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Injuries to the auditory nerve: a study in monkeys

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Summary The effect of traction injury to the eighth nerve on the compound action potentials (CAPs) recorded from the exposed nerve in response to tonebursts and click sounds was compared to responses elicited by continuous tones and noise that were amplitude-modulated with pseudorandom noise. Responses to the continuous sounds were presented in the form of cross-correlograms between the averaged response, with the averager locked to the periodicity of the noise and one period of the noise. While the wave form of these cross-correlograms was similar to the wave form of the response to the same, but unmodulated, stimulus when presented in short bursts when the nerve was intact, these two measures changed in different ways as a result of slight injury to the nerve. Thus, the N₁ peak of the CAP in response to clicks and tones or noisebursts became prolonged when the nerve was stretched, while the first peak in the cross-correlograms was essentially unchanged. The second peak in the cross-correlogram was obliterated, but the N₂ peak in the CAP was clearly present, although attenuated. More severe injury resulting in a nearly total conduction block, however, produced similar changes in the CAPs and cross-correlograms.

Key words: Auditory nerve; Nerve injury; Compound action potentials; Cross-correlation; Pseudorandom noise

In previous studies we correlated changes in auditory nerve compound action potentials (CAPs) caused by slight injury to the auditory nerve in dogs (Sekiya and Møller 1987a) and monkeys (Sekiya and Møller 1987b, 1988) with histological changes in the auditory nerve. In the present study, we compare CAPs recorded from the eighth nerve in monkeys in response to clicks and tonebursts with cross-correlograms of the response to continuous pseudorandom noise, and to tones and noise that were amplitude-modulated with pseudorandom noise before and after surgical manipu-

lation of the eighth nerve. We used data analysis techniques similar to those used in our previous studies (Møller 1973, 1974, 1983a, 1987).

Our earlier studies have shown that the wave forms of correlograms of the responses from the auditory nerve and the cochlear nucleus are similar to the CAPs obtained in response to tonebursts or clicks (Møller 1981a, b, 1985, 1987). However, there are certain important differences between the results obtained when continuous noise is used as the stimulus and when transient sounds are used as stimuli. For example, the latency of the cross-correlograms of the response to continuous sounds does not decrease when stimulus intensity is increased, as does the latency of the CAP in response to such transient sounds as clicks and tonebursts. This is advantageous when conduction times in neural pathways are studied, and this feature of the method has been useful in studies of the peripheral auditory system (Møller 1975, 1985).

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The latency of the response to transient sounds from single auditory nerve fibers and single nerve cells in the nuclei of the ascending auditory pathway decreases with increasing stimulus intensity. In contrast, the latencies of the cross-correlograms obtained when using continuous sounds that are amplitude-modulated are independent of the stimulus intensity. These results have been interpreted to show that it is the increase in rate of rise of generator potentials in the receptor cells and excitatory postsynaptic potentials (EPSP) in relay neurons that causes the decrease in latency of the response to transient sounds, and that the other components of the system that contribute to the latency, such as neural conduction time and synaptic transmission time, are independent of the stimulus intensity (Møller 1975). The response from the auditory nerve to continuous sounds is less dependent on the rate of rise of the generator potentials, and therefore the latency of the cross-correlations becomes independent of the stimulus intensity.

In the present study, we show that surgical manipulation (mainly stretching) of the eighth cranial nerve results in changes in the wave form of the CAPs recorded from the eighth nerve in response to transient sounds, and that these changes differ from the changes that occur in the wave forms of the cross-correlograms of the responses to continuous sounds. Thus, while there is great similarity between the wave forms of the cross-correlograms of the response to continuous sounds and the CAPs elicited in response to tones and noisebursts when the nerve is intact, there is a substantial difference between these two types of wave form when the nerve is slightly injured.

Materials and methods

Because the experimental techniques used in the present study were detailed in previous reports (Møller 1983a; Sekiya and Møller 1987a), they will be described only briefly here. Monkeys were anesthetized using pentobarbital, thiopental, and a fentanyl-droperidol mixture. In some cases, animals were paralyzed with pancuronium. Brainstem auditory evoked potentials (BAEPs) were

recorded from the earlobe or ear canal and vertex using a non-cephalic reference in response to tonebursts and click sounds before the operation and during the entire experiment.

The auditory nerves were exposed by performing a retromastoid craniectomy, and monopolar recordings from the eighth cranial nerve were obtained using Teflon-insulated silver wires with a reference electrode placed non-cephalically.

The stimuli were delivered through miniature stereo earphones placed in the ear of the monkey and sealed with plastic adhesive tape. Click stimuli were generated by applying rectangular impulses of 20 μ sec duration to the earphones.

Pseudorandom noise was generated by low-pass filtering ternary m-sequences that were generated by simulating a shift register with 19,682 steps on a computer. These sequences were digitally low-pass filtered (2.5 kHz cutoff frequency and an attenuation of 36 dB/octave), and the number of datapoints was reduced to 2048 by linear interpolation before conversion to an analog signal (12-bit). The analog signal was low-pass filtered (3.4 kHz cutoff frequency and an attenuation of 36 dB/octave) (Møller 1983a). Tonebursts and continuous tones were generated by function generators, and random noise was generated by an analog device and high-pass filtered (5.6 kHz cutoff frequency and an attenuation of 36 dB/octave). Amplitude-modulated sounds were generated by means of an analog multiplier; the modulation depth was 25% root mean square (RMS) when tones were used as carriers and 70% RMS when high-pass filtered noise was used. The amplitude-modulated sounds, as well as the pseudorandom noise, were presented as continuous sounds when used as stimuli, and the responses from the auditory nerve to these sounds were averaged over one period of the pseudorandom noise, and cross-correlated with one period of the noise using the methods described earlier (Møller 1974, 1983a, 1987).

The recorded potentials were amplified at bandpass filter settings of 3–3000 Hz (6 dB/octave rolloff). Responses were sampled at intervals of 30 μ sec, and each record contained 512 datapoints when clicks and tonebursts were used. When continuous sounds were used the sampling inter-

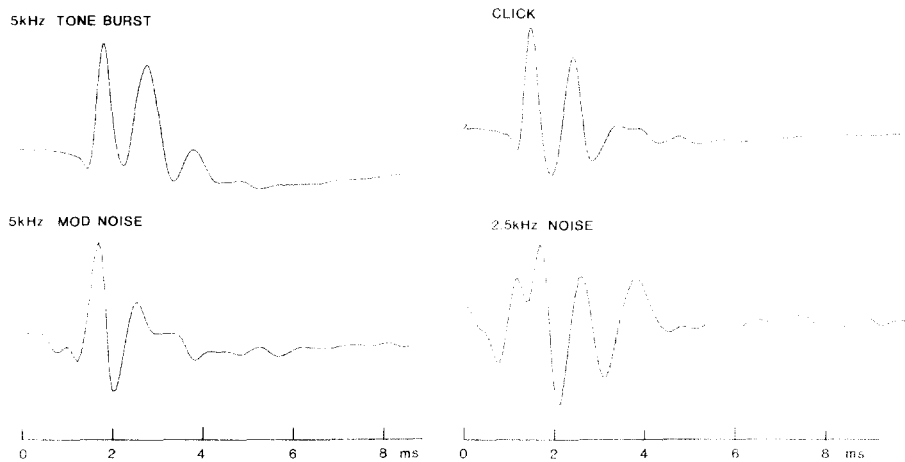


Fig. 1. Responses from the intact eighth nerve of a rhesus monkey to 5 kHz tonebursts (92 dB SPL) and to condensation clicks (107 dB peak equivalent (pe) SPL) compared with the cross-correlograms of the responses to a continuous 5 kHz tone that was amplitude-modulated with pseudorandom noise and to low-pass filtered pseudorandom noise (85 dB SPL).

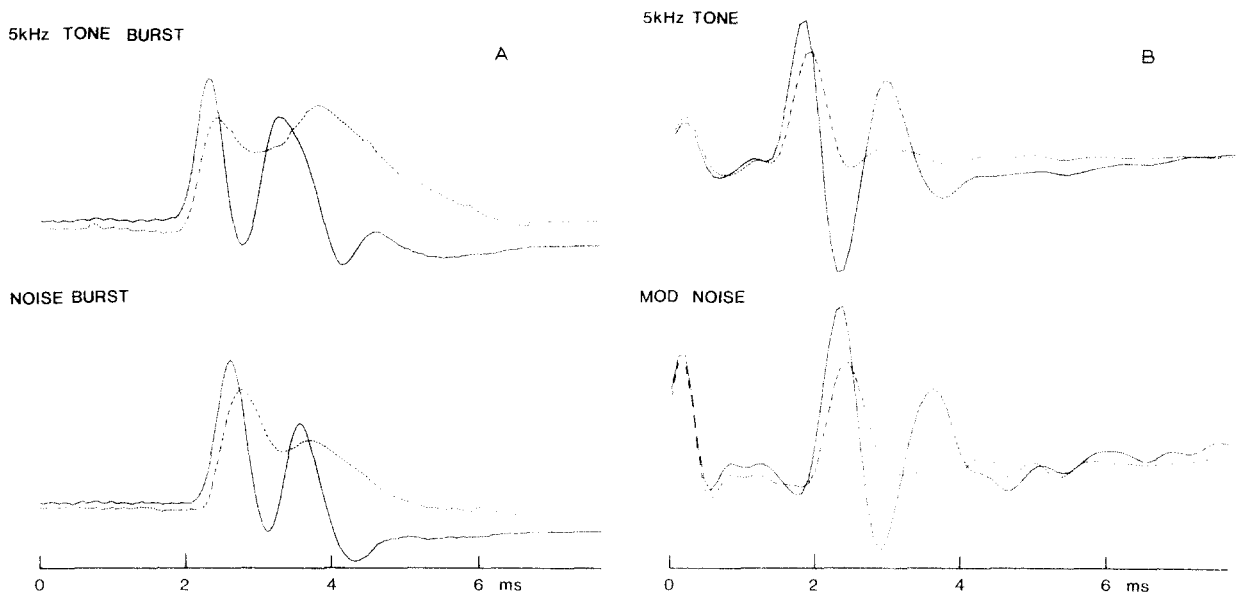


Fig. 2. A: responses to tonebursts and noisebursts before (solid lines) and after (dashed lines) the eighth nerve was injured by retraction. B: cross-correlograms of the responses to continuous tones that were amplitude-modulated with pseudorandom noise before (solid lines) and after (dashed lines) retraction. The recordings of the potentials evoked to tonebursts and noise bursts were obtained at about the same time as the responses to continuous amplitude-modulated tones were obtained. The solid lines in both graphs show results obtained in a monkey after the auditory nerve was exposed but before any injury was caused to the nerve. The intensity of the tones was 92 dB SPL, and that of the noise was 82 dB SPL. The results were obtained in the same animal as shown in Fig. 1.

val was 80 μ sec, and the response to one period of the pseudorandom noise contained 2048 data-points.

Results

The results of the present study are based on interpretation of recordings made in 8 monkeys. In Fig. 1, the wave forms of the response from an intact auditory nerve in a monkey to tonebursts and clicks are shown, along with the cross-correlograms of the responses to tones that were amplitude-modulated with pseudorandom noise. In addition, Fig. 1 shows a cross-correlogram of the response to the pseudorandom noise itself. It may be seen that the responses to tonebursts and clicks of the intact auditory nerve have 2 negative peaks (N_1 and N_2), and that the wave forms of the

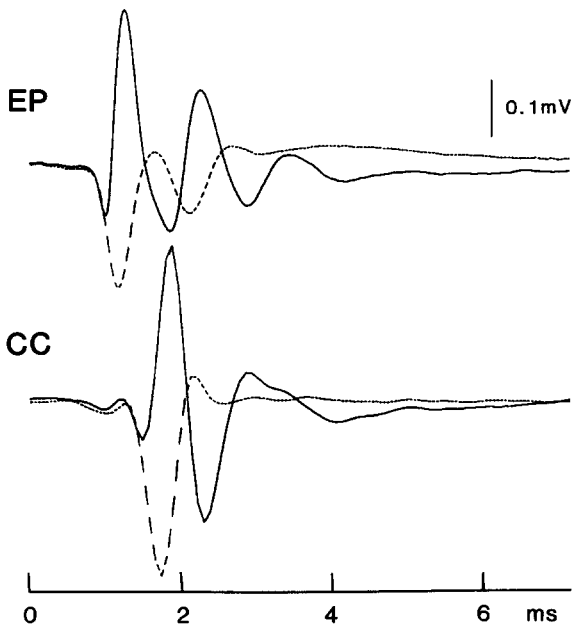


Fig. 3. Typical responses to rarefaction clicks recorded from the distal part of the eighth nerve (EP) before (solid lines) and after (dashed lines) stretching of the eighth nerve in another monkey, shown with the cross-correlograms of the response to continuous amplitude-modulated noise (CC) obtained at about the same time as the CAP (EP) before (solid line) and after (dashed line) the eighth nerve was injured by traction. The intensity of the tones was 92 dB SPL and that of the clicks was 107 dB pe SPL.

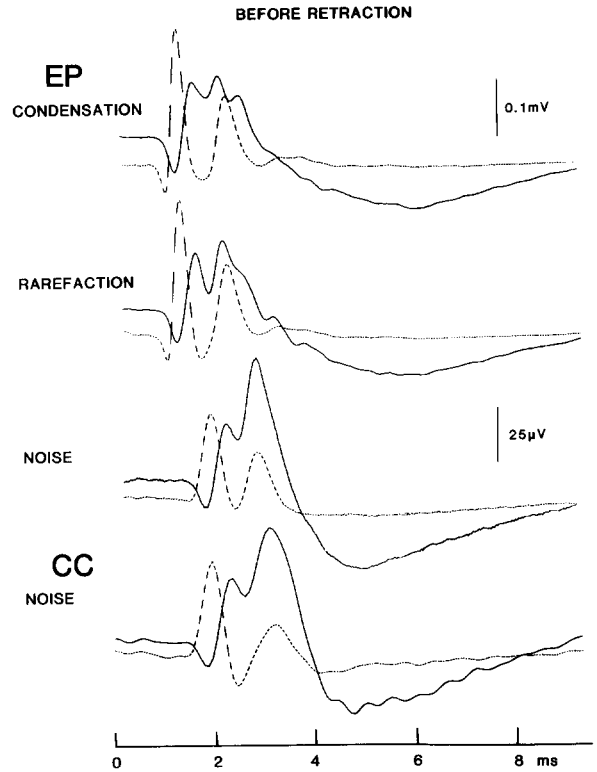


Fig. 4. Comparison of evoked potentials (EP), obtained in another monkey, recorded from the eighth nerve near the porus acusticus (dashed lines) and near the brain-stem (solid lines) using click stimuli and noisebursts together with cross-correlograms of the response to amplitude-modulated noise (CC). The intensity of the noise was 82 dB SPL and that of the clicks was 107 dB pe SPL.

responses to tonebursts are similar to the correlograms of the responses to the noise-modulated 5 kHz tone. The cross-correlogram of the response to the pseudorandom noise itself has 3 main peaks, with the first peak being preceded by a small additional peak. The far-field responses recorded from the scalp before the beginning of the operation were compared to those at the time of these recordings to ensure that the nerve was not injured during nerve exposure.

Slight retraction of the eighth nerve caused widening of the N_1 peak of the CAP in response to tonebursts and noisebursts (Fig. 2A) and a reduction in amplitude of the N_2 peak which appeared superimposed on the long tail of the N_1 peak after the injury. However, the first peak of

the cross-correlogram of the response to amplitude-modulated sounds was nearly unchanged (Fig. 2B), while the second peak in the cross-correlogram was practically eliminated. Before injury, the wave forms of the responses to tonebursts and the cross-correlograms of the responses to amplitude-modulated tones were similar, but after injury there was a large difference between the wave form of the CAP and that of the cross-correlogram.

Fig. 3 shows both the change that occurred in the CAP in response to click sounds and the change that occurred in the cross-correlograms as a result of injury to the auditory nerve. In this animal, the injury was more severe, and it caused

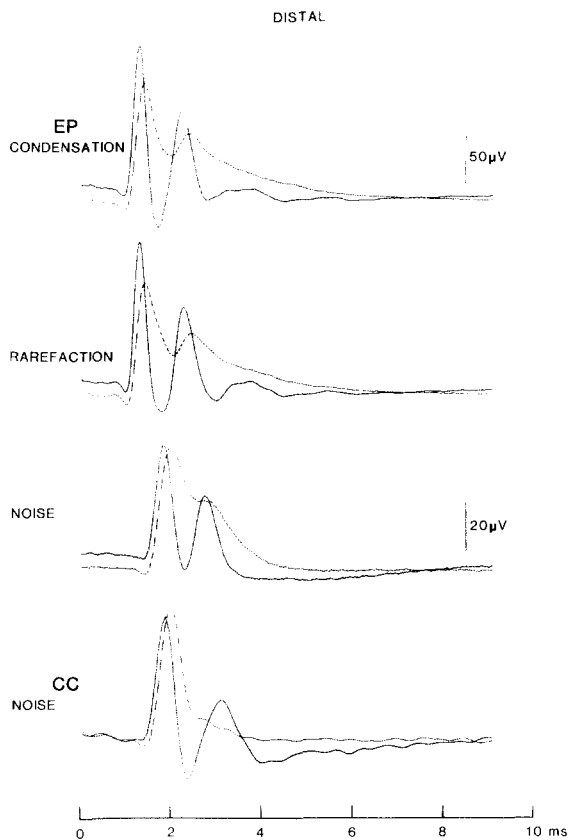


Fig. 5. Compound action potentials (EP) and cross-correlograms (CC) obtained from the distal part of the eighth nerve in the same animal as shown in Fig. 4, shown with the results obtained before (dashed lines) and after (solid lines) retraction. The stimuli were the same as in Fig. 4.

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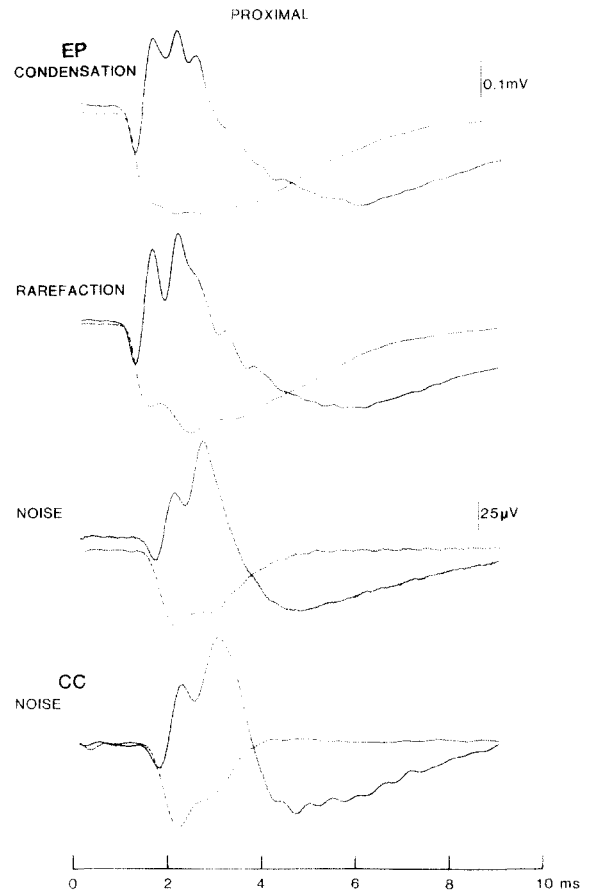


Fig. 6. Results similar to those shown in Fig. 5, but recorded from the proximal part of the eighth nerve.

the CAPs from rarefaction clicks to change to a large positive deflection followed by a small N_1 peak. This injury reduced the cross-correlograms of the response to noise-modulated noise to nearly a single positive peak (Fig. 3).

Responses to clicks and sound bursts obtained from the auditory nerve at a location near the porus acusticus and also from the nerve close to the brain-stem were different in several ways. For example, there was a slight decrease in the latency of the N_1 peak when the electrode was moved from a proximal to more distal location on the nerve. In addition, the amplitude of the second peak increased while its latency remained the same, and that change was most evident when noise was used as the stimulus. A similar change may also be

seen in the correlograms of the responses to continuous noise that was amplitude-modulated with pseudorandom noise (Fig. 4). Thus, the wave form of the responses to noisebursts was similar to that of the cross-correlogram of the responses to amplitude-modulated noise, both when the recordings from the nerve were made at a location near the porus acusticus and when they were made at a location close to the brain-stem.

After retraction, the latency of the N_1 peak of the potentials recorded at a distal location in response to clicks or noisebursts increased, the N_1 peak broadened, and there was a marked decrease in the amplitude of the second peak (N_2) (Fig. 5). The trough between the two peaks was much smaller after retraction and the second peak appeared only as a small hump on the tail of the N_1 peak, similar to what was seen in Fig. 2. The correlograms of the responses recorded near the porus acusticus to noise-modulated continuous noise showed changes similar to those shown in Fig. 1, with little or no change in the latency time of the first peak and only a slight increase in the

width of the first peak, but with obliteration of the second peak.

The potentials recorded from a proximal location on the eighth nerve changed dramatically as a result of retraction (Fig. 6). The potentials evoked by clicks and noisebursts changed from being negative deflections with two distinct peaks preceded by a small positivity before retraction to broad, positive potentials. These changes indicate that there was an almost complete conduction block in the eighth nerve, and that this block was located somewhere between the two recording locations. The cross-correlograms of the responses to amplitude-modulated noise recorded from the proximal part of the auditory nerve showed a similar change, as did the responses to noisebursts.

The responses to 5 kHz tonebursts at 3 different intensities, and correlograms of the responses to a 5 kHz amplitude-modulated tone at the same 3 different intensities (Fig. 7), show a similar pattern of change. While the 2 negative peaks in the potentials evoked by short tonebursts became

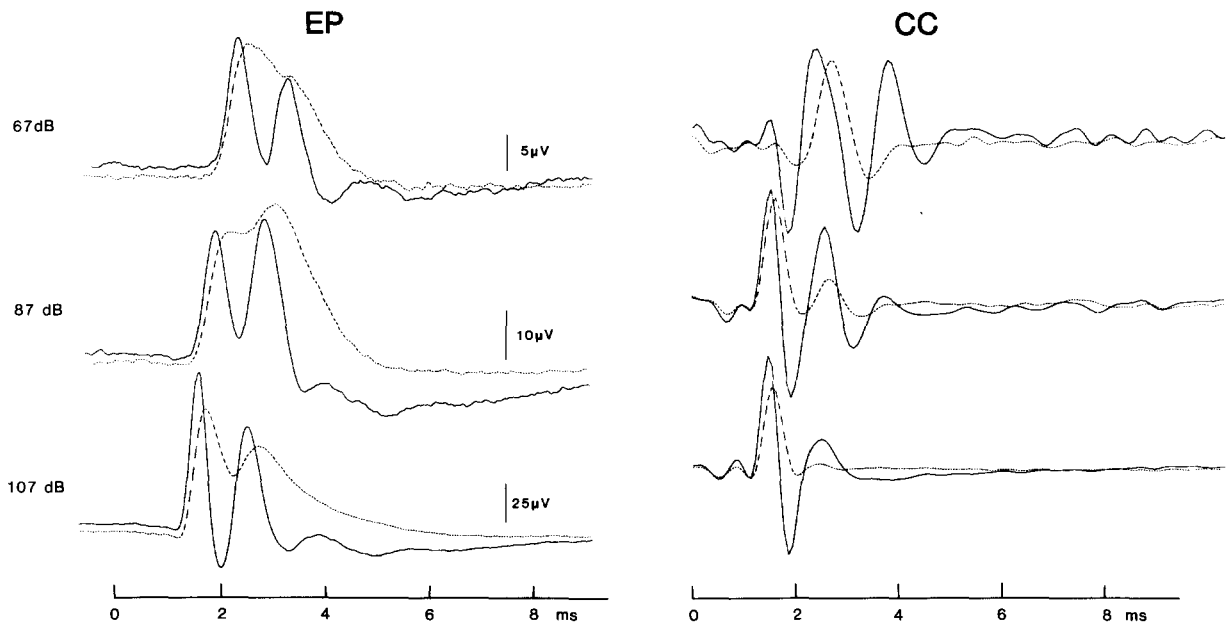


Fig. 7. Responses to 5 kHz tonebursts (EP) before (solid lines) and after (dashed lines) retraction of the eighth nerve for 3 different sound intensities (given in dB SPL as legend numbers), together with cross-correlograms (CC) of the responses to amplitude-modulated 5 kHz tones obtained in the same way.

fused with a small latency shift of the N_1 peak after retraction, the initial peak in the cross-correlograms was almost unchanged. However, the second peak became attenuated or was virtually absent as a result of retraction. This is similar to what can be seen in Figs. 2–6. Retraction also resulted in a slight increase in the latency of the first peak in the correlogram.

Discussion

The results of this study show that the cross-correlograms of the responses to continuous sounds change in a different way than responses to tonebursts and click sounds from surgical manipulation of the eighth nerve. Thus, while the N_1 peak in the response to tonebursts or clicks is widened and fused with the second peak (N_2) and there is a prolonged negativity following the second peak, the first peak in the cross-correlograms remains nearly unchanged after the nerve is stretched. The consequence of this is that the wave forms of the CAPs and of the cross-correlograms are different when recorded from a slightly injured nerve, whereas they are nearly identical when recorded from a normal nerve. The reasons for these observations are not obvious. The generator of the second peak in the cross-correlogram (as well as the N_2 peak in the CAP) is assumed to be the cochlear nucleus (Møller 1983b), and the decrease in amplitude in the second peak in the CAP as well as in the correlograms may be explained by a decrease in the number of auditory nerve fibers that conduct activity to the cochlear nucleus.

The broadening of the N_1 peak in the CAP, on the other hand, may result from dispersion of neural activity caused by larger differences in conduction velocity of individual nerve fibers in the auditory nerve. However, this broadening could also result from prolongation of the wave forms of the discharges in the individual nerve fibers. Both of these hypotheses seem to be contradicted by the finding that the first peak in the cross-correlogram is nearly unchanged in the slightly injured nerve while the N_1 peak in the CAP is broadened. Since the cross-correlograms are assumed to represent the summation of neural discharges in many nerve

fibers analogous to the CAPs in response to transient sounds, a change in the wave forms of individual neural discharges should affect the wave forms of the cross-correlations in ways similar to how the CAP is affected. If the change in wave form of the CAP was a result of temporal dispersion of discharges in individual nerve fibers, then the wave forms of the cross-correlograms would most likely change in a similar way. A more plausible hypothesis would be that the slightly injured nerve fibers that conduct somewhat more slowly than intact nerve fibers are not capable of sustaining a response to continuous stimulation and, therefore, do not respond to continuous sounds. That is, the cross-correlograms only represent the neural activity in intact nerve fibers.

When nerve injury is so severe that the CAP recorded in response to clicks and tonebursts indicates nearly total conduction block, the wave forms of both the CAPs and the cross-correlograms reflect the 'cut end' responses of the nerve fibers.

It is interesting that the wave form of the CAP recorded from the injured auditory nerve in response to tonebursts differs much more from the wave form of the cross-correlograms of the responses to amplitude-modulated tones and noise than it does from the wave forms of normal nerve. These results indicate that a slightly injured nerve responds fundamentally differently to transient and continuous stimuli, and it may indicate that the responses to continuous test sounds are more sensitive to changes in neural conduction than the response to transient sounds. Further, this shows that the method used in the present study may be superior to that using transient sounds as stimuli when the purpose is to detect small abnormalities in neural conduction. However, more studies are needed before any definite conclusions can be made in this respect.

The changes in wave forms of the CAPs and the cross-correlograms that occur when the recording electrode on the eighth nerve is moved from a location near the porus acusticus (distal) to a location near the brain-stem (proximal) are almost identical. The prolongation of the latency of the earliest peak in the cross-correlogram and the CAP is likely to be a result of the longer traveling time of activity in the eighth nerve. That there is

no prolongation in the latency of the second peak when the recording electrode is moved indicates that this peak is generated by a stationary source, probably the cochlear nucleus (Møller 1983b). The increase in its amplitude is likely to be a result of the recording electrode being placed closer to the source of this peak.

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