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EARLY EVOKED POTENTIALS IN PATIENTS WITH ACOUSTIC NEUROMA †

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In the process of growth, acoustic neuromas initially produce mechanical distortions of axons which may reversibly interfere with normal axonal functions. Later the tumor may produce disruption or actual destruction of axons. At any moment the degree of functional impairment of auditory nerve represents the sum of these effects. Early in the development of the neuroma the functional impairment is often difficult to assess with behavioral (audiometric) tests. However, the disparity between thresholds for continuous and intermittent stimulation, characteristic of Type III Bekesy tracings, can provide an indication that impairment exists (Jerger 1963).

With auditory nerve pathology, perceptual responses to intermittent stimulation are particularly sensitive to the interval between stimuli (Davis, 1962). A gradual deterioration of threshold may appear if this interval becomes less than 400 msec. Deterioration accelerates abruptly and a stable threshold can no longer be maintained if the inter-stimulus interval (ISI) becomes less than some 'critical' duration. The magnitude of this 'critical off-time' varies with frequency and intensity, however it appears independent of stimulus duration (Dallos and Tillman 1966; Jerger and Jerger 1966).

The brain-stem evoked potential (BSR) varies with parameters such as these. Under normal conditions, brief transient ('click') stimulation elicits a series of 5—7 waves with characteristic latencies and morphology, all appearing within 10 msec (Picton et al. 1974). The effects of precipitous high-frequency hearing loss (Davis and Hirsch 1974) and the effects of masking with variously filtered, continuous-noise on the latency and amplitude of wave V (Hecox 1974) indicate that this response arises from middle and high frequency fibers with little or no contribution from low frequency fibers. The sensitivity to rise-time but not to duration or fall-time of the stimulus indicates that this is an 'onset response' (Hecox et al. 1974). Stimulation with brief phase-locked tone-bursts also evokes a series of waves, the sum of which can resemble the acoustic stimulus, yielding the so-called human 'frequency-following response' (FFR). Based on evidence from audiometric studies with acoustic neuroma, one would anticipate marked distortion in the BSR if the magnitude of ISI becomes less than the 'critical off-time'. One would also predict that these effects would be more marked with tone bursts which represent limiting cases of iterative stimulation (Daly et al. 1976).

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Methods

We have studied four patients with acoustic neuroma subsequently confirmed at operation; two patients were also re-examined twelve days after the initial studies. In each patient, audiometric tests were carried out immediately before the evoked potential studies.

Acoustic stimuli consisted of 500 msec square waves presented at ISI of 320, 80 and 63 msec, and of 250 or 500 c/sec coherent tone-bursts 14 msec in duration with 5 msec rise-fall times presented at ISI of 180 msec. Stimuli were presented monaurally to each ear at 50, 60 and 70 dB SL, re: ISI 320 msec for clicks and 180 msec for tones. We used MX41-AR cushions attached to a coupler system (Gerken et al. 1975) designed to isolate the patient from the electrical stimulus applied to the driver (Telephonics, TDH 49). This coupler introduced an echo which extended the duration of the stimuli by several milliseconds.

EEG was recorded from gold electrodes affixed at C_z, A_1 and A_2 of the 10—20 system. A ground electrode was placed on one forearm. Recordings were made using vertex-earlobe deviations; in addition, recordings were made from each earlobe and the vertex using a common sterno-spinal reference electrode (Stephenson and Gibbs

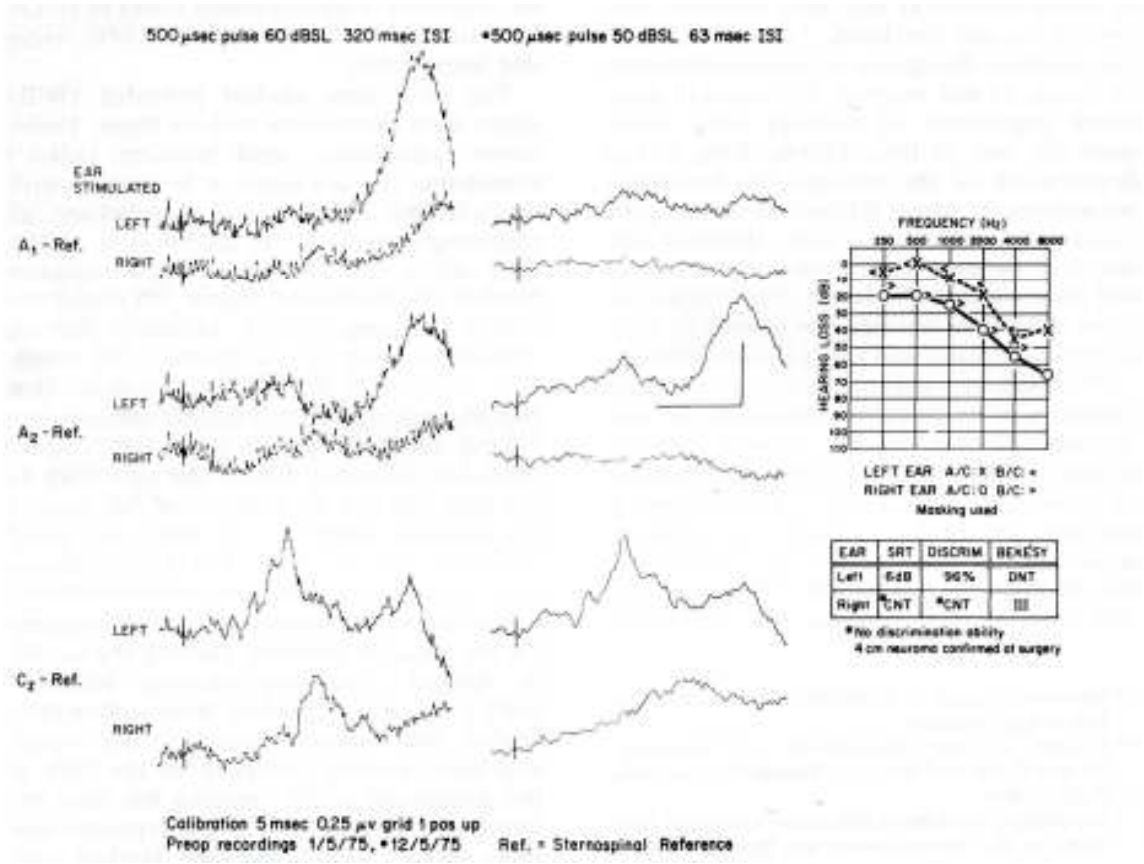

Fig. 1. Referential recordings from Case 1, showing the effect of ISI on click-evoked potentials. Vertical line marks acoustic stimulus. Audiometric data are shown to right. A/C, air conduction; B/C bone conduction; SRT, speech reception threshold; Discrim, speech discrimination score.

1951; Lehtonen and Koivikko 1971; Wolpaw and Penry 1975). EEG was amplified with Tektronix 122 amplifiers modified to band pass 1 c/sec to 3.5 kc/sec and cascaded to provide an overall gain of 10^8. The amplified EEG was digitized and summed on a Nicolet 1072-4 Signal Averager. Summed responses were traced with an X-Y plotter (Mosley 2D2AM). Each click-evoked response consisted of 2048 individual potentials; each tone-evoked response of 1024.

Results

General

Although all subjects initially perceived the click and the tone-burst simuli, each showed markedly altered evoked potentials with stimulation of the ear ipsilateral to the lesion. The alterations evident with tone-burst stimuli did not correlate with low frequency threshold sensitivity in that ear. These alterations persisted in the two patients who were retested.

Case 1. A 58-year-old woman had a right acoustic neuroma. Pure tone audiometry showed a mild high frequency sensorineural hearing loss in the left ear and a mild to moderate sensorineural hearing loss in the right ear. The patient was unable to discriminate speech in the right ear. Bekesy audiometry showed a Type III tracing in that ear, and the patient also exhibited significant tone decay.

With clicks presented to the left ear BSR were well-defined; with clicks at ISI of 320

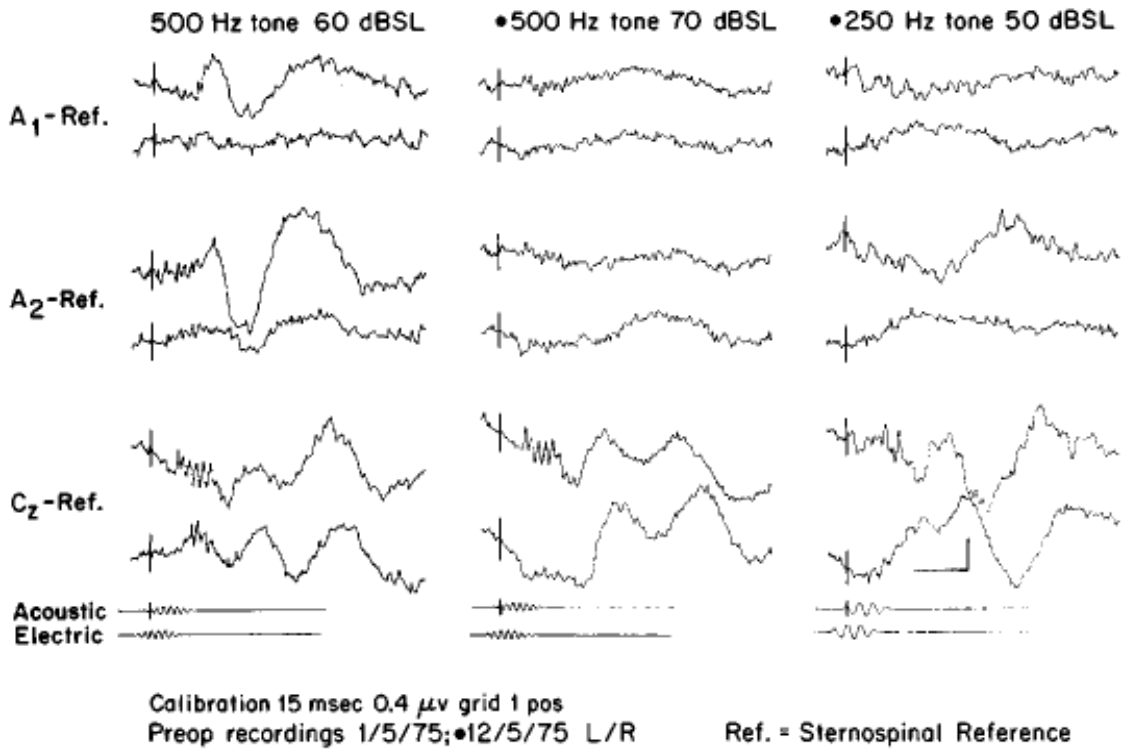

Fig. 2. Tone-evoked potentials recorded from Case 1 using a common sterno-spinal reference electrode. In each pair the upper recording is from left ear stimulation and the lower recording from right ear stimulation. Averaged acoustic stimuli, recorded using a condenser microphone and an artificial ear, illustrate delay and brief low-amplitude echo introduced by the acoustic coupler. Note several peaks in the C_z-Ref derivation following right ear stimulation at 500 c/sec (60 dB SL). Attenuation persisted over testing sessions on separate days.

msec presented to the right ear BSR were attenuated, becoming virtually inapparent at ISI of 63 msec (Fig. 1).

Responses to tone-bursts presented to the left ear were well defined. These responses appeared largest in voltage at C_z (Fig. 2);ipsi-lateral-contralateral amplitude differences were evident with the A_rA_2 derivation (Fig. 3). The 250 c/sec stimuli elicited a response with peaks at 2 msec intervals. Differences between the onset of the 250 and 500 c/sec responses were not substantially greater than those which factors such as stimulus rise-time might produce (Figs. 2 and 3).

Responses to tone-bursts presented to the right ear were markedly altered. The responses to 250 c/sec stimuli contained a sinusoidal wave form which occurred later than the FFR and which was not apparent in the responses to left ear stimulation (Fig. 3).

Case 2. A 35-year-old man had a right acoustic neuroma. Pure tone audiometry showed a slight high frequency sensorineural hearing loss at 4000 c/sec in the left and a mild sensorineural hearing loss in the right ear. Speech audiometry gave normal findings in the left ear; the patient was unable to discriminate speech in the right ear. Bekesy audiometry showed a Type III tracing in the right ear; the patient also exhibited significant tone decay.

BSR for clicks presented to the left ear were well-defined; BSR for clicks presented to the right ear were markedly attenuated. With

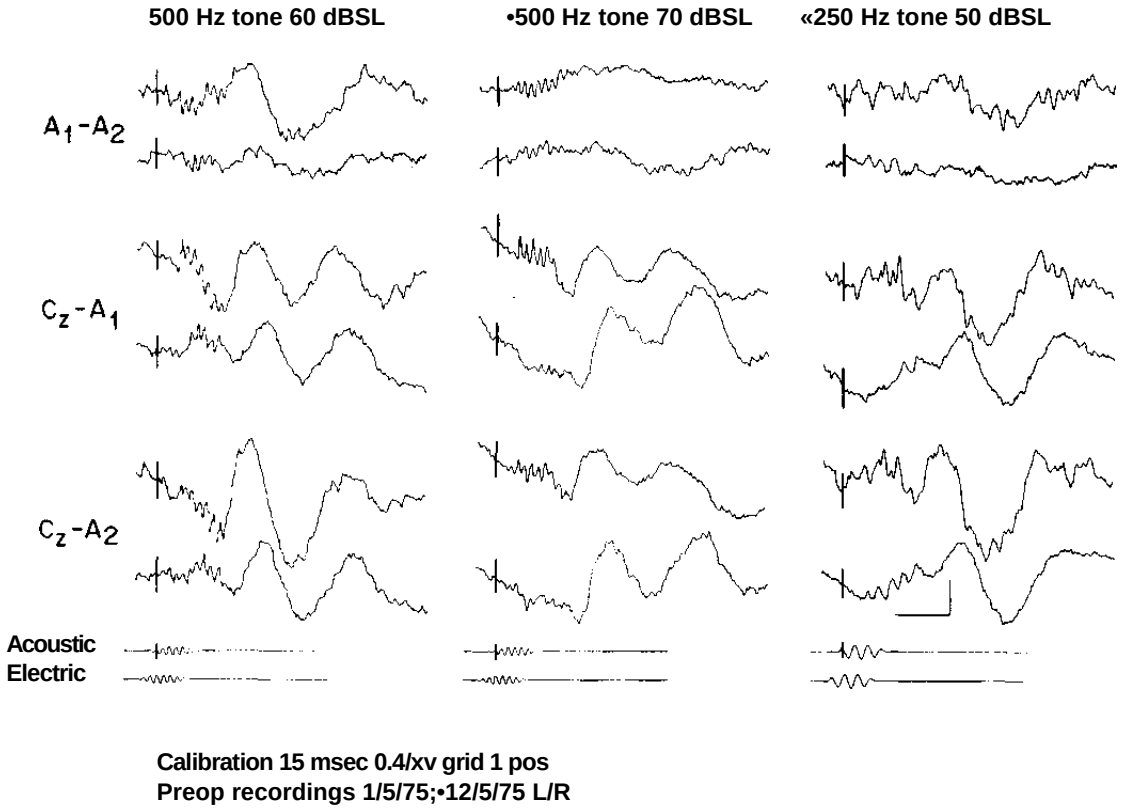

Fig. 3. Tone-evoked potentials derived from referential recordings in Fig. 2 (Case 1) by computer subtraction of digitized responses. In each pair, the upper recording is from left ear stimulation, the lower recording from right ear stimulation. Peaks appear at 2 msec intervals in C_z-A_1 and C_Z-A_2 derivations following left ear stimulation at either 250 or 500 c/sec. In contrast, a sinusoid appears in A_1-A_2 and later in C_Z-A_2 derivations, but not in C_z-A_1 derivation following right ear stimulation at 250 c/sec.

tone-bursts at lower intensities, a well-defined response could be observed after left ear stimulation but not after right ear stimulation. Stimulation of the impaired ear at higher intensities elicited a response resembling the cochlear microphonic potential (Sohmer and Pratt 1976). This response began and ended earlier than did the FFR from the unimpaired ear (Fig. 4). This response remained unchanged over 8 runs in 2 separate testing sessions.

Case 3. A 31-year-old man had a left acoustic neuroma. Two weeks previously, audio-metry had shown impairments consistent with acoustic neuroma. However, on the day of our study pure-tone audiometry, speech reception thresholds and speech discrimination scores showed normal findings in both ears. Acoustic reflexes were elevated at 2000 and 4000 c/sec, and significant reflex decay was observed in the impaired ear.

For clicks presented to the right ear BSR were well-defined; for clicks presented to the left ear BSR were markedly attenuated at shorter ISI. For tone-bursts presented to the right ear responses were well-defined, but for tone-bursts presented to the left ear responses were markedly attenuated (Fig. 5).

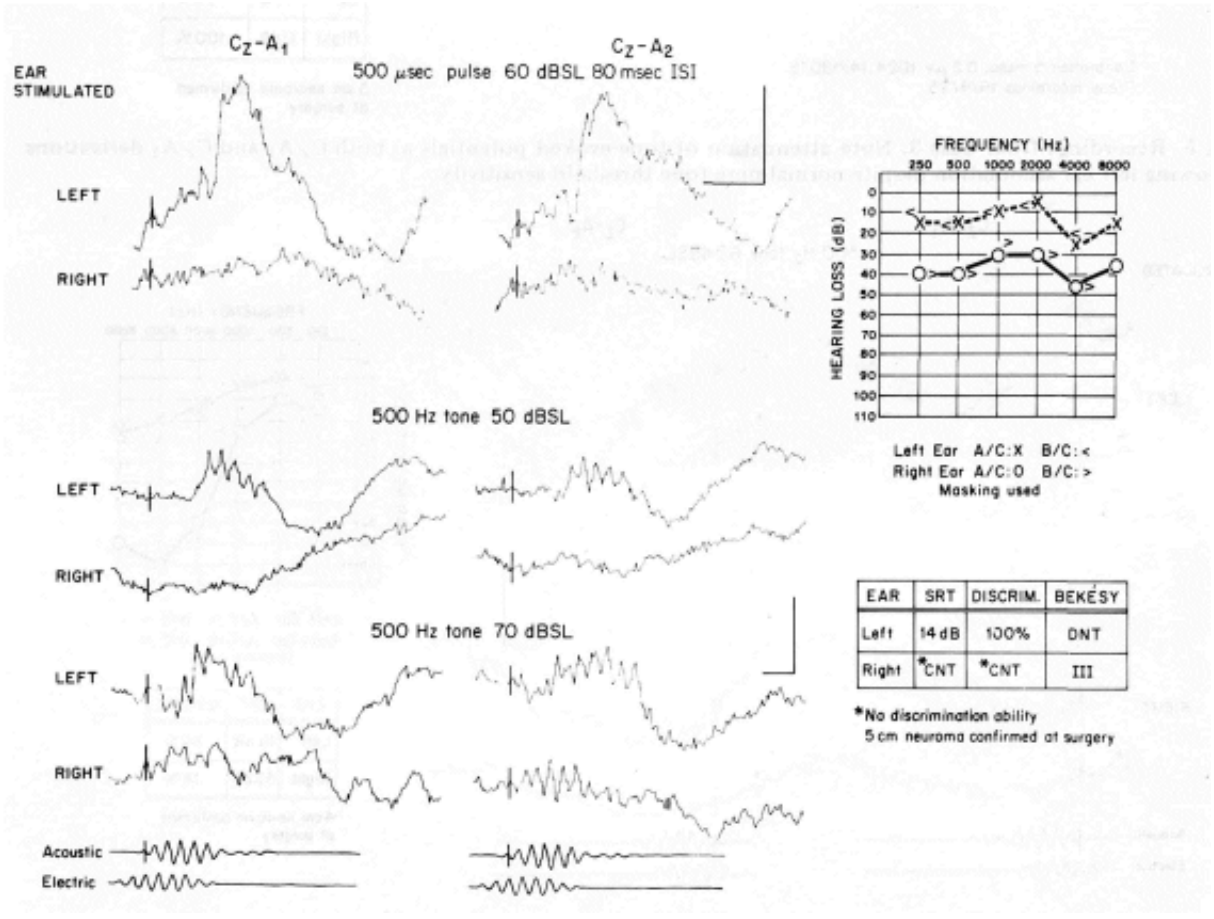

Fig. 4. Recordings from Case 2. Note response resembling cochlear microphonic potential in bottom tracings. This potential appeared after left ear as well as right ear stimulation.

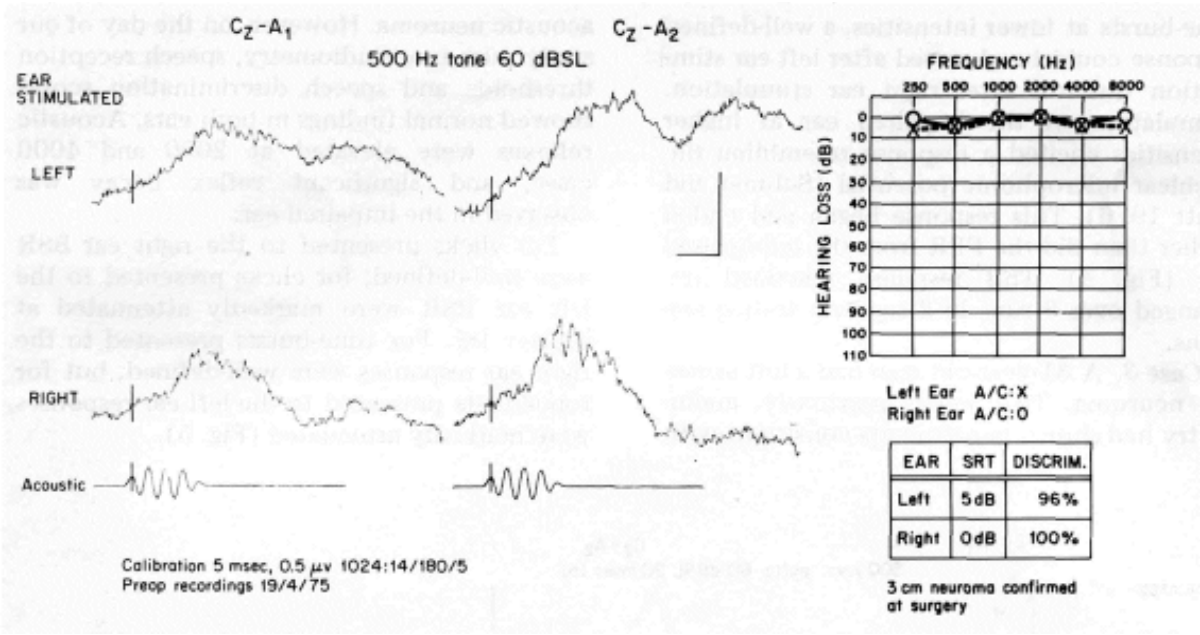

Fig. 5. Recordings from Case 3. Note attenuation of tone-evoked potentials at both C_Z-A] and C_Z-A2 derivations following left ear stimulation despite normal pure-tone threshold sensitivity.

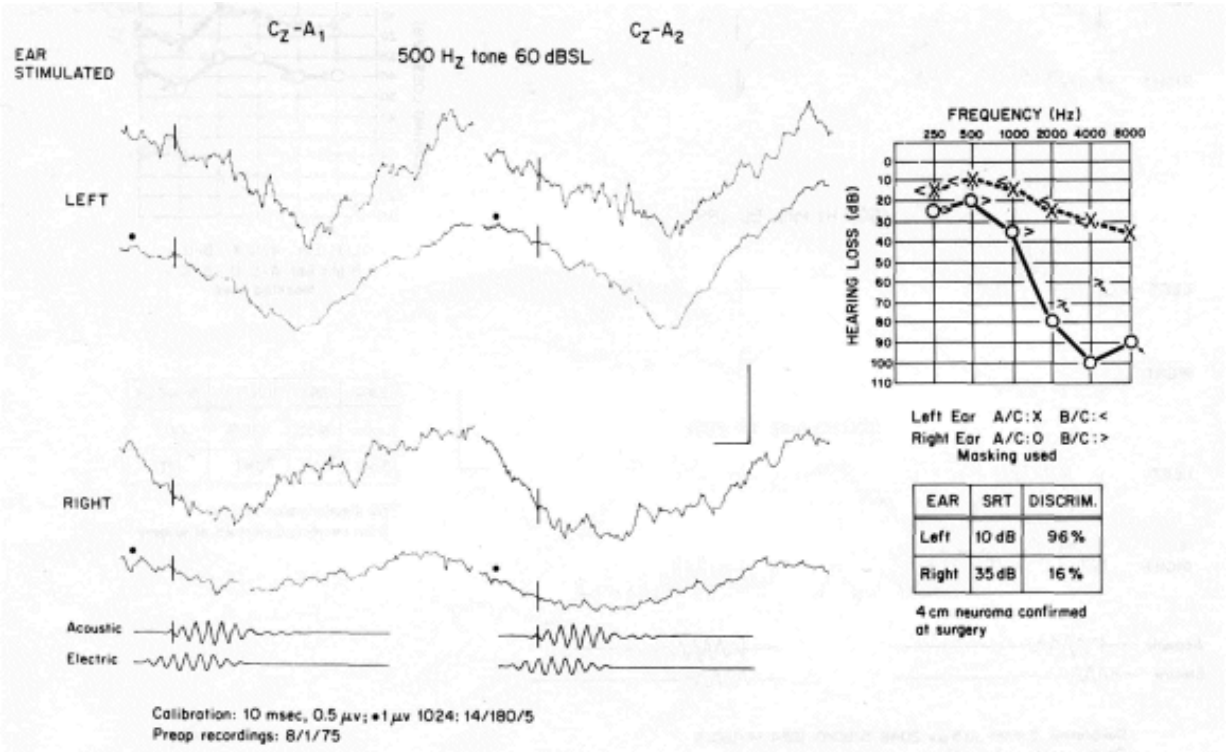

Fig. 6. Recordings from Case 4. Note attenuation of tone-evoked potentials at the C_z-Ai and C_Z-A_2 derivations after left ear and after right ear stimulation. The neuroma was large enough to produce evidence of brain stem dis--placement.

Case 4. A 48-year-old woman had a right acoustic neuroma of sufficient size to produce evidence of brainstem displacement both clinically and on posterior fossa contrast studies. Pure tone audiometry showed sloping sensorineural hearing loss, mild in the left ear and mild to severe in the right ear. With speech audiometry the left ear was within normal limits, but the right ear showed severely impaired speech discrimination.

BSR to stimulation of either ear were consistently attenuated, more so with stimulation of the ear ipsilateral to the lesion (Fig. 6).

Discussion

These studies suggest that BSR may provide a stable, independent, noninvasive measure of auditory nerve function useful in the early detection of acoustic neuroma. Early in the development of an acoustic neuroma, results of behavioral (audiometric) tests may be variable or indeed misleading; however, alterations in BSR occur despite such behavioral fluctuation as was seen in Case 3. The ability to record cochlear potentials by far-field technique also permits evaluation of cochlear integrity. Further, BSR may provide information useful in determining size of the lesion and the possibility of brainstem displacement, as was seen in Case 4. Finally, recording of BSR requires only minimal cooperation by the patient.

These preliminary findings encourage the development of families of stimuli which selectively exploit features of behavioral tests. For example, the use of click stimuli permits variation of the interstimulus interval to induce alterations in evoked potentials at shorter ISI. Since with far-field techniques cochlear potentials are apparent in response to low-frequency sounds (Sohmer and Pratt 1976), tone-bursts may permit evaluation of cochlear function (Elberling and Salomon 1973). These two types of stimuli might be combined into a single stimulus type consisting of coherent bursts of two or three cycles at appropriate frequencies.

The findings of the present study also contribute to an understanding of the so-called human FFR. On stimulation of the unimpaired ear (Fig. 3) the amplitude-phase differences observed in the A_1A_2 derivation are consonant with observations on ipsilateral-contra-lateral amplitude differences following monaural stimulation in normal subjects and in patients with unilateral hearing-loss (Daly et al. 1976). Both bipolar (vertex-ear) and referential recordings from the vertex reveal similar morphology in the responses at 250 and 500 c/sec. Although the responses at both frequencies exhibit a periodicity of 2 msec, the 250 c/sec responses do not correspond with the morphology of the acoustic stimulus, a true sine wave. The amplitude differences which appear between alternate peaks at 250 c/sec are inapparent at 500 c/sec. (Figs. 2 and 3). Comparable differences in the spatial and temporal distribution of potentials evoked by clicks have been described by Picton et al., (1974).

The responses observed after stimulation of the impaired ear indicate that neither the presence of the response, nor its amplitude and 'latency' relate to behavioral threshold sensitivity. In fact, in Case 3, pure-tone threshold sensitivity was normal for those frequencies of tone-bursts stimuli which revealed markedly attenuated FFR. In all cases, alterations of BSR appeared to correlate better with ISI. Because peaks did appear in the tone-evoked potential (Figs. 2 and 3) it seems unlikely that the altered FFR results solely from temporal dispersion attenuating the averaging process. However, if the successive waves of the tone-burst stimulus act as individual stimulus events, then the duration of a single cycle could be viewed as the ISI. These findings would be compatible with the observations of Hecox et al., (1974) that the BSR is an 'onset response' and that rise-time is a critical feature of the stimulus.

In Case 1 stimulation of the impaired ear at 250 c/sec revealed a sinusoidal form in A_1A_2

and C_Z-A_2 derivations but not in C_z-A_1 (Fig. 3). This response has a different spatial and temporal distribution and different morphology than the so-called human FFR. The hypothesis that FFR results from the 'collective activity of phase-locked single units' in a 'compact neural source' (Gerken et al. 1975) fails to explain these findings. However, this sinusoidal form closely resembles the response reported by Davis and Hirsch (1974) in normal subjects when high-pass noise was used for masking. Presumably, in recordings from normal subjects under circumstances designed to elicit FFR, such responses are obscured by the earlier and high amplitude activity from other sources.

Given these results a parsimonious hypothesis would view the tone evoked potential as a summated response consisting of a component reflecting response to iterated stimuli, in which each wave of the tone burst constitutes a stimulus event, and a component more closely reflecting the locus of activity on the basilar membrane. We feel that a more non-committal term than the 'human FFR' should be used to designate these responses.

Summary

Using clicks with varying interstimulus intervals and coherent tone-bursts, early components of the auditory evoked potential (brain stem responses) were studied in four patients with confirmed acoustic neuroma. Abnormalities in responses appeared with shorter interstimulus intervals and with tone-bursts delivered monaurally to the involved ear; bilateral alterations occurred in one patient with brain stem displacement. The results indicate that BSR can provide a stable, independent, noninvasive measure of auditory nerve function useful in the early detection of acoustic neuroma. The results contribute to the understanding of the so-called human FFR.

Resume

Potentiels evoques precoces chez des malades avec neurinome de racoustique

A 1'aide de clicks avec intervalles interstimulations variables et bouffees sonores coherentes, les composantes precoces du potentiel evoque auditif (reponses du tronc cerebral) ont ete etudiees chez 4 malades atteints de neurinome de 1'acoustique confirme. Les anomalies des reponses apparaissent pour les intervalles interstimuli plus courts et pour des salves de bruits delivrees de fagon monaurale du cote de la lesion; des alterations bilaterales one ete observees chez un sujet avec deplacement du tronc cerebral. Ces resul-tats indiquent que les BSR peuvent fournir une mesure stable independante, specifique de la fonction du nerf auditif, utile dans le detection precoce du neurinome de 1'acoustique.

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References

Dallos, P.J. and Tillman, T.W. The effects of parameter variations in Bekesy audiometry in a patient with acoustic neuroma, JSHR, 1966, 9: 557—572.

Daly, D.M., Roeser, R.J. and Daly, D.D. Early evoked responses in patients with acoustic neuroma. J. Acoust. Soc. Amer., 1976, 59: S17.

Daly, D.M. Roeser, R.J. and Moushegian, G. The frequency-following response in subjects with profound unilateral hearing loss. Electroenceph. clin. Neurophysiol., 1976, 40: 132—142.

Davis, H. A functional classification of auditory defects. Acta Oto-rino-laryng. Belg., 1962, 71: 692-704.

Davis, H. and Hirsch, S.K, Interpretation of the human frequency-following response. J. Acoust. Soc. Amer., 1974, 56: S63.

Elberling, C. and Salomon, G. Cochlear microphonics recorded from the ear canal in man. Acta Oto-laryng. (Stockh.), 197, 75: 478—495.

Galambos, R. and Hecox, K. Clinical applications of the human brainstem responses to auditory stimuli. In J. Desmedt (Ed.), Proceedings of the international symposium on cerebral evoked potentials in man, Oxford University Press, New York, 1975.

Gerken, G.M., Moushegian, G., Stillman, R.D. and Rupert, A.L. Human frequency following responses to monaural and binaural stimuli. Electroenceph. clin. Neurophysiol., 1975, 38: 379—386.

Hecox, K. Frequency specificity of brainstem evoked responses in man. J. Acoust. Soc. Amer. 1974, 56: S63.

Hecox, K., Squires, N. and Galambos, R. The dependence of human brainstem evoked potentials on signal duration and rise-fall time. J. Acoust. Soc. Amer., 1974, 56: S63.

Jerger, J. Audiological manifestations of lesions in the auditory nervous system. Laryngoscope, 1960, 70: 417-425.

Jerger, J. and Jerger, S. Critical off-time in Vlllth Nerve Disease. JSHR, 1966, 9: 573—583.

Lehtonen, J.B. and Koivikko, M.J. The use of a non-cephalic reference electrode in recording cerebral evoked potentials in man. Electroenceph. clin. Neurophysiol., 1971, 31: 154-156;

Picton, T., Hillyard, S., Krausz, H. and Galambos, R. Human auditory evoked potentials. I. Evaluation of components. Electroenceph. clin. Neurophysiol., 1974, 36: 179—190.

Sohmer, H. and Pratt, H. Recordings of the cochlear microphonic potential with surface electrodes. Electroenceph. clin. Neurophysiol., 1976, 40: 253-260.

Stephenson, S.A. and Gibbs, F.A. A balanced non-cephalic reference electrode Electroenceph. clin. Neurophysiol., 1951, 3: 237-240.

Wolpaw, J.R. and Penry, J.K. A temporal component of the auditory evoked response. Electroenceph. clin. Neurophysiol., 1975, 39: 609—620.