MAGNITUDE-SQUARED COHERENCE APPLIED TO MLAEP DURING STIMULATION AT DIFFERENT SOUND PRESSURE LEVELS

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Abstract: The need for a better approach for auditory screening is due to pathologies that can affect higher auditory centers. In this context, the Middle Latency Auditory Evoked Potential (MLAEP) was investigated in the frequency domain by applying Magnitude-Squared Coherence (*MSC*) to the EEG of ten adults during click stimulation with different sound pressure levels. Results indicate the most characteristic frequency band in MLAEP for high intensity levels (85 and 60 dB_{NHL}) to coincide with the gamma band (30-100 Hz). For intensities close to the psycho-acoustic threshold, the band 30-60 Hz was identified. Detection was obtained in 100% of the volunteers for stimulation levels varying from 85 down to [L+18] dB_{NHL} and in 80% for [L+10] dB_{NHL}. These findings indicate the potentiality of *MSC* in detecting MLAEP response of low intensity in adults. Thus, this technique might be used as an auxiliary tool for determining objectively the individual neurophysiologic acoustical threshold level.

Introduction

Among the objective techniques employed for auditory test, the brainstem auditory evoked potential (BAEP) is useful to assess the integrity of the auditory pathway from the inner hair cells (IHC) up to the inferior colliculus in the midbrain (brainstem). An audiometry test based on the wave V of BAEP, named BERA, has good correlation with the tonal audiometry, indicating the lowest stimulus pressure level that is able to produce auditory response [1]. The Otoacoustic Emissions (OAE) [2] have been employed in order to assess the integrity of the auditory bioamplification system of the outer hair cells (OHC) in the cochlea. Hence, one can point out these techniques as a neurophysiologic threshold measure. Furthermore, automatic methods using BERA (AABR – automated auditory brainstem response) have also been used and, more recently, the steady-state auditory evoked potential (SSAEP) has been investigated [3].

However, some pathologies may also affect higher auditory centres, i.e. those above the inferior colliculi, hence leading to the dysfunction of these structures to be not detected through current auditory tests [4,5]. For instance, the Auditory Neuropathy (AN) diagnosis, which is also named auditory desynchronisation, does not specify in neonates (NN) the dysfunctional site of deafness neither the neuropathological aspects [4]. Hence, the Mid-latency Auditory Evoked Potential (MLAEP) could be employed, since it reflects the activity of structures above the inferior colliculi up to the primary auditory cortex [6].

The detection criterion usually employed in auditory evoked potentials is based on the response morphology (particularly the amplitude and latency of peaks). The use of objective response detection (ORD) techniques in frequency domain, particularly the *MSC* (Magnitude-Squared Coherence), has shown superior performance in comparison with morphological criteria [7,8,9], reducing the exam time [10]. Nevertheless, the choice of the harmonics of the stimulation frequency that characterize the response presence is commonly performed heuristically [7]. This work applies *MSC* to the MLAEP of normal subjects under stimulation at several sound pressure levels, including the psycho-acoustic threshold, aiming at investigating the frequency bands that better characterize the evoked response.

Materials and Methods

Magnitude-Squared Coherence – MSC

MSC has been used as an ORD technique applied to EEG under stimulation [10], providing a significance level α of false-negative detection [8]. The *MSC* between one deterministic periodic signal (pulse train of stimuli) and another random one (observed EEG) depends only on this latter and can be estimated as [8]:

$$\hat{\kappa}^2(f) = \left|\sum_{j=1}^{M} \tilde{X}_j(f)\right|^2 \Bigg/ M\sum_{j=1}^{M}\left|\tilde{X}_j(f)\right|^2 , \quad (1)$$

where $\tilde{X}_j(f)$ is the Discrete Fourier Transform (DFT) of the j^{th} epoch of EEG signal ($x_j[n]$) sampled at f_s with N samples, $f = k.f_0$ (for k = 0, 1,…, N-1 and $f_0 = f_s/N$) and M is the number of epochs.

Assuming $x[n]$ to be a Gaussian white noise, the statistical distribution of $\hat{\kappa}^2(f)$ for the null hypothesis of no response (H_0) is related to the *F*-distribution [8] and this can be used to detect responses by comparing the value of $\hat{\kappa}^2(f)$ to critical values, according to:

$$\hat{\kappa}^2_{crit} = \frac{F_{crit\ 2,2M-2,\alpha}}{M-1+F_{crit\ 2,2M-2,\alpha}} , \quad (2)$$

where $F_{crit\,2,2M-2,\alpha}$ is the critical value of the *F*-distribution for a significance level α. In the presence of

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stimulus-synchronized response, positive detections occur whenever $\hat{\kappa}^2(f) > \hat{\kappa}^2_{crit}$. In the case of no response or for no stimulation, a false positive detection rate α is expected in all frequencies.

Casuistry

The EEG signal was collected from 10 normal volunteers aging from 21 to 57 years (mean: 35.3 years), in dorsal decubitus, completely relaxed and comfortable in silent ambient. Each acquisition lasted about 60 minutes. All volunteers signed up a consent agreement form.

Experimental Protocol

The exams were carried out using the two-channel evoked potential equipment *Nihon Koden* MEB 9102 (Japan), which performed the EEG pre-amplification and digital filtering (20 Hz high-pass at 6 dB/octave, 2000 Hz low-pass at 12 dB/octave, and 60 Hz *notch*). Ag/AgCl electrodes were positioned according to the 10-20 international system in order to acquire the derivation [Cz-Mi] (vertex-ipsilateral mastoid: left), grounded at Fpz. Impedance was kept below 2 kΩ during the whole experiment.

Rarefaction 100 µs-wide clicks were driven by the MEB 9102 equipment at 9 Hz (frequency band around 1-4 kHz [2]), and transduced via earphone *Elega* model DR-531B-14. Sound pressure level was measured in dB_{NHL} (0 dB_{NHL} = 30 dB_{peSPL} in this equipment). Only left ear was stimulated, while right ear received masking white noise at 40 dB below the stimulation level employed.

The number of stimuli lied between 600 and 2000, depending on the sound pressure level. Higher number of stimuli was applied for lower level stimulation, aiming at maintaining response detection even for low signal-to-noise ratio (SNR). Initially, the auditory threshold (L) was determined for each volunteer (varied from 0 to 11 dB_{NHL}, average of 7 dB_{NHL} = 37 dB_{peSPL}) and, then, EEG was collected without stimulation for circa 90 s. Then, 600 stimuli at 85 dB_{NHL} were applied, followed by two sessions of 1000 stimuli (60 and [L+26] dB_{NHL} − i.e. 26 dB above individual threshold) and a third session of 1200 stimuli at [L+18] dB_{NHL}. Another session of pure EEG was collected for 110 s, followed by two sessions of 1200 stimuli ([L+15] and [L+12] dB_{NHL}). The remaining sessions consisted of 2000 stimuli each one (sound pressure levels of [L+10], [L+8], [L+5], [L+2], [L] and [L-2] dB_{NHL}). The stimulation at 2 dB_{NHL} below threshold was considered as pure EEG.

Acquisition

The EEG derivation and the stimulation *trigger* were digitalized at 6 kHz (DAQPad 1200) via acquisition *software* developed in LabVIEW (*National Instruments*, Austin, USA). During acquisition, epochs containing samples with amplitude higher than 20 µV were considered as artefact contaminated and hence were automatically rejected, while the averaged waveform was visually monitored on the equipment screen.

Evoked Potential and MSC Estimation

The epochs were averaged in order to estimate the auditory evoked potential (AEP) waveform. In the AEP of Figure 1a, referring to stimulation at 85 dB_{NHL}, one can recognize the waves V from BAEP and N_0, P_0, Pa, Na, Pb, Nb from MLAEP.

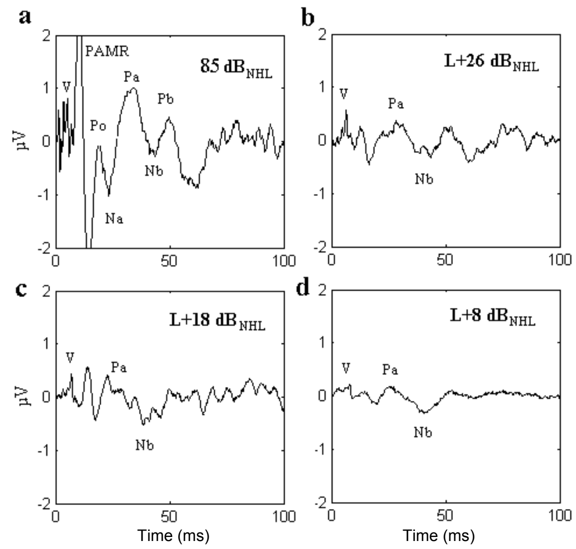

Figure 1: AEP from volunteer #1 (L = 11 dB_{NHL}) during stimulation at 9 Hz: a) 85 dB_{NHL} and $M = 600$; b) [L+26] = 37 and $M = 1000$; c) [L+18] = 29 and $M = 1200$; d) [L+8] = 19 dB_{NHL} and $M = 2000$.

The high-amplitude wave after wave V is the Post-Auricular Muscle Response (PAMR – usually found at high pressure level stimulation). As exemplified in Figure 1, the amplitude and definition of the AEP is directly related to the stimulation level, although the number of epochs considered was $M = 600$ for 85 dB_{NHL}, 2000 for [L+8] and 1200 for intermediate levels.

Discrete Fourier Transform (DFT) was applied to 110 ms long EEG epochs triggered to the stimuli, resulting in spectral resolution of circa 9 Hz. A Tukey window (10 ms lateral transitions) was applied to each epoch, aiming at attenuating responses beyond the expected MLAEP interval (10-100 ms). $\hat{\kappa}^2(f)$ was then estimated using (1). The value of $\hat{\kappa}^2_{crit}$ for α = 0.01 was calculated from (2), where one can note its dependence on M.

Results

Figure 2 illustrates the results from *MSC* application to the EEG of volunteer #1 during stimulation at 9 Hz. For sound pressure level of 85 dB_{NHL} and $M = 600$

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(Figure 2a), the null hypothesis of no response could be rejected in the band between 30 and 180 Hz ($\hat{\kappa}^2(f) > \hat{\kappa}^2_{crit}$), with the auditory response more pronounced from 30 to 60 Hz. By reducing the stimulation level to 19 dB_{NHL} ([L+8], that is, 8 dB_{NHL} above the individual threshold) and $M = 2000$, the null hypothesis could also be rejected within 30-60 Hz, although detection could still occur in higher frequencies up to about 100 Hz (Figure 2d). Similar results were achieved among all volunteers, particularly at 36, 45 and 54 Hz, even for low stimulation levels.

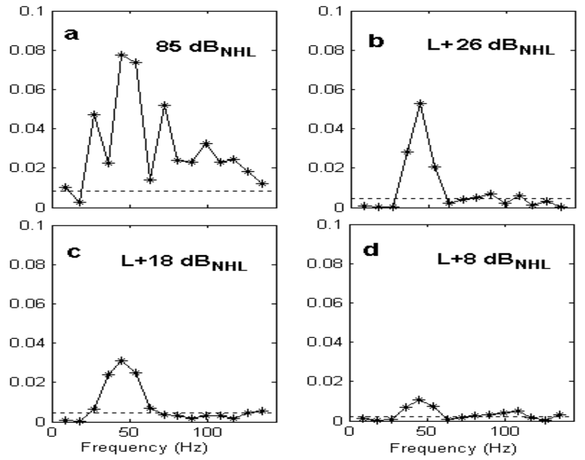

Figure 2: *MSC* from volunteer #1 (L = 11 dB_{NHL}) during stimulation at 9 Hz: a) 85 dB_{NHL} and $M = 600$; b) [L+26] = 37 and $M = 1000$; c) [L+18] = 29 and $M = 1200$; d) [L+8] = 19 dB_{NHL} and $M = 2000$. Horizontal line refers to $\hat{\kappa}^2_{crit}$ for $\alpha = 0.01$.

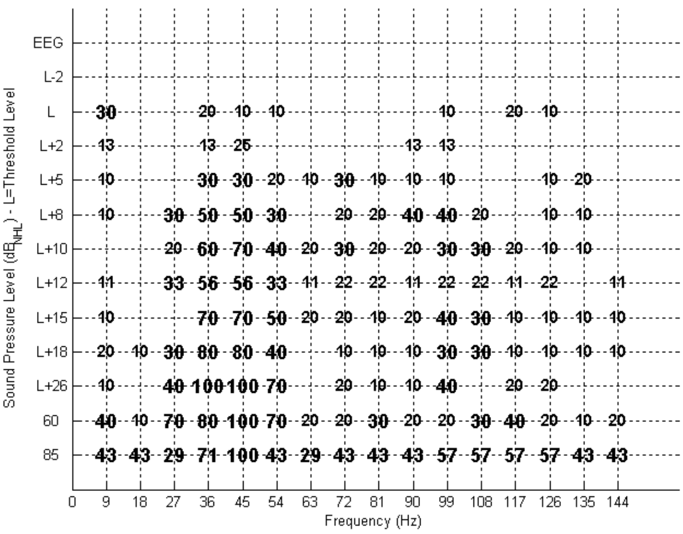

Figure 3: Frequency-related detection rate ($\hat{\kappa}^2(f) > \hat{\kappa}^2_{crit}$, $\alpha = 0.01$), considering all volunteers stimulated with several sound pressure levels.

In Figure 3, considering all volunteers, the higher detection percentage (superior to 40%) occurs in frequencies 36, 45 and 54 Hz for stimulation level between 85 and [L+10] dB_{NHL}. Even for [L+5] dB_{NHL}, detection occurs for 50% of the volunteers in the frequencies 36 and 45 Hz.

By defining the detection criterion as the rejection of the null hypothesis in any of the three frequencies within 36 to 54 Hz, the response could be detected in all volunteers stimulated with sound pressure level between 85 and [L+18] dB_{NHL} (Figure 4a). With stimulation at [L+15] dB_{NHL}, detection occurred in 90% of the volunteers, and decreased to 40% for stimulation at [L+5] dB_{NHL}.

For the frequency band from 81 to 99 Hz, the maximum percentage of volunteers for whom the null hypothesis of no response could be rejected (60%) occurred for stimulation at 85, [L+15] and [L+8] dB_{NHL} (Figure 4b).

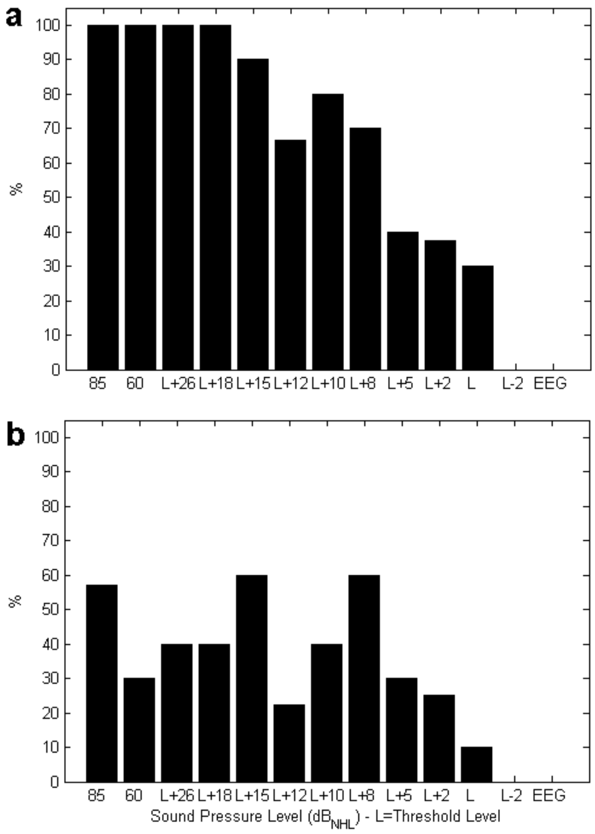

Figure 4: Percentage of volunteers for whom auditory response to stimulation at with several sound pressure levels was detected: a) 30-60 Hz band; b) 80-100 Hz.

Discussion

The MLAEP amplitude reduction for lower stimulation levels was clearly noted (it behaves similarly to the BAEP, as described in [1]), and the wave Nb was usually the last to be suppressed. On the other hand, there is a minor increase in the latencies of MLAEP waves by lowering the stimulation level. Contrastingly, the latency of the wave V of BAEP is considerably augmented under low sound pressure levels [2].

Using the *MSC*, the frequency band 30-60 Hz (corresponding to the low gamma band) resulted in

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more pronounced response detection even for low stimulation levels. This band has been considered as part of the MLAEP characteristic band [6]. Furthermore, this finding is in accordance with [11], for whom the gamma band, particularly the frequency 40 Hz, composes the evoked responses at cortical level. Moreover, recent works also point out the dominance of this band in the cortical auditory response in humans with different protocols: "human-speech" and "non-human-speech" sounds at 60 dB_{SL} (equivalent to [L+60] dB_{NHL}) [12]; pure tones at 55 dB_{SPL} (equivalent to 25 dB_{NHL}) [13]; and *tone burst* at 85 dB_{NHL} [14].

Besides the band 30-60 Hz, auditory response detection was occasionally achieved in frequencies from 70 to 120 Hz (high gamma band), even for sound pressure levels close to the individual psycho-acoustic threshold. Using *tone burst* stimulation at 85 dB_{NHL}, Artieda *et al.* [14] have also described that there is response in the high gamma band (but from 80 up to 120 Hz). Moreover, these authors have suggested that this activity is originated in the brainstem. Nevertheless, applying the *MSC* to the brainstem auditory response (but stimulating with clicks at 85 dB_{NHL}), Ramos *et al.* [7] and Azevedo *et al.* [15] have reported those frequencies within the range between 800 and 1100 Hz as those with higher sensitivity and specificity detection.

In the present work, the estimated neuro-physiological auditory threshold has shown results between L and [L+15] at 36, 45 and 54 Hz. The detection rate of 100% was obtained at levels from 85 down to [L+18] dB_{NHL}. For stimulation level of [L+10] dB_{NHL}, detection occurred in 80% of the volunteers. The sound pressure level of 15 dB higher then the psycho-acoustic threshold is also reported in [16] but using a MLAEP expert-based morphological detection.

MSC was also applied to steady-state auditory evoked potentials elicited by clicks at 39.1 Hz in [17], where the average psycho-acoustic threshold (37.5 dB_{peSPL}) is close to that obtained in our work (37 dB_{peSPL}). Whereas a 95% detection rate for stimulation at 10 dB_{SL} in normal adults was observed, full detection occurred at 20 dB_{SL} (equivalent to [L+20] dB_{NHL}).

On the other hand, with sound pressure levels above 50 dB_{NHL}, a 90% detection rate has been reported in [18], where amplitude-modulated tone at 500 Hz has been employed to produce the 40 Hz AEP in 10 normal adults. Moreover, Dobie & Wilson [18] pointed out that psycho-acoustic tonal thresholds are considerably lower than those obtained with click stimulation, resulting in apparently higher AEP detection thresholds.

Considering the high gamma band (80-100 Hz), our work achieved MLAEP detection in 60% of the volunteers at stimulation level of [L+8] dB_{NHL}. On the other hand, stimulating with tones amplitude-modulated at 78 to 95 Hz and using the T^2 statistic (a technique similar to *MSC*), Picton *et al.* [19] detected response within the stimulation band at the level of [L+21] dB_{NHL}, but did not specify the detection rate. Another work using steady-state evoked potentials included normal adults and babies (within 1 and 10 months) stimulated with different modulated tone frequencies [20]. By applying also the T^2 statistic to detect responses to 500 Hz tones modulated at 77 Hz in the adults, these authors obtained an average estimated threshold corresponding to [L+14] dB_{NHL}, which is close to that obtained in our work using low gamma band. For the babies, these authors estimated an average threshold of 45 dB_{SPL}, and suggested this method as useful for frequency-specific audiometry in early infancy.

Conclusion

The *MSC* was able to detect MLAEP with low stimulation levels, even close to the individual perception threshold. Frequencies between 30 and 60 Hz, within the gamma band, have shown to lead to the highest detection consistency. Thus, this technique might be used as an auxiliary tool in determining objectively the individual neurophysiologic acoustical threshold level. Moreover, the results suggest this method to be investigated in neonates.

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