Recording of auditory brainstem response at high stimulation rates using randomized stimulation and averaging

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The recording of auditory brainstem response (ABR) at high stimulation rates is of great interest in audiology. It allows a more accurate diagnosis of certain pathologies at an early stage and the study of different mechanisms of adaptation. This paper proposes a methodology, which we will refer to as randomized stimulation and averaging (RSA) that allows the recording of ABR at high stimulation rates using jittered stimuli. The proposed method has been compared with quasi-periodic sequence deconvolution (QSD) and conventional (CONV) stimulation methodologies. Experimental results show that RSA provides a quality in ABR recordings similar to that of QSD and CONV. Compared with CONV, RSA presents the advantage of being able to record ABR at rates higher than 100 Hz. Compared with QSD, the formulation of RSA is simpler and allows more flexibility on the design of the pseudorandom sequence. The feasibility of the RSA methodology is validated by an analysis of the morphology, amplitudes, and latencies of the most important waves in ABR recorded at high stimulation rates from eight normal hearing subjects. © 2012 Acoustical Society of America. [http://dx.doi.org/10.1121/1.4764511]

I. INTRODUCTION

The objective evaluation of hearing is currently a widely used practice in hospitals and clinics around the world. A universal newborn hearing screening is compulsory in most of the United States and it is recommended in Europe (Grandori and Lutman, 1999; American Academy of Pediatrics, 1995). Auditory brainstem responses (ABRs), along with otoacoustic emissions, are objective measurements commonly applied for hearing screening (Erenberg *et al.*, 1999; Kennedy *et al.*, 1991). ABR signals represent the electrical activity of the brainstem associated with an auditory stimulus. This biological response is described by a series of waves that occur during the first 10 ms after the stimulus. These waves are identified with Roman numerals as proposed in Jewett and Williston (1971). The study of ABR is of great interest from an audiological point of view, since it allows the analysis of some of the mechanisms involved in the process of hearing (e.g., Hall, 2007; Katz, 1994).

The methodology for an ABR recording consists of the presentation of auditory stimuli to the subject and the recording of their associated electrical response by electrodes placed on the skin in different places of the head. The low amplitude of these potentials (usually less than 1 μV at the electrodes) requires a high amplification in the recording process. Additionally, the signals are contaminated by artifacts of diverse origin, such as neuromuscular activity of the subject, noise from the amplifier, electromagnetic interference, etc. In order to reduce these artifacts, the response to a large number of stimuli is recorded. If the response to each stimulus can be assumed to be linear and time invariant (LTI), the signal-to-noise ratio (SNR) improves by averaging a large number of sweeps (e.g., Wong and Bickford, 1980; Webster and Clark, 1995).

The conventional (CONV) technique for ABR recording consists of the averaging of several sweeps whose corresponding stimuli are periodically presented, i.e., with a constant inter-stimulus interval (ISI). This technique has the important limitation that the ISI must be greater than the averaging window in order to avoid the contamination of the recording by an adjacent response (e.g., Zollner *et al.*, 1976; Kjaer, 1980). Therefore, the CONV technique cannot be used to record ABR at rates higher than 100 Hz.

The recording of ABR at high stimulation rates (higher than 80 Hz) may present a number of advantages, as reported by several authors. Thornton and Slaven (1993) and Leung *et al.* (1998) argue that the presentation of stimuli with a low ISI could reduce the necessary recording time, which is a critical parameter in certain situations such as investigating children and other non-cooperative subjects (e.g., Burkard *et al.*, 1990; Bell *et al.*, 2001). Several authors agree that the use of high stimulation rates would allow a more detailed study of the phenomenon of adaptation (e.g., Lasky, 1997; Burkard *et al.*, 1990). Leung *et al.* (1998) states that the use of high stimulation rates may help to improve accuracy in estimating the hearing threshold of a subject. Finally, many researchers have found that the use of high stimulation rates

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could be useful for detecting certain pathologies at an early stage (e.g., Don *et al.*, 1977; Stockard *et al.*, 1978; Yagi and Kaga, 1979; Jiang *et al.*, 2000; Thornton *et al.*, 2006).

Several techniques which are able to record ABR at high rates of stimulation have emerged with the intention of breaking with the limitation imposed by the CONV technique. These methods estimate the biological response through the use of pseudorandom stimulation sequences that are repeated periodically. The *jitter* of a stimulation sequence is a measure that indicates the magnitude of dispersion of the ISI. All techniques only recover the LTI-like component of the total response, while ignoring deviations from LTI behavior. However, as the stimulation rate increases, the morphology of responses changes (Bohorquez and Ozdamar, 2006). Therefore, the jitter of a stimulation sequence could be a critical parameter to be considered when assuming that each click evokes the same response (e.g., Jewett *et al.*, 2004). The most relevant techniques proposed for recording ABR at high stimulation rates are maximum length sequences (MLS), quasi-periodic sequence deconvolution (QSD), and continuous loop averaging deconvolution (CLAD).

The MLS technique was developed by Eysholdt and Schreiner (1982). In this technique, the deconvolution of overlapping responses is performed using bursts of pseudorandom pulses whose ISIs are adjusted to De-Brujin sequences. This technique has not only been used to record ABRs at high stimulation rates (e.g., Leung *et al.*, 1998; Bohorquez and Ozdamar, 2006) but also to record mid-latency auditory evoked potentials (e.g., Lavoie *et al.*, 2010) and other biological signals such as transient evoked otoacoustic emissions (e.g., Hine *et al.*, 2001; Thornton, 1993; de Boer *et al.*, 2007). The stimulation technique based in Legendre sequences (LGS) is also adjusted to the De-Brujin sequences. This methodology has also been used to obtain ABRs at high rates of stimulation. MLS and LGS present a similar performance, as reported by Burkard *et al.* (1990). The main difficulties with both methodologies are their high jitter and the restrictions imposed on the stimulation sequences.

The QSD model, developed by Jewett *et al.* (2004), describes the conditions that sequences of low jittered pulses have to fulfill in the frequency domain in order to allow deconvolution of overlapping responses at high rates of stimulation. The main difficulty with this technique resides in the search for an optimal stimulation sequence, which usually requires a high computational effort (e.g., Jewett *et al.*, 2004; Wang *et al.*, 2006). The frequency domain analysis described in the QSD model opened a new framework that has influenced the approach of other methodologies.

In the CLAD methodology, devised by Ozdamar *et al.* (2003a,b) and Delgado and Ozdamar (2004), deconvolution of overlapping responses is achieved through time-domain matrix algebra processing. A frequency domain formulation of this technique was described by Ozdamar and Bohorquez (2006). The Wiener filtering theory can be applied to the CLAD methodology to improve the SNR of the recordings (Wang *et al.*, 2006). Although the most important application of the CLAD deconvolution method is the recording of ABR, it has also been used to record electrocochleograms and auditory middle latency responses at high stimulation

rates (e.g., Bohorquez *et al.*, 2009; Millan *et al.*, 2006). The main advantage of this method with respect to MLS relies on a significant relaxing of the stimulation sequences restrictions. However, CLAD presents two important limitations: The convolution matrix, generated from the stimulation sequence, must be invertible (i.e., not singular) and the power spectral density of the stimulation sequence must accomplish the noise attenuation requirements exposed in the QSD model. Indeed, CLAD is a methodology that can be used to implement QSD (Jewett *et al.*, 2004).

The purpose of the present study is to present a new methodology that allows the recording of ABR signals at high stimulation rates using jittered stimulation sequences. We have called this methodology randomized stimulation and averaging (RSA). The RSA technique consists of the averaging of auditory responses corresponding to stimuli whose ISI varies randomly according to a predefined probability distribution. This method [for which fundamentals were described in Alvarez *et al.* (2010) including some preliminary results] is described in detail in this paper and compared with QSD and CONV in terms of quality of the responses. ABR responses obtained with RSA present a similar quality as those with QSD and CONV. In comparison with CONV, RSA allows the recording of ABR at rates higher than 100 Hz; furthermore, the restrictions imposed to QSD, CLAD, or MLS sequences are not necessary in RSA, which makes the implementation of RSA easier and allows more flexibility in the selection of the probability distribution of the ISI. This allows more control in the jitter of the sequences used for RSA. The reliability of the RSA technique has also been assessed by an analysis of the morphology, amplitudes, and latencies of the main waves in ABR recorded from eight subjects at different stimulation rates, obtaining results consistent with previous studies.

II. RSA

In contrast to the CONV stimulation technique, in which stimuli are presented at a constant period greater than the averaging window [Fig. 1(A)], the RSA technique consists of averaging auditory responses, corresponding to a burst of stimulation pulses, in which the ISI varies randomly according to a predefined probability distribution. The RSA technique involves a digital blanking process and non-uniform averaging in order to minimize the effect of the stimulus artifact in overlapped responses. The digital blanking process consists of considering null values those samples of the EEG in which stimulus artifact occurs. Figure 1(B) shows a frame of a RSA stimulation signal of ISI_{4-8}, in which the ISI randomly varies according to a uniform distribution between 4 and 8 ms. Figure 1(C) shows a histogram of the ISI for the selected random sequence. When RSA is applied, two important differences can be observed with respect to CONV stimulation: The rate of stimulation can be higher and two or more consecutive responses can be overlapped; both effects depend on the selected probability distribution of the ISI.

In order to obtain the ABR response in the RSA framework, a non-uniform averaging is applied to the raw electroencephalogram (EEG), after a digital blanking process. Let
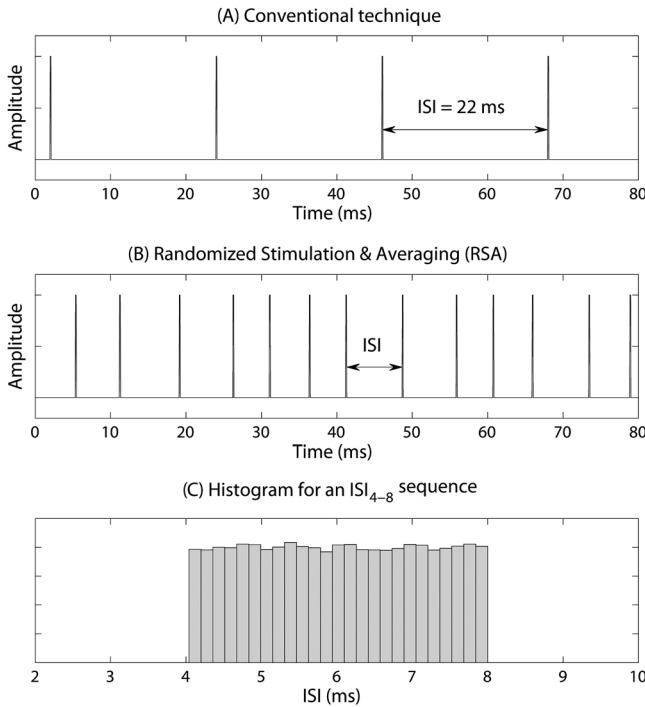
FIG. 1. (A) Example of a stimulation signal in CONV mode. Stimuli are presented at a constant period of 22 ms, greater than the averaging window ($A_w = 10$ ms). (B) Example of stimulation signal in the RSA technique at ISI_{4-8}. In this case, ISI is smaller than the averaging window. (C) Histogram of the ISI when a uniform distribution between 4 and 8 ms is considered to generate the sequence (ISI_{4-8}).

$y(n)$, $b(n)$, and $s(n)$ ($n = 1,...,N$) be, respectively, the digitized EEG, the blanking signal, and the synchronization signal (that indicates with the value of 1 the samples in which stimulation starts and 0 otherwise). For an EEG in which K stimuli are presented, the index of the samples in which each stimulus starts can be represented with $m(k)$ ($k = 1,...,K$). Therefore, $s(m(k)) = 1$. The blanking signal $b(n)$ differences valid samples of EEG (value 1) from samples contaminated with a stimulation artifact (value 0). The digital blanking process considers null values 0.2 ms before and 0.8 ms after each stimulus [Eq. (1)]. The ABR signal $\hat{x}(j)$ is estimated in RSA by averaging of the biological responses corresponding to the K stimuli presented to the subject, without considering in the averaging process those segments of EEG affected by stimulation artifact [Eq. (2)]

$$b(n) = \begin{cases} 0 & \text{if } n \in [m(k) - 0.2\,\text{ms} \cdot f_s, \\ & m(k) + 0.85\,\text{ms} \cdot f_s], \forall k \quad n = 1,...,N, \\ 1 & \text{otherwise,} \end{cases}$$

(1)

$$\hat{x}(j) = \frac{\sum_{k=1}^{K} b(m(k) + j) \cdot y(m(k) + j)}{\sum_{k=1}^{K} b(m(k) + j)}, \quad j = 1,...,J,$$

(2)

where J and N represent, respectively, the length of the averaging window and the total number of samples of the EEG. Figure 2 shows an example to illustrate the calculation of the

ABR response when RSA is applied. A real ABR response (obtained with 10 000 sweeps) was used to artificially synthesize an EEG. A stimulation sequence was generated at ISI_{8-12} (i.e., with a uniform distribution between 8 and 12 ms). Figures 2(A) and 2(B) show, respectively, the beginning of the stimulation signal and the synchronization signal $s(n)$. The synchronization signal $s(n)$ was convolved with the ABR response and white noise was added at $SNR = 13$ dB in order to obtain the synthesized EEG $y(n)$ [Fig. 2(C)]. Figure 2(D) shows the effect of the digital blanking process, $y(n) \cdot b(n)$. Those segments of the EEG with a stimulus artifact are removed from averaging. Finally, Fig. 2(E) shows the ABR response $\hat{x}(j)$ averaged according to the RSA technique. The sampling rate in this example was $f_s = 25$ kHz. Although in ABR recordings the EEGs present a typical SNR below -10 dB, in this example the synthesized EEG was contaminated with less noise in order to allow the identification of biological responses.

In contrast to the rest of the techniques able to record ABR at high stimulation rates, RSA does not perform deconvolution. In the RSA methodology, there basically exist three types of artifacts involved in the process of ABR
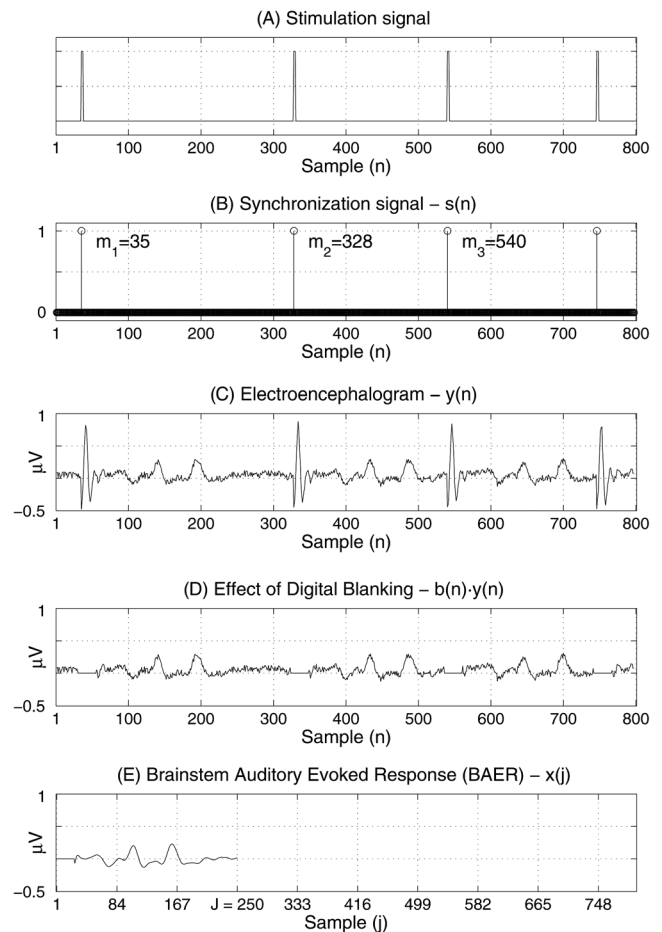

FIG. 2. An illustration of the estimation of the ABR response based on RSA. (A) RSA stimulation signal for ISI_{8-12}. (B) Synchronization signal $s(n)$. (C) Raw EEG $y(n)$ (in this example, the EEG was synthesized from a real ABR response). (D) Effect of digital blanking, $b(n) \cdot y(n)$. Segments of EEG with stimulation artifacts removed from averaging. (E) Estimation of the ABR response $\hat{x}_K(j)$. Sampling frequency: $f_s = 25$ kHz; length of the averaging window: $J = 250$ samples (10 ms).

recording: Stimulus artifact, noise unlocked with stimuli, and noise associated with overlapping responses. The digital blanking and averaging processes minimize, respectively, the effect of the first two types of artifacts. The noise associated with overlapping responses can be minimized by averaging and an adequate selection of the jitter in the stimulation sequence. The RSA technique is able to retrieve the ABR to a single click as long as the jitter of the stimulation sequence is large enough. However, very high jittered stimulation sequences could lead to obtain inaccurate ABR signals since auditory responses of different morphology would be averaged, and therefore, considered the same evoked response. The jitter of a stimulation sequence should be chosen carefully, reaching a compromise between these two aspects. Moreover, since the use of the digital blanking technique produces a non-uniform number of averaged responses inside the averaging window, we consider that an adequate jitter should allow a number of averaged responses over a threshold of the 70% of the total number of available responses all along the averaging window. Averaging a number of responses below such threshold could produce a noticeable difference in terms of quality between different segments of the response.

III. METHODS

A. Acquisition of EEG

The evaluation of the RSA method was based on the analysis of ABR recorded from different subjects. The stimulation of the auditory system was performed by 0.1 ms clicks presented at an intensity of 70 dBnHL. Zero dBnHL was established considering the threshold level (stimulation level at which the stimulus is just detectable) for a burst of clicks presented at a rate of 20 per second in a group of 15 subjects (9 male and 6 female) ranging in age between 24 and 31 yr, with no self-reported history of auditory dysfunction (normal hearing subjects). The equivalent 0 dBnHL under such typical stimulus conditions is 36.4 dB peak sound pressure level and 29.9 dB peak-to-peak equivalent sound pressure level (Burkard, 1984; Klein and Teas, 1978; Stapells et al., 1982). Duration clicks of 0.1 ms were used as stimuli in order to evoke synchronous firing of a large number of neurons, especially those in the 1000 to 4000 Hz region (Hall, 2007). The recording sessions were held in a room isolated from acoustical and electromagnetic interferences. During the process of ABR recording, subjects were seated in a comfortable and relaxed position to minimize electromyogenic noise. Auditory stimuli were presented to the subjects through standard circumaural headphones (Pro-550, Ultrasone, Wielenbach, Germany). The biological evoked responses associated with the stimuli were recorded from three Ag/AgCl surface electrodes placed on the skin at different positions on the head. Active, reference, and ground electrodes were situated at the high forehead, the ipsilateral mastoid, and on the low forehead, respectively. Interelectrode impedances were always below 10 kΩ. The biological signal was 70 dB amplified and band pass filtered (100 to 3500 Hz). Both the biological signal and the stimulation signal were sampled at 25 kHz and represented with 16 bits/sample (with a two-channel analog-to-digital con-

verter). Digital signals were processed with algorithms implemented in MATLAB (The Mathworks, Inc., Natick, MA). The recorded EEG had been digital filtered using a sixth order bandpass Butterworth filter (150 to 3000 Hz). The synchronization signal $s(n)$ had been obtained from the recorded stimulation signal. A full description of the ABR recording system can be found in Valderrama et al. (2011).

B. Recording of RSA, QSD, and CONV responses

This study involves the recording of ABR signals over a group of 8 normal hearing adults (5 males and 3 females; aged between 22 and 36 yr) using the RSA, QSD, and CONV techniques. These subjects were volunteers and were informed in detail about the experimental protocol and possible side effects of the test. A jitter of 4 ms was used in the stimulation sequences of RSA and QSD methodologies. Sweeps (20 000) were recorded from each subject using the RSA and QSD techniques at the stimulation rates corresponding to ISI_{20-24}, ISI_{16-20}, ISI_{12-16}, ISI_{10-14}, ISI_{8-12}, ISI_{6-10}, ISI_{4-8}, and ISI_{2-6}. The same number of sweeps were recorded using the CONV technique at the stimulation rates ISI_{22}, ISI_{18}, ISI_{14}, ISI_{12}, and ISI_{10}.

The RSA stimulation sequences were randomly generated with a uniform probability distribution of the ISI between two limits. RSA responses were obtained according to the procedure exposed in Sec. II. In this work the stimulation sequences in QSD (q-sequences) are composed of 16 stimuli with ISI in a range between two limits. These sequences are periodically repeated to provide the required number of sweeps. In order to obtain efficient q-sequences, for each ISI condition 3 million sequences with ISI in the specified range were randomly generated, and the magnitude of the fast Fourier transform (FFT) was evaluated for each sequence. The selected q-sequence was the one which maximizes the minimum value of the FFT magnitude in the band of interest (150 to 3000 Hz). This way the selected q-sequence minimizes the amplification of noise when deconvolution is applied to obtain the ABR responses. QSD responses corresponding to each block of 16 stimuli were averaged. The final QSD response was obtained by deconvolution and filtering of the averaged block of responses. A more detailed description of the QSD methodology can be found in Jewett et al. (2004).

A basic artifact rejection procedure has been applied to RSA, QSD, and CONV recordings. In RSA and CONV, the response to each stimulus was evaluated after the digital blanking process and those sweeps whose instantaneous voltage exceeded 10 μV were removed from averaging. In the case of QSD, the analysis was similar but estimation of the instantaneous voltage is referred to each block of 16 stimuli. The blocks with instantaneous voltage higher than 10 μV after digital blanking were not considered for deconvolution or averaging. This way, the artifact rejection procedure removes the noisiest parts of the EEG from the final ABR response.

C. Quality assessment of ABR responses

This article evaluates and compares the performance of the RSA, QSD, and CONV techniques. An objective assessment of the quality of recordings is performed in this study

through the correlation coefficient (r) methodology. This parameter points out the grade of similarity between two ABR signals. A high positive correlation coefficient would indicate a high quality ABR recording when the two signals are recorded in the same conditions (Mason *et al.*, 1977; Schimmel *et al.*, 1974; Weber and Fletcher, 1980). In comparison with the objective quality assessment methodologies for ABR recordings based on the variance ratio and multiple pre-post Z, the correlation coefficient is considered a more consistent technique to score the quality of ABR recordings (Arnold, 1985).

In order to evaluate the performance of the RSA, QSD, and CONV techniques at different stimulation rates, we have split the 20 000 sweeps of each recording into five groups of 4000 sweeps. Then, we have obtained the ABR signals in each group applying the corresponding methodology (RSA, QSD, or CONV). Therefore, 5 different ABR signals of 4000 sweeps, recorded on the same conditions, are obtained from each recording. The correlation coefficient was calculated between all possible combinations of these five ABR signals. Thus, the total number of statistics per recording is ten, that is, combinations of five elements taken two at a time. Finally, the quality of each technique in each stimulation rate can be parameterized with the mean and standard deviation of the statistics of the eight subjects in each scenario.

D. ABR amplitudes and latencies

This paper presents an analysis of the amplitudes and latencies of the main waves of ABR signals obtained using the RSA, QSD, and CONV techniques at different stimulation rates over a group of eight normal hearing subjects. The latencies and amplitudes of waves I, III, and V were measured on ABR recordings obtained using 20 000 sweeps, applying the RSA and QSD techniques at the stimulation rates ISI_{20-24}, ISI_{16-20}, ISI_{12-16}, ISI_{10-14}, ISI_{8-12}, ISI_{6-10}, ISI_{4-8}, and ISI_{2-6}, and using the CONV technique at the stimulation rates ISI_{22}, ISI_{18}, ISI_{14}, ISI_{12}, and ISI_{10}. Latencies were measured as a difference in milliseconds between the stimulus onset and the top of the peaks. Amplitudes were measured in microvolts as a difference between the top of the peak and the following trough for all waves. The mean and standard deviation of the amplitudes and latencies among the eight subjects were calculated at each stimulation rate, and the effect of the stimulation rate over amplitudes and latencies was analyzed by linear regression in the RSA technique. The results obtained in this study were contrasted with previous literature in order to test the efficiency of the RSA technique when recording real ABR signals.

IV. RESULTS

A. Selection of the stimulation sequence

The q-sequence in the QSD methodology must be chosen carefully in order to successfully deconvolve the evoked potentials. The power spectral density of an efficient q-sequence avoids frequency components near zero in the passband (Jewett *et al.*, 2004). On the other hand, RSA sequences are not affected by such restrictions. In order to evaluate the importance of the

selected sequence in QSD, ABR responses have been compared for different RSA and QSD sequences. Figure 3 shows ABRs from subject 2 involving 10 000 sweeps in the RSA and QSD techniques, using ISI_{10-14} stimulation signals. Signals A1, A2, and A3 are examples of auditory evoked potentials deconvolved by the QSD methodology using three different efficient q-sequences. These recordings are of high quality. When the former premise is not accomplished and the value of any frequency component is near zero in the passband, the noise at that frequency is increased in the process of deconvolution. Signals B1 and B2 in Fig. 3 are examples of auditory evoked potentials deconvolved by the QSD methodology using two different non-efficient q-sequences. The q-sequences used to deconvolve these signals have a component near 0 at 2.29 kHz (B1) and at 1.64 kHz (B2) and, as a result, the noise at that frequency is significantly increased. Such noise can be identified in the B1 and B2 evoked potentials despite the use of a large number of averaged sweeps. The most important waves can still be distinguished in B1 and B2 signals. However, if the q-sequence had a close to 0 component near 500 Hz, the evoked potentials would not be successfully deconvolved since the main waves of ABR have their major energy around that frequency (Delgado and Ozdamar, 1994). Graphic B3 presents the deconvolved signal using a q-sequence with a very close to 0 component at a frequency of 481.6 Hz. No evoked potentials can be identified in that signal. Signals B1, B2, and B3 show the consequences of non-efficient stimulation sequences in the QSD technique. In the RSA technique, no attention is required to the frequency components of the stimulation sequence since evoked potentials are obtained through an averaging process. Signals C1, C2, and C3 show examples of ABR responses obtained using the RSA technique with different random sequences (from the same subject, at the same stimulation level, and with the same number of sweeps on average). The most important waves
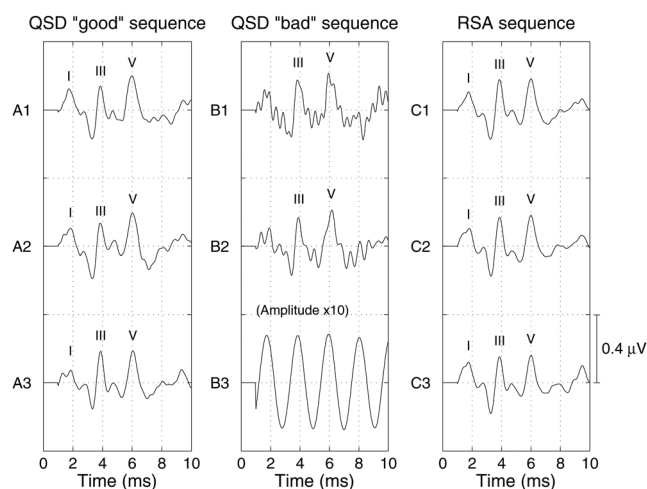

FIG. 3. Examples of ABR responses obtained using the QSD and RSA methodologies on one subject (subject 2) in the same recording conditions using ISI_{10-14} stimulation signals. Efficient (A1–A3) and non-efficient (B1–B3) q-sequences are considered in QSD. Responses obtained with 10 000 sweeps. The amplitude of the B3 signal is divided by a factor of 10 to fit onto the graph. While selection of the q-sequence is critical in QSD, no significant differences are observed for different RSA sequences (C1–C3).

Valderrama *et al.*: Randomized stimulation and averaging

can be identified in all three recordings and the quality of the recordings is similar for C1, C2, and C3, independent of the random sequence used.

B. RSA/QSD/CONV comparison

The performance of the RSA, QSD, and CONV techniques is compared in this section. Each ABR used in this study considered 4000 sweeps in the averaging process. Figure 4 shows examples of ABRs from subject 1 obtained using the RSA, QSD, and CONV techniques at different stimulation rates. Waves I, III, and V can be easily identified in these recordings at all stimulation rates, which suggests that use of such a number of sweeps is appropriate to obtain ABR recordings of enough quality at every stimulation rate considered in this study.

Table I presents the results of the quality evaluation test performed over the RSA, QSD, and CONV techniques as a function of stimulation rate. Table I shows the mean and standard deviation of the correlation coefficient (r) calculated between all possible combinations of 5 recordings of 4000 sweeps, taking 2 at a time (i.e., 10 parameters per subject) at each technique and stimulation rate. Since 8 subjects are considered in this study, the total number of parameters in each scenario is 80. Table I demonstrates the great efficiency of the three methods to successfully obtain high quality ABR signals. Table I highlights that the performance of the RSA technique is very similar to CONV but with the advantage of being able to record ABR at rates higher than 100 Hz. Table I also shows that RSA presents a slightly better performance than QSD, especially at high stimulation rates. In general terms, the quality of recordings decreases as the stimulation rate increases in all techniques. This deterioration of clarity of recordings with increasing stimulation rate is a common phenomenon as a consequence of adaptation, as has been reported in previous studies (e.g., Don et al., 1977; Kjaer, 1980; Lasky, 1984). The low standard

TABLE I. Analysis of the correlation coefficient (r) calculated between all possible combinations of 5 recordings of 4000 sweeps, taking two at a time (i.e., 10 parameters per subject) at each technique and stimulation rate. Eight subjects are considered in this study; thus, the total number of parameters in each scenario is 80. Mean (and standard deviation in parentheses) are indicated for each condition. The mean of the rate for each experiment is indicated in the first column.

Experiment	RSA	QSD	CONV
$ISI_{20–24/22}$ (45.5 Hz)	0.95 (0.04)	0.88 (0.08)	0.95 (0.05)
$ISI_{16–20/18}$ (55.5 Hz)	0.93 (0.07)	0.86 (0.09)	0.95 (0.05)
$ISI_{12–16/14}$ (71.4 Hz)	0.93 (0.06)	0.80 (0.18)	0.93 (0.06)
$ISI_{10–14/12}$ (83.3 Hz)	0.93 (0.04)	0.79 (0.18)	0.90 (0.08)
$ISI_{8–12/10}$ (100 Hz)	0.89 (0.09)	0.68 (0.29)	0.90 (0.08)
$ISI_{6–10/8}$ (125 Hz)	0.89 (0.09)	0.69 (0.22)	
$ISI_{4–8/6}$ (166.7 Hz)	0.84 (0.10)	0.68 (0.20)	
$ISI_{2–6/4}$ (250 Hz)	0.80 (0.14)	0.63 (0.25)	

deviation in all techniques at low stimulation rates points out a steady measure of quality among recordings in such conditions. The variability of quality increases with the stimulation rate in all techniques. This variation is more remarkable in the QSD technique, where its standard deviation increases to a greater extent than in RSA and CONV, which suggests that QSD is more sensitive to noise than the other two techniques.

C. Analysis of amplitudes and latencies measured with RSA

ABR recordings of 20 000 auditory responses were recorded from 8 subjects for this experiment at different stimulation rates using the RSA, QSD, and CONV techniques. Figure 5 shows the recordings corresponding to the RSA methodology. Waves I, III, and V are labeled in Fig. 5. These waves can be easily recognized at most of the stimulation rates, being more difficult the identification of waves I and III
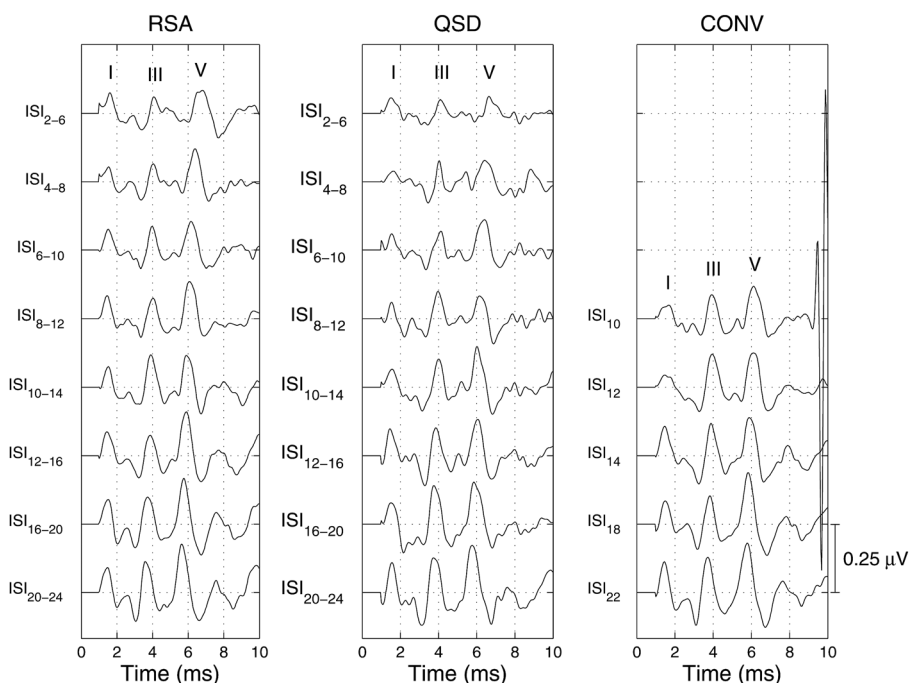

FIG. 4. Examples of ABR from subject 1 obtained using the RSA, QSD, and CONV techniques at different stimulation rates, considering 4000 auditory responses in the averaging process.
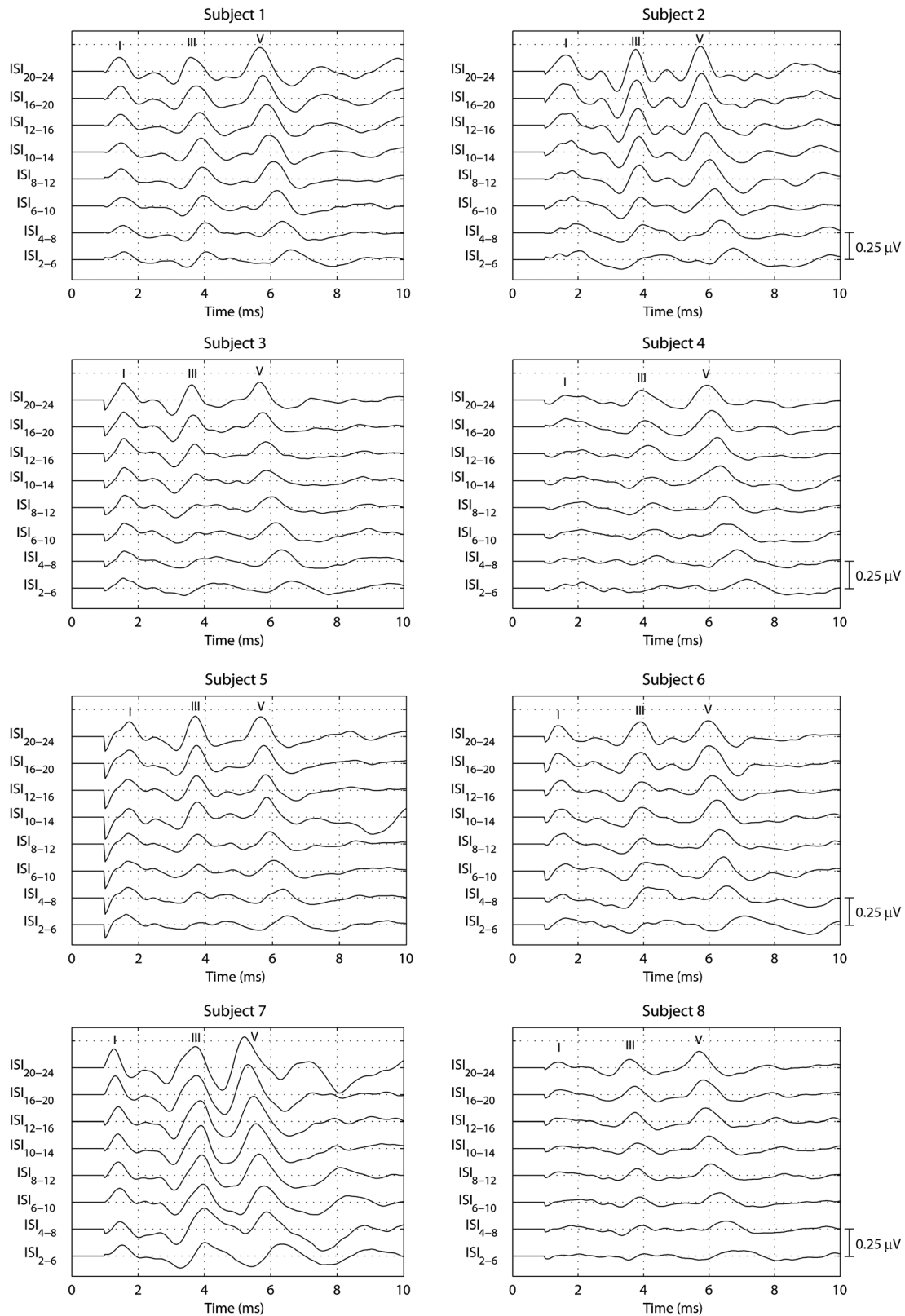
FIG. 5. ABRs recorded from eight normal hearing subjects. These responses were obtained using the RSA technique at the stimulation rates ISI_{20-24}, ISI_{16-20}, ISI_{12-16}, ISI_{10-14}, ISI_{8-12}, ISI_{6-10}, ISI_{4-8}, and ISI_{2-6}, considering 20 000 sweeps in the averaging process.

at higher stimulation rates. Wave V was identified in all subjects at all stimulation rates. Waves I and III could be identified at least in six subjects at each stimulation rate, except wave III at the stimulation rate ISI_{2-6}, which could only be

identified in four subjects. The amplitudes and latencies of waves I, III, and V were measured to perform this test. The morphology of the waves, the amplitudes, and the latencies of the most important waves in these recordings are very similar

Valderrama *et al.*: Randomized stimulation and averaging

with other studies (e.g., Yagi and Kaga, 1979; Lasky, 1984; Lina-Granade *et al.*, 1993; Leung *et al.*, 1998; Jiang *et al.*, 2009; Stone *et al.*, 2009).

Table II shows the mean and standard deviation of the latencies and amplitudes of waves I, III, and V on ABR obtained using the RSA, QSD, and CONV techniques at different stimulation rates. A comparison of the mean and standard deviation of these parameters between different techniques indicates that the latencies and amplitudes of the main waves of ABR using the RSA, QSD, and CONV techniques at all stimulation rates are statistically comparable. In addition, the results of the analysis of the amplitudes shown in Table II point out that the amplitude of all waves, on average, decreases as stimulation rate increases. Wave V presents the largest amplitude at all stimulation rates. The large standard deviation of these results points out a significant variability among subjects in terms of amplitudes. The linear regression analysis performed in the RSA technique (A_I: $r = 0.44$, $p < 10^{-3}$; A_{III}: $r = 0.49$, $p < 10^{-4}$; A_V: $r = 0.56$, $p < 10^{-5}$) indicates that the stimulation rate is a statistically significant factor that influences the amplitude of ABR signals, as stated in previous literature (e.g., Lasky, 1984, 1997; Leung *et al.*, 1998; Thornton and Slaven, 1993).

The analysis of latencies of waves I, III, and V on ABRs obtained at different stimulation rates using the RSA technique is presented in Fig. 6. Figure 6 shows the mean and standard deviation of the latencies of the eight subjects at each stimulation rate. Figure 6 also shows the correlation coefficient (r) and the p-value (probability of the null hypothesis of statistical independence between ISI and latency) of a linear regression analysis of the data. According to this analysis, the latency of wave I is hardly affected by an increase in stimulation rate ($r = -0.33$; $p = 0.018$), the
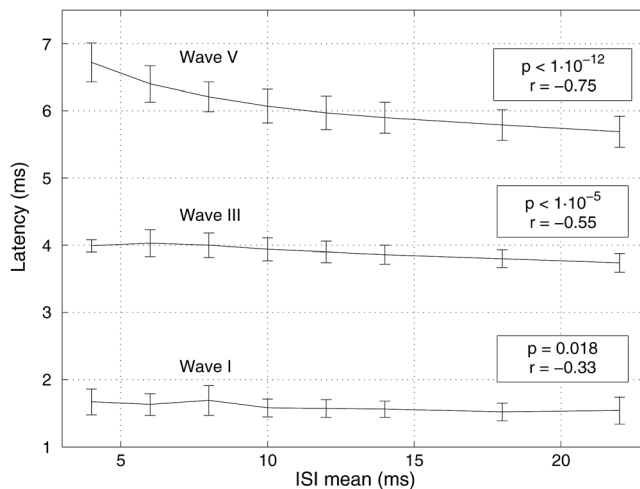

FIG. 6. Latencies of waves I, III, and V recorded using the RSA technique at different stimulation rates. The plots represent the mean values for eight subjects and the error bars represent standard deviations. The correlation coefficient r and the p-value are shown in the plots.

latency of wave III undergoes a slight shift ($r = -0.55$; $p < 10^{-5}$), and the latency of wave V is a deeper shift ($r = -0.75$; $p < 10^{-12}$). A statistically significant effect is observed in waves III and V. The correlation coefficients are relatively high in the case of waves III and V, and the dependence of latency on ISI is clear (despite the low number of subjects included in the study and the inter-subject variability). This analysis highlights that the stimulation rate influences the central components of the auditory system in a greater extent than peripheral components, as has already been reported in previous studies (e.g., Pratt and Sohmer, 1976; Yagi and Kaga, 1979; Jiang *et al.*, 2009).

TABLE II. Mean (and standard deviation in parentheses) of the latencies (L) measured in ms and amplitudes (A) measured in μV on ABR recorded from eight normal hearing subjects using the RSA, QSD, and CONV methodologies at different stimulation rates, considering 20 000 sweeps in the averaging process. The ABR corresponding to the RSA technique are shown in Fig. 5.

	RSA			QSD			CONV		
	L_I	L_{III}	L_V	L_I	L_{III}	L_V	L_I	L_{III}	L_V
$ISI_{20-24/22}$	1.54 (0.20)	3.74 (0.14)	5.69 (0.23)	1.52 (0.15)	3.79 (0.15)	5.75 (0.24)	1.54 (0.16)	3.77 (0.11)	5.75 (0.26)
$ISI_{16-20/18}$	1.52 (0.13)	3.80 (0.13)	5.79 (0.23)	1.53 (0.15)	3.82 (0.13)	5.83 (0.24)	1.54 (0.15)	3.83 (0.16)	5.83 (0.27)
$ISI_{12-16/14}$	1.56 (0.12)	3.86 (0.14)	5.90 (0.23)	1.57 (0.16)	3.89 (0.11)	5.97 (0.25)	1.57 (0.14)	3.90 (0.16)	5.94 (0.26)
$ISI_{10-14/12}$	1.57 (0.13)	3.90 (0.16)	5.97 (0.25)	1.63 (0.16)	3.94 (0.16)	6.02 (0.22)	1.58 (0.14)	3.90 (0.12)	6.02 (0.27)
$ISI_{8-12/10}$	1.58 (0.13)	3.94 (0.17)	6.07 (0.25)	1.58 (0.22)	3.97 (0.15)	6.15 (0.25)	1.59 (0.17)	3.90 (0.09)	6.04 (0.25)
ISI_{6-10}	1.69 (0.22)	4.00 (0.18)	6.21 (0.22)	1.64 (0.18)	4.05 (0.23)	6.27 (0.25)			
ISI_{4-8}	1.63 (0.16)	4.03 (0.20)	6.40 (0.27)	1.64 (0.19)	3.98 (0.03)	6.41 (0.21)			
ISI_{2-6}	1.67 (0.19)	3.99 (0.09)	6.72 (0.29)	1.65 (0.23)	4.38 (0.23)	6.73 (0.35)			
	A_I	A_{III}	A_V	A_I	A_{III}	A_V	A_I	A_{III}	A_V
$ISI_{20-24/22}$	0.24 (0.09)	0.24 (0.08)	0.28 (0.07)	0.25 (0.08)	0.23 (0.09)	0.31 (0.08)	0.24 (0.09)	0.23 (0.06)	0.29 (0.09)
$ISI_{16-20/18}$	0.23 (0.08)	0.21 (0.08)	0.28 (0.09)	0.23 (0.07)	0.20 (0.08)	0.26 (0.09)	0.22 (0.07)	0.21 (0.08)	0.28 (0.10)
$ISI_{12-16/14}$	0.23 (0.05)	0.19 (0.07)	0.25 (0.07)	0.23 (0.06)	0.20 (0.10)	0.23 (0.07)	0.24 (0.06)	0.18 (0.09)	0.25 (0.08)
$ISI_{10-14/12}$	0.21 (0.05)	0.17 (0.09)	0.24 (0.07)	0.22 (0.03)	0.16 (0.08)	0.23 (0.05)	0.16 (0.04)	0.19 (0.09)	0.22 (0.08)
$ISI_{8-12/10}$	0.21 (0.03)	0.15 (0.08)	0.21 (0.07)	0.19 (0.05)	0.15 (0.08)	0.22 (0.07)	0.19 (0.09)	0.15 (0.06)	0.21 (0.08)
ISI_{6-10}	0.17 (0.05)	0.15 (0.07)	0.18 (0.06)	0.17 (0.05)	0.12 (0.04)	0.21 (0.05)			
ISI_{4-8}	0.16 (0.03)	0.13 (0.06)	0.18 (0.08)	0.17 (0.07)	0.11 (0.03)	0.19 (0.05)			
ISI_{2-6}	0.16 (0.03)	0.11 (0.07)	0.15 (0.03)	0.15 (0.05)	0.10 (0.04)	0.12 (0.05)			

V. SUMMARY AND CONCLUSIONS

This paper describes the RSA technique, a new methodology that can be used to obtain ABR responses evoked by jittered stimuli at high stimulation rates. In this work, the performance of the RSA technique is compared with the QSD and CONV techniques. The search for an optimal stimulation sequence in QSD may accomplish frequency-domain restrictions in order to successfully deconvolve ABR. Otherwise the evoked response would be contaminated by noise in the deconvolution process (Jewett *et al.*, 2004). In contrast to these restrictions, RSA does not impose any frequency-domain constraints on the stimulation sequence, leading to an easier and more flexible implementation of RSA.

The quality of ABR responses acquired with RSA has been compared with that corresponding to QSD and CONV, in terms of the correlation coefficient between pairs of ABR signals recorded in similar conditions. This test has been performed at stimulation rates up to 250 Hz (ISI_{2-6}) in the QSD and RSA methodologies, and up to 100 Hz (ISI_{10}) in the CONV technique. The results of this study suggest: (1) That the quality degrades when the ISI decreases (when the stimulation rate increases) because of the reduction of the amplitude of the response; (2) that the quality of ABR signals recorded using RSA and CONV is very similar but with the advantage for RSA of being able to record ABR at rates higher than 100 Hz; and (3) that the quality of the responses recorded with RSA is slightly better than that of the QSD responses, especially at higher stimulation rates.

Two mechanisms could be involved in the improvement of RSA with respect to QSD. On one hand, the quality of QSD is strongly influenced by the selected sequence, since noise could be amplified at specific frequencies. In this sense, RSA responses seem to be more stable and independent of the selected stimulation sequence. On the other hand, the procedure selected for artifact rejection has different effects on RSA and QSD: Since QSD responses are obtained from deconvolution of blocks of 16 responses the artifact rejection procedure accepts or rejects each whole block depending on the evaluation of the noise affecting it. However, in the case of RSA, the response to each stimulus can be independently accepted or rejected by the artifact rejection procedure. This results in a more flexible application of the artifact rejection procedure in the case of RSA, since the portions rejected for averaging are smaller in RSA than in QSD. As a consequence, for similar SNRs of the EEG in RSA and QSD recordings, the average SNR of the accepted part of the EEG would be slightly higher in RSA than in QSD, leading to better quality in the resulting ABR responses. Furthermore, RSA provides more accurate ABR signals than CONV at stimulation rates near 100 Hz because the use of a fixed ISI will systematically contaminate the ABR with later components of adjacent responses that are time-locked with the stimulus, and therefore its effect cannot be diminished by averaging (Kjaer, 1980). The jitter of stimulation sequences in RSA or QSD may avoid this undesired effect.

A comparison of amplitudes and latencies measured on high quality ABRs obtained using the RSA, QSD, and CONV techniques at different stimulation rates indicates that ABR recordings obtained with different stimulation techniques are statistically comparable. The RSA technique was also applied to perform an analysis of the influence of the stimulation rate on the amplitudes and latencies of ABRs obtained at different stimulation rates. The results of this analysis are consistent with those reported in previous literature when other methods are applied for recording ABR at high stimulation rates.

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