Proceedings of the 28th IEEE
EMBS Annual International Conference
New York City, USA, Aug 30-Sept 3, 2006

Acquisition and Analysis of High Rate Deconvolved Auditory Evoked Potentials during Sleep

*Jorge Millan, *Member, IEEE*, Özcan Özdamar, *Member, IEEE*, and Jorge Bohórquez, *Member, IEEE*

***Abstract*—Auditory Evoked Potentials (AEPs) have been recorded at high stimulus rates during sleep using Continuous Loop Averaging Deconvolution (CLAD) sequences. AEP transient signals are obtained via frequency domain deconvolution of overlapped responses. Simultaneous acquisition of Auditory Brainstem Response (ABR), Middle Latency Response (MLR), and Long Latency Response (LLR) is obtained at an average stimulation rate of 39.1 Hz, using 10, 20 and 100 second electroencephalography (EEG) recordings. Deconvolved responses confirm previous observations on the reduction and disappearance of the P1 MLR component during stage III and IV, obtained with standard averaging and stimulation methods. Results indicate that auditory stimulation at high rates during sleep, using short time sweeps, may help correlating the sleep EEG indicative of different arousal levels, with corresponding AEPs.**

I. Introduction

AUDITORY evoked potentials (AEPs) are electrical signals originated within structures of the cochlea, auditory nerve and auditory pathways in the brain in response to an external auditory stimulus. Evoked potential (EP) components reveal specific neurological conditions, states and pathologies, making the functional testing of many sensory and motor neural pathways possible in both normal and disease states. Extraction of AEPs from the background EEG requires the averaging of a synchronized (time-locked) set of post stimulus responses. The maximum stimulus rate is dictated by the duration of the evoked response component under study to avoid overlapping of responses. During long acquisition times or during sleep, the EEG activity does not remain stationary and variations in the AEP responses are commonly observed.

A viable alternative to conventional stimulation is to present auditory stimuli at high rates. Although overlapping of responses occurs, if the stimuli are delivered in a certain time sequence, the single transient responses can be recovered from overlapped responses. Eysholdt and Schreiner [9] introduced a solution to the overlapping problem by using maximum length sequences (MLSs) to deconvolve overlapped ABR responses. The method uses the correlation property of the MLS sequence to extract the transient response. The method was later applied to other classes of AEPs and otoacoustic emissions (OAEs) [1], [2], [3], [11], [14], [16]. The interstimulus interval (ISI) patterns of the MLS sequences, however, are fixed and cannot be changed. They contain a wide but uneven distribution of ISIs which may generate different results than the regularly spaced conventional stimulus sequence due to adaptation characteristics of AEP components [4], [5].

A more general deconvolution method, continuous loop averaging deconvolution (CLAD), has been recently introduced to generate high rate stimulus sequences and extract transient responses from overlapped evoked responses [7], [12]. CLAD formulates a matrix linear equation to obtain the transient response from the stimuli sequence and the averaged overlapped response. If the conditions for a unique solution are present, the equations are solved and a deconvolution matrix is generated [7]. An alternative method [13] formulates the CLAD as a frequency domain deconvolution filtering process operated on the overlapped responses. This method offers the advantage of predicting the effect of the stimulus sequence on the signal-to-noise-ratio (SNR) of the evoked response calculation [13]. Extraction of overlapped ABR and MLR components has been demonstrated using the CLAD deconvolution method [2], [7], [12], [13].

High stimulation rates have been proven useful in clinical environments and research settings [3], [5], [14]. Evoked responses can detect pathologies and abnormal ABRs if the stimulus repetition-rate is high [10]. For situations where the testing time needs to be reduced such as in testing children or in intra-operative monitoring situations, stimulation at high rates is desirable to reduce acquisition times.

Auditory evoked potential analysis during sleep has the potential to unveil important relationships between arousal and consciousness levels. Reduction and disappearance of the middle latency P1 component during stage III and IV [8], indicate a connection between the background EEG activity and the AEPs. Since MLR and LLR responses are associated with auditory sensory and cognitive information processing, in this study we aimed to develop and test a tool for the acquisition and analysis of AEPs at high rates during the various sleep stages and compare these results with previous findings using conventional methods [6], [8]. Stimulation at high rates opens the possibility to examine

Manuscript received April 24, 2006.

*Jorge Millan is with the Department of Biomedical Engineering, University of Miami, Coral Gables, FL 33146 USA (phone: 305-284-5272, fax: 305-284-6494; e-mail: jorgemillan@bellsouth.net).

Ozcan Ozdamar is with the Department of Biomedical Engineering, University of Miami, Coral Gables, FL 33146 USA, with second affiliation in Departments of Pediatrics, Otolaryngology, and Neuroscience, University of Miami, Miami, FL 33136 USA (e-mail: oozdamar@miami.edu).

Jorge Bohorquez is with the Department of Biomedical Engineering University of Miami, Coral Gables, FL 33146 USA (e-mail: jbohorquez@miami.edu).

responsiveness of the sensory information processing centers to frequent stimuli. Stimulation during sleep permits evaluating the morphology of the responses during various awareness levels. An investigation of this relationship will be useful in a variety of clinical and research applications such as anesthesiology, neurology and behavioral sciences.

II. Methodology

To record and deconvolve overlapped responses obtained at high stimulus rates during sleep, we have developed an AEP system that implements the CLAD Deconvolution method. The system allows simultaneous recording of EEG, (electromyographic) EMG and electrooculographic (EOG) signals for sleep staging, and all major AEP components. ABR serves as a landmark to indicate the presence of auditory stimulus in the brainstem, whereas the MLR and LLR indicate the responses of the various brain structures in the ascending auditory pathway and their relative changes during the sleep cycle. Due to the variable EEG activity during the sleep stages, CLAD-AEP acquisition is performed in short AEP acquisition windows (10, 20, or 100 seconds) for proper EEG-AEP correlation analysis.

A. CLAD Formulation

Let $a(t)$, $t = 0, \ldots, T-1$, be a transient response of time length T in response to a single auditory stimulus. Assuming that T is large enough so that $a(t)=0$ for $t>T$, and the presence of N auditory stimulus, then the acquired response is

$$v(t) = \sum_{n=1}^{N} a(t) \cdot \delta(t - t_n) \qquad (1)$$

By defining a time vector T where v(t) is contained, having P opportunities for a stimulus presentation, then after the time T is reached, the time sequence is wrapped around in a circular fashion with period T [7]. This allows any number of time vectors T to be added. The acquisition of the data is continuously done throughout the sequence until the stimulus sequence starts again. The process converts a long time vector into a circular buffer where all elicited stimulus in the finite sequence are repetitively added in the exact position within the circular buffer without any jitter in time. Equation (1) can be converted into a time convolution form as

$$v(t) = a(t) * s(t) \qquad (2)$$

Where $s(t)$ is the stimulus sequence function. The Fourier transformation of (2) is

$$V(f) = A(f)S(f) \qquad (3)$$

$a(t)$ can then be resolved from (3) as

$$a(t) = FT^{-1}\left(\frac{V(f)}{S(f)}\right); \text{ if } \left[S(f) \neq 0\right]\forall f \qquad (4)$$

The solution exists if the frequency domain transfer function $S(f)$ does not have any zero values. Fig. 1 illustrates a stimulus sequence used in this study and the corresponding deconvolution filter frequency response. The SNR improvement of the deconvolution process is determined by the frequency response magnitude [13].

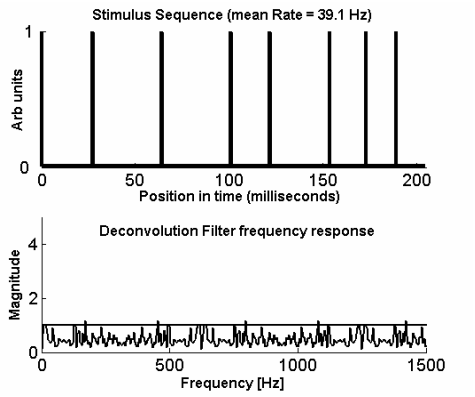

Fig. 1. Auditory stimulus sequence and corresponding filter frequency response. Sweep duration is 204.8 msec. The designed sequence has an overall noise reduction effect on the overlapped responses.

B. System Description

The AEP monitoring system consists of a computer station, a 16-bit 200 KS/s USB analog IO data acquisition board, and a multichannel bioamplifier system, arranged as shown in Fig. 2. The EEG, EMG and EOG signals are bandpass filtered (0.3 - up to 1000 Hz) and amplified with a gain of 10,000. The stimulus signal is continuously digitized to synchronize the stimulus onset along the acquired EEG epochs. The computer application is designed to acquire, process and continuously record the EEG, EMG and EOG signals. A real time EEG FFT display is implemented to graphically detect any unwanted noise such as 60 Hz power interference. The EEG/EMG/EOG signals are used for visual classification of sleep episodes into stage awake, I, II, III, IV and REM sleep, following standard staging criteria [15]. The system acquires and displays in real time physiological data and continuously process and displays CLAD deconvolved evoked responses. Auditory stimulus is PC generated as a wave sound file delivered to the subject via insert earphone EARTONE 3A.

C. Recordings

To validate the AEP-EEG system AEP recordings were acquired from two healthy female volunteer subjects (A: age 21 and B: age28), with no history of audiological or neurological hearing problems. Informed consent was signed according with approved IRB protocols. Electrode montages included EEG at Cz+, ipsi mastoid-, and ground at forehead, EOG, and EMG at chin. Electrode impedances were less than 3k ohm. The subject was placed in a sound-isolated chamber and asked to lay relaxed in a supine position with the eyes closed. Auditory monaural (right ear)

rarefaction clicks were elicited at 60-dB nHL, with an average repetition rate of 39.1 Hz. The acquisition window was 204.8 ms for each individual epoch. The duration of each session was about one hour.

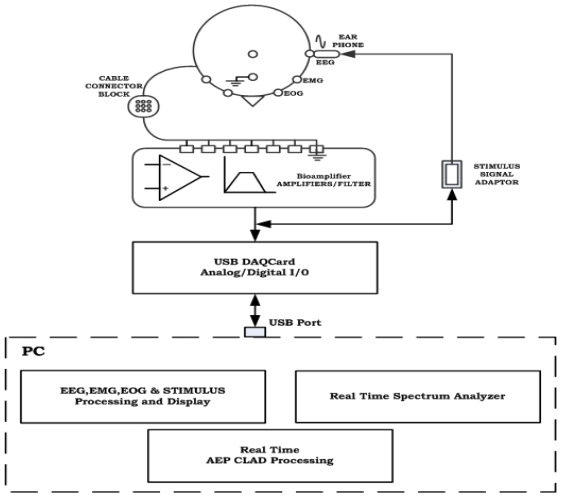

Fig. 2. AP system block diagram illustrating electrode montage, amplifier, data acquisition and software processing modules.

III. Results

Figures 3 - 7 illustrate sample recorded EEG and AEP waveforms from subject A. The AEP shown in Fig. 3 corresponds to a 10 second EEG recorded during stage I. Remarkably, clear V, VI, No, Po, Na, Pa, Nb, P1, N1, P2 and N2 waves were extracted within this short time window. Fig. 4 and 5 illustrate sample 100-second processed AEP waveforms for awake through stage IV, and their corresponding recorded EEG epochs. As observed, the P1 component is reduced during stage III and disappears during stage IV. Amplitude and latency measurements are illustrated in Fig. 6 and 7. ABR latency remained fairly constant around 6.90 ± 0.17 msec during the sleep session. Pa latency was 30.66 ± 1.43 msec, and P1 latency was 57.47 ± 3.25 msec. P1 was not detectable during stage III and IV (t > 24 minutes). Similar recordings were observed from subject B.

IV. Discussion

Detection of ABR, MLR and LLR components at high stimulation rates during sleep opens the possibility to investigate the correlation between brain responses to auditory stimulus, background EEG activity, and arousal and consciousness levels. As observed in Fig. 5, 6 and 7, ABR responses were constantly obtained without being significantly affected by the various stages of sleep. This confirms the view as being exogenous responses, reflecting the activity in the peripheral auditory nerve and brainstem relay centers. The background EEG activity is uncorrelated to the AEP ABR components during the entire sleep period. The MLR component, on the other hand, showed a variation in P1. Pa remained fairly stable during the recording but changing morphology during stages III and IV. This finding also confirms the view of MLRs as closely related to the arousal state of the subject. The MLR generating system includes auditory regions such as the thalamo-cortical pathway and the reticular formation, which modulate the general state of arousal and receptiveness to sensory input. The background EEG activity recorded during sleep was correlated to the AEP response. The LLR showed variations in the N1 and P2 components during stage III and IV. From Fig. 5, the N1 wave disappears at stage IV but not during Stage III, where a latency shift occurs. P2 also disappears at stage IV. The LLR component is therefore strongly correlated with the sleep EEG activity during stages III and IV, and less affected during awake and stages I and II. Further studies need to include the role of individual sleep EEG frequencies and morphologies during each sleep stage in the AEP response. The system's ability to process AEPs from short EEG buffers helps to reduce the inherent EEG variability found during long recordings and sleep stage transitions. Short segments are required to study the effects of K-complexes and sleep spindles in the processed AEP response.

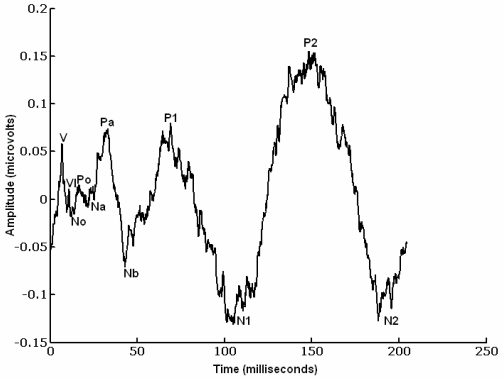

Fig. 3. CLAD deconvolved auditory evoked potential from a 10-second EEG recording. ABR, MLR and LLR components are identified.

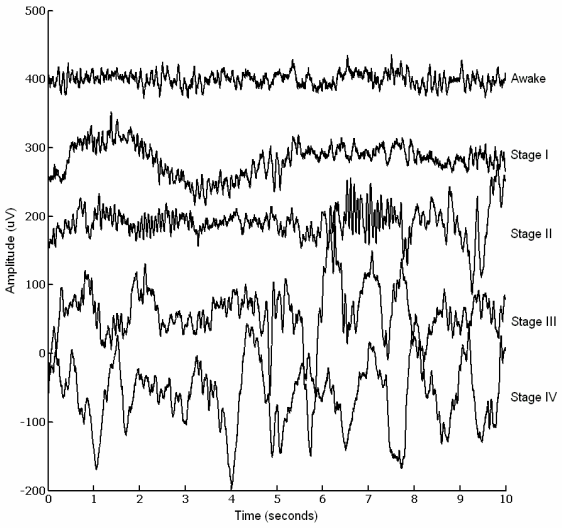

Fig. 4. Sleep EEG recordings for awake, and sleep stages I-IV. Note various EEG frequencies and wave patterns during the sleep cycle. Each EEG trace corresponds to 10 seconds.

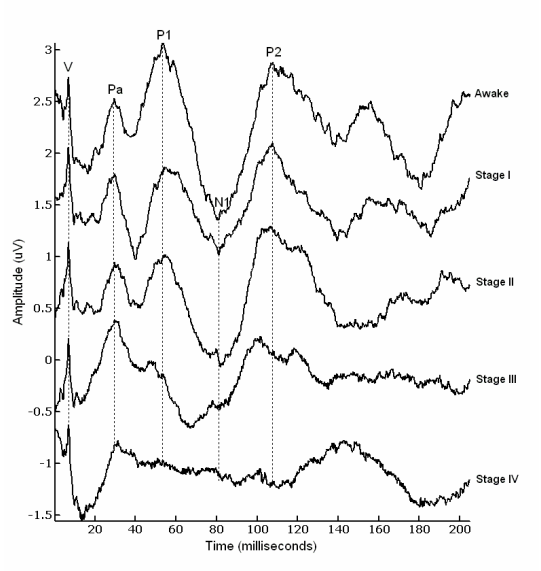

Fig. 5. Deconvolved AEP responses from EEG recordings during a sleep cycle. All major AEP components are identified.

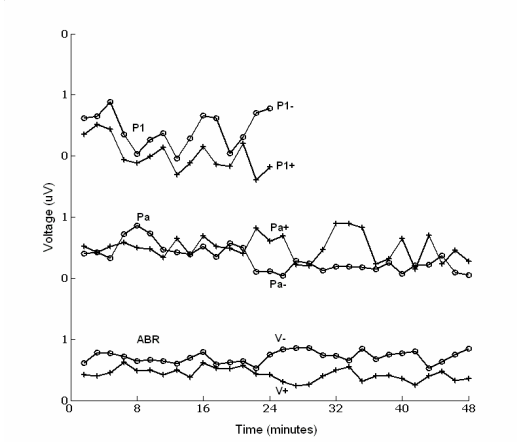

Fig. 6. Amplitudes of waves V, Pa and P1 components measured from preceding through to peak (+), and from preceding peak to through (-). After t=24 min, P1 wave disappeared and no amplitudes were measured for that component.

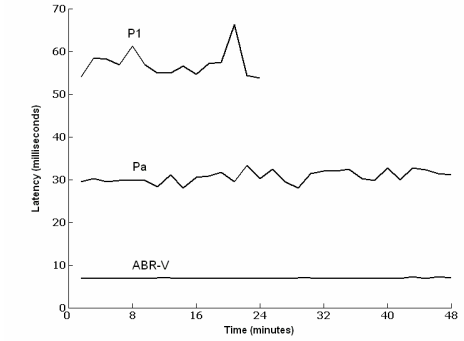

Fig. 7. Wave V, Pa and P1 peak latencies. After 24 minutes, P1 wave disappeared and no latencies were annotated for that component.

V. Conclusion

This study demonstrates the feasibility of simultaneous recording of AEP components at high stimulus rates during sleep. Using CLAD sequences and frequency deconvolution of overlapped responses, short EEG recordings can be used, reducing the large EEG variability encountered during sleep. EEG activity during sleep stages III and IV reflect various levels of arousal and information processing affecting the evoked response generation.

References

[1] S. L. Bell, R. Allen, and M. E. Lutman, "The feasibility of maximum length sequences to reduce acquisition time of the middle latency response", *J. Acoust. Soc. Am*. vol. 109, no. 3, pp. 1073-1081. 2001.

[2] J. Bohórquez, and Ö. Özdamar, "Signal-to-noise ratio analysis of maximum length sequences (MLS) deconvolution of overlapping evoked responses". *J. Acoust. Soc. Am.,* in press, 2006.

[3] R. Burkard, Y. Shi, and K. E. Hecox, "A comparison of maximum length sequences and Legendre sequences for the derivation of brainstem auditory evoked responses at rapid rates of stimulation." *J. Acoust. Soc. Am*. vol. 87, no. 4, pp. 1656-1664. 1990.

[4] R. Burkard, J. McGee, and E. J. Walsh, "Effects of stimulus rate on the feline brain-stem auditory evoked response during development I. Peak latencies," *J. Acoust. Soc. Am*. vol. 100, no. 2, pp. 978–990. 1996.

[5] R. Burkard, J. McGee, and E. J. Walsh, "Effects of stimulus rate on the feline brain-stem auditory evoked response during development. II. Peak amplitudes," *J. Acoust. Soc. Am*., vol. 100, no. 2, pp. 991–1002. 1996.

[6] K. B. Campbell, and I. M. Colrain, "Event-related potential measures of the inhibition of information processing: II. The sleep onset period". *International Journal of Psychophysiology,* vol. 46, pp. 197–214. 2002.

[7] R. E. Delgado, and Ö. Özdamar, "Deconvolution of evoked responses obtained at high stimulus rates". *J. Acoust. Soc. Am.,* vol. 115, no.3, pp. 1242-1251. 2004.

[8] R. Erwin, and J. S. Buchwald, "Middle Latency Auditory Evoked Responses: Differential Effects of Sleep in the Human". *Electroencephalogr. Clin. Neurophysiol.*, vol. 65, pp. 383-392. 1986.

[9] U. Eysholdt, and C. Schreiner, "Maximum Length Sequences - a fast method for measuring brainstem evoked responses". *Audiology,* vol. 21, no. 3, pp. 242-250. 1982.

[10] D. Z. Jiang, M. D. Brosi, X. M. Shao, and A. R. Wilkinson, "Maximum length sequence brainstem auditory evoked responses in term neonates who have perinatal hypoxia – ischemia". *Pediatric Research*, vol. 48, pp. 639-645. 2000.

[11] R. E. Lasky, J. Perlman, and K. E. Hecox, "Maximum Length Sequence Auditory Evoked Brainstem Responses in Human Newborns and Adults," *J. Am. Acad. Audiol.,* vol. 3, pp. 383–389. 1992.

[12] Ö. Özdamar, R. E. Delgado, K. V. Thombre, E. Yavuz, E., and M. Anderson, "Acquisition of ABRs at very high stimulation rate using CLAD (Continuous Loop Algorithm Deconvolution)," ARO Abstr. 40, 44. 2003.

[13] Ö. Özdamar, and J. Bohórquez, "Signal-to-noise ratio and frequency analysis of continuous loop averaging deconvolution (CLAD) of overlapping evoked potentials". *J. Acoust. Soc. Am.,* vol. 119, no. 1, pp. 429-438. 2006.

[14] T. W. Picton, S. C. Champagne, and A. J. C. Kellet, "Human auditory evoked potentials using maximum length sequences," *Electroencephalogr. Clin. Neurophysiol.*, vol. 84, pp. 90–100. 1992.

[15] A. Rechtschaffen, and A. Kales, "A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages in Human Subjects". Los Angeles: Brain Information Service/Brain Research Institute. 1968.

[16] A. R. D. Thornton, "High rate otoacoustic emissions" *J. Acoust. Soc. Am*., vol. 94, pp. 132–136. 1993.