Hearing Research 309 (2014) 63–74

Contents lists available at ScienceDirect

Hearing Research

journal homepage: www.elsevier.com/locate/heares

Research paper

Vestibular receptors contribute to cortical auditory evoked potentials☆

Neil P.M. Todd [a,*], Aurore C. Paillard [a], Karolina Kluk [a], Elizabeth Whittle [a], James G. Colebatch [b]

[a] The University of Manchester, UK
[b] University of New South Wales, Australia

ARTICLE INFO

Article history:
Received 13 August 2013
Received in revised form
8 October 2013
Accepted 26 November 2013
Available online 7 December 2013

ABSTRACT

Acoustic sensitivity of the vestibular apparatus is well-established, but the contribution of vestibular receptors to the late auditory evoked potentials of cortical origin is unknown. Evoked potentials from 500 Hz tone pips were recorded using 70 channel EEG at several intensities below and above the vestibular acoustic threshold, as determined by vestibular evoked myogenic potentials (VEMPs). In healthy subjects both auditory mid- and long-latency auditory evoked potentials (AEPs), consisting of Na, Pa, N1 and P2 waves, were observed in the sub-threshold conditions. However, in passing through the vestibular threshold, systematic changes were observed in the morphology of the potentials and in the intensity dependence of their amplitude and latency. These changes were absent in a patient without functioning vestibular receptors. In particular, for the healthy subjects there was a fronto-central negativity, which appeared at about 42 ms, referred to as an N42, prior to the AEP N1. Source analysis of both the N42 and N1 indicated involvement of cingulate cortex, as well as bilateral superior temporal cortex. Our findings are best explained by vestibular receptors contributing to what were hitherto considered as purely auditory evoked potentials and in addition tentatively identify a new component that appears to be primarily of vestibular origin.

1. Introduction

In many fish and amphibian species the otolith organs (the saccule and utricle) are important for the detection of sound, as well as serving a vestibular function (Lewis and Narins, 1999). Throughout vertebrate evolution, new structures evolved for the detection of sound culminating in the cochlea (Manley et al., 2004). Nevertheless, an acoustic sensitivity of the otolith organs has been conserved in all classes of vertebrate, including primates (Young et al., 1977; McCue and Guinan, 1994; Curthoys et al., 2006). In humans, acoustic sensitivity of the otolith organs can be demonstrated by vestibular-dependent effects like nystagmus (Lackner and Graybiel, 1974) or evoked electromyographic (EMG) signals (Bickford et al., 1964). Such EMG responses can be measured either from muscles of the neck, e.g. the sternocleidomastoid muscle, reflecting the vestibular-collic reflex pathways (the vestibular evoked myogenic potential or VEMP: Colebatch et al., 1994) or from extra-ocular eye muscles, reflecting activation of the vestibular ocular reflex pathways (ocular VEMP or OVEMP: Rosengren et al., 2005; Todd et al., 2007). Although the neck response is often now referred to as a cervical VEMP (or CVEMP), in the rest of this text we use the original acronym VEMP.

The use of vestibular evoked EMG methods has enabled considerable advances in our knowledge of the sensitivity of the human otolith organs to acoustic stimulation. Within the literature there is, however, considerable confusion in the use of terms, especially with the introduction of the mini-shaker (e.g. model 4810, Bruel & Kjaer, Denmark) as a means of stimulation, along with the usual head-phones for the delivery of air-conducted (AC) sound, and the more conventional audiological vibrator (e.g. model B71, Radioear Corp., USA) for bone-conducted (BC) sound. The principal source of confusion is that the nature of the skull response changes as a function of stimulus frequency. At the higher frequencies typically employed in audiometry, the skull response is primarily a function of its reactive, i.e. elastic, properties, but for low-frequencies, less than about 800–1000 Hz, the skull response is characterised as whole-head quasi-rigid vibration in which there is zero phase between stimulus and response (Stenfelt et al., 2000; McKnight et al., 2013). This is further complicated by the existence of several skull resonances near 500 Hz. In order to

* Corresponding author. Faculty of Life Science, University of Manchester, Manchester M13 9PL, UK. Tel.: +44(0)161 306 5770.
E-mail address: neil.todd@manchester.ac.uk (N.P.M. Todd).

0378-5955/$ – see front matter © 2013 The Authors. Published by Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.heares.2013.11.008

distinguish these response regimes we use here the terms BC sound vs. low-frequency vibration, with the transition placed at around 200 Hz, just below the skull resonances.

In response to sound and vibration the two otolith organs appear to have distinct tuning properties, with the saccule and utricle tuned to approximately 500 Hz and 100 Hz respectively (Todd and Cody, 2000; Todd et al., 2009), likely a consequence of underlying biomechanical properties. Recently, Zhang et al. (2011, 2012) showed that stimulation with both head-phones and mini-shaker may produce distinct resonances at about 100 Hz and 500 Hz, suggesting that the two resonance peaks are specific to the different dynamic responses of the two end-organs. Sound and vibration modes of stimulation also have distinct threshold properties. For 500 Hz AC sound activation, vestibular thresholds are found at about 80 dB above the auditory thresholds (Todd et al., 2008b), while using 100 Hz vibration, vestibular thresholds may be as low as 15 dB *below* the auditory threshold (Todd et al., 2008a).

Having made some progress in establishing the natural frequencies and appropriate modes of stimulation of the otolith organs, these sensitivities may be used as a tool to investigate the central pathways, i.e. by stimulating at best frequency for the receptors one is maximally likely to excite higher order neurons. Several attempts have now been made to measure vestibular evoked potentials (VsEPs) of neurogenic origin. Following a study by de Waele et al. (2001), which showed the existence of short-latency potentials (8–15 ms) in response to electrical stimulation, Todd et al. (2003) demonstrated a similar response to 500 Hz BC sound. These acoustically evoked short-latency VsEPs were confirmed as being vestibular as they were absent in avestibular patients but present in deaf subjects with intact VEMPs (Rosengren and Colebatch, 2006). A later study by Todd et al. (2008b) used a source analysis to confirm that the short-latency VsEPs are dominated by the pathways underlying the vestibular-ocular reflex, but also suggested activity in frontal cortex. More recently McNerney et al. (2011) used an alternative source analysis method to suggest that a wider range of vestibular cortical areas contribute to the short-latency potentials activated by sound. Such studies complement animal work using linear or rotational whole body acceleration to evoke short-latency vestibular responses (Sohmer et al., 1999; Jones et al., 2011).

While there is agreement on the existence of short-latency vestibular evoked effects, and some progress made in elucidating the sub-cortical and cortical generators in humans, a question which has not been addressed is the contribution, if any, made by vestibular receptors to the late auditory evoked potentials (LAEPs). These are characterised by a series of potentials, which are usually measured at the vertex, between about 50 and 250 ms, i.e. the P1, N1 and P2 (although the P1 is sometimes considered as a Pb wave following the mid-latency response (MLR) Na, Pa and Nb waves (Picton, 2011)). Source analysis indicates that the primary generators are bilateral tangential and radial sources in superior temporal cortex, with additional generators in the frontal cortex (Naatanen and Picton, 1987; Scherg et al., 1989). The aim of the present study was to address the above question by looking for evidence of changes in 500 Hz AC sound evoked LAEP when stimuli are presented at intensities above vestibular threshold and to carry out a source analysis.

2. Methods

2.1. Subjects

Fourteen healthy subjects were selected for this study (mean age = 28.3; SD = 6.9; 5 females and 9 males). All subjects were first screened for any neurological, vestibular and hearing impairment. Prior to any testing, all participants gave written informed consent according to the Declaration of Helsinki. The University of Manchester Research Ethics Committee approved the study.

2.2. Stimuli

The experimental stimuli employed for obtaining vestibular responses were AC 2-ms, 500-Hz, single cycle tone pips. AC stimuli were delivered by insert earphones (3A insert earphone, E-A-RTone Gold, Guymark UK Limited). The maximum input voltage, which was set to 1 V pp, resulted in a maximum output on the amplifier equivalent to a peak SPL of 135.9 dB re 20 μPa (as measured by the LLpk parameter with linear frequency weighting) and an RMS SPL of 115.4 dB re 20 μPa (measured by the LAI parameter, with A-frequency weighting and impulse time weighting). Stimulus calibration was carried out using a GRAS IEC711 Coupler (RA0045) and a pressure-field microphone (Model 4134) with a 2260 Investigator (Brüel and Kjaer, Naerum, Denmark). The stimuli were generated using customised software with a laboratory interface (power 1401, Cambridge Electronic Design, Cambridge, UK) and a commercial or custom amplifier.

2.3. Procedure

In normally hearing subjects use of AC stimuli will give rise to evoked potentials of cochlear origin, i.e. auditory evoked potentials (AEPs), and thus any vestibular evoked potentials (VsEPs) would be mixed in with AEPs. For this reason after obtaining the subjects' VEMP thresholds we recorded EEG responses both below and above the VEMP threshold in two separate sessions. The VEMP threshold is necessarily higher than the receptor threshold due to synaptic attenuation, but is convenient to use as it fairly easy to obtain and changes in the infra-ocular waveforms, i.e. presence and absence of OVEMPs, are clearly recognizable above and below this level. However although this threshold does not guarantee that the EEG response is free from vestibular influence we expected that they would be predominantly cochlear in origin.

2.4. Auditory thresholds

Audiograms were obtained for both ears using an Amplivox audiometer (Amplivox Ltd, UK) with Telephonics TDH 49 earphones (Telephonics Corp., Farmingdale, NY, USA). Each subject satisfactorily achieved pure tone air conduction thresholds of $\leq$20 dB HL at 125, 250, 500, 1000, 2000, 4000 and 8000 Hz bilaterally, according to British Society of Audiology (BSA) (2011) recommended procedures. The subjects had no history of otological or neurological pathology.

Psychophysical auditory thresholds of the stimulus used for evoked response recording were determined using PsyLab (v2.0, Hansen, 2006) using 3-alternative forced choice (3AFC), one-up two-down adaptive method to track the 79.4% point on the psychometric function (Levitt, 1971). The signal, i.e. 2-ms, 500-Hz, single-cycle tone-pip, was randomly presented to the subject in one of the three intervals and delivered unilaterally through insert earphones (3A insert earphone, E-A-RTone Gold, Guymark UK Limited). The initial signal level was set to 81 dB LLpk; this was reduced by 4 dB after two successive correct responses and increased by 4 dB after an incorrect response. After four reversals the measurement phase began and the step size was reduced to 1 dB. The threshold was taken as an average of the last four reversals.

2.5. Vestibular thresholds

Vestibular thresholds were obtained by means of VEMPs. Subjects were tested lying supine on a couch, with the backrest to