A Programmable Acoustic Stimuli and Auditory Evoked Potential Measurement System for Objective Tinnitus Diagnosis Research

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***Abstract*— This paper presents the development of a single platform that records auditory evoked potential synchronized to specific acoustic stimuli of the gap prepulse inhibition method for objective tinnitus diagnosis research. The developed system enables to program various parameters of the generated acoustic stimuli. Moreover, only by simple filter modification, the developed system provides high flexibility to record not only short latency auditory brainstem response but also late latency auditory cortical response. The adaptive weighted averaging algorithm to minimize the time required for the experiment is also introduced. The results show that the proposed algorithm can reduce the number of the averaging repetitions to 70% compared with conventional ensemble averaging method.**

I. Introduction

Tinnitus is the subjective perception of sound with no physical acoustic stimulus in the ears. Currently in clinic, tinnitus evaluation questionnaires such as the tinnitus handicap inventory are performed to determine the presence and the degree of tinnitus [1]. However, the reliability of those tests is being argued, especially in malingering cases, because they rely on only patients' self-reporting [2]. For the objective tinnitus assessment, gap prepulse inhibition of acoustic startle (GPIAS) method was proposed and has been evaluated in some animal studies [3-5]. This method measures the behavioral response which is the acoustic startle reflex (ASR) of normal or tinnitus-induced animals to sudden loud acoustic pulses. As shown in Fig.1, the acoustic stimulus in GPIAS method is composed of a continuous background noise and a startle noise with or without a short silent gap preceding the startle pulse. In normal animals, the stimulus with a silent gap induced lower amplitude of the ASR than the stimulus without a silent gap. It is postulated that normal animals could expect the startle pulse by perceiving the silent gap and this expectation might inhibit ASR. In tinnitus-induced animals, on the other hand, the inhibition rarely occurred presumably because the tinnitus fills in the silent gap and then the ability to detect the silent gap has decreased.

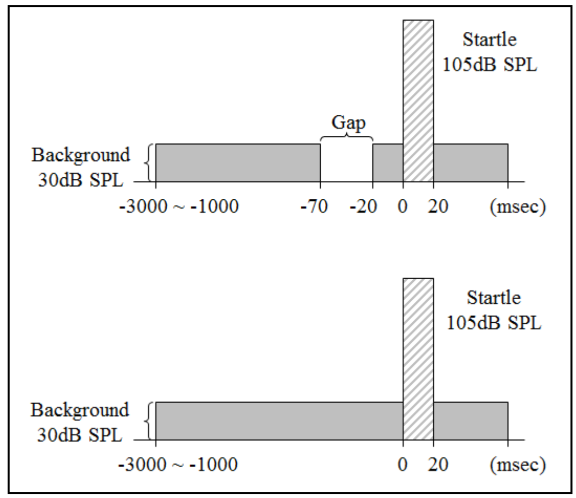

Figure 1. Typical GPI acoustic stimuli with/without a silent gap

Regarding to the application to humans of GPIAS method, recently Fournier et al. measured the electromyogram activity of eye blink instead of ASR, as a response of gap prepulse inhibition (GPI) stimuli [6]. However, behavioral responses such as ASR or eye blink have some limitations to be applied for clinical diagnosis because behavioral responses could be manipulated by patient's intention. We assumed that auditory evoked potential (AEP) could be an objective response to GPI in humans based on the hypothesis that ASR and AEP are elicited from the same acoustic sensory input pathway [7]. AEP is an electrical potential of the auditory pathway to the brain following the onset of the acoustic stimulus. Auditory brainstem response (ABR) which occurs within first 10ms after the acoustic stimulus has about 0.1-1uV amplitude with the frequency bandwidth of 30-3000Hz. On the other hand, late latency response (LLR) after 80ms which reflects the cortical response usually shows relatively larger amplitudes (1-10uV) and narrower frequency bandwidth (1-300Hz) [8].

In order to investigate our hypothesis, the development of a research platform is necessary to record AEP which is synchronized to the specific acoustic stimuli of the GPI method. The high flexibility of the acoustic stimuli generation should be achieved to find the optimal GPI parameters for humans, such as the type of background noise or the length of

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startle pulse. In addition, high flexibility of filter gain and cut-off frequency modification is necessary to observe full range of AEP because AEP includes various main waves in different amplitudes and frequency bandwidths. When recording AEP from surface electrodes, the signal averaging methods are generally used because the amplitude of AEP is relatively very small compared with the amplitude of spontaneous background noise. In clinic, commonly over 1000 sweeps with the repetition rate of about 7-11 acoustic stimuli/second are performed to achieve the high signal quality of AEP [8]. However, as shown in Fig.1, the duration between startle pulses in the GPI method has random several seconds to avoid the patient's prediction to the next stimulus. This causes the time required for the GPI experiment to be much longer than the time of general AEP test. Longer experiment time leads to inconvenience for subjects and also produces higher induced noise in AEP measurement. Therefore, decreasing the required time is essential for high signal quality of AEP in GPI method. This paper presents not only the development of a single platform for the acoustic stimuli generation of the GPI method and the AEP measurement but also the development of fast averaging algorithm to reduce the time required for the experiment.

II. Materials and Methods

A. AEP Measurement System with GPI Acoustic Stimuli Generation

Fig.2 shows the block diagram of the developed PC based system. The system was designed as a single platform without additional devices such as DAQ modules and audio/pre amplifiers to increase system stability and controllability. All components of the developed system were commercially available. The developed system was composed of two main blocks: Digital to Analog (DAC) for GPI acoustic stimuli generation and Analog to Digital (ADC) for AEP measurement. The specification of the developed system was decided based on the requirements of the acoustic stimuli and the characteristics of the AEP. DAC featured 18 bits monotonicity which enables the wide dynamic range of output with 20-110dB SPL of the acoustic stimuli. To generate the high frequency background noise such as 12kHz, the sampling frequency of the DAC was selected to 40KSPS. Regarding to the ADC, 16KSPS sampling frequency was chosen to guarantee wide frequency bandwidth measurement, especially for ABR which has up to 3000Hz. Moreover, high 24 bits ADC resolution was used to record very small potential amplitude below 1uV. The dynamic range of the ADC was programmed regarding the AEP amplitude and the applied filter gains. For the synchronization between ADC and DAC, the trigger signal was sent from DAC to ADC when each acoustic stimulus was generated.

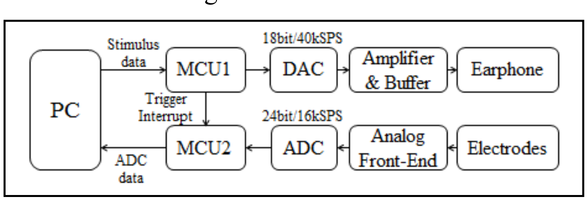

Figure 2. Block diagram of the developed system

As shown in Fig.3, the acoustic stimulus setting and the plotting of recorded AEP was performed in PC based User Interface(UI) programmed in Labview (National Instruments, Austin, TX, USA). To prevent the habituation of subjects about the presence of a silent gap, stimuli with/without a silent gap were randomly generated and then, the AEP responses to each type of stimulus were separately acquired and averaged.

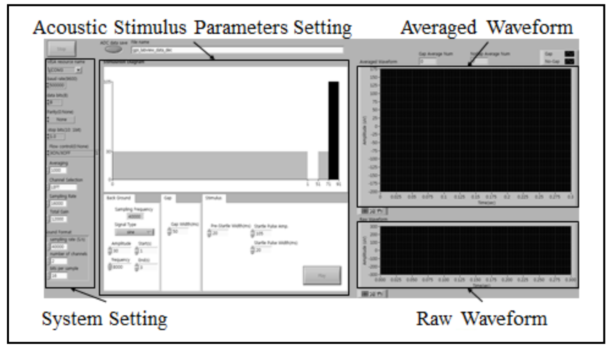

Figure 3. PC based user interface

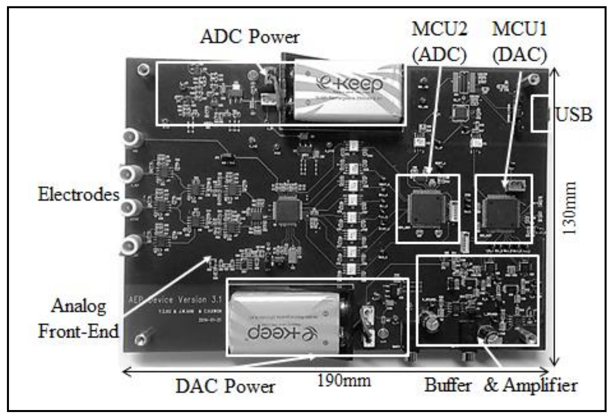

Figure 4. GPI acoustic stimuli generation and AEP recording platform

Fig.4 shows the hardware for the GPI acoustic stimuli generation and the AEP measurement. Because the amplitude of the ABR, one of our target signals, is below 1uV, the technique for the low noise circuit was applied. Two different batteries were used to minimize the interference between ADC and DAC. Moreover, the effects between the analog part and the digital part decreased by using the optocouplers on all interface signals. In the analog front-end circuit, a DC offset high pass filter with 0.1Hz cut-off frequency and an anti-aliasing filter with 3000Hz cut-off frequency were implemented. Other filter characteristics could be modified depending on the scope of the AEP waves. Negative feedback circuits were also applied to enhance the common mode rejection among surface electrodes.

B. Adaptive Weighted Averaging Algorithm

When recording ABR signals from surface electrodes, the time-domain signal averaging techniques are exploited because the single recorded SNR is very low (-20 to -30 dB) [9]. The time-locked ensemble averaging by the sweep repetitions is practically applied based on following assumptions. The main assumptions are that signal and noise are statistically uncorrelated and the signal strength is constant while the noise is random with a mean of zero and constant variance in every sweep.

$$SNR = \frac{nS}{\sqrt{n\sigma^2}} = \sqrt{n}\frac{S}{\sigma} \qquad (1)$$

Under these assumptions, the SNR of n repetitive trials has increased to √n times as shown in Eq. (1), where s denotes the signal strength and σ denotes the variance of the noise.

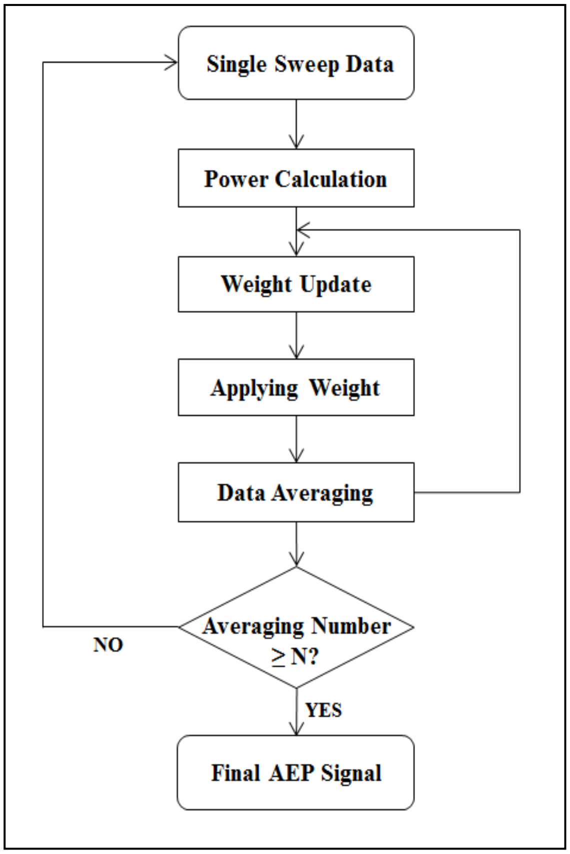

Figure 5. Block diagram of the proposed averaging algorithm

In the actual AEP measurement, however, the conventional averaging method was susceptible to sudden background noises such as eye blink and patient's motions which have non-constant variances. To compensate this problem, a weighted averaging method was proposed [9]. This method approximates that the signal of single sweep equals to the noise component because the SNR of single sweep signal is very low. Then, the weight, the inverse of the signal power is applied to the single sweep signal. Because the weighted method could reflect the noise power of each sweep, it usually showed better performance than the conventional method. However, the weighted averaging method should be performed iteratively after finishing the repetitions because this method intrinsically underestimates the overall magnitude of the signal. In this study, in order to avoid the signal underestimation and the iterative procedure, the modified weight calculation method was proposed as shown in Fig. 5.

$$W(n) = \frac{1}{P(N_n(t))} = \frac{1}{P(S_n(t)) - P(A_{n-1}(t))} \qquad (2)$$

Weighting W(n) is inverse of the difference between the power of the single sweep signal $S_n(t)$ and the power of the current averaged signal $A_{n-1}(t)$. The new averaged signal is updated as

$$A_n(t) = \frac{\sum_{i=1}^{n} W(i) S_i(t)}{\sum_{i=1}^{n} W(i)} \qquad (3)$$

In the proposed method, the signal estimation from the single sweep is performed based on not only the single signal power but also the power of the current averaged signal. Therefore, the underestimation of the signal component in the general weighted averaging method could be compensated.

III. RESULTS AND DISCUSSIONS

The noise amplitude of the developed system was measured by connecting an active electrode, a reference electrode, and a ground electrode. Fig.6 shows the averaged system noise on 1000 repetitions. The system SNR was 42.4dB compared with the average peak to peak amplitude of ABR signal. In this level of SNR, it was considered that the developed system was suitable to measure target signals. Then, actual ABR and LLR measurement trials were performed to subjects. An active electrode was located on the vertex position (Cz) and left/right mastoids (A1/A2) were used as reference electrodes for both ears. A ground electrode was attached on the forehead (G). In the ABR recording, the 0.1ms click sound with 105 dB SPL was used as the startle pulse while the 20ms white noise with 105dB SPL was generated to record the LLR. In both ABR and LLR measurements, the high reproducibility within the same subject was confirmed as shown in Fig.7. The main features of ABR waveforms (wave I, III, and V) were significantly distinct in both stimuli with/without a silent gap. The N1 and P2 peaks of the LLR waveforms from 100ms to 200ms after the presence of acoustic stimulus also appeared in both stimuli with/without a silent gap.

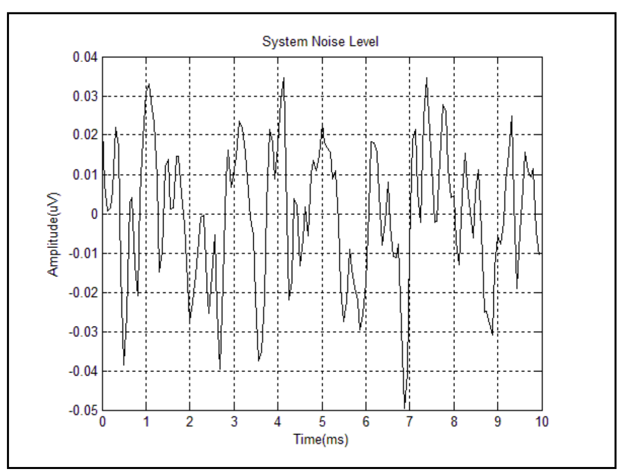

Figure 6. Measured system noise level

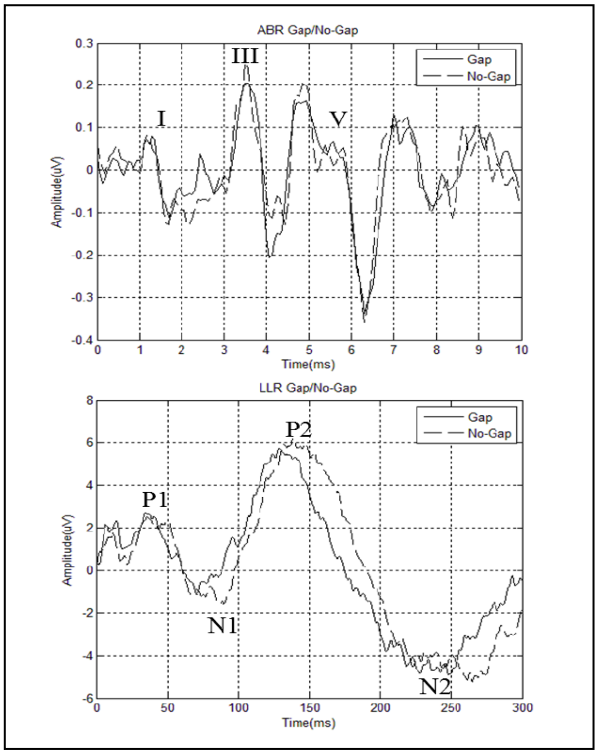

Figure 7. Recorded ABR and LLR waveforms

Fig.8 shows the averaged correlation changes of three subjects among the conventional ensemble averaging method, the weighted averaging method with no iteration, and the proposed adaptive weighted averaging method. The signal achieved by 500 repetitions in each method was used as the reference signal for the correlation calculation. As shown in an example in Fig.9, the morphology distortion in the ABR main waves did not occur in the proposed method. The required averaging number in the proposed method was about 320 when the target correlation was 0.95. However, the conventional averaging method required over 450 repetitions. Moreover, relatively large correlation decrease frequently appeared even with over 350 repetitions in the conventional averaging method. This result was not found in the proposed method because the adaptive weighting method is less sensitive to sudden large background noises due to the noise compensation.

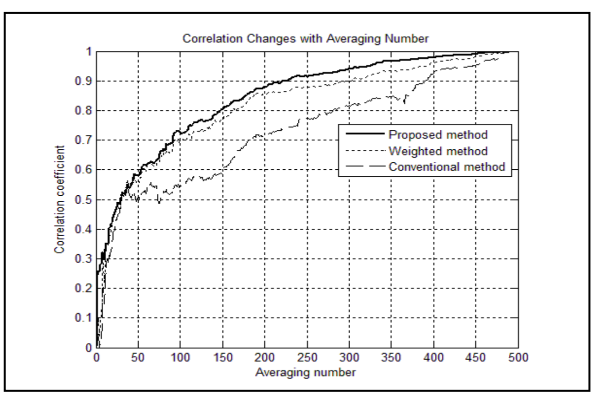

Figure 8. Correlation changes with averaging number

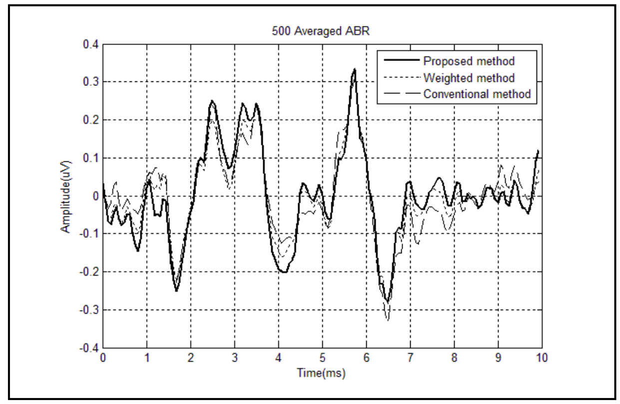

Figure 9. Comparion of the 500 averaged ABR waveforms

IV. Conclusion

A PC based single platform for objective tinnitus diagnosis research was developed to record AEP which is synchronized to the specific acoustic stimuli of the GPI method. High flexibility of the developed system was achieved in the GPI acoustic stimuli generation and the AEP measurement. Moreover, the time required to perform the GPI method was reduced to 70% with the proposed adaptive weighted averaging algorithm. The developed system was feasible for the further study that finds optimal parameters of the acoustic stimuli and the diagnosis features in various AEP waves.

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