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Intermediate latency evoked potentials of cortical multimodal vestibular areas: Acoustic stimulation

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HIGHLIGHTS

- Multimodal vestibular network 3-D EEG dipoles mapped with BESA program.
- Specific evoked and induced cortical potentials 20–150 ms.
- Corresponding deep brain electrode data in epilepsy patient.

ABSTRACT

Objective: Loud acoustic stimuli at 500 Hz activate the vestibular system. Intermediate-latency vestibular cortical potentials of multimodal cortex regions were investigated, beyond the 20 ms time range.
Methods: Eighteen healthy subjects with 32-channel EEG and one epilepsy patient with right-sided intracortical electrodes received three types of stimuli: tone bursts capable of evoking vestibular evoked myogenic potentials (VEMP) in neck muscles and sham stimuli matched for either frequency or amplitude, which cannot evoke myogenic responses.
Results: VEMP-capable stimuli activated anterior insula and posterior operculum bilaterally at 20, 30, 60 and 110 ms, frontal brain regions at 70 and 110 ms, determined by Brain Evoked Source Analysis BESA. Recordings from intracranial electrodes revealed corresponding peaks at identical latencies. Stimulus-locked high and low beta and mu band modulations were found in vestibular, parietal and occipital regions, beyond 20 ms. Sham stimuli only evoked late acoustic potentials. Corresponding vestibular potentials were also seen in an eight-channel bipolar Laplacian montage.
Conclusions: The sequentially appearing cortical potentials evoked by VEMP-capable stimuli co-locate with data from functional imaging studies. Frequency-specific activity (induced potentials) in these areas may reflect multimodal proprioceptive and visual sensory crosstalk.
Significance: Vestibular cortical evoked potentials may see clinical use in vertigo disorders.

1. Introduction

Vestibular information ascends through vestibular nuclear complex, medio-lateral fascicule (MLF) and thalamus (Büttner-Ennever, 1992; Brandt and Strupp, 2005; Büttner and Büttner-Ennever, 2006; Lopez and Blanke, 2011). The "vestibular cortex" is distributed bilaterally around an "inner vestibular circle" without a solitary primary sensory cortex (Guldin et al., 1992; Guldin and Grüsser, 1998; Lopez and Blanke, 2011), including the bilateral parietal opercula and the bilateral anterior insular margin (Guldin et al., 1992; Guldin and Grüsser, 1998; Fasold et al., 2002; Kahane et al., 2003; Dieterich et al., 2003, 2005a,b; Stephan et al., 2005; Schlindwein et al., 2008; Miyamoto et al., 2007; Hüfner et al., 2009; Lopez and Blanke, 2011). An overall subjective body-in-space perception is generated in this network, by combining particularly vestibular, visual and proprioceptive information in a multisensory array (Brandt and Strupp, 2005; Lopez and Blanke, 2011). The vestibular network, unlike other sensory systems, unites different input modalities at an early stage of cortical processing and is considered to be involved in sensory re-afference loops.

Loud acoustic stimuli can excite the saccular vestibular epithelium (Nong et al., 2002; Todd et al., 2003; Miyamoto et al., 2007)

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and evoke a biphasic response in the ipsilateral pre-activated sternocleidomastoid (SCM) muscle (acoustic vestibular evoked cervical myogenic potentials VEMP or cVEMP) through descending vestibulo-spinal pathways. Loud click stimuli, short tone bursts and bone vibration of the mastoid at 500 Hz have been used throughout the literature. Stimulation of higher frequencies or lower amplitudes has been extensively and repeatedly shown to elicit no specific vestibular-related response beyond mere acoustic stimulation (e.g. Sheykholeslami et al., 2001). At 95 dB(A) NHL (equivalent to 125 dB(A) SPL), the P13-N24 VEMP amplitude of the SCM typically exceeds 100 μV in compliant healthy subjects with a sufficiently pre-innervated SCM muscle (e.g. Sheykholeslami et al., 2001; Wang and Young, 2006; Sandhu and Bell, 2009). Other vestibular stimulation techniques, such as physical motion (Li et al., 1993, 1995; Rodionov et al., 1996; Sichel et al., 2000[1]) or galvanic stimulation (Bense et al., 2001) preferentially excite the semicircular canals or multiple vestibular end-organs simultaneously.

Early potentials, likely related to vestibular nerve, vestibular nuclear or even certain early cortical activations (Li et al., 1993, 1995; Elidan et al., 1995), were described as multiple sharp waves within the first 10–20 ms of vestibular stimulation, especially as "short latency vestibular evoked potentials SL-VsEP" (Li et al., 1993; Elidan et al., 1995; Sichel et al., 2000). Ascending cortical potentials associated with acoustic vestibular stimulation have been investigated by distributed source LoRETA (low resolution electromagnetic tomography analysis, McNerney et al., 2011) and basic discrete source analysis (Todd et al., 2003, 2007, 2008; McNerney et al., 2011), all focused on potentials prior to 20–30 ms. At present, these early potentials are discussed to be related to intraorbital presaccadic activity, different from motions of the eye dipole by certain authors. They are either referred to as "oculomotor oVEMP" (Todd et al., 2007, 2008; Sandhu and Bell, 2009; Rosengren et al., 2005, 2009a,b, 2010a,b, 2011) or "medium-latency vestibular evoked potentials ML-VsEP" (Leibner et al., 1990; Rodionov et al., 1996; Miyamoto et al., 2007). Some authors relate potentials <20 ms after a specific vestibular stimulus already to vestibular cortical activity (DeWaele et al., 2001; McNerney et al., 2011). In this field with disputed origin of early potentials, this study focused on the spatial and temporal characteristics of intermediate to long latency cortical potentials associated with VEMP-capable acoustic stimuli particularly *beyond* 20 ms, which have not been described previously. Sources of such potentials were compared to areas of vestibular activations found in previous functional imaging and anatomical studies and suggested to be part of the vestibular multimodal network. EEG data from healthy volunteers and intracortical potentials from one subject undergoing diagnostic epilepsy recordings were investigated.

2. Materials and methods

2.1. Subjects

Eighteen healthy right-handed individuals (11 male, 7 female; age 23–35, average 28; Edinburgh handedness inventory ⩾90% towards right) without any history of vestibular, hearing or other neurological disorders were recruited from university personnel. None of the subjects were re-educated from left-handedness at childhood.

Additionally, a 22yo, 100% naturally right-handed female with frontal epilepsy of the non-dominant right hemisphere since age 15 was investigated. Surface EEG showed inter-ictal and ictal epileptic discharges in the right temporal and frontal regions, remote from posterior operculum and anterior insula. Nine deep-brain recording electrodes (T08 Pt/Ir microelectrodes, DIXI medical, Besançon, www.diximedical.com) were implanted into the frontal lobe, posterior operculum and temporal structures (Fig. 1a–d) for possible epilepsy surgery indication. The study was approved by the University's ethics committee (Decision 142/04 of the Ethikkommission der Medizinischen Fakultät der Ludwig-Maximilians-Universität). All of the involved subjects gave their written informed consent in accordance with the Helsinki Declaration.[2]

2.2. Acoustic stimuli

Three different acoustic tone burst stimuli types (Table 1) were applied while recording either neck EMG or EEG potentials. One VEMP-evoking stimulus was compared to two 'sham stimuli': frequency sham used a higher frequency at ISO-loudness-adapted amplitude; amplitude sham was lower amplitude at identical frequency. Inter-stimulus intervals were randomized between 300 and 500 ms. Comparison to avestibular or deaf subjects was omitted in this study due to extensively rich literature, describing the VEMP-capable stimulation as vestibular-related in comparison to the aforementioned sham stimuli (e.g. Sheykholeslami et al., 2001).

Stimuli were created with Matlab R2009b (The MathWorks Inc., www.mathworks.com) on a personal computer connected to a Phase26 USB sound card (TerraTec Electronic GmbH, www.terratec.net) and a stereo amplifier (Pioneer A-109, Pioneer Corporation, www.pioneer.jp), then delivered by Beyer Dynamic DT 48 headphones (Beyer Dynamic GmbH & Co KG, www.beyerdynamic.de). The entire setup was calibrated for peak sound amplitudes through a 4152 artificial ear with a dB(A)-filtered 2260 device (ISO calibration using a 4294 device, all instruments by Brüel and Kjær, www.bksv.com).

The amplitude sham stimuli (85 dB) were always presented in a block before the randomly scrambled presentation of the loud 127 and 118.5 dB stimulus trains, both during the neck VEMP and later during the EEG recording trials, avoiding temporary threshold shifts and thus possibly masking amplitude sham effects. Stimuli in a block were always randomized for side (amplitude sham) or for side *and* type of stimulus (combined frequency sham and VEMP stimuli block).

2.3. Experimental schedule

Two series of tests were conducted with each participant. First the presence of neck VEMPs in the SCMs was determined bilaterally, indicating an intact peripheral vestibular organ, vestibular nuclei and descending vestibulo-spinal tracts. Subjects were positioned in a chair with the rake flexed back to 45°. Eyes were closed (Sandhu and Bell, 2009) and the jaw slightly opened with closed mouth to minimize oculomotor, blink and masticatory artifacts. To activate the SCM muscle, the head had to be actively lifted from the surface. Then 270 stimuli of each type and side were delivered.

Bilateral Ag/AgCl ring electrodes over the upper two-thirds of the SCM muscles were referenced to an electrode over the top of the sternum. Impedances <20 kΩ were obtained with Abralyt high-chloride gel. A BrainAmp DC amplifier recorded EMG at 10 μV/500 Hz amplitude and temporal resolution, filtered DC – 2.5 kHz. All EMG and EEG equipment is distributed by Brain Products GmbH (www.brainproducts.com).

Then the same sequence of stimuli with 1000 iterations each was applied during the recording of a 32-channel EEG, with pauses every 3 min and without head lifting. In the one patient, recordings were obtained from the intracranial electrodes; an EOG channel was added externally. Participants were sitting upright with straight

[1] http://www.ncbi.nlm.nih.gov/pubmed/10733183.

[2] http://www.wma.net/en/30publications/10policies/b3/.