Neural processing of high-rate auditory stimulation under conditions of various maskers.
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ABSTRACT
This study investigated a new auditory evoked-response, G-waves, being the response to tone pip stimuli delivered at a rate of 40/sec. These waves were detected using the QSD (Q-Sequence Deconvolution) method, which utilizes circular convolution and deconvolution on a quasi-periodic stimulus sequence to recover the transient response to each stimulus in the train. Thus, the G-waves recorded to stimuli delivered at 40/sec show the transient responses that underlie the "40Hz steady-state response". Based upon initial data showing differences in masker effects as a function of stimulus repetition rate, we studied several maskers, showing that at the 40/sec rate white noise maskers affect the waveforms, whereas music masking at the same intensity does not.

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Keywords auditory evoked potentials, auditory middle latency response, G-waves, QSD, auditory masking

1. Introduction

We initially compared the G-waves with AMLR (Auditory Middle Latency Responses) recorded with the same 30-150 Hz passband, but stimulating at 4/sec. Since we found statistically-significant waveform differences due to the presence of a continuous music masker, we undertook a parametric study of masker properties at the higher stimulus repetition rate, since the characteristics of the G-waves, being a new measure of auditory function, might be of interest.

2. Methods.

A total of eleven healthy human subjects (19-40 years of age, 4 female, 7 male) with normal hearing participated in full knowledge of all procedures, having read and signed an informed consent approved by our institutional IRB. Subjects were reimbursed for participation. Subjects were fitted with gel-based surface electrodes (10-20 array, recorded channels C4-A1, C3-A2, F3-P4 and F4-P3). Electrode pairs were impedance matched to improve common mode rejection.

Subjects were seated comfortably on a reclining chair in a sound-attenuating shielded chamber (Lindgren). Auditory stimuli were tone-pips (2 kHz, 8 msec duration, 25% skew (rapid rise, slower descent), Blackman-windowed) that were delivered binaurally (4 or 40/sec., run duration = 20 min or 7.5 min respectively) from a centrally located loudspeaker (63 dBSL) placed about 1 meter in front and above the meridian of the reclining subject. Subjects were asked to attend to this stimulus in all conditions. The stimulus sequence jittered +/-12% around 40/sec, had a duration of about 500 ms, and was continuously outputted (100% duty cycle) creating a circular average.

Masker stimuli were delivered from an eccentrically located loudspeaker placed about 30 degrees off the midline to the left and below the subject's meridian. Auditory evoked potentials were recorded from the four bipolar channels (16-bit A/D accuracy, 48 kHz per channel), averaged, and G-waves recovered using Q-sequence deconvolution (QSD, Abratech Corp.) method (Jewett et al., 2001, 2002) . Resultant data was filtered (30-150 Hz) then averaged over two trials for each comparison. For purposes of display and analysis, data recovered from each independent channel was vector-summed (see Figure 1B). The choice of a vector summation of all recorded channels is particularly useful for initial surveys of far-field responses because a single channel may not detect all dipolar activity within the volume (see Martin et al., 1987; Sininger et al., 1987). For each quad vector, peak amplitudes and latencies-to-peak were measured for each G-wave using an automated analysis program developed in-house (IGOR Pro Carbon, Wavemetrics). All latencies are measured from 5 ms before the onset of the tone-pip. The exact time of stimulation within a tone-pip is not readily ascertained, but the pips were the same throughout all data runs. Statistical significance was assessed using the Wilcoxan matched-pairs signed-rank test (Prism, GraphPad software, Inc.).

Experimental series. Based upon the results of the first experiments (q.v.), we elected to parametrically study masker frequencies, as well as any possible differences between music and white noise. The various conditions are listed in Table 1.

TABLE 1

Paradigm	Experimental condition	Description	Abbreviation
#1	Control	Auditory stimulus alone	ST(ST)
#2	CD Full spectrum	Music (CD) without filtering	CDFS(ST)
#3	CD band reject	CD filtered to remove 1-3 kHz frequencies	CDBR(ST)
#4	CD band pass	CD filtered to include only 1-3 kHz frequencies	CDBP(ST)
#5	White noise full spectrum	Full spectrum white noise (WN)	WNFS(ST)
#6	White noise band reject	WN filtered to remove 1-3 Khz frequencies	WNBR(ST)
#7	White noise band pass	WN filtered to include only 1-3 kHz frequencies	WNBP(ST)

A Krohn-Hite analog filter (set for 24 dB/octave roll-off) was used to adjust the passband of the masking stimuli. White noise (to 20 kHz) was created by a Bruel & Kjaer Type 1405 Noise Generator. The music-masker intensity was 16 dBSL at a 4/sec stimulus rate, and 23 dBSL at the 40/sec rate, in an attempt to compensate for possible middle-ear contractions at the higher rate of tone-pip stimulation. The intensity of the white noise masker was 23 dBSL for all conditions. The music masker was computer-generated "Techno" music filtered as described in Table 1.

3. Results.

The fundamental difficulty with auditory stimuli presented at high rates ($\geq$ 20/sec) lies in the overlap of the recorded electrical response in the AMLR latency range (filters 30-150 Hz). This difficulty is overcome by QSD, which shows transient evoked G-wave responses lasting about 80 ms, despite the fact that the stimuli occur about every 25 ms at

40/sec (Figure 1). The initial positivity recorded on a single bipolar channel, is termed G0 and represents a waveform due to a "leaky integrator" that includes the classic auditory brainstem responses (ABR inset, Fig.1A).

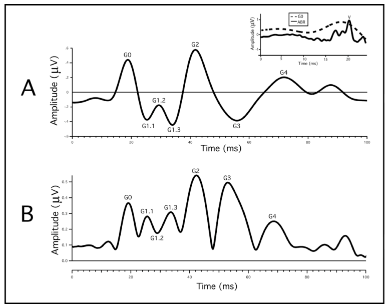

Figure 1. G-wave recordings. A. Representative response recorded from one channel (electrode pair C3-A2), showing the naming convention. [inset: G0 (filtered 30-150 Hz, solid line) represents a "leaky-integrator" measure of the auditory brainstem response (ABR, dashed line, filtered 120-2000 Hz) due to the G0 filtering.] B. Quad vector of 4 bipolar channels.

Initially we studied the effects on G2 amplitude and latency of the presence of the music masker, studying both the 4/sec AMLR and the 40/sec G-wave. In one subject the results were so noisy that the comparison could not be made. In the remaining 10 subjects, this pilot study showed 6 subjects in which there was a difference between stimulus alone and stimulus plus masker. In the same subjects, only one showed a difference when the stimulation rate was 40/sec. When this 2x2 data was analyzed using Fisher's Exact test, the probability was 0.027. This significant rate-difference motivated us to devise a parametric study of masker effects.

Unfortunately, with a research design involving 6 waves, and at least six comparisons against the "no masker" control condition, the Bonferroni correction is p= 0.05/36 = 0.0014. Thus, this study can be considered only as an exploratory, pilot study looking for trends.

We tested each of the seven conditions (experimental series of Table 1) and no condition, when compared with the "no masker" condition, reached the Bonferroni p-level. No significant effect on either amplitude or latency was noted in any condition using a music masker (conditions 2-4). Between subjects there was a tendency for early G-waves (G0-G1.3) to be reduced in amplitude in the presence of full-band white noise, and a notable reduction in waves G3 (81±5.7% control, p<0.1) and G4 (84±5.4% control, *p*<0.05). The greatest effects were seen in the presence of the band-reject the white noise masker (WNBR, see Figure 2), where peak amplitudes were reduced in G0 (81±7.9% control, *p*<0.05), G1.3 (73±7.9% control, *p*<0.01), G2 (85±6.8% control, *p*<0.05) and G3 (86±6.2% control, *p*<0.05). Under no conditions were significant changes in latency noted when the data for all subjects was considered.

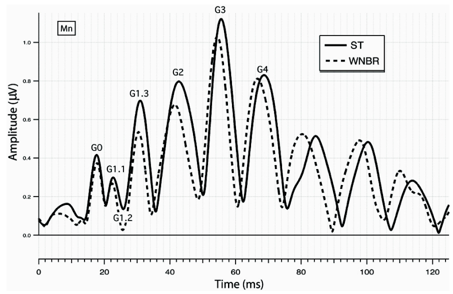

Figure 2. The recordings showing the response in one subject to the conditions in which the greatest reduction in G-wave responses were noted between subjects: responses in the presence of a band-reject white noise (WNBR) masker. No significant shifts in latency-to-peak were noted when all subjects were considered.

4. Discussion

The initial observation, that a music masker seemed to have little effect at 40/sec although there was an effect at 4/sec, has been confirmed by our study of the seven conditions of Table 1. We found no consistent effects of the music masker, compared with the "no masker" condition.

White noise masking interfered with G-wave processing to a greater extent than music. There was a tendency for G0 to be reduced in the presence of white noise masking, and this effect was largest in the WNBR condition. These results are entirely consistent with masker effects that are in the brainstem, though there are also effects in G3 and G4. Based on some preliminary results using magnetoencephalography, we believe that G2 represents primary auditory cortex. Hence, there are effects due to masking that may occur in secondary cortex at the 40/sec stimulation rate.

Our results suggest that there may be differences in auditory processing as a function of repetition rate.

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BIOSKETCH

Linda J. Larson-Prior received her Ph.D. in neurobiology in 1980. She did her postdoctoral work in electrophysiology at Northwestern University College of Medicine. She then took a research faculty position at the University of Chicago, and is currently Professor of Neuroscience at Touro University College of Osteopathic Medicine and senior scientist at Abratech Corporation, where her research focuses on auditory evoked responses in human subjects.

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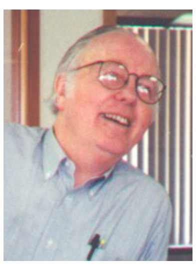

Don L. Jewett received his M.D. from UCSF (University of California, San Francisco) in 1960 and his D. Phil. from Oxford University in 1963. He went on to do postdoctoral work in neurophysiology at Yale where he did early studies of the ABR in cats. In 1964, he joined the UCSF faculty where he did early ABR studies in humans, and studied the 3-CLT in animals. He is currently the Director of Research at Abratech Corporation and Professor Emeritus at UCSF.