overview of ABR amplitude and latency reliability across a six month period, using 72 dB nHL (72 dB above the normal adult hearing threshold) monaural clicks in 10 listeners. No significant differences emerged between sessions for any wave amplitudes or latencies, or for wave I/V ratios. Using a mean-squared-difference approach, it was found that the participant contributed most variability to the measured responses, followed by ear, session (different days), and run (different acquisition on the same day); however, this was only estimated using wave latency. Lauter and Loomis (1986, 1988) tested seven listeners in eight separate weekly sessions and all waves (I-V) were evaluated. The data show high repeatability across the different testing sessions for both amplitude and latency. Rather than a formal assessment of reliability, the approach used the coefficient of variation (CoV; standard deviation divided by the mean) as a marker of "stability" and used ANOVAs to determine that between-subject variability was significantly greater than within-subject variability. Munjal et al. (2016) evaluated the long-term test-retest reliability of the ABR in 50 normal hearing listeners at 3, 6 and 12 month intervals. Only latencies and inter-peak latencies were studied, which demonstrated good reliability overall, although there were differences in the absolute latency of wave I across the different test intervals.

The studies discussed above all used either linear correlations or ANOVAs to estimate the reliability of ABR responses across multiple sessions. These statistical tools are not formal methods of quantifying reliability, unless the ANOVA is set up in an appropriate manner (Zaki et al., 2013; Kim, 2013). A more appropriate method is to use the intra-class correlation coefficient (ICC; Shrout and Fleiss, 1979), which estimates the proportion of the total variance that can be attributed to between-subject variability. Recently, Bidelman et al. (2017) used the ICC to study the test-retest reliability of sub-cortical and cortical auditory evoked potentials. Wave V of the ABR was evaluated, in response to an 80 dB nHL click stimulus, and the amplitude and latency ICCs were 0.65 and 0.76 respectively, reflecting good test-retest reliability.

The primary motivation for the current study was to determine the test-retest reliability of ABR wave I, to evaluate its suitability for measuring auditory nerve function in individual human listeners. There were also a number of secondary questions which the present study was able to address in parallel to the main research question. By using two different EEG montages, a scalp-mounted mastoid electrode and a canal tiptrode (a gold-wrapped foam insert which records the electrical potential from the ear canal), we were able to determine the extent to which reliability is improved by recording from closer to the neural generator of wave I. A canal tiptrode is known to produce a larger wave I response than a scalp-mounted mastoid electrode (Bauch and Olsen, 1990), and it was therefore predicted that the canal tiptrode would produce a more reliable response by virtue of an enhanced signal-to-noise ratio. Furthermore, by using a tiptrode (which emphasizes the SP) we were able to measure the reliability of the SP/AP ratio (utilized by Liberman et al., 2016), and thus evaluate the potential clinical utility of this measure for the detection of synaptopathy.

Finally, the study recruited groups of low- and high-noise exposed female listeners to determine whether changes in the ABR or SP/AP are associated with noise exposure in a single-sex cohort in which audiometric function is tightly controlled. It was predicted that high-noise exposed listeners would yield smaller wave I amplitudes, and larger SP/AP ratios, than low-noise exposed controls.

2. Methods

2.1. Participants and test sessions

Thirty female participants were tested, all with clinically normal audiometric thresholds (see section 2.3 and Fig. 1). Participants were recruited into two equal-sized groups based on noise exposure histories (see section 2.2). The mean age of participants in the low-exposure group was 23.87 years (range, 19–31) and in the high-exposure group was 24.87 years (range, 20–34). The study was approved by the University of Manchester Research Ethics Committee (project number 16206) and informed, written consent

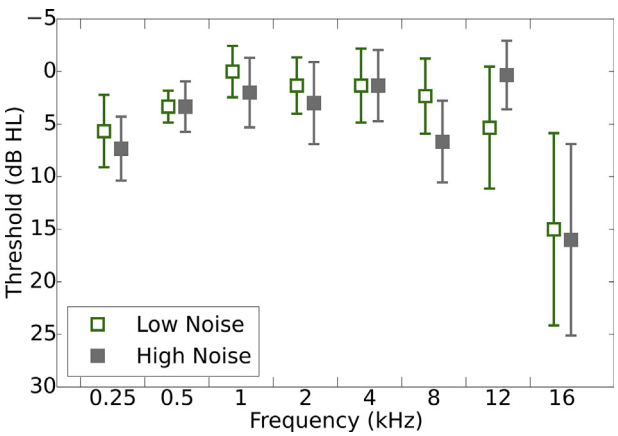

Fig. 1. Pure tone air-conduction audiometric thresholds. Thresholds are shown for the test ear, with 95% confidence intervals, for the two groups of listeners. N = 15 in each group.

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