AUDITORY FREQUENCY SELECTIVITY IN PERIPHERAL NEURONS

AN ELECTROPHYSIOLOGICAL STUDY IN THE CAT BEFORE AND AFTER INDUCEMENT OF AN ACUTE NOISE TRAUMA

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PROEFSCHRIFT

TER VERKRIJGING VAN DE GRAAD VAN DOCTOR IN DE WISKUNDE EN NATUURWETENSCHAPPEN AAN DE RIJKSUNIVERSITEIT TE UTRECHT, OP GEZAG VAN DE RECTOR MAGNIFICUS PROF. DR. O. J. DE JONG, VOLGENS BESLUIT VAN HET COLLEGE VAN DECANEN IN HET OPENBAAR TE VERDEDIGEN OP WOENSDAG 7 DECEMBER 1983 DES NAMIDDAGS TE 2.30 UUR

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EVERT VAN HEUSDEN

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PROMOTORES: PROF. DR. G.F. SMOORENBURG
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COREFERENT: PROF. DR. J.J. EGGERMONT
(Katholieke Universiteit te Nijmegen)

J'avais fait ceci et je n'avais pas fait cela.
Je n'avais pas fait telle chose alors que
j'avais fait cette autre. Et après ?

Albert Camus : L'étranger

Ik draag dit proefschrift op
aan mijn Ouders.

Het in dit proefschrift beschreven onderzoek werd verricht in de afdeling Audiologie, hoofd Prof. dr. ir. R. Plomp, van het Instituut voor Zintuigfysiologie TNO te Soesterberg.
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Aan allen die meegewerkt hebben aan het tot stand komen van dit proefschrift betuig ik mijn oprechte dank.

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INTRODUCTION

CHAPTER I

INTRODUCTION

When people are confronted with hearing-impaired persons, they raise their voice to compensate for the impairment. A hearing aid compensates in a similar way by amplifying the received sound. In spite of this sound amplification the hearing impaired, especially those who suffer a sensorineural hearing loss, complain that they are seriously handicapped in noisy environments. This indicates that hearing impairement may be associated not only with reduced sensitivity to sound, but also with reduced discrimination of sounds that they do hear. A reason for this reduced ability to discriminate speech from ambient noise may be that the frequency filters in the damaged ear are less selective than those in the normal ear. This is the proposition we have investigated. The results of this investigation are described in this thesis.

Since the above mentioned complaints mostly arise when the loss is located in the cochlea, it is useful to determine the transfer function of the cochlear filters. Hence, we have to measure, at the output of the cochlea, neural activity evoked by a well defined sound stimulus.

Candidates for recording neural activity at the output of the cochlea (eighth nerve) are:

a) extracellular potentials of single nerve fibers;

b) synchronous responses of groups of nerve fibers.

ad a) Single fibers can be recorded from by placing a micro-electrode in the eighth nerve. The importance of recordings from single fibers is that the results reflect the activity of a restricted cochlear region because most of these fibers innervate only one sensory cell.

ad b) Synchronous responses of a group of nerve fibers (compound eighth-nerve action potentials, AP) can be measured by means of an electrode in the vicinity of the round window membrane. This means that the AP can be recorded from the human ear relatively simply by penetrating the eardrum with an electrode. AP recordings are of clinical importance for otological and audiological diagnosis. However, AP recordings are less suited to study detailed aspects of frequency selectivity, because the AP reflects the activity of a group of fibers, corresponding to a relatively broad cochlear region.

When recording from single fibers there are indications that the stimulus frequency for which a fiber has its lowest excitation threshold (the characteristic frequency, CF) may change because of the inducement of a hearing loss. This means, that comparison of fibers having the same CF before and after inducement of the hearing loss is not allowed because these fibers may innervate different cochlear regions. Therefore, we found it a methodological requirement to record from the same fiber both before and after inducement of the hearing loss. This requirement had repercussions on the recording site and on the technique to induce the hearing loss. To record from the same fiber both before and after inducement of the loss, a long recording time is required.

For eighth-nerve fibers such a long recording time is (almost) impossible to realize. But it is possible to realize long recording times for neurons in the antero-ventral part of the cochlear nucleus (AVCN), the next stage in the auditory chain. Since AVCN neurons show responses which are comparable to eighth-nerve fiber responses, we found it justified to record from the AVCN neurons instead of eighth-nerve fibers.

The way we induced the hearing loss was also determined by the requirement to record from the same neuron before and after inducement of the hearing loss. The trauma needed to be induced in a short period of time and during the experiment.

The structure of this thesis is as follows. Chapter II presents results of a pilot study on the effects of an acute noise trauma on cochlear frequency selectivity. Measurements reported here include the selectivity of frequency tuning curves measured for the AP and for single units in the AVCN. Absolute threshold and synchronisation of action potentials to the stimulus waveform are also presented. Furthermore, cochlear response latency for single units and APs is derived. Cochlear response latency for single units appeared to be almost unaffected by the noise exposure. Therefore we investigated whether it is possible to use latency instead of CF to determine the cochlear region innervated by that neuron (Chapter III).

In view of the clinical importance of the AP, we studied the possibility to derive APs which stem from a restricted cochlear region. Chapter IV describes properties of APs evoked by single-frequency tonebursts. It concerns AP threshold, latency and amplitude before and after inducement of the trauma. Effects of parameters of the test-tone such as frequency, level, rise time and

inter-stimulus interval are presented. It appeared to be possible to record frequency specific APs. In Chapter V we developed a method to measure tuning curves by forward masking of the AP. We investigated potentials and limitations of this method in providing us with a measure of frequency selectivity before and after inducement of the trauma. The action potential tuning curves were measured as a function of several test-tone and masker parameters. Finally, Chapter VI gives responses of AVCN units before and after inducement of the trauma. In both conditions measures of frequency selectivity are given using sinusoidal, click and noise stimuli. Furthermore, unit threshold, cochlear response latency and phase locking to the stimulus waveform are presented. The relation between single unit results and AP results is discussed.

CHAPTER II

EFFECTS OF ACUTE NOISE TRAUMATA ON WHOLE-NERVE AND SINGLE-UNIT ACTIVITY

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Effects of Acute Noise Traumata on Whole-nerve and Single-unit Activity*

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Summary. This paper gives some preliminary results of a research program on the effects of noise traumata on cochlear functioning. Measurements reported here include: the latency of the whole-nerve (compound) action potential (AP), the selectivity of frequency-tuning curves (e.g., the Q_{10}-values) measured for the AP (with a forward-masking technique) and for single units in the antero-ventral cochlear nucleus (AVCN), the degree of phase-locking of the action potentials of these units to the stimulus waveform, and the phase of the stimulus waveform to which these potentials are locking. The noise traumata were induced during the experiments. After inducement of the traumata we found:

– an increase of AP latency, if a sinusoidal stimulus was presented at the same sound pressure level as before the trauma,

– no effect on AP latency (for most stimulus frequencies), if the latency values measured at the pre- and post-trauma thresholds were compared,

– a decrease of the Q_{10}-values of the AP frequency-tuning curves, (the pre-trauma Q_{10}-values were small in comparison with single nerve fiber data),

– a decrease of the Q_{10}-values of the single-unit frequency-tuning curves,

– no effect on the degree of phase-locking of the single-unit potentials to the stimulus waveform,

– an increase of cochlear response time calculated from the phase of the stimulus waveform to which the single-unit potentials are locking as a function of stimulus frequency.

Key words: Noise trauma – Tuning curve – Compound action potential – Single-unit response

In this paper we present some preliminary results of a research program on the effects of noise traumata on cochlear functioning. Noise traumata were induced halfway into the experiments in order that data before and after the inducement of

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the noise trauma could be compared. The experimental animal, the cat, was anesthetized with sodium pentobarbital. Experiments lasted for about 50 h. Recordings were made of the whole-nerve (compound) action potential (AP) measured in the vicinity of the round window and of the extracellular potentials of single units in the anteroventral cochlear nucleus (AVCN). The AVCN, rather than the primary nerve, was chosen as the recording site because recordings from AVCN units can be made for a longer period of time before the unit is lost and most units in the AVCN show responses similar to those of primary nerve fibers (Rose et al., 1974; Smoorenburg et al., 1976). The recording site was ipsilateral to the stimulated ear.

The type of data that will be reported in this paper are: AP thresholds and latencies, AP frequency-tuning curves measured with a forward masking technique, single unit frequency-tuning curves and the temporal pattern of the single-unit potentials. All AP data in this paper were obtained from one cat; the single-unit data from several cats.

1. Description of the Noise

The noise used to induce the trauma was synthesized from 127 harmonics spaced at 160 Hz intervals. The sound pressure level (SPL) of the first harmonic was 98 dB, the levels of the higher harmonics were lower according to a −3 dB/oct slope. This slope was chosen to obtain a constant intensity per octave. The total sound pressure level was 105.3 dB. (Sound pressure levels are specified at the eardrum.) The noise was presented to the animal for 30 min. The phases of the 127 harmonics were chosen such that the noise as a function of time had as small a crest factor (peak factor) as possible.

2. AP Threshold and Latency

AP thresholds and latencies were measured in response to a sine-wave stimulus, 5 ms in duration (except for 0.5 kHz, 10 ms), and starting at zero phase. A gradual onset of the stimulus, often used to reduce spread of energy to adjacent frequencies, was not used in these threshold and latency measurements. Careful experiments, in which the contributions from different frequency regions to the AP were selectively masked with a forward masking technique (see sec. 3), showed that for cats without a pathology the threshold and latency values were not affected by the frequency spread in our stimulus. If there is no effect of frequency spread, it is advantageous to refrain from using a gradual stimulus onset because the gradual onset affects the measured latency of the AP. The AP was measured by averaging the responses to 100 stimuli presented at a rate of 10/s (except for 5 kHz, 5/s). The threshold criterion was a 2.5 μV amplitude of the AP. AP latency was measured from the onset of the stimulus to the top of the AP (or, at low frequencies, to the first peak of a frequency-following AP). In the latency data a 0.2 ms accoustic delay of the stimulus system is included.

AP thresholds measured before the noise trauma was induced, immediately after inducement of the trauma and 6 h later are given in Fig. 3. (The other data in this figure will be discussed in the next section.) Although a wide-band noise with a

constant intensity per octave was used, we find a frequency-dependent increase of the threshold with a maximum loss at 2 kHz. This frequency is not quite typical of all our data. Usually, the greatest losses are found in the 4 kHz region. Neither is the recovery of the threshold quite typical of all our data. In most cases there is virtually no recovery within the first 6 h after the noise trauma has been induced and the recovery is limited to about 6 dB over a 24-h period.

AP latencies as a function of SPL are given in Fig. 1. The latencies measured before the noise trauma was induced (solid curves) show a familiar type of behavior. Near threshold and orderly decrease of the latency is found with increasing frequency. The latency values agree with cochlear response times estimated from primary-nerve and AVCN data. The decrease of the latency with increasing SPL is due to contributions to the AP from cochlear regions that, at low stimulus levels, respond only to frequencies higher than the stimulus frequency. These regions are stimulated progressively when stimulus level is raised (e.g., de Boer, 1975). After inducement of the noise trauma (dashed curves) an increase of the latency values is found. Except for the 2 kHz stimulus the latency values at the (increased) threshold levels are similar to the normal threshold values. This suggests that the AP stems from the cochlear region corresponding to the stimulus frequency. The threshold latency found for 2 kHz after inducement of the noise trauma is much smaller than the normal threshold value. The small value suggests that the AP stems from the 8–15 kHz region of the cochlea. This implies that the threshold for the 2 kHz region

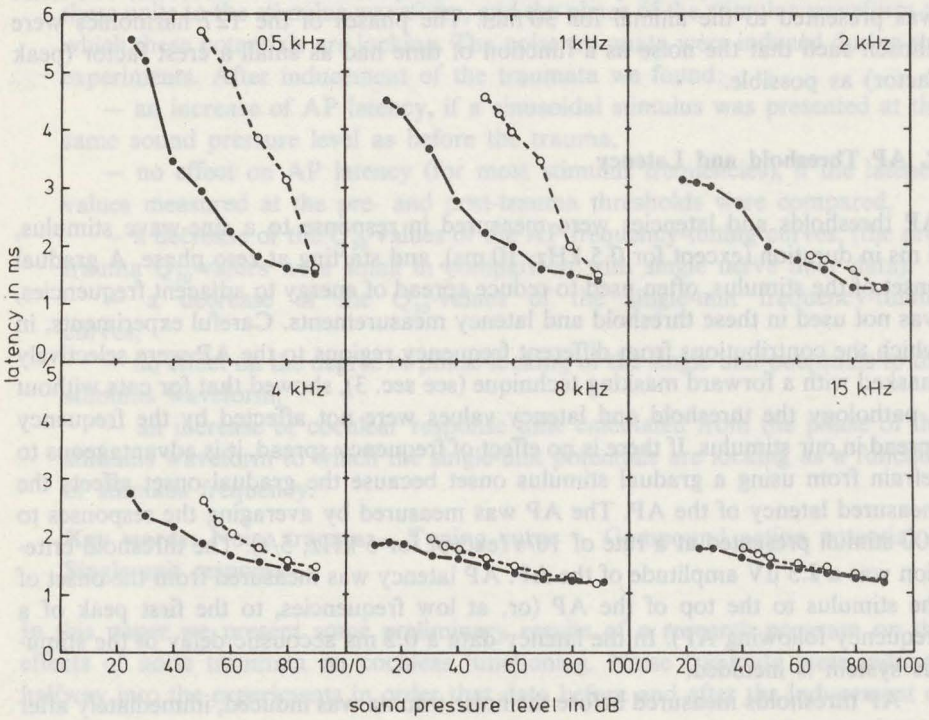

Fig. 1. AP latency as a function of SPL measured before (solid curves) and after (dashed curves) inducement of the noise trauma

is probably higher. This higher value, however, was not measured since higher frequency regions of the cochlea respond before the 2 kHz region responds.

The next sections will show that frequency tuning of the cochlea deteriorates after inducement of the noise trauma. Less selective frequency tuning might imply a faster response of the cochlear filter and, hence, smaller latencies. The results just discussed do not support this view.

3. AP Frequency-tuning Curves

AP frequency-tuning curves were obtained with a forward masking technique. The AP can be masked completely or suppressed partly if the tone burst evoking the AP (the test signal) is preceded by another signal (the masker). Maximum suppression of the AP is found if the masker frequency equals the frequency of the test signal. When the masker frequency is changed a higher level of the masker is required to maintain the same amount of suppression. This technique was used also by Dallos and Cheatham (1976). In our experiments we used a masker of 20 ms duration, followed by a 16 ms silent period and a 5 ms test signal. Figure 2 shows some results where the level of the test signal was chosen such that an AP amplitude of 6 μV was obtained (frequency and level of the test signal are indicated by means of a triangle) and where the frequency-tuning curves represent, as a function of frequency, the level of the masker at which the AP-amplitude was reduced to 4 μV. Solid and dashed curves represent results collected before and after the noise trauma was induced. Figure 3 shows another set of tuning curves at higher levels. In this case the AP amplitudes evoked by the test signal alone were 18, 28, 90, and 82 μV before

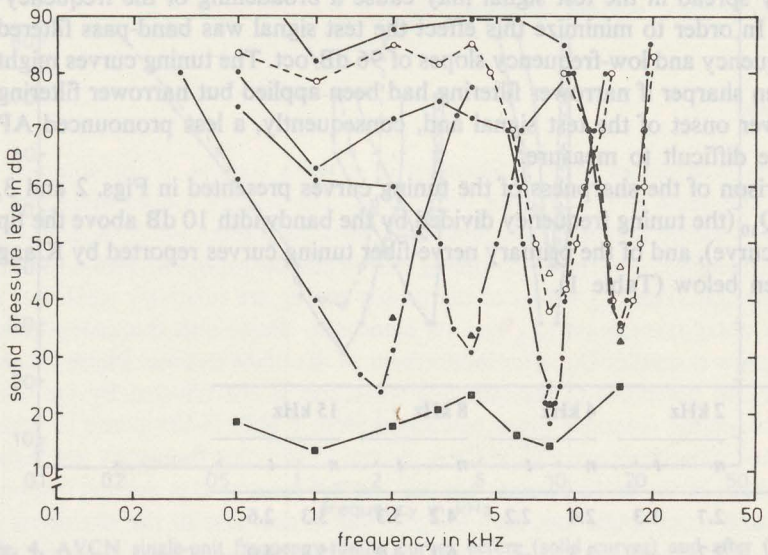

Fig. 2. AP frequency-tuning curves measured before (solid curves) and after (dashed curves) inducement of the noise trauma. The test signal frequencies and levels are indicated by triangles. The pre-trauma threshold is given by the solid curve connecting squares

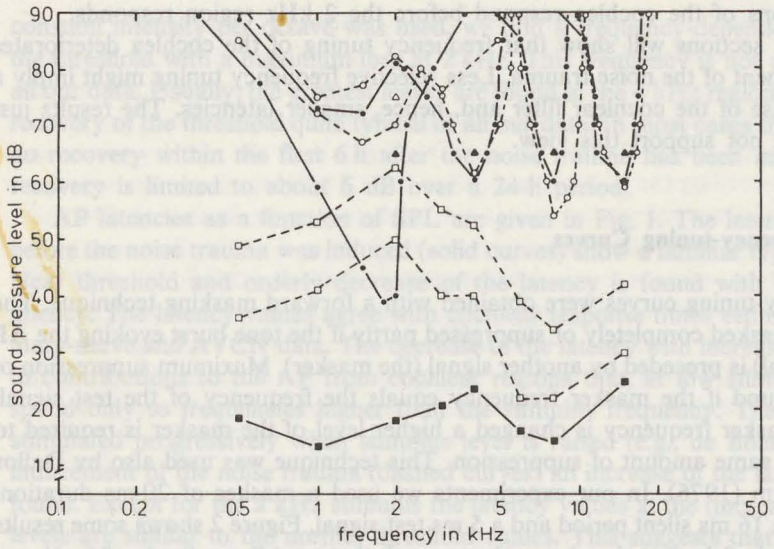

Fig. 3. As Fig. 2, but for higher levels. Two thresholds measured after inducement of the noise trauma are indicated by squares connected by means of dashed lines. The highest threshold was measured immediately after inducement of the trauma, the lower one 6 h later

inducement of the noise trauma and 5.0, 5.8, 48, and 38 μV after its inducement, both sets of data for 2, 4, 8, and 15 kHz, respectively. The masker suppressed the AP amplitude to 2/3 of its original value.

Frequency spread in the test signal may cause a broadening of the frequency-tuning curve. In order to minimize this effect the test signal was band-pass filtered with high-frequency and low-frequency slopes of 96 dB/oct. The tuning curves might have been even sharper if narrower filtering had been applied but narrower filtering implies a slower onset of the test signal and, consequently, a less pronounced AP which is more difficult to measure.

A comparison of the sharpness of the tuning curves presented in Figs. 2 and 3, expressed in Q_{10} (the tuning frequency divided by the bandwidth 10 dB above the tip of the tuning curve), and of the primary nerve-fiber tuning curves reported by Kiang (1965) is given below (Table 1).

Table 1

	2 kHz		4 kHz		8 kHz		15 kHz	
	n	*t*	*n*	*t*	*n*	*t*	*n*	*t*
AP, high-level	2.7	1.3	2.4	2.2	4.2	3.3	3.3	2.6
AP, low-level	2.2	–	3.3	–	6.1	3.0	5.8	4.0
Kiang, primary nerve fibers	4	–	8	–	11	–	13	–

n = normal; *t* = trauma

The AP Q_{10}-values measured at low levels appear to be smaller than the Q_{10}-values reported by Kiang for single-fiber tuning curves. Higher AP Q_{10}-values may be found for stimuli with less frequency spread but they are not expected to quite meet the primary fiber Q_{10}-values because an AP is measured only if a number of fibers is stimulated. After inducement of the noise trauma our results show wider AP tuning curves (smaller Q_{10}-values) than those measured for normal ears.

4. Single-unit Frequency-tuning Curves and Some Temporal Aspects of Single-unit Firing

Since we have not yet got sufficient data to compare results for one population of units measured before inducement of the noise trauma with another population of units measured after its inducement, we shall on this occasion show some results for three units, each of which could be measured before and after inducement of the noise trauma. Of course, each experiment offers the possibility of recording from only one such unit if one is lucky enough to keep the recording micro-electrode in contact with the unit for the period of time required. Figure 4 shows (solid curves) three threshold tuning curves giving the level of the stimulus, as a function of stimulus frequency, that is needed to increase the firing rate of the unit to just above its spontaneous rate, and two tuning curves respresenting specific higher firing rates. Three higher firing rates are chosen such that the tips of these tuning curves coincide with the tips of the threshold tuning curves measured after inducement of the noise

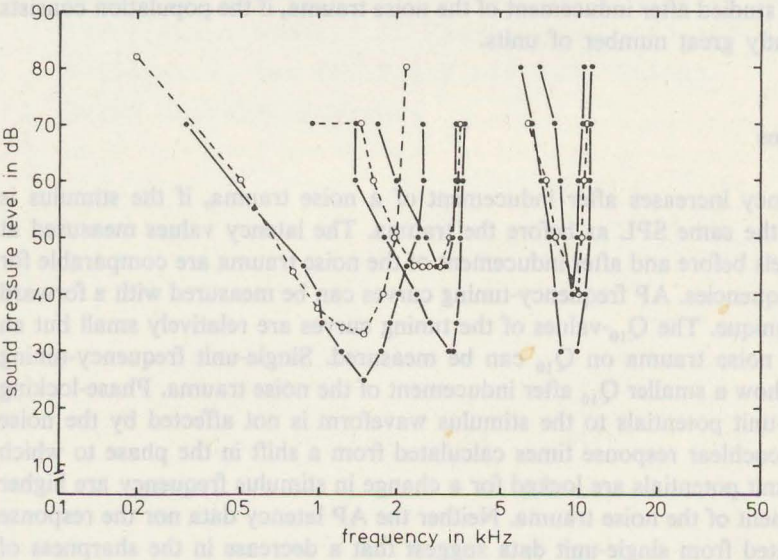

Fig. 4. AVCN single-unit frequency-tuning curves before (solid curves) and after (dashed curves) inducement of the noise. Three solid tuning curves represent a just-noticeable increase of firing rate above the spontaneous rate (threshold tuning curves), the other two represent higher firing rates such that their tips coincide with the tips of the threshold tuning curves for the traumatized ear

trauma (dashed curves). (In fact, the two tuning curves representing higher firing rates have been chosen from a set of isorate tuning curves.) The Q_{10}-values measured before and after inducement of the noise trauma are (units indicated by their tuning frequencies or best frequencies, BF): BF = 1.5 kHz, Q_{10} = 1.7 and 1.4; BF = 3 kHz, Q_{10} = 3.0 (both tuning curves) and 2.0; BF = 9.5 kHz, Q_{10} = 9.0 (upper tuning curve) and 4.8, respectively. A clear decrease of frequency selectivity is found after inducement of the noise trauma. The Q_{10}-values of these AVCN tuning curves for the normal ear correspond to the lowest Q_{10}-values found by Kiang (1965) for primary nerve fibers.

In addition to the measurements of the tuning curves, the timing of the single-unit potentials with respect to the stimulus waveform was studied. Responses phase-locked to the stimulus were found before and after inducement of the noise trauma. For example, the unit with BF = 3 kHz showed in both cases equally good phase-locking up to 3700 Hz, the high-frequency edge of the tuning curve. From the phase at which most single-unit potentials occur as a function of stimulus frequency we can calculate the cochlear response time. As mentioned before in the last paragraph of sec. 2, a smaller response time may be expected with deteriorating frequency selectivity after inducement of the noise trauma. In contrast, we found an increase of the response time of 0.2 ms for the unit with BF = 1.5 kHz and of 0.5 ms for the unit with BF = 3 kHz. (The third unit is tuned to frequencies for which no phase-locked responses are found.) The effect of the nouse trauma on the calculated response times is on the order of the variability in the response times calculated for different units with about the same BF and no noise trauma. This effect will therefore only show up in a study in which one population of units is studied before, and another population is studied after inducement of the noise trauma, if the population consists of a sufficiently great number of units.

5. Conclusions

The AP latency increases after inducement of a noise trauma, if the stimulus is presented at the same SPL as before the trauma. The latency values measured at threshold levels before and after inducement of the noise trauma are comparable for almost all frequencies. AP frequency-tuning curves can be measured with a forward masking technique. The Q_{10}-values of the tuning curves are relatively small but an effect of the noise trauma on Q_{10} can be measured. Single-unit frequency-tuning curves also show a smaller Q_{10} after inducement of the noise trauma. Phase-locking of the single-unit potentials to the stimulus waveform is not affected by the noise trauma, but cochlear response times calculated from a shift in the phase to which most single-unit potentials are locked for a change in stimulus frequency are higher after inducement of the noise trauma. Neither the AP latency data nor the response times calculated from single-unit data suggest that a decrease in the sharpness of tuning found after inducement of the noise trauma is accompanied by a decrease of cochlear response times.

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CHAPTER III

EFFECTS OF ACUTE NOISE TRAUMATA ON COCHLEAR RESPONSE TIMES IN CATS

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EFFECTS OF ACUTE NOISE TRAUMATA ON COCHLEAR RESPONSE TIMES IN CATS

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INTRODUCTION

In this paper we present preliminary results of a study on the effect of excessive noise stimulation on cochlear response times measured for single cells in the Antero-Ventral Cochlear Nucleus (AVCN).

"Any correlation of auditory physiology with cochlear histology is based on the premise that the best frequency (BF) dimension in the auditory nerve maps in some continuous way onto the longitudinal dimension of the cochlea" (Kiang *et al* , 1976). In the pathological ear there were doubts about this premise because excessive noise and ototoxic agents result in a shift to higher SPLs of the sharply tuned segment of a fiber's frequency tuning curve (FTC), and sometimes fibers become hypersensitive at low frequencies (Kiang *et al.*, 1976; Liberman and Kiang, 1978). Consequently, lower BF values will be assigned to these fibers. Robertson and Johnstone (1979) found this apparent BF shift to lower frequencies in spiral ganglion recordings of kanamycin-damaged guinea pig cochleas. In these animals the normal tonotopic pattern of organization in the cochlea was greatly disrupted.

For neurons whose discharges are phase-locked to the stimulus, timing of discharges with respect to the phase of the stimulus waveform can be measured. The slope of the cumulative phase shift as a function of stimulus frequency approximates a straight line. The slope of this line is a measure of the time delay between stimulus waveform and the corresponding waveform in the period histogram of the discharges (Anderson *et al*, 1971). For AVCN neurons the time delay between stimulus and response measured from the cumulative phase as a function of frequency is a monotonic function of BF (Gibson *et al*, 1977). In the traumatized ear this time delay (cochlear response time) measured in single cells in the AVCN may be a better indicator of the place along the basilar membrane innervated by those cells than the BF is. This hypothesis led us to perform experiments experiments on the cochlear response time before and after inducement of a noise trauma.

METHODS

Young healthy adult cats were anesthetized with sodium pentobarbital. The recording site was the AVCN ipsilateral to the stimulated ear. Stimuli were presented through an electrodynamic transducer (Beyer DT 48) connected to the cat's external meatus. The transducer was calibrated by measuring sound pressure level (SPL) and phase of sinewave stimuli with a calibrated probe tube microphone near the tympanic membrane.

Experiments lasted for about 50 h. Noise traumata were induced halfway through the experiments by exposing the ear for 30 minutes to 105.3 dB SPL pink noise. Such exposure resulted in a threshold shift which remained fairly steady during the experiment.

Cochlear response time is calculated from the phase shift revealed by the period histogram as a function of stimulus frequency and weighted according to firing rate (Goldstein *et al*, 1971).

EXPERIMENTS

Fig. 1 shows tuning curves of unit 760304 before and after inducement of a noise trauma. Frequency selectivity has decreased after inducement of the trauma. The FTC before the trauma at high SPL (higher spike-rate criterion) shows that the decrease in selectivity is not simply an SPL effect, because the tip of this curve is also sharper than the tip of the FTC measure after inducement

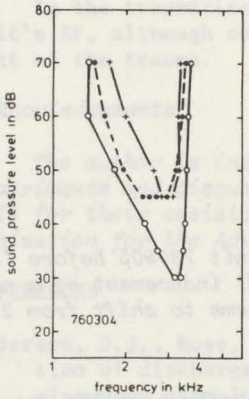

Fig. 1 FTCs of unit 760304 before (solid curves) and after (dashed curve) inducement of a noise trauma. The curves indicated by open circles and with dots, represent a just-noticeable increase in firing rate above the spontaneous rate (threshold tuning curves). The third curve (+) represents an FTC before the trauma at a higher firing rate such that its tip coincides with the tip of the threshold tuning curve for the traumatized ear.

of the trauma. Figure 2 shows for unit 760304 the cumulative phase of the discharges with respect to the stimulus waveform as a function of stimulus frequency at two SPLs before and after inducement of the trauma. After inducement of the trauma we see no effect on the degree of phase locking of single cell potentials to the stimulus waveform. The cochlear response times derived from these functions were 2.9 ms before and 3.5 ms after inducement of the trauma.

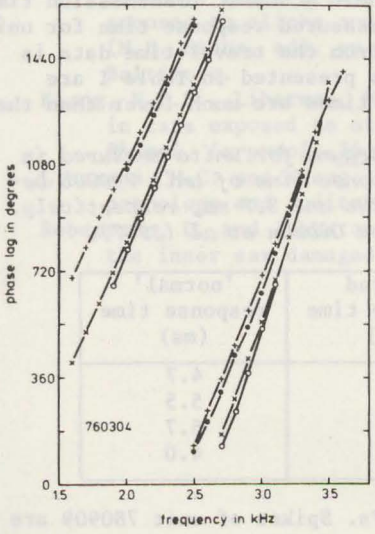

Fig. 2 Cumulative phase between stimulus waveform and the corresponding waveform in the period histogram of the discharges of unit 760304. The phase is plotted modulo 1560 degrees. The curves before the trauma (+, 60 dB SPL and •, 30 dB SPL) are shallower than the curves of the same unit after inducement of the trauma (×, 60 dB SPL and ○, 45 dB SPL);

The effect of stimulus SPL on cochlear response time is small. In three more cats, where we succeeded to keep the recording electrode in contact with a unit for the period of time required, we found an increased response time after inducement of the trauma, while frequency selectivity has decreased. The effect of excessive stimulation on the cochlear response time is on the order of the variability in the response times found for different cells with about the same BF and no noise trauma.

Fig. 3 shows tuning curves for unit 780905 before and after inducement of

the trauma. The sharply tuned segment of the FTC has shifted markedly to higher SPLs. Furthermore, this unit became hypersensitive at low frequencies. Consequently, the BF seems to shift from 2.4 to 0.7 kHz. The cochlear response time for this unit increased from 2.7 to 3.3 ms after inducement of the trauma.

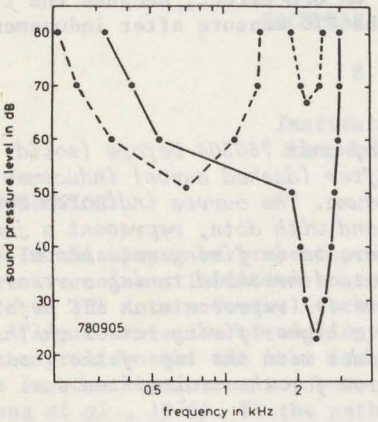

Fig. 3 FTCs of unit 780905 before (solid) and after (dashed) inducement of a noise trauma. The BF seems to shift from 2.4 kHz to 0.7 kHz.

With our angle of approach to the AVCN in each penetration BFs are found in a restricted frequency range in the normal ear. We expect these units to innervate a restricted region on the basilar membrane. Table I shows response time data for four units (unit 780905 included) measured in one penetration of the AVCN. In order to obtain cochlear response time data as a function of BF comparable to our response time data (eardrum to AVCN unit) we adapted travel-time data from Gibson *et al* (1977) and corrected these data for frequency-independent delays reported by them (1.5 ms) minus their acoustic transmission time estimated by us (0.3 ms). In the normal ear the measured response time for unit 780905 is 2.7 while the response time estimated from the travel-time data is 2.9 ms. The estimated response times of the units presented in Table I are shown in the right column. The measured response times are much lower than the

Table I Response times after inducement of the trauma for units measured in one penetration of the AVCN. BF and response time of unit 780905 before inducement of the trauma were 2.4 kHz and 2.7 ms, respectively. 'Normal' response times were adapted from Gibson et al (1977).

unit nr	BF (kHz)	measured response time (ms)	'normal' response time (ms)
780905	0.7	3.3	4.7
780907	0.4	3.1	5.5
780908	0.36	3.3	5.7
780909	1.1	2.6	4.0

estimated response times based on the assigned BFs. Spikes of unit 780909 are so-called fast negative discharges. Response times of this type of spike were omitted by Gibson *et al* (1977), since many of these spikes yielded delays at the lower extremes of the distribution. The interpretation given by those authors is that this type of spike represents discharges of presynaptic terminals of auditory nerve fibers and hence might be expected to have time delays less than AVCN neurons by the amount of one synaptic delay. Unit 780909 indeed showed lower response time than other units in this track.

The fact that the units are found in one track and that their response times are similar led us to conclude that they must have had BFs close to 2.4 kHz in the normal ear. An additional indication of a decreased BF after induce-

ment of the trauma is that discharges of units in Table I show phase locking to the stimulus (80 dB SPL) at frequencies higher than 2 kHz. In the normal ear we have seldom found phase locking above 2 kHz for BFs lower than 1.1 kHz. The shift of the BF to lower frequencies in the acoustically traumatized ear is in agreement with the results reported by Robertson and Johnstone (1979) in the kanamycin-damaged ear.

In the traumatized ear response time seems to be a good indicator of a unit's BF, although cochlear response time proves to be increased after inducement of the trauma.

Acknowledgements

The author is indebted to Guido Smoorenburg for his participation in the experiments and discussion of the results and to Nel Blokland and Evert Agterhuis for their assistance. This research was supported by the Netherlands Organization for the Advancement of Pure Research (ZWO).

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CHAPTER IV

EIGHTH-NERVE ACTION POTENTIALS EVOKED BY TONE BURSTS IN CATS BEFORE AND AFTER INDUCEMENT OF AN ACUTE NOISE TRAUMA

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EIGHTH-NERVE ACTION POTENTIALS EVOKED BY TONE BURSTS IN CATS BEFORE AND AFTER INDUCEMENT OF AN ACUTE NOISE TRAUMA

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Properties of eighth-nerve action potentials (AP) evoked by single-frequency tone-bursts (test tone) were studied in cats. Curves representing AP threshold as a function of test-tone frequency have a shape similar to behavioral and single-fiber threshold curves. The absolute level of AP thresholds is higher than that of behavioral and single-fiber thresholds. Cats were exposed to broad-band noise (equal intensities per octave) halfway into the experiments. This exposure resulted in a long-term temporary threshold shift (TTS) which remained fairly steady during the measurements. APs were measured before and during an acute noise trauma in the same animal. After inducement of the trauma the greatest threshold shift is found between 2 and 6 kHz. Curves representing AP amplitude as a function of stimulus SPL are displaced to higher stimulus SPLs. Sometimes the slope of the curve is steeper after the noise exposure than before. AP latency at threshold did not change due to the excessive noise exposure. AP-latency values compared at equal sound pressure levels before and after inducement of the trauma showed higher values during the trauma than before.

Key words: eighth-nerve action potential; thresholds; latency; acute noise trauma.

1. INTRODUCTION

In this paper we present results from a study on properties of the eighth-nerve action potential (AP), from which we can deduce frequency-specific information concerning the state of the cochlea both before and after inducement of a noise trauma.

In cochlear electrical responses evoked by click or tone-burst stimulation one may distinguish summating potentials (SP), cochlear microphonics (CM) and compound or eighth-nerve action potentials (AP).

Little research has been done on the summating potentials after excessive sound stimulation. Curves representing SP, measured near the round window of humans suffering sensorineural hearing loss, as a function of stimulus level are displaced to higher SPLs compared to curves for normal ears [14].

Cochlear microphonics, on the other hand, has often been used to study noise traumata. Anatomical injury of the cochlea correlates well with a decrease in CM sensitivity and in maximum CM amplitude, if CM is recorded at the place in the cochlea corresponding to exposure frequency [8]. If cochlear microphonics is measured with an electrode near the round window, which is easier than with intra-cochlear electrodes, responses to low-frequency tones are obscured by contributions from CM generators in the basal (high-

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frequency) part of the cochlea. There are considerable differences in the degree of correlation between behavioral and CM thresholds measured near the round window [18]. Simmons and Beatty [39] found in the cat that CM measured near the round window only properly reflects cochlear partition damage within a few millimeters of the round window (16 kHz and above).

Compound action potentials are frequency dependent when they are evoked by tonal stimuli presented at low to moderate sound pressure levels (SPL) [6,14,15,25,44]. In the following we shall use the term *test tone* for a single-frequency tone burst evoking an AP. The shape of the curves representing AP threshold as a function of test-tone frequency is quite similar to the shape of behavioral threshold curves for both normal and abnormal ears [7,15,26,35]. Furthermore, Dallos et al. [7] found in normal chinchillas and in Kanamycin-treated animals that the single-fiber threshold at the characteristic frequency (CF), averaged over octave bands, and AP threshold (AP amplitude at about 1 μV) are within 10 dB of one another throughout the frequency range. Johnstone et al. [26] observed in guinea pigs that single-fiber thresholds are 0–20 dB lower than AP thresholds (5 μV criterion).

AP was found to be more susceptible to acoustic trauma than CM [4,8]. AP depression can even be observed when CM appears to be normal [32,36]. Also, the AP threshold seems to be more susceptible to acoustic trauma than the behavioral threshold. After a continuous 24-day exposure to an octave band of noise centered at 4 kHz, there was a loss of AP amplitude (intra-cochlear measurement), whereas no permanent shift of behavioral threshold was found [18]. After dissection anatomical injury was apparent but the extent of the injury could not account for the amount of AP amplitude loss. Loss of synchrony of primary auditory nerve fiber responses, which were thought to constitute the AP, has been mentioned as the origin of the reduced AP amplitude. After excessive noise stimulation Benitez et al. [4] observed in chinchillas that threshold shift of the (intra-cochlear) AP exceeded behavioral shift during long-lasting temporary threshold shift (TTS), while Pugh et al. [36] observed in monkeys that behavioral shift was larger than AP (round-window) threshold shift in a permanent threshold shift (PTS) situation. A review of the literature on the relation between anatomical injury of behavioral threshold after excessive noise stimulation and cochlear electrophysiological potentials is given by Durrant [10].

It is commonly accepted [1,9,17,23,29,33,34,44] that the AP is built up from nearly simultaneous contributions of a population of primary auditory neurons. This means that neuron properties such as adaptation affect the AP. The neural output of the mammalian cochlea is organized tonotopically, by which is meant that nerve fibers emanating from a given region of the organ of Corti are most sensitive to a particular stimulus frequency. Hence, by using a single-tone test stimulus at low to moderate SPLs we expect contributions to the AP from a limited area of the organ of Corti excited by the stimulus. However, the rapid onset of a test tone necessary to evoke an AP produces energy at spurious frequencies, which means that the AP might be affected by contributions from spuriously excited areas.

The sparseness of frequency-specific data on action potentials in the cat before and during noise traumata led us to perform the present experiments using single-frequency tone-burst stimuli. Effects of inter-stimulus time interval (ISI), onset time and filtering are considered.

Since we intended to perform experiments on the same animal both before and after excessive noise stimulation, we induced the acoustic trauma by means of a 30 min exposure to an intense noise level. Miller et al. [31] showed that this type of noise stimulation produces a long-lasting TTS which is probably of cochlear origin.

2. METHODS

Healthy adult cats were anaesthetized with sodium pentobarbital (Nembutal). After an initial intraperitoneal injection of Nembutal (45 mg/kg) and an intramuscular injection of Atropine (0.5 mg), supplementary doses of Nembutal were administered intravenously to maintain the animal at a surgical level of anaesthesia during the experiment. Every 8 hours an intramuscular injection of Atropine Sulfate (0.5 mg) was given. All animals were tracheotomized. Arterial blood pressure, heart beat frequency and percentage of carbon dioxide in expired air were monitored in order to check the general state of the animal. Rectal temperature was maintained at approximately 38°C by means of a thermostatically controlled heating blanket.

Surgical preparations for electrophysiological recordings included resecting the pinna and opening the bulla to provide access to the round-window membrane. A silver-ball

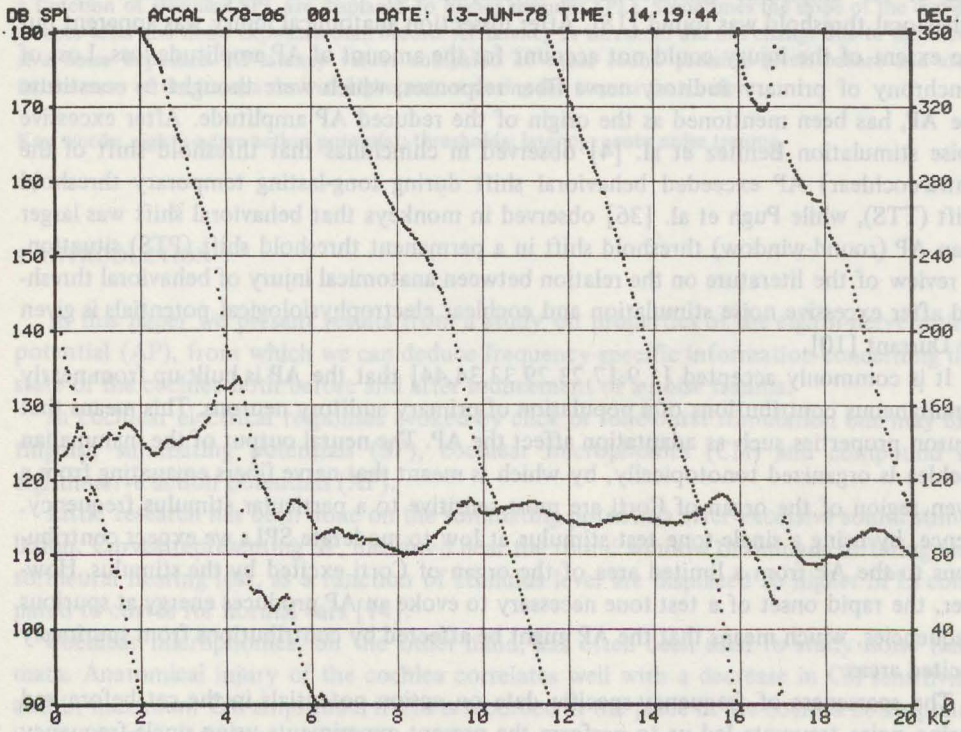

Fig. 1. Sound pressure and phase calibration curves for cat 7806. Pressure and phase are measured near the tympanic membrane. Input to the electrodynamic transducer was 2.8 V peak to peak. The amplitude and phase data were corrected for the transfer function of the probe microphone measuring system.

recording electrode was placed in the vicinity of the round window, while the indifferent electrode was placed in the neck muscles. The recording site was ipsilateral to the stimulated ear. In a number of experiments single-cell recordings in the antero-ventral cochlear nucleus (AVCN) were also made. AVCN was made visible by aspirating the overlying cerebral cortex, white matter and cerebellum.

Experiments were performed in a room especially constructed for acoustic insulation and electric shielding. Stimulus generation, cochlear-response averaging, and response storage were fully controlled by a computer (PDP 11-10).

Stimuli were presented through an electrodynamic transducer (Beyer DT 48) connected to the cat's external meatus. The transducer was calibrated by measuring SPL and phase of sinewave stimuli with a probe tube microphone near the tympanic membrane. The calibration signals covered the frequency range of 40 Hz to 20 kHz in steps of 40 Hz (Fig. 1). SPL and phase data were stored in the computer and were used to calculate the electrical stimulus required to produce a desired acoustic stimulus at the tympanic membrane.

Cochlear responses from the round-window electrode were amplified 10 000X and bandpass filtered between 1 and 30 000 Hz. To obtain compound action potential data,

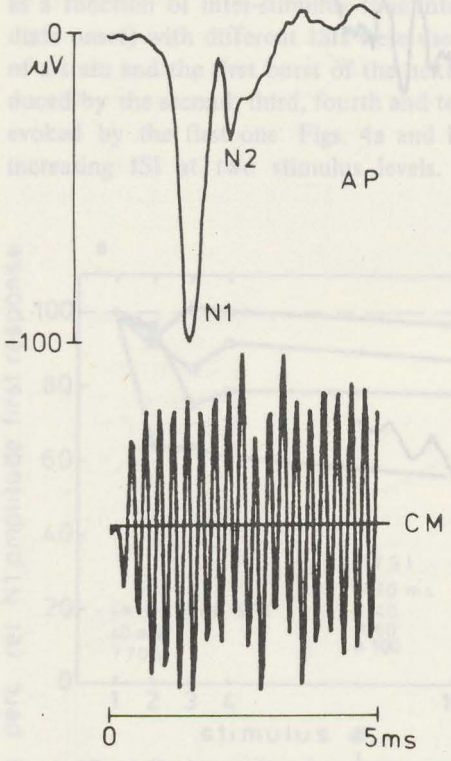

Fig. 2. Example of AP and CM produced by a 5 ms test tone of 4 kHz and 70 dB SPL. AP and CM are obtained by starting the test tone from d.c. level alternately with 0 or 180° phase, and by addition (AP) or subtraction (CM) of paired responses.

100–1000 responses to a test tone were averaged. Responses were only recorded during the presentation of the test tone. This means that test-tone duration determined the time window of the response. To separate CM from AP, the test tones were started alternatively from d.c. level with 0 or 180° phase. As a result, CM could be obtained by subtraction, and AP by addition of successive responses (Fig. 2), because CM follows the test-tone phase while AP polarity is independent of this phase. In general we could distinguish two negative peaks (N_1 and N_2) in the whole-nerve action potential. We defined AP amplitude as the difference between the baseline (level just prior to stimulus delivery) and the N_1 peak. The SPL of a test tone producing an AP amplitude of 2.5 μV was defined as the AP threshold. Furthermore, we defined AP latency as the time delay between stimulus onset at the tympanic membrane and the occurrence of the N_1 peak. An AP following stimulus frequency cycle by cycle could be found for stimuli up to about 1.0 kHz. We digitally filtered this frequency following response in order to facilitate calculation of AP latency (Fig. 3).

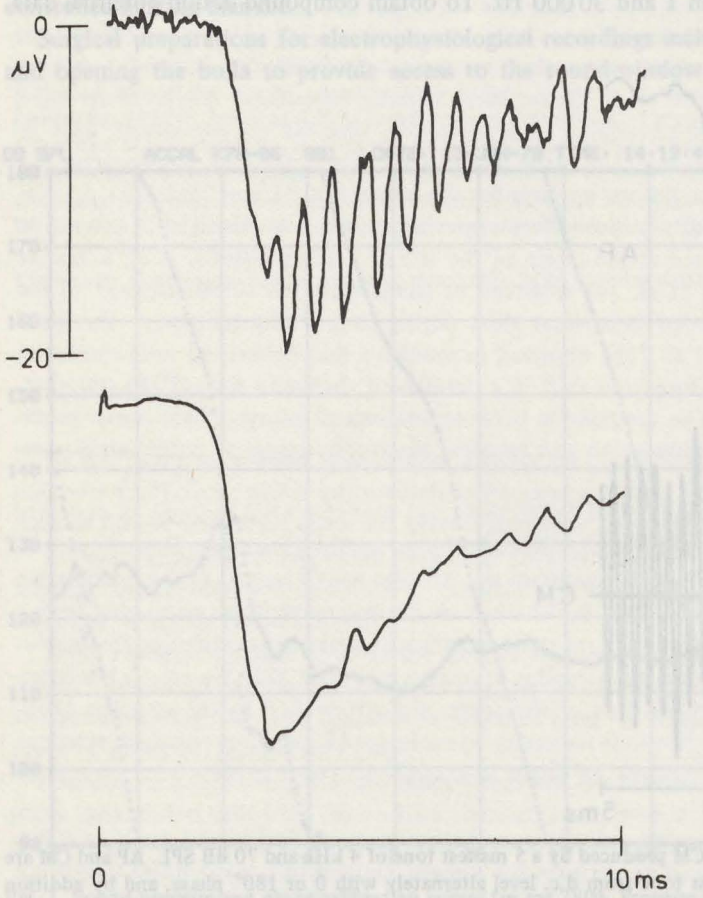

Fig. 3. Example of an AP following stimulus frequency and its digitally filtered version. Test tone of 1 kHz and 35 dB SPL. Filtering of the response was performed to facilitate calculation of AP latency.

Halfway into the experiments cats were exposed to broad-band noise for half an hour. In order to induce the acoustic trauma by means of noise having a spectrum which is well defined at the tympanic membrane irrespective of the transfer function between transducer and tympanic membrane, we synthesized the noise from 127 harmonics spaced at 160-Hz frequency intervals. The SPL of the first harmonic was 98 dB and the levels of the higher harmonics were lower in accordance with a −3 dB/oct slope. This slope was chosen to obtain a constant intensity per octave as a function of frequency. The total SPL was 105.3 dB. Phases of the 127 harmonics were chosen such that the noise as a function of time had as small a crest factor (peak factor) as possible [38].

3. EXPERIMENTS

In the following we present experiments performed to derive frequency-specific information from APs evoked by test tones. These experiments were preceded by pilot studies which were performed to optimize stimulus parameters.

3.1. Choice of inter-stimulus time interval

To investigate how adaptation of fibers affects the AP we measured the AP amplitude as a function of inter-stimulus time interval (ISI). Trains of ten stimulus bursts (immediate onset) with different ISIs were used. For all ISIs the interval between the last burst of a train and the first burst of the next train was 1 s. We expressed the amplitude produced by the second, third, fourth and tenth stimulus bursts as a percentage of amplitude evoked by the first one. Figs. 4a and b show the increase of the AP amplitude with increasing ISI at two stimulus levels. Adaptation increases when the stimulus level

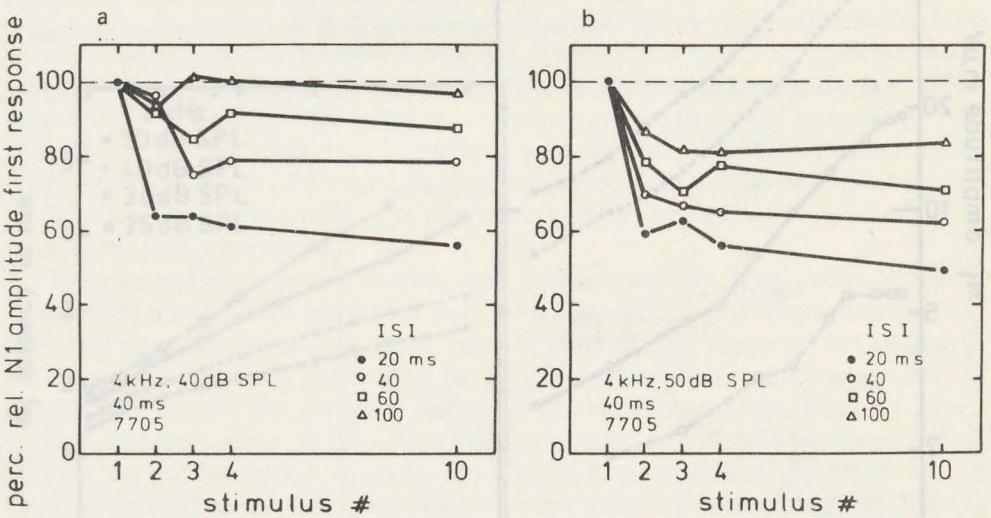

Fig. 4. AP amplitude as a function of test-tone number as a result of stimulation with trains of (10) tone bursts. AP amplitudes produced by the second, third, fourth and tenth stimuli are expressed in percentages of the N_1 amplitude produced by the first stimulus burst. AP amplitudes for 40 ms test tones (4 kHz) are shown for 40 dB SPL (left panel) and 50 dB SPL (right panel). ISI is a parameter.

increases. For a stimulus duration of 40 ms, there is no adaptation for a stimulus level of 40 dB SPL and a 100 ms ISI. A 200 ms ISI is sufficient to produce no adaptation at 50 dB SPL stimuli of 40 ms in duration. At 50 dB SPL and 100 ms ISI no adaptation is found if stimulus duration is only 5 ms (not shown). These observations were made at several stimulus frequencies and were verified in one more cat. For 0.5 and 1.0 kHz stimuli (10 ms duration) no adaptation is found for ISIs of 200 ms.

At high stimulus SPLs and for longer trains of test tones adaptation might have an effect on AP amplitude.

3.2. Choice of stimulus for a frequency-specific AP

To derive frequency-specific information from the AP it is necessary to use stimuli with a narrow-frequency spectrum. However, AP is essentially an onset phenomenon. The rapid onset of a test tone necessary to evoke an AP implies energy at spurious frequencies, which means that the excitation area of the onset of the test tone is wider than the excitation area of a steady-state tone. The stimulus evoking an AP should be carefully

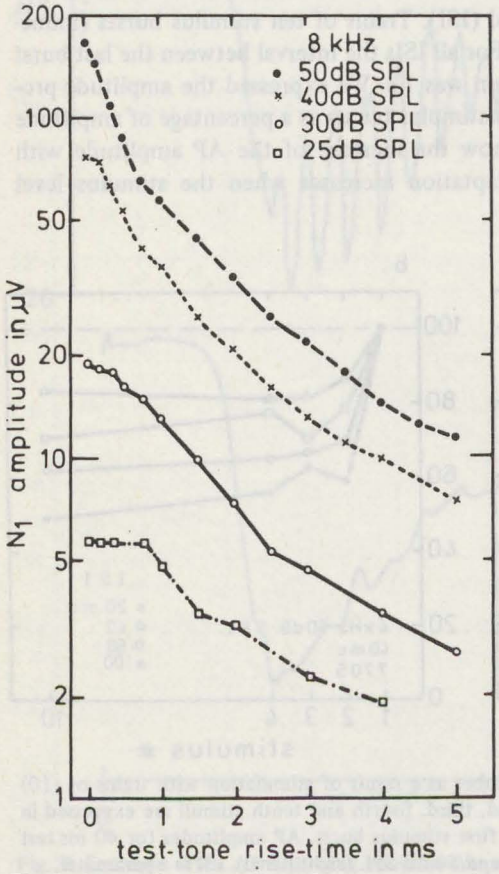

Fig. 5. AP amplitude as a function of test-tone rise time for several SPLs. The envelope of the onset is cosine shaped.

chosen since we want the cochlear filter and not the spectral characteristics of the test tone to determine the AP. By means of temporal shaping and spectral filtering one can restrict the energy spread to a particular frequency region. In measurements of the eighth-nerve action potential temporal shaping is often used. Advantages of filtering over temporal shaping are that the limits of the frequency spread are better defined. Filtering was used to study the effect of frequency limitation on AP threshold and AP latency. However, in filtering the test tone we had no direct control of the rise time. We therefore used temporal shaping of the test tone to study the effect of test-tone rise time on AP. A method to derive APs generated in a restricted frequency region is to mask APs by adding high-pass filtered noise to the stimulus [44]. By means of this technique, so-called derived narrow-band APs can be obtained. We performed derived narrow-band masking experiments to find the 'true' AP latency at threshold.

3.2.1. Effect of test-tone rise time on the AP. To study the effect of stimulus rise time (0–100%) on the AP, we performed experiments with a cosine-shaped gradual onset of the test tone. APs were measured by averaging 500 responses to test tones presented at a rate of 10 per second. The test tone was 5 ms in duration. Fig. 5 shows the AP amplitude produced by an 8 kHz test tone as a function of test-tone rise time for several SPLs. At the lowest level (25 dB SPL) the amplitude begins to decrease when the rise time exceeds 0.75 ms. At higher SPLs decrease in AP amplitude sets in immediately. Fig. 6 shows the effect of gradual onset on AP latency for the 8 kHz test tone at several SPLs. It is apparent that the effect of rise time on latency becomes smaller when stimulus level increases. A third characteristic of the AP waveform, its width, also changes as a function of rise time. We measured AP width at 50% of the AP amplitude. The results obtained with an 8 kHz test tone at several SPLs are shown in Fig. 7. The effect on AP width is largest for

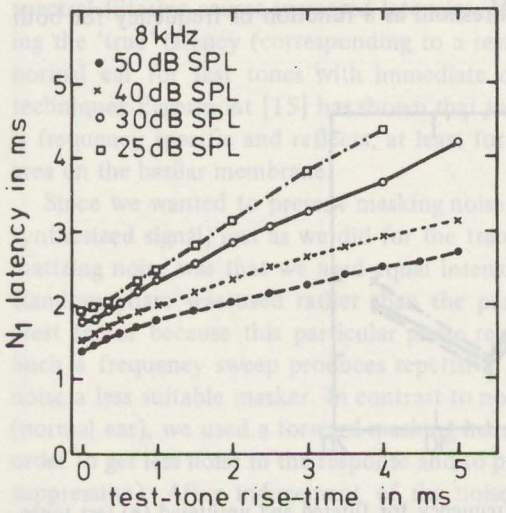

Fig. 6. AP latency as a function of test-tone rise time for several SPLs.

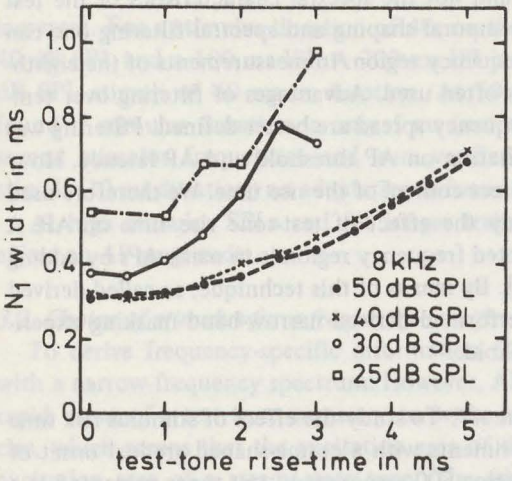

Fig. 7. AP width as a function of test-tone rise time for several SPLs.

low stimulus levels. The curves for 40 dB and 50 dB SPL test-tone levels are close to each other and follow a similar course.

3.2.2. Effect of test-tone filtering on AP threshold and AP latency. Fig. 8 shows the AP threshold as a function of test-tone frequency. The results for test tones filtered by a combination of low- and high-pass filters are also shown (cut-off frequency at test-tone frequency, slopes of 48 and 96 dB/oct, respectively). Filtering does not affect the shape of the threshold curve from 2 to 15 kHz. Increase of threshold due to test-tone filtering is less than 5 dB.

Fig. 9 shows the AP-latency values at threshold as a function of frequency for both

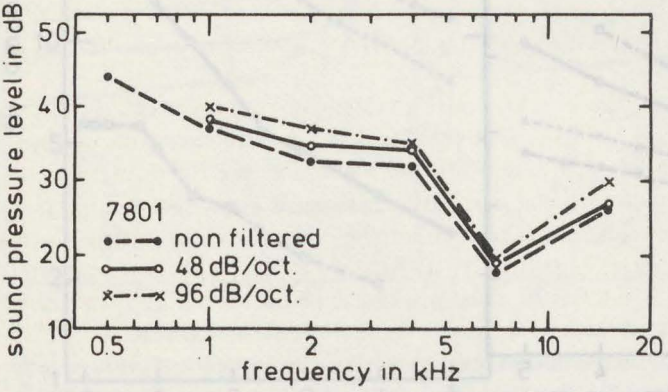

Fig. 8. AP threshold as a function of test-tone frequency for filtered and unfiltered (•) test tones. Test tones are filtered by a combination of low- and high-pass filters. Cut-off frequency of the filters is at test-tone frequency, while both slopes are 48 dB/oct (○) or 96 dB/oct (X).

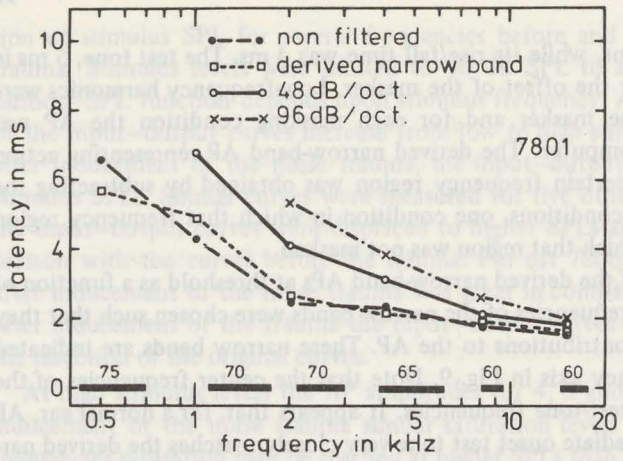

Fig. 9. AP latency as a function of test-tone frequency for filtered and unfiltered test tones at threshold given in Fig. 8. Derived narrow-band latencies are also shown. The frequency region from which the derived narrow-band response is obtained is indicated by bars along the frequency axis. The numbers close to the bars indicate the SPL of the masking noise required to mask the AP completely in a forward-masking procedure.

filtered and unfiltered test tones. We see that filtering causes an increase in latency. For the 48 dB/oct-filtered 8-kHz test tones, rise time was 0.8 ms, while it was 1.0 ms for the 96 dB/oct ones. From these values and Fig. 6 we expected the latency of the AP produced by the non-filtered 8 kHz test tone to increase by 0.35 and 0.5 ms due to filtering with 48 and 96 dB/oct, respectively. Since we expected the cochlear filter to be steeper than 48 dB/oct we did not use filters with shallower slopes.

3.2.3. Latency of derived narrow-band APs. We saw that test-tone temporal shaping or spectral filtering causes increased latencies. Masking experiments may be helpful in finding the 'true' latency (corresponding to a restricted area on the basilar membrane) in the normal ear for test tones with immediate onsets. By means of filtered noise-masking techniques Eggermont [15] has shown that the AP evoked by a single-frequency test tone is frequency specific and reflects, at least for the normal ear, the activity of a restricted area on the basilar membrane.

Since we wanted to present masking noise with an essentially flat spectrum, we used a synthesized signal, just as we did for the traumatizing noise. A difference with the traumatizing noise was that we used equal intensities and random phases for the harmonics. Random phase was used rather than the particular phase relation producing a minimal crest factor because this particular phase relation implied a repetitive frequency sweep. Such a frequency sweep produces repetitive AP activity which makes the minimal crest noise a less suitable masker. In contrast to noise-masking experiments reported until now (normal ear), we used a forward-masking instead of a simultaneous-masking technique, in order to get less noise in the response and to prevent masker–test tone interaction (lateral suppression). After inducement of the noise trauma we sometimes used simultaneous masking because we were unable to mask the AP in a forward-masking situation. The

masker had a duration of 20 ms, while its rise/fall time was 4 ms. The test tone, 5 ms in duration, followed 16 ms after the offset of the masker. Low-frequency harmonics were successively removed from the masker and for each masking condition the AP was recorded and stored in the computer. The derived narrow-band AP representing action potentials originating from a certain frequency region was obtained by subtracting the masked APs for two masking conditions, one condition in which that frequency region was masked and the other in which that region was not masked.

Fig. 9 shows the latencies of the derived narrow-band APs at threshold as a function of frequency. Width and center frequencies of the narrow bands were chosen such that they covered the most important contributions to the AP. These narrow bands are indicated by solid bars along the frequency axis in Fig. 9. Note that the center frequencies of the narrow bands are higher than test-tone frequencies. It appears that, for a normal ear, AP latency measured with an immediate onset test tone very closely matches the derived narrow-band latency. Thus, the spread of energy to spurious frequencies due to the immediate onset does not affect latency near threshold.

3.3. AP amplitude before and after inducement of the trauma

Fig. 10 shows, for one cat (7806), the AP amplitude evoked by a test tone, as a func-

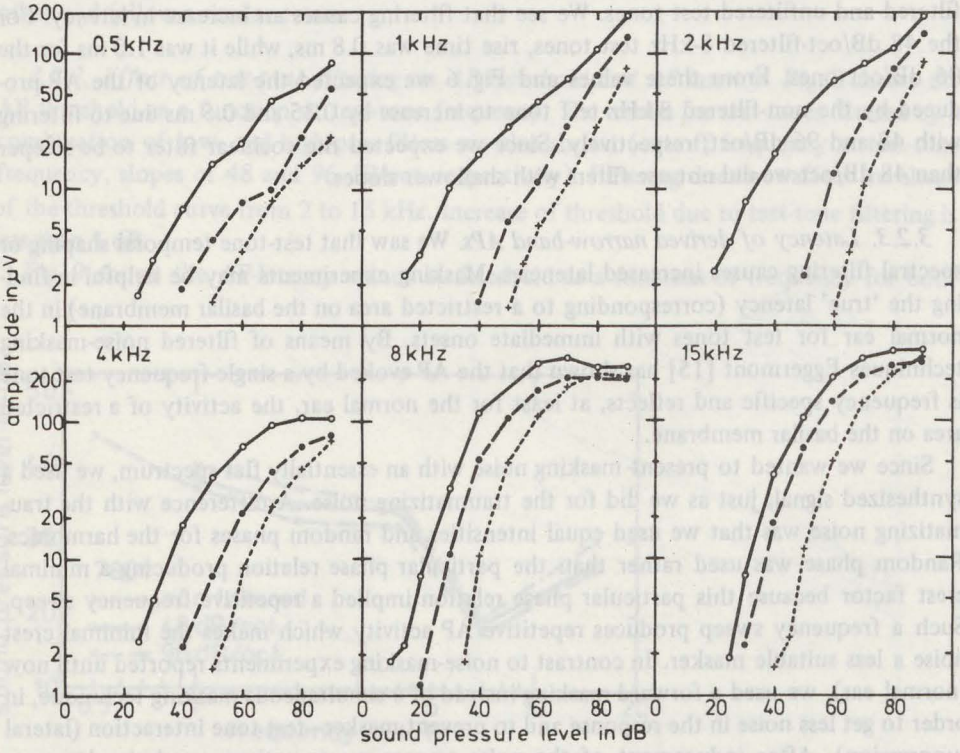

Fig. 10. AP amplitude as a function of test-tone SPL for several frequencies before and after inducement of the noise trauma for one cat (7806). ○, before the trauma; +, just after excessive noise stimulation; ·, six hours after the noise exposure.

tion of stimulus SPL for several frequencies before and after inducement of the noise trauma. Stimulus levels were limited to 90 dB SPL to avoid overstimulation. The amplitude–SPL function depends upon stimulus frequency. At low stimulus SPLs the slopes of the input–output curves increase from low to high stimulus frequencies. Immediately after inducement of the noise trauma, the input–output curves are displaced to higher stimulus SPLs. Similar curves were measured for five other cats. For 1 and 2 kHz stimuli the input–output curves were displaced to higher SPLs and also became steeper in comparison with the curves before the trauma. For cat 7806 recovery of the AP amplitude after inducement of the noise trauma was great in comparison with other cats. Six hours after inducement of the trauma the input–output curves of cat 7806 had shifted back in the direction of the original curves.

At high stimulus levels the AP amplitudes for 4, 8 and 15 kHz stimuli saturate. After inducement of the noise trauma similar saturation levels are found. For lower stimulus frequencies saturation may be reached at higher SPLs than the ones we used.

3.4. AP threshold before and after inducement of the noise trauma

A 2.5 μV AP amplitude was defined as the AP threshold. This amplitude criterion is well above the visual detection criterion when averaging 100 responses to the test tone. Fig. 11 shows the average AP threshold as a function of frequency (11 cats). The results

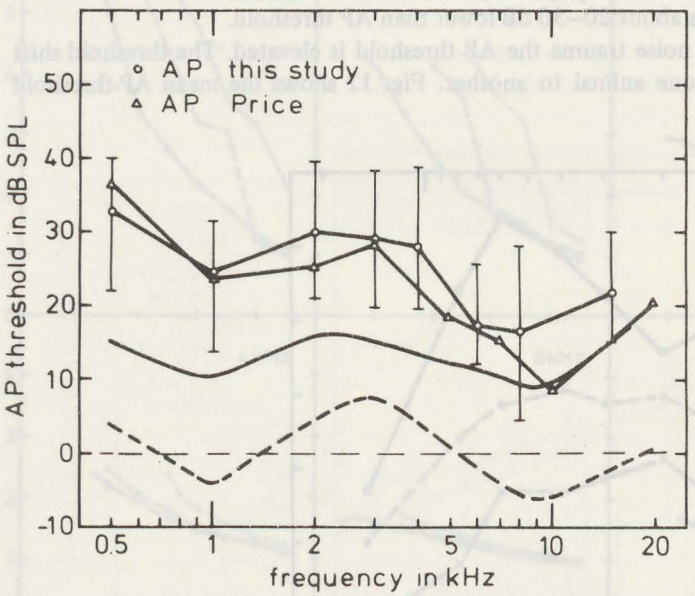

Fig. 11. Mean AP threshold as a function of test-tone frequency (○). The bars represent the range of AP thresholds found in 11 cats. AP-threshold data of Price (0 μV criterion) are converted to a 2.5 μV criterion using his mean rate of growth curves for test-tone SPLs close to the AP threshold. These converted AP thresholds are given in the figure (△). Behavioral data, presented by Miller et al. [31] corrected for the transfer from free field to tympanic membrane [47] and for opening the bulla [24], are also shown (- - - - -). Furthermore, mean threshold of high spontaneous-rate eighth-nerve fibers as found by Liberman and Kiang [30] was added to the figure (———).

are compared with a survey of behavioral data presented by Miller et al. [31] (solid/dashed curve). These data have been corrected for the transfer from free field to tympanic membrane [47] and for opening the bulla [24]. Furthermore, the mean threshold (34 cats) for high spontaneous rate eighth-nerve fibers (rates greater than 18 spikes/s) was added to Fig. 11 [30]. Price [35] obtained AP thresholds by extrapolating the curves representing AP amplitude as a function of SPL to zero amplitude. From the mean rate of growth of the AP amplitude (μV per dB) for test-tone SPLs near AP threshold (his Fig. 3, [35]) we derived the AP thresholds Price would have found had he used a criterion of 2.5 μV. These thresholds are also plotted in Fig. 11. The data adapted from Price [35] are not in agreement with our results for test-tone frequencies above 8 kHz. The rate of growth of the AP amplitude in μV per dB measured by Price [35] for test-tone frequencies between 7 and 20 kHz, shows that a 2.5 μV criterion threshold is about 1 dB higher than a zero-amplitude threshold. For 4 cats we measured AP threshold using a 1 μV and a 2.5 μV criterion. At 15 kHz the 1 μV threshold was 4 dB (7 dB at 0.5 kHz) lower than the 2.5 μV threshold. Although these data are from only 4 cats, the AP-threshold shift of 4 dB at 15 kHz suggests a smaller rate of growth of the AP amplitude than that found by Price. The shapes of the AP-threshold curves are rather close to the mean single-fiber threshold and to the behavioral threshold curve. A local maximum at 3 kHz is visible in each threshold curve. For low-frequency test tones the difference between fiber and AP threshold is about 15 dB, while for high-frequency stimuli the difference is about 10 dB. The behavioral threshold is about 20–30 dB lower than AP threshold.

After inducement of a noise trauma the AP threshold is elevated. The threshold shift varies considerably from one animal to another. Fig. 12 shows the mean AP-threshold

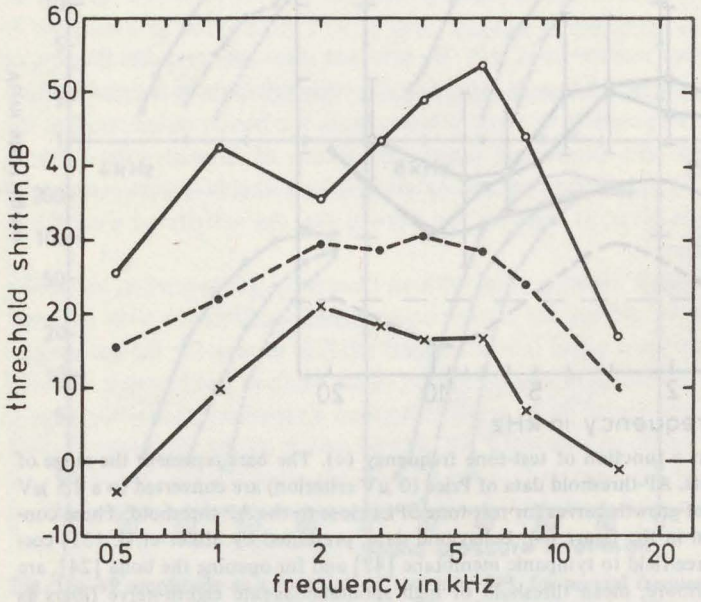

Fig. 12. AP-threshold shift due to excessive noise stimulation. The three curves represent: mean (8 cats) threshold shift (•), and shifts for the cats with largest (○) and smallest (×) overall shift.

shift (8 cats) produced by excessive noise stimulation (see Methods). Furthermore, threshold shifts for the cats with the smallest and the largest mean threshold shift are shown. Threshold shift is largest between 2 and 6 kHz. Twelve hours after inducement of the trauma we observed at 4 kHz an average recovery from TTS of about 5 dB.

3.5. AP latency before and after inducement of the trauma

AP latency depends on stimulus frequency, as can be seen in Fig. 13, which shows for one cat (7806) the latency–SPL curves before and after inducement of a noise trauma. The effect of stimulus SPL on latency decreases from low to high frequencies. At high stimulus SPLs, AP latency converges to one value for all stimulus frequencies (about 1.0 ms). Similar curves were measured for five other cats.

After inducement of the trauma, AP latency appears to increase if we compare the data at the same SPL. For cat 7806 the latency values at the increased AP thresholds, however, are similar to the normal threshold values except for the 2 kHz stimulus. The threshold latency found for the 2 kHz stimulus after inducement of the trauma is smaller than the normal threshold value. Six hours after inducement of the noise trauma the latency-SPL curves have shifted in the direction of the normal curves. The latencies at AP

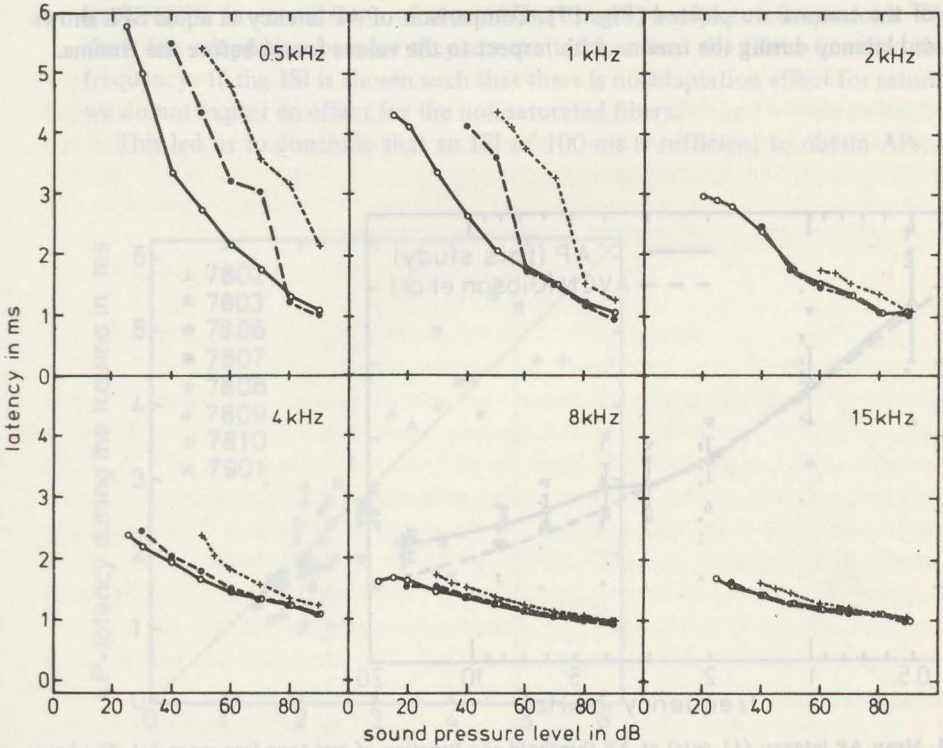

Fig. 13. AP latency as a function of test-tone SPL for several frequencies before and after inducement of the noise trauma for one cat (7806). ○, before the trauma; +, just after excessive noise stimulation; •, six hours after the noise exposure.

threshold have remained similar to the normal threshold values except at 2 kHz, where the latency at threshold still deviates from normal.

3.6. AP latency at threshold before and after inducement of the trauma

In Fig. 14 we see for 11 cats the latency at threshold as a function of frequency. Furthermore, the travel time curve of Gibson et al. [21] for single units in the AVCN shifted +0.7 ms along the latency axis, accounting for frequency independent delays (see Discussion) is shown. After this shift the two sets of data match. The small dots represent individual (8 cats) latencies at threshold after inducement of the trauma.

Fig. 15 shows AP latency at threshold after inducement of the trauma as a function of AP latency before the trauma (8 cats). Fig. 16 shows the same data, but here test-tone frequency is the parameter. In the area with largest losses (2–6 kHz) the latency values vary considerably, as does the threshold for this area. For test-tone frequencies between 2 and 8 kHz there is a tendency towards lower latency values at threshold during the trauma. Some AP latencies after inducement of the trauma are shorter than the shortest latencies found at 15 kHz before inducement of the trauma. For cat 7810 such short latencies were found. This cat showed the largest loss (see open circles in Fig. 12) of the eight animals we studied. For 3 cats latency values at equal SPL before and after inducement of the trauma are plotted (Fig. 17). Comparison of AP latency at equal SPL shows increased latency during the trauma with respect to the values found before the trauma.

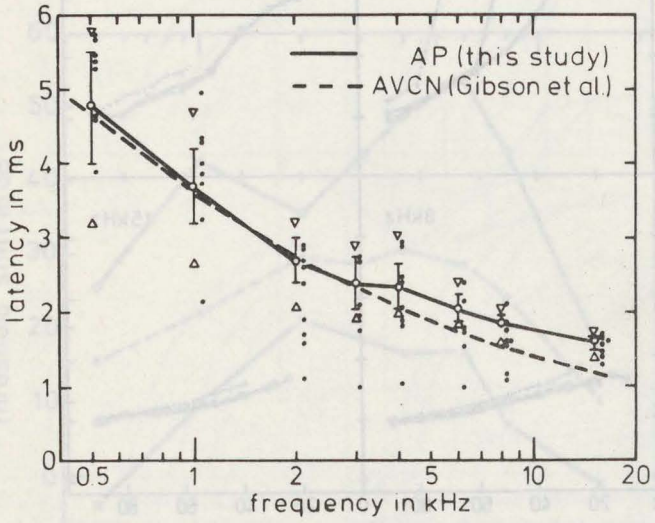

Fig. 14. Mean AP latency (11 cats) at AP threshold as a function of test-tone frequency (○). The bars represent the standard deviations. The upper limit (▽) and the lower limit (△) of the measured latencies are indicated. The small dots represent individual latencies at threshold after excessive noise stimulation. The dots are shifted somewhat to the right. The dashed line represents the travel time for AVCN units as given by Gibson et al. [21], shifted 0.7 ms upward along the latency axis.

4. DISCUSSION

4.1. Choice of inter-stimulus time interval

A large number of stimulus presentations is required to obtain an acceptable signal-to-noise ratio for the average AP. To save time one is tempted to use a high presentation rate. However, this produces the risk of driving the auditory neurons into a state of adaptation which results in a decrease in AP amplitude. Eggermont and Spoor [12,13] and Spoor et al. [43] performed adaptation experiments on both guinea pigs and humans. They found a large species difference in ISIs required to avoid build-up of adaptation (guinea pigs 100 ms and humans 500 ms). Pilot experiments on adaptation (2 cats) showed that 5-ms test tones at 2, 4 and 8 kHz, and at the highest SPL used in this pilot experiment (50 dB SPL), do not build-up adaptation if the ISI is 100 ms. For guinea pigs and humans, ISIs that avoid adaptation at 45 dB SPL also avoid adaptation at higher SPLs. We assume that this also holds for the cat. The reason that higher stimulus SPLs do not cause adaptation might be due to saturation. According to Smith [40,41] the amount of short-term adaptation of an auditory-nerve fiber at a certain instant in time is proportional to the fiber's excitation produced by a stimulus preceding that instant. As a result, maximum adaptation is obtained when at a certain stimulus level (about 50 dB SPL) the firing rate of fibers tuned to the stimulus-frequency saturates. An increase in stimulus level results in recruitment of more fibers tuned to adjacent frequencies. These fibers show less adaptation because they are excited less than the fibers tuned to the test-tone frequency. If the ISI is chosen such that there is no adaptation effect for saturated fibers, we do not expect an effect for the non-saturated fibers.

This led us to conclude that an ISI of 100 ms is sufficient to obtain APs, evoked by

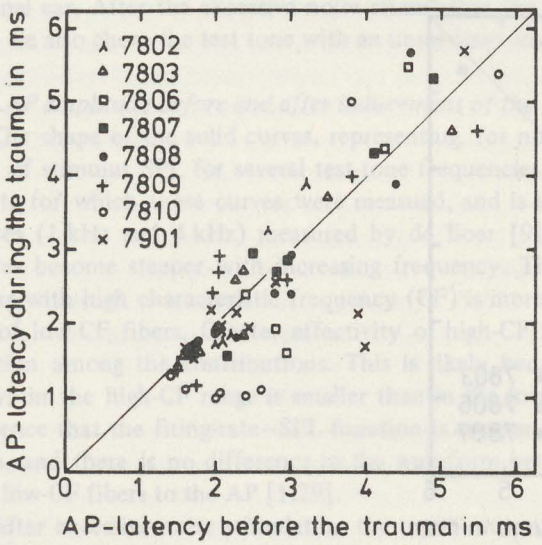

Fig. 15. AP latency at threshold after inducement of the trauma (small dots in Fig. 14) as a function of the latency at threshold before the trauma for 8 cats.

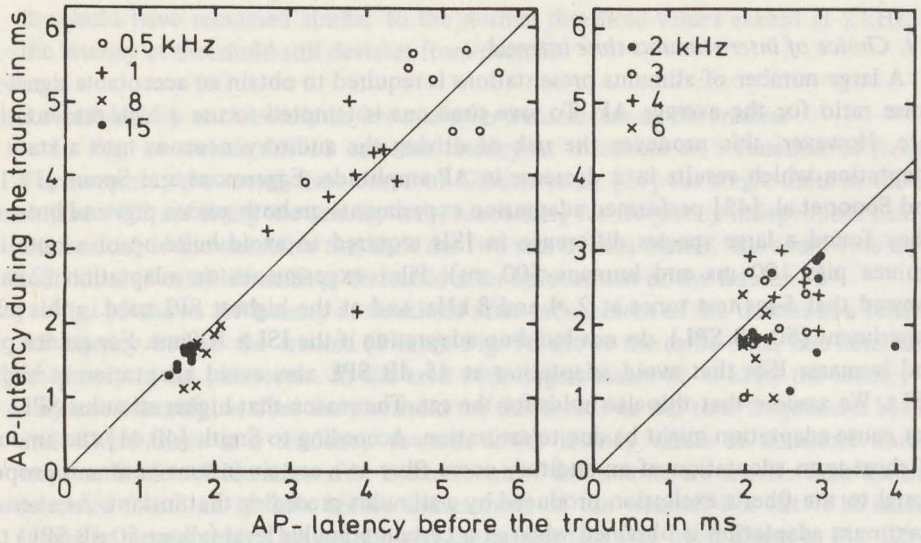

Fig. 16. The same AP latency data as in Fig. 15 are shown for frequencies which are least affected by the excessive noise exposure (left panel) and for frequencies in the region with largest threshold shift (right panel).

5-ms test tones over a large SPL range, and which are only slightly affected by adaptation. However, for longer trains of test tones used in the main body of experiments adaptation might not be limited by saturation at high stimulus levels.

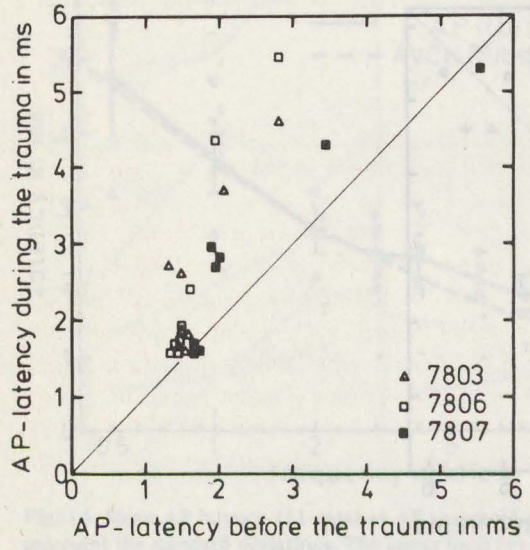

Fig. 17. AP latency after inducement of the trauma as a function of AP latency before the trauma, for three cats and for 8 test-tone frequencies. Test-tone SPL before and after inducement of the trauma is the AP threshold after inducement of the trauma.

4.2. Choice of stimulus for a frequency-specific AP

In order to obtain frequency-specific APs we want a restricted population of fibers all tuned to about the same frequency to contribute to the AP. But an AP is generated at the onset of a stimulus, which implies energy spread over a frequency region, particularly for rapid onsets. Temporal shaping of the test tone is often used to keep the energy from spreading to spurious frequency regions. A disadvantage of a gradual onset in comparison with an immediate onset is that a gradual onset produces smaller (Fig. 5) and wider (Fig. 7) APs, which have prolonged latencies (Fig. 6). As a result, one has to find experimentally a compromise between spectral 'splatter' on the one hand and reduced AP amplitude and prolonged AP latency on the other [9]. In searching for such a compromise it it wrong to consider the spectrum of the whole stimulus. Only the short-term aspects of the stimulus at about stimulus onset time determine the population of fibers contributing to the AP. De Boer [9] found, by trial and error, a rise time that shows a satisfactory compromise between spectral splatter on the one hand and AP amplitude on the other. The rise time he found for a 4 kHz stimulus was 0.25 ms. For this rise time none of the output envelopes of the filters he used in his model showed more than 50% overshoot during the onset transient. Assuming filter width to be proportional to center frequency, a 0.125 ms onset would be satisfactory for the 8 kHz stimulus we used in the pilot experiments. However, we found an increase in AP latency at rise times as short as 0.1 ms, the shortest rise time in our pilot experiments (Fig. 6).

An optimal way of reducing energy splatter without affecting latency is to use filters matched to the cochlear filter. However, for this purpose there is no adequate information on the cochlear filter (e.g. the problem of the second filter, non-linear aspects; see also Goldstein et al. [22]). Morever, the cochlear filter of the traumatized ear is unknown and may differ from cat to cat. Since the derived narrow-band AP latencies are equal to the AP latencies produced by immediate onset tones we chose for immediate onset in the normal ear. After the excessive noise stimulation the choice is arbitrary. For that condition we also chose the test tone with an immediate onset.

4.3. AP amplitude before and after inducement of the trauma

The shape of the solid curves, representing, for normal cats, N_1 amplitude as a function of stimulus SPL for several test-tone frequencies shown in Fig. 10, is typical of the 5 cats for which these curves were measued, and is in agreement with the shape of the curves (1 kHz and 4 kHz) measured by de Boer [9]. The slopes of the input–output curves become steeper with increasing frequency. This reflects the fact that the set of fibers with high characteristic frequency (CF) is more effective in producing AP than the set of low-CF fibers. Greater effectivity of high-CF fibers may be due to a better time relation among the contributions. This is likely because the latency dispersion among fibers in the high-CF range is smaller than in the low-CF one. Furthermore, there is no evidence that the firing-rate–SPL function is steeper for high-CF fibers than for low-CF ones, and there is no difference in the waveform between the contributions from high- and low-CF fibers to the AP [1,29].

After excessive noise stimulation the input–output curves are shifted to higher SPLs, while the maximum N_1 amplitude remains equal. Uziel et al. [46] also found unaffected maximum AP amplitudes in guinea pigs when AP-threshold shifts due to Kanamycin

treatment were less than 50 dB. In a number of cases the input–output curves of Fig. 10 are steeper after inducement of the trauma. This might be the electrophysiological equivalent of an effect which is known as abnormal growth of loudness or loudness recruitment. Loudness of a stimulus might reflect the total firing activity of fibers excited by that stimulus. In pathological ears it is observed that the low-frequency tail of single-fiber tuning curves often is normal or even hypersensitive, while the tip is broader and has shifted to higher SPLs [19,20,27,28,30]. Evans [20] explains recruitment by broader tuning of pathological fibers. Broader tuning implies a faster growth of the number of active fibers with increasing SPL. These considerations do not hold for wide-band stimuli because the increase of the number of fibers firing is not due to a spread of neural activity, since wide-band stimuli cover the whole CF range. In addition to the fast growth of the number of active fibers, cochlear pathology serves to increase the steepness of the discharge-rate–SPL functions at the fiber's CF [19]. However, it is not possible to predict simply how these effects are reflected by the AP amplitude because of the complex character of the AP. For instance, after inducement of a trauma an AP evoked by a test tone might be built up from fibers with higher CFs than before the trauma. In such a case steeper input–output curves may be expected, while the magnitude of the number of fibers excited by the test tone is not necessarily larger.

4.4. AP threshold before and after inducement of the noise trauma

As expected from the experiments of Miller et al. [32], our type of excessive noise stimulation caused threshold shifts which differed considerably from one animal to another. They reported a recovery from TTS 12 hours after noise exposure of 7 dB at 4 kHz. This value is comparable with the recovery we found (5 dB at 4 kHz). The difference might be explained by inter-individual variation or by the fact that our animals were under anaesthesia during and after the noise exposure. The greatest threshold shift was found between 2 and 6 kHz. This is sometimes ascribed to the middle-ear transfer characteristic. Tonndorf [46], for example, explains the largest (broad-band) noise-induced hearing loss (PTS) in the 4 kHz region (in man) by resonance at that frequency in the outer ear canal. Our results for cats do not fully support this view, because the traumatizing noise used in our experiments is essentially flat at the tympanic membrane.

In the traumatized ear the AP-amplitude criterion for the definition of threshold has an effect on the shape of the curve representing threshold shift as a function of test-tone frequency, because in pathological ears input–output curves are sometimes steeper than in normal ears. We do not follow Price's method of extrapolating to zero amplitude because this extrapolation is not uniquely defined. We prefer measuring around the AP-amplitude criterion.

4.5. AP latency before and after inducement of the trauma

The solid curves representing AP latency for normal cats as a function of test-tone SPL (Fig. 13) are typical of the results collected for 5 cats. Just after inducement of the trauma higher latency values are found for each condition. These longer latencies probably reflect the fact that higher frequency regions, which are activated in the normal ear, are not activated in the traumatized ear. High-pass noise masking of the AP as a tool for finding the place of origin of the AP in the traumatized ear is questionable. A problem

with the derived narrow-band AP is the center frequency of the narrow band. See the position of the bars, relative to the test-tone frequency in Fig. 9. The center frequency depends upon (a) noise level relative to single-fiber thresholds, and (b) the low-frequency slope of the excitation pattern produced by the noise masker. Both factors are unknown after inducement of the acoustic trauma. An additional problem is that in the traumatized ear we did not succeed in masking the AP produced by a tone burst having a frequency for which the threshold is increased. Even simultaneous masking with masker levels up to 80 dB SPL per component was not successful.

4.6. AP latency at threshold before and after inducement of the trauma

The curve representing average AP latency at threshold (11 cats) as a function of test-tone frequency (Fig. 14) shows a gradual decline for increasing frequency. To compare latency data of AVCN neurons with AP-latency data, we corrected the travel-time data of Gibson et al. [21] with the total frequency-independent delay (1.5 ms) minus the estimated acoustic transmission (0.3 ms) and one synaptic delay (0.5 ms). After these corrections, latency data of AVCN neurons [21] are in agreement with the average AP-latency data.

AP-latency values at 3 and 4 kHz are equal. The 4 kHz latency seems to be too high by about 0.2 ms. This might be due to the transfer function from earphone to sound pressure at the tympanic membrane. This function (Fig. 1) shows a narrow peak at about 4 kHz, which means that the 4 kHz test tone has a small onset time at the tympanic membrane instead of an immediate onset.

AP-latency values at threshold (8 cats) after inducement of the trauma are about equal to the values measured before the trauma (Figs. 15 and 16). In a few cases AP-latency values in the traumatized ear are considerably shorter than for the normal ear in particular with cat 7810. Shifts in latency correspond to shifts of the excited area to the nearest intact area on the basilar membrane [2,3]. Uziel et al. [46] found normal or larger latencies in Kanamycin-treated guinea pigs. The treatment resulted in a high-frequency hearing loss. So, larger latencies are due to a shift of the excitation area to an area that responds to lower frequencies. However, Eggermont [16] found that, for human ears which show loudness recruitment and which also show a W-shaped waveform of the derived narrow-band AP produced by a click, the narrow-band latency is smaller in comparison with the normal ear (equal SPL of the click). This is in agreement with our findings in cat 7810. This cat showed, after inducement of the trauma, short latencies accompanied by a W-shaped waveform of the AP produced by tone bursts. The threshold shift after excessive noise stimulation is the largest we found for the eight cats measured (upper curve, Fig. 12). The group of recruiting ears in the study of Eggermont [16] which showed no W-shaped narrow-band waveform had AP latencies equal to the normal ear. Eggermont assumes that the decrease in the narrow-band AP latency is due to wider tuning of the cochlear filter.

We agree that broader filters may have shorter response times, but we did not find shorter response times for single neurons in the AVCN [42], which showed broader tuning curves (equal SPL at the tip, hence different firing rates) after excessive noise stimulation. These response times were calculated for phase-locked units which could be measured both before and after inducement of the trauma. These measurements do not

exclude the possibility that shorter response times can be found for larger threshold shifts than we found in our experiments. Salvi et al. [37] observed in auditory-nerve fibers of noise-treated chinchillas (5 days, octave centered at 0.5 kHz and 95 dB SPL) that latencies of the first peak in the post-stimulus-time histogram of firing produced by a click is equal to the latencies found for the normal ear, provided that the SPL of the click is equal in both cases.

From the above-mentioned studies it is not clear whether the short latency at threshold we found, for instance as shown for the 2 kHz test tone in cat 7806, stems from high-BF fibers or reflects a wider cochlear filter.

5. CONCLUSIONS

For the normal ear the shape of curves representing AP threshold as a function of test-tone frequency is similar to behavioral and single-fiber threshold curves.

AP thresholds are higher than behavioral and single-fiber thresholds.

AP latency at threshold (normal ear) for an immediate-onset test tone is equal to the derived narrow-band AP latency.

Even for the shortest test-tone rise time used (0.1 ms), an increased AP latency is found with respect to AP latency measured by means of immediate-onset test tones.

After exposure for half an hour to broad-band noise (equal intensity per octave) at 105.3 dB SPL, the largest threshold shift is found between 2 and 6 kHz.

AP-latency values at threshold before and after inducement of the trauma are not significantly different.

Comparison of AP latency before and after inducement of the trauma at equal SPL showed increased latencies, whereas for a minority of responses after inducement of the trauma lower latencies at threshold are found than before.

It is not yet clear whether the responses before and after inducement of the trauma stem from the same population of auditory-nerve fibers or whether the responses after inducement of the trauma stem from another fiber population innervating the nearest intact area on the basilar membrane excited by the test tone.

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CHAPTER V

EIGHTH-NERVE ACTION-POTENTIAL TUNING CURVES IN CATS BEFORE AND AFTER INDUCEMENT OF AN ACUTE NOISE TRAUMA

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EIGHTH-NERVE ACTION-POTENTIAL TUNING CURVES IN CATS BEFORE AND AFTER INDUCEMENT OF AN ACUTE NOISE TRAUMA

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Potentials and limitations of eighth-nerve action-potential tuning curves (APTC) in providing us with a measure of frequency selectivity are studied in cats. APTCs are measured, using a forward-masking technique. They are essentially wider than auditory-nerve fiber tuning curves. Width of APTCs is dependent upon test-tone sound pressure level (SPL) and masking criterion. This can be explained by assuming that APs are formed by discharges of fibers with different CFs. Acoustic traumata are induced halfway into the experiments in order to measure APTCs before and during the trauma in the same animal. This broad-band noise exposure resulted in a long-lasting temporary threshold shift which remained fairly steady during the experiment. In the traumatized ear APTCs are wider than in the normal ear. This widening, also observed in auditory-nerve fibers, is not simply an SPL effect.

Key words: eighth-nerve action potential; frequency selectivity; acute noise trauma.

1. INTRODUCTION

An electrode placed in the vicinity of the round-window membrane records the compound activity of primary auditory-nerve fibers. The compound response following click or tone-burst stimulation measured with this electrode is called compound or whole-nerve action potential (AP). Several masking techniques have been used in order to show that the AP evoked by low-level tone bursts is built up from contributions of primary auditory-nerve fibers which have characteristic frequencies (CF) in a narrow frequency range [5,8,9,14,30,31]. By means of a tone-on-tone masking technique it has been demonstrated that it is possible to obtain compound action-potential tuning curves (APTC) in the normal ear, which are quite similar to auditory-nerve iso-rate curves also known as frequency tuning curves (FTC) [5,13,14]. An APTC represents level as a function of frequency of those pure-tone maskers which reduce, by a fixed amount, the amplitude of the first negative peak of the AP (N_1) evoked by a tone with fixed SPL and frequency. Hence, an APTC is an iso-masking contour.

From psychophysical studies we know that the perception of a tone (probe) can be masked by another signal (masker) immediately preceding that tone. This type of masking is often used and is called forward masking. A review on non-simultaneous masking technique is given by Duifhuis [7]. Using forward-masking paradigms one avoids non-linear distortion effects such as lateral suppression and combination-tone generation, which occur during simultaneous presentation of two tones [15,28].

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Smith [26] showed at the primary auditory fiber level that a fiber's firing rate produced by a tone (probe) decreases if this tone is preceded by another signal (masker). This phenomenon is known as short-term adaptation. A fiber's firing rate evoked by a probe (frequency at fiber's CF) decreases by an amount which is proportional to the firing rate produced by the preceding masker [1,13,26,27]. The constant of proportionality is a function of masker duration and masker-probe time interval, but is not, on the other hand, a function of masker frequency and level. Furthermore, the firing rate evoked by the probe decreases by an amount independent of the probe level. From this it follows that for single-fibers iso-masking contours are equivalent to iso-firing-rate contours.

Based on these single-fiber experiments a simplified model of the mechanisms underlying APTCs can be constructed. We define a test tone as a sinusoidal stimulus evoking an AP. If we present a test tone to the ear at a sound-pressure level (SPL) just above fiber's threshold, only fibers with CF at test-tone frequency will fire. These fibers may constitute an AP which can be measured close to the round window. The collection of pure-tone maskers that reduce the AP amplitude by a fixed amount form, by definition, an APTC. Because the averaged amplitude of the AP reflects each fiber's probability of firing at the onset of the stimulus and the synchrony across the active ensemble, we assume the results presented by Smith [26,27], Harris [13] and Abbas [1] concerning firing rates to be valid for the probability of firing during the onset of a tone. Maskers reducing AP amplitude by a fixed amount excite fibers, with CF at test-tone frequency, at fixed firing rates. In other words, by means of masking the AP we indirectly measure the excitation of fibers, with CF at test-tone frequency, produced by the masker. The set of those pure-tone stimuli that excite a fiber with a fixed amount form, by definition, a frequency tuning curve (FTC). Hence, APTCs should be equivalent to FTCs, assuming that only fibers with CF at test-tone frequency constitute the AP.

In practical conditions we will see that this model does not adequately predict the results, because the fibers contributing to the AP do not all have the same CF. The reason is that the AP is a gross potential measured far away from its origin. The response of one fiber measured at the round window is about 0.05 μV [2,20]. To evoke a 'threshold' response (about 2 μV, averaging 100 responses) it is necessary for a number of fibers to fire nearly simultaneously. The amplitude of an AP built up from contributions of a population of fibers increases if the probability of firing during the onset of the test tone increases. The amplitude of an AP also increases if the dispersion of the firing moments decreases. The probability of firing increases if the test-tone SPL increases, and the dispersion of firing moments decreases if test-tone onset time decreases. However, increasing test-tone SPL implies that the number of fibers excited by the test tone also increases because the extent of the excitation pattern increases [22]. Furthermore, a rapid test-tone onset time which is used in order to ensure that firing moment dispersion is low, results in splatter of tone-burst energy over spurious frequency bands. Energy over spurious frequencies stimulates fibers with CF, corresponding to the splattered tone-burst energy which then contribute to the AP. Hence, using a non-simultaneous masking technique, we present the potentials and limitations of the APTC in the cat, in providing us with a measure of frequency selectivity of both the normal and the acoustically traumatized ear.

2. METHODS

Healthy adult cats were anaesthetized with sodium pentobarbital (Nembutal). After an initial intraperitoneal injection of Nembutal (45 mg/kg) and an intramuscular injection of Atropine (0.5 mg), supplementary doses of Nembutal were administered intravenously to maintain the animal at a surgical level of anaesthesia during the experiment. Every 8 hours an intramuscular injection of Atropine Sulfate (0.5 mg) was given. All animals were tracheotomized. Arterial blood pressure, heartbeat frequency, and percentage of carbon dioxide in expired air were monitored in order to check the general state of the animal. Rectal temperature was maintained at approximately 38°C by means of a thermostatically controlled heating blanket.

Surgical preparations for electrophysiological recordings included resecting the pinna and opening the bulla to provide access to the round-window membrane. A silver-ball recording electrode was placed in the vicinity of the round window, while the indifferent electrode was placed in the neck muscles. The recording site was ipsilateral to the stimulated ear. In a number of experiments single-cell recordings in the antero-ventral cochlear nucleus (AVCN) were also made. AVCN was visualized by aspirating the overlying cerebral cortex, white matter, and cerebellum.

Experiments were performed in a chamber especially constructed for acoustic insulation and electric shielding. Stimulus generation, cochlear-response averaging, and response storage were fully controlled by a computer (PDP 11-10).

Stimuli were delivered through an electrodynamic transducer (Beyer DT 48) connected to the cat's external meatus. The transducer was calibrated by measuring sound pressure level and phase of sine-wave stimuli with a probe-tube microphone near the tympanic membrane. The calibration signals covered the frequency range from 40 Hz to 20 kHz in steps of 40 Hz. SPL and phase data (both specified at the tympanic membrane) were stored in the computer and were used to calculate the electrical stimuli required to produce the desired acoustic stimuli at the tympanic membrane.

Cochlear responses from the round-window electrode were amplified 10,000X and bandpass filtered between 1 and 30,000 Hz. To obtain compound action potential data, 100 to 1000 responses to a test tone were averaged. Responses were only recorded during presentation of the test tone. To separate CM from AP the test-tones were started from d.c. level alternately with 0 or 180° phase. As a result, CM can be obtained by subtraction and AP by addition of two successive responses, because CM follows the test-tone phase while AP polarity is independent of this phase. Responses to masker and test tone were also measured separately. Unless otherwise specified, we measured APTCs in standard conditions. These conditions were: (a) forward masking; (b) low test-tone SPL (10 μV AP amplitude); (c) 25% masking criterion; (d) test tones (immediate onset and offset) filtered by high- and low-pass filters with cut-off frequencies at test-tone frequency (both slopes 96 dB/oct). The timing sequence used in the experiments is depicted in Fig. 1. The test tone, 5 ms in duration (immediate onset and offset) followed 16 ms after the offset (signal still at 100%, 10.4 ms after completed offset, signal 0%) of the masker. The masker had a duration of 20 ms, while its rise/fall time was 4 ms (between 10 and 90% of full amplitude with cosine shaping).

In general we may distinguish two successive negative peaks in the whole-nerve action

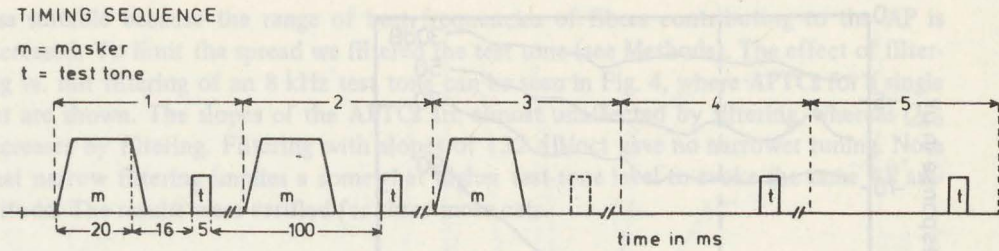


Fig. 1. Timing sequence of the stimuli used in the forward-masking paradigm to measure AP tuning curves. In each stimulus cycle (525 ms) AP following test-tone onset is measured twice with (1 and 2), and twice without (4 and 5) a preceding masker. In between (3), the response produced by the masker is measured at the time of the test tone, which is not present then. Responses to test tones are measured twice in order to remove cochlear microphonics from the recordings (the two test tones have opposite polarities).

potential (N_1 and N_2). We define AP amplitude as the difference between the baseline (level just prior to test-tone delivery) and the N_1 peak. Furthermore, we define AP latency as the time interval between stimulus onset at the tympanic membrane and the moment that N_1 reaches its peak value. Frequency selectivity is expressed in Q_{10}, which is the ratio of test-tone frequency and the bandwidth 10 dB above the tip of the APTC. Halfway into the experiments cats were exposed to broad-band noise for half an hour.

In order to induce the acoustic trauma by means of noise having a spectrum which is well defined at the tympanic membrane, irrespective of the transfer function from transducer to the membrane, we synthesized this noise from 127 harmonics spaced at 160 Hz frequency intervals. The SPL of the first harmonic was 98 dB and the levels of the higher harmonics were lower according to a −3 dB/oct slope. This slope was chosen to obtain a constant intensity per octave as a function of frequency. The total SPL was 105.3 dB. Phases of the 127 harmonics were chosen such that the noise as a function of time had as small a crest factor (peak factor) as possible [25].

3. RESULTS

3.1. Slow after-response evoked by a masker

The forward-masking experiments show that maskers produce a slow negative after-response. This after-response becomes greater if the masker SPL increases. This can be seen in Fig. 2, where the slow after-response is shown for an 8 kHz masker at several SPLs. Different masker frequencies produce different after-responses. Fig. 3 shows after-responses for several frequencies of the masker at 70 dB SPL. The greatest effect is found at 1 kHz.

In order to minimize interaction between masker and test-tone a large interval is needed. However, the masking effect decreases with increasing interval between masker and test-tone [5]. For a good compromise we chose an interval of 16 ms.

Assuming linear superposition of after-response and test-tone response, we measured separately the after-response to the masker, and obtained the response to the test tone by

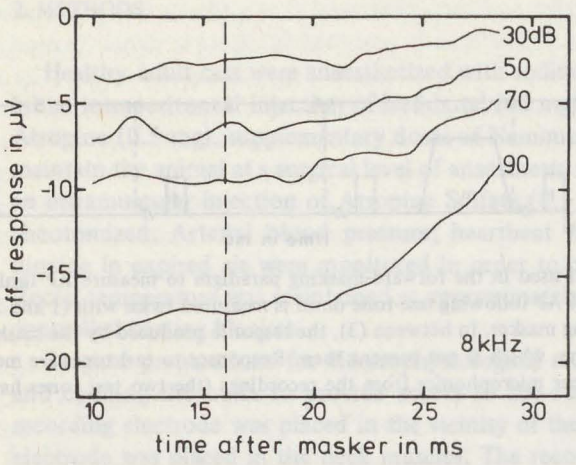


Fig. 2. Amplitude of the slow after-response produced by an 8 kHz masker at several SPLs. The dashed line represents the moment at which the test tone is switched on during forward-masking experiments.

subtracting the after-response from the compound response to test tone and masker. The slow after-response is not due to the recording system, as the time constant of the system is greater than 1 s. Recently Harris [14] also reported a slow response following the masker, and he also assumed linear superposition.

3.2. Effect of test-tone filtering on APTC

The rapid onset of the test tone necessary to produce an AP response produces spread of test-tone energy over a frequency band. This spread makes a test tone with rapid onset

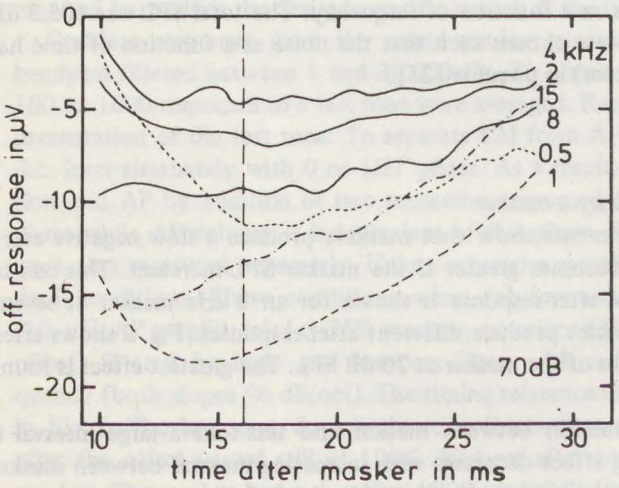


Fig. 3. Amplitude of the slow after-response produced by 70 dB SPL maskers at several frequencies. The dashed line represents the moment at which the test tone is switched on during forward-masking experiments.

less suitable because the range of best frequencies of fibers contributing to the AP is increased. To limit the spread we filtered the test tone (see Methods). The effect of filtering vs. not filtering of an 8 kHz test tone can be seen in Fig. 4, where APTCs for a single cat are shown. The slopes of the APTCs are almost unaffected by filtering, whereas Q_{10} increases by filtering. Filtering with slopes of 132 dB/oct gave no narrower tuning. Note that narrow filtering implies a somewhat higher test-tone level to evoke the same AP amplitude. The results were verified for three more cats.

3.3. Simultaneous and forward masking

Simultaneous masking is more complex than forward masking because interactions between masker and test tone such as lateral suppression and combination tone generation may play a role in the results. Fig. 5 presents APTCs obtained with simultaneous- and forward-masking techniques. Test-tone SPL and frequency are equal in both experiments (30 dB SPL, 8 kHz).

It is clear that the masking criterion (25%) is met at lower masker SPLs during simultaneous masking than during forward masking. Furthermore, the APTC measured by

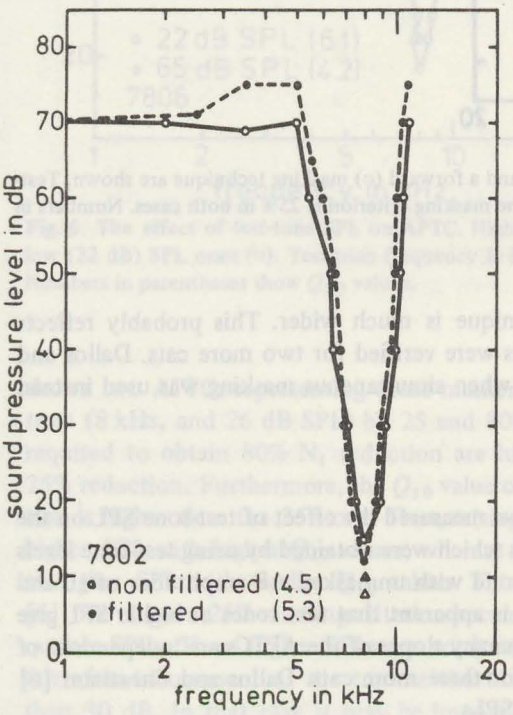


Fig. 4. The effect of test-tone filtering on APTCs. The curves represent those maskers which reduce the amplitude of the AP produced by the test tone from 2.6 to 2.0 μV. The curves represent APTCs obtained by means of unfiltered (○) and filtered (●) test tones. The test tone is low- and high-pass filtered, with slopes of 96 dB/oct and cut-off frequency at test-tone frequency. Test-tone level and frequency are indicated by means of open and closed triangles for unfiltered and filtered test tones, respectively. The masking criterion is 25% in both cases. Numbers in parentheses show Q_{10} values.

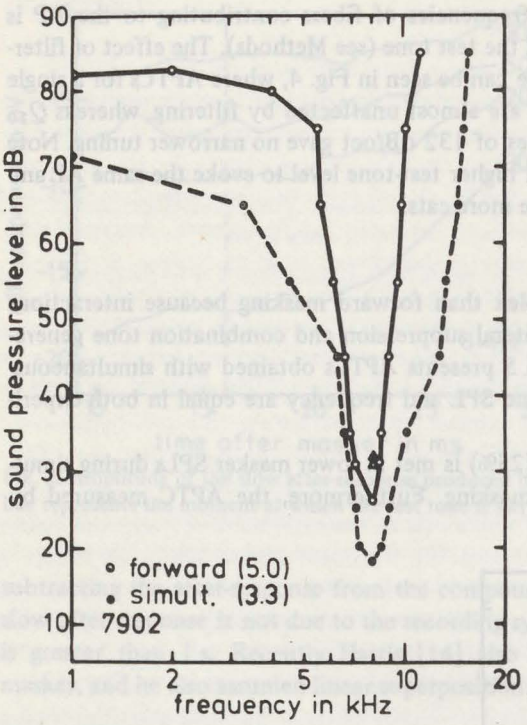


Fig. 5. APTCs obtained with a simultaneous (•) and a forward (○) masking technique are shown. Test-tone frequency and SPL are 8 kHz and 30 dB. The masking criterion is 25% in both cases. Numbers in parentheses show Q_{10} values.

means of the simultaneous masking technique is much wider. This probably reflects effects of test-tone suppression. The results were verified for two more cats. Dallos and Cheatham [6] also reported wider APTCs when simultaneous masking was used instead of forward masking.

3.4. Effect of test-tone SPL on APTC

Using a fixed masking criterion (25%), we measured the effect of test-tone SPL on the APTC. Fig. 6 shows for one cat two APTCs which were obtained by using test-tone levels of 22 and 65 dB SPL. These levels correspond with unmasked AP amplitudes of 10 and 90 μV. Test-tone frequency was 8 kHz. It is apparent that test tones at higher SPL give wider APTCs, while the low- and high-frequency slopes of the APTCs are independent of test-tone level. The results were verified for three more cats. Dallos and Cheatham [6] also found wider APTCs at higher test-tone SPLs.

3.5. Effect of masking criterion on APTC

The amount of masking depends on the amount of excitation of the fibers also excited by the test tone. This means that more masking of the AP response results in an APTC corresponding to the tuning curve of a fiber responding with a higher firing rate. Fig. 7

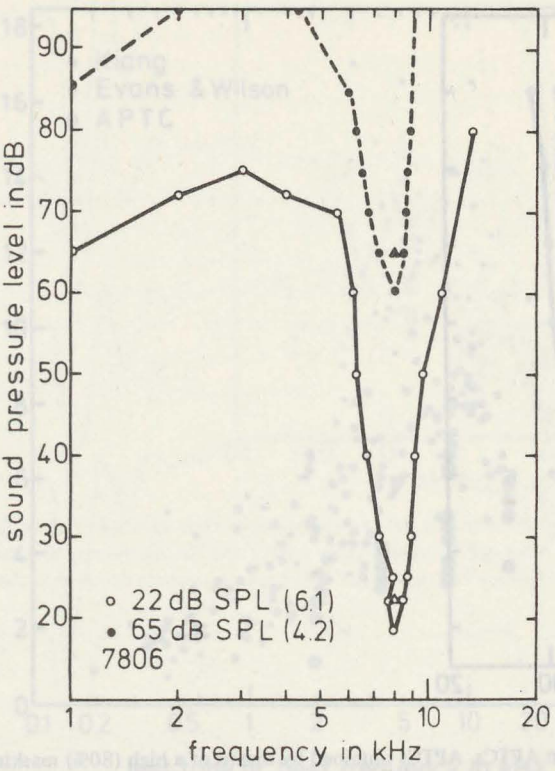


Fig. 6. The effect of test-tone SPL on APTC. High (65 dB) test-tone SPL APTCs (•) are wider than low (22 dB) SPL ones (○). Test-tone frequency is 8 kHz. The masking criterion is 25% in both cases. Numbers in parentheses show Q_{10} values.

shows two APTCs representing those maskers which reduce the AP response to the test tone (8 kHz, and 26 dB SPL) by 25 and 80%, respectively. Of course the masker levels required to obtain 80% N_1 reduction are higher than the masker levels which produce 25% reduction. Furthermore, the Q_{10} value of the APTC corresponding to 80% N_1 reduction is higher than the 25% one. Thus, raising the masking criterion gives tuning curves at higher SPL with higher Q_{10} values, whereas increasing test-tone SPL gives tuning curves at higher SPL with smaller Q_{10} values. This is in agreement with Dallos and Cheatham [6]. We chose a 25% masking criterion because higher masking criteria also lead to higher masker SPLs. These higher SPLs are no drawback in measuring APTCs for a normal ear, but after inducement of the trauma the tuning-curve tips may shift upward over more than 30 dB. In that case it may be impossible to obtain APTCs at masker levels lower than 90 dB SPL.

3.6. Differences between APTC and FTC

In Fig. 8 we show the Q_{10} values for primary-auditory-nerve fibers as found in the cat by Kiang [17] and by Evans and Wilson [10]. Furthermore, we plotted the Q_{10} values of

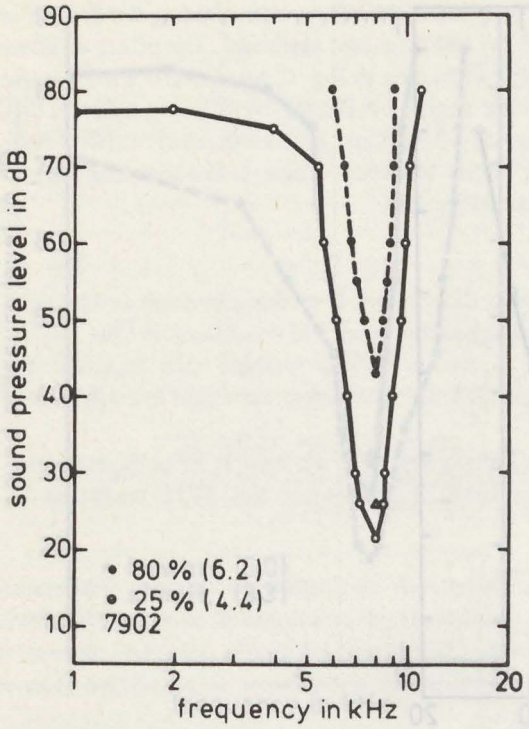


Fig. 7. The effects of masking criterion on APTCs. APTCs obtained by means of a high (80%) masking criterion (•) are narrower than APTCs obtained by using a low (25%) criterion (○). Test-tone frequency and SPL are 8 kHz and 26 dB. Numbers in parentheses show Q_{10} values.

APTCs which where found for an AP amplitude decrease from 10 to 7.5 μV. It is clear that the APTC Q_{10} is lower than or equal to the lowest Q_{10} values found for single fibers. Evans and Wilson [10] also obtained low-frequency slopes from FTCs in the cat. Fig. 9 shows low-frequency slopes measured between 5 and 25 dB from the tip of single-fiber FTCs [10] and from the tip of APTCs (this study). Low-frequency slopes of low-frequency APTCs are shallower than single-fiber slopes. For high-frequency APTCs the low-frequency slope is about equal to or perhaps greater than single-fiber slopes at 15 kHz.

3.7. Tip shift of APTC

Fig. 10 depicts the reduction in N_1 amplitude, expressed as a percentage of the non-masked (control) N_1 amplitude, as a function of masker frequency for several masker SPLs. Test-tone frequency and SPL were 4 kHz and 45 dB. With increasing masker SPLs the frequency causing greatest reduction decreases. An interesting case is seen in Fig. 11. Test-tone frequency and SPL were 8 kHz and 70 dB. AP responses masked by pure tones are presented for two masker SPLs and several masker frequencies. For 80 dB SPL maskers the first negative peak (N_1) is divided into two components if the masker frequency is near the test-tone frequency (8 kHz). If the masker frequency is lower than the

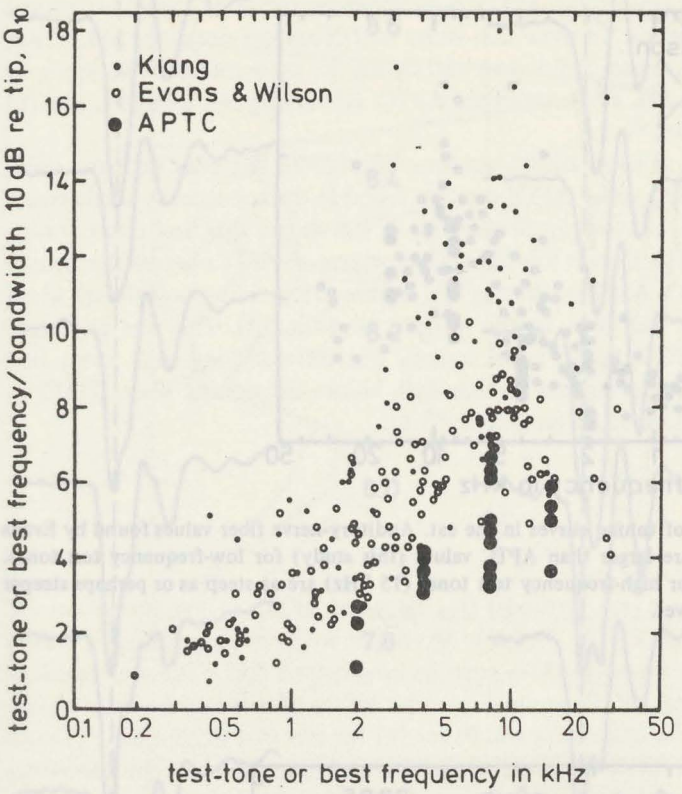


Fig. 8. Frequency selectivity expressed in Q_{10} for auditory-nerve fibers and APTCs in the cat. The fiber values found by Kiang [17] and Evans and Wilson [10] are greater than the APTC values found in this study.

test-tone frequency, the amplitude of the short-latency peak increases, while for higher masker frequencies the long-latency peak becomes more pronounced. The effect is less clear for 50 dB SPL maskers. When the masker level is at 50 dB SPL the masker frequency for which the short- and the long-latency peak amplitudes are equal, is higher than the test-tone frequency. This phenomenon has also been observed in other cats but is not always as clear as shown in Fig. 11.

3.8. APTCs in the acoustically traumatized ear

APTCs were measured before and after inducement of noise traumata. The results are shown in Figs. 12a–d for two cats. Test-tone SPLs (unfiltered) required to produce a threshold response (2.5 μV) both before and after excessive noise stimulation are also plotted. For both cats in Figs. 12a–d the tips of the APTC are broader and the slopes of the APTC are shallower when the test-tone frequencies are in the traumatized (increased threshold) region. The tips of the APTCs have undergone a greater upward shift than the tails. For one cat, 8 kHz (Fig. 13a) and 15 kHz (Fig. 13b) APTCs after partial recovery

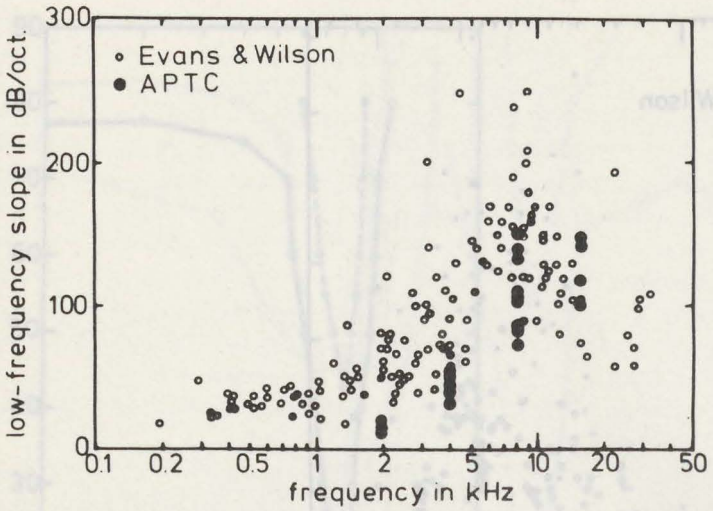


Fig. 9. Low-frequency slopes of tuning curves in the cat. Auditory-nerve fiber values found by Evans and Wilson [10] in the cat are larger than APTC values (this study) for low-frequency test tones. APTC low-frequency slopes for high-frequency test tones (15 kHz) are as steep as or perhaps steeper than slopes of fiber tuning-curves.

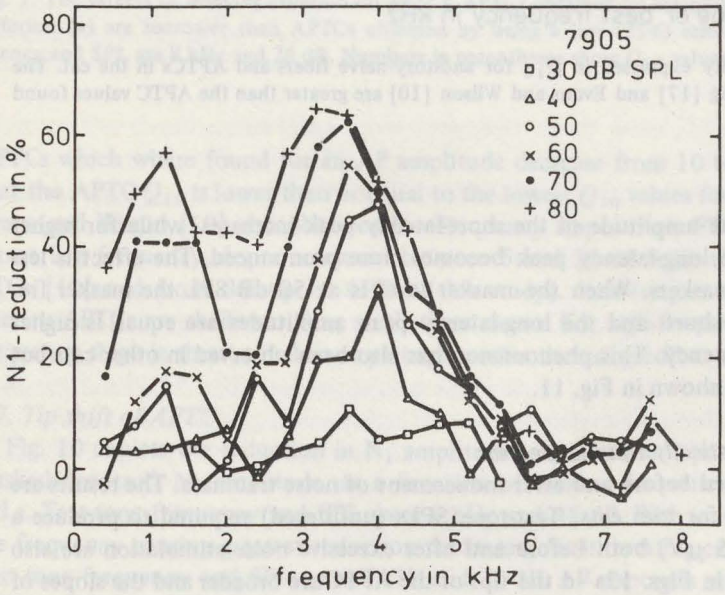


Fig. 10. N_1 reduction due to the masker (relative to the non-masked N_1) as a function of masker frequency for several masker SPLs. Test-tone frequency and SPL are 4 kHz and 45 dB. The frequency for maximum N_1 reduction shifts to lower frequencies with increasing masker SPL.

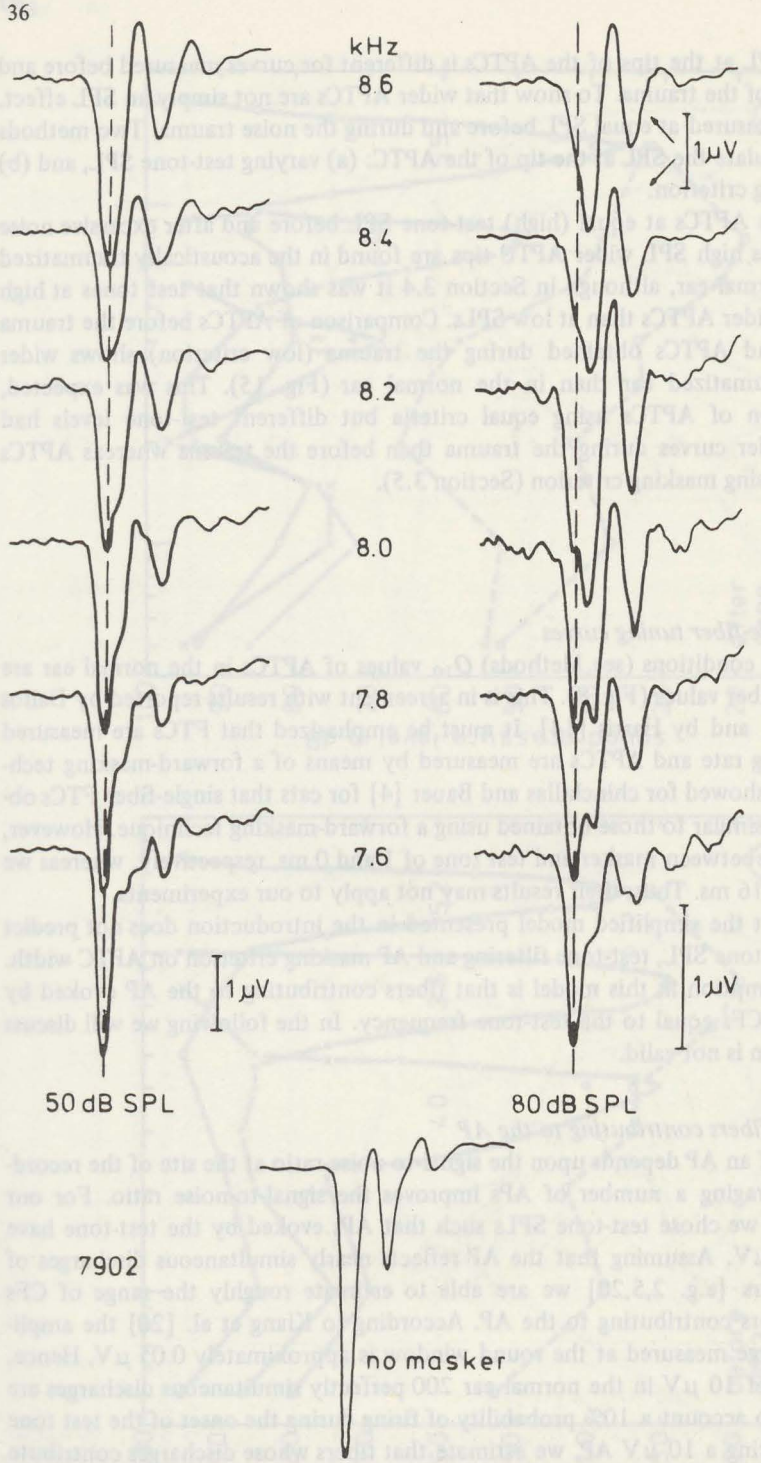


Fig. 11. An interesting case of an AP masked by pure tones. Test-tone frequency and SPL are 8 kHz and 70 dB. Masker frequency and level are shown. The dashed line represents the latency of the non-masked AP. Note that for the 80 dB SPL masker at test-tone frequency, N_1 is divided into two components.

are shown. The SPL at the tips of the APTCs is different for curves measured before and after inducement of the trauma. To show that wider APTCs are not simply an SPL effect, APTCs are also measured at equal SPL before and during the noise trauma. Two methods are used to manipulate the SPL at the tip of the APTC: (a) varying test-tone SPL, and (b) varying AP masking criterion.

Fig. 14 presents APTCs at equal (high) test-tone SPL before and after excessive noise stimulation. At this high SPL wider APTC tips are found in the acoustically traumatized ear than in the normal ear, although in Section 3.4 it was shown that test tones at high SPLs give rise to wider APTCs than at low SPLs. Comparison of APTCs before the trauma (high criterion) and APTCs obtained during the trauma (low criterion) shows wider APTCs in the traumatized ear than in the normal ear (Fig. 15). This was expected, because comparison of APTCs using equal criteria but different test-tone levels had already shown wider curves during the trauma than before the trauma whereas APTCs narrow with increasing masking criterion (Section 3.5).

4. DISCUSSION

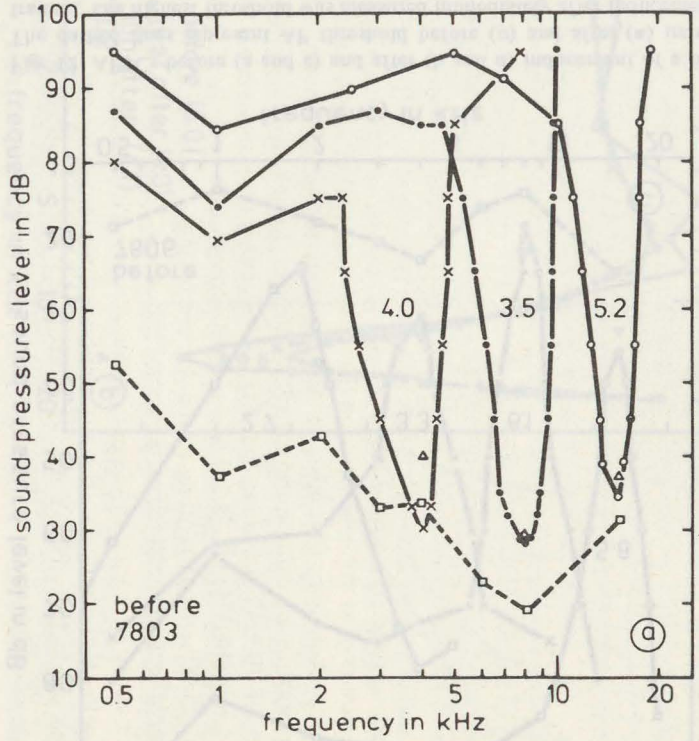
4.1. AP versus single-fiber tuning curves

Under standard conditions (see Methods) Q_{10} values of APTCs in the normal ear are lower than single-fiber values (Fig. 8). This is in agreement with results reported by Dallos and Cheatham [5] and by Harris [14]. It must be emphasized that FTCs are measured directly using firing rate and APTCs are measured by means of a forward-masking technique. Harris [13] showed for chinchillas and Bauer [4] for cats that single-fiber FTCs obtained directly are similar to those obtained using a forward-masking technique. However, they used intervals between masker and test tone of 1 and 0 ms, respectively, whereas we used an interval of 16 ms. Thus, their results may not apply to our experiments.

It is evident that the simplified model presented in the introduction does not predict any effects of test-tone SPL, test-tone filtering and AP masking criterion on APTC width. An important assumption in this model is that fibers contributing to the AP evoked by the test tone have CFs equal to the test-tone frequency. In the following we will discuss why this assumption is not valid.

4.2. Population of fibers contributing to the AP

The detection of an AP depends upon the signal-to-noise ratio at the site of the recording electrode. Averaging a number of APs improves the signal-to-noise ratio. For our APTC experiments we chose test-tone SPLs such that APs evoked by the test-tone have amplitudes of 10 μV. Assuming that the AP reflects nearly simultaneous discharges of auditory-nerve fibers [e.g. 2,5,20] we are able to estimate roughly the range of CFs covered by the fibers contributing to the AP. According to Kiang et al. [20] the amplitude of one discharge measured at the round window is approximately 0.05 μV. Hence, to produce an AP of 10 μV in the normal ear 200 perfectly simultaneous discharges are needed. Taking into account a 10% probability of firing during the onset of the test tone at the levels producing a 10 μV AP, we estimate that fibers whose discharges contribute to the AP (2000 fibers) cover a CF range of about half an octave.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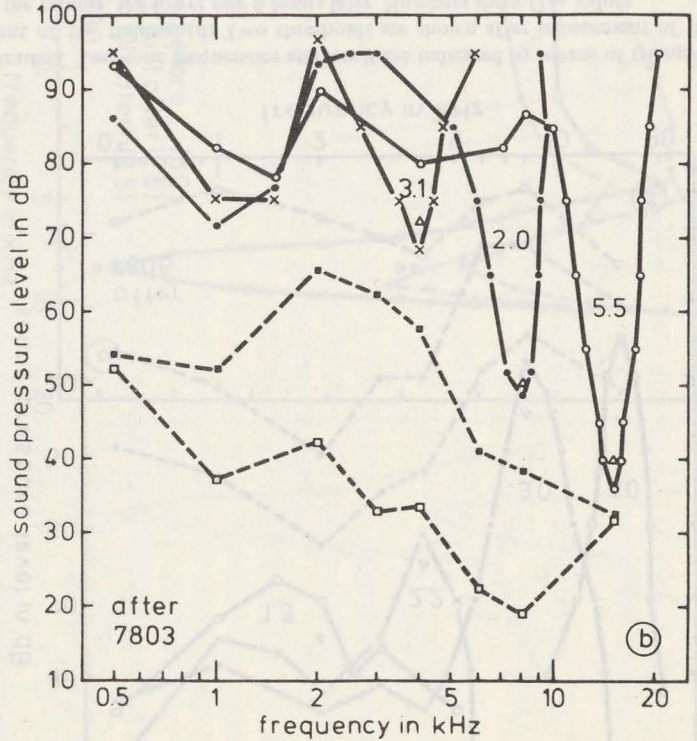
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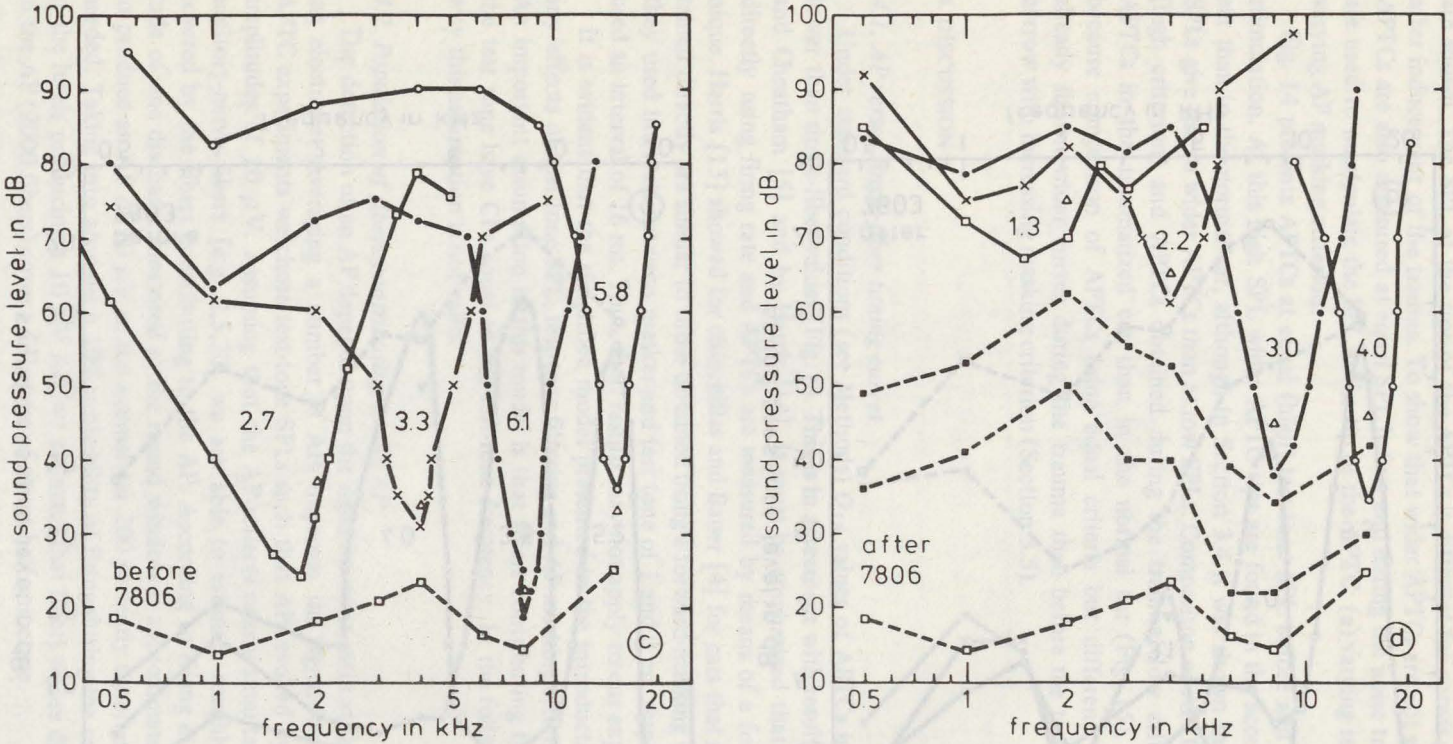

Fig. 12. APTCs before (a and c) and after (b and d) inducement of a noise trauma. Test-tone frequencies and levels are indicated by means of triangles. The dashed lines represent AP threshold before (□) and after (■) inducement of the trauma. (d) Two thresholds are shown after inducement of the trauma. The highest threshold was measured immediately after inducement of the trauma, the lower one 6 hours later. Numbers show Q_{10} values.

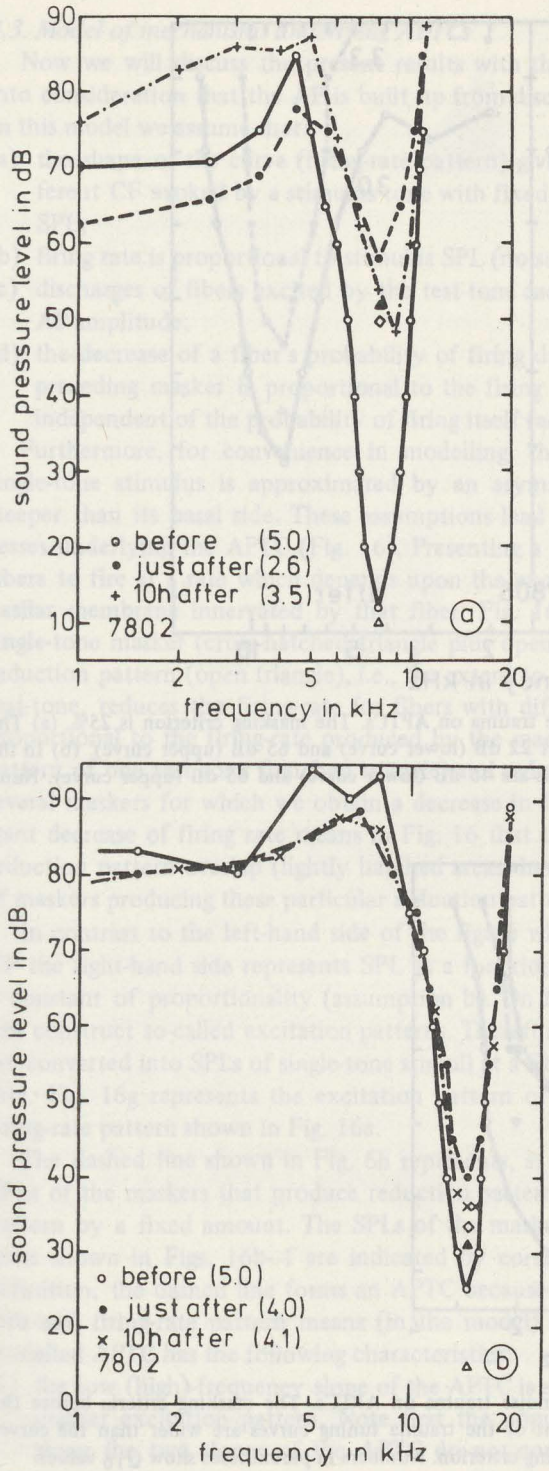

Fig. 13. Two examples of partial recovery of APTCs. Test-tone frequencies and levels are indicated by means of triangles. Numbers in parentheses show Q_{10} values.

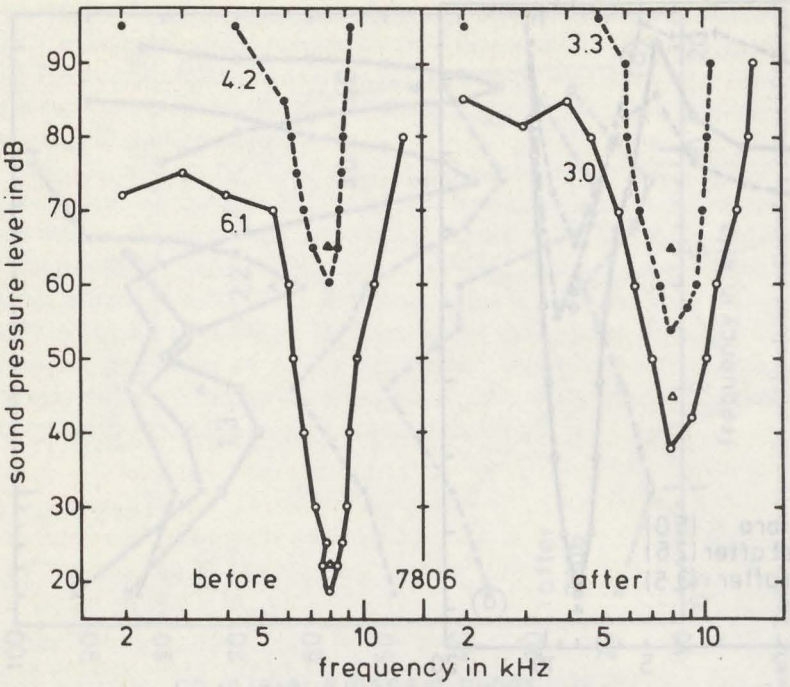

Fig. 14. Effect of test-tone SPL and noise trauma on APTCs. The masking criterion is 25%. (a) The test tone is presented before the trauma at 22 dB (lower curve) and 65 dB (upper curve). (b) In the acoustically traumatized ear test-tone levels are 45 dB (lower curve) and 65 dB (upper curve). Numbers show Q_{10} values.

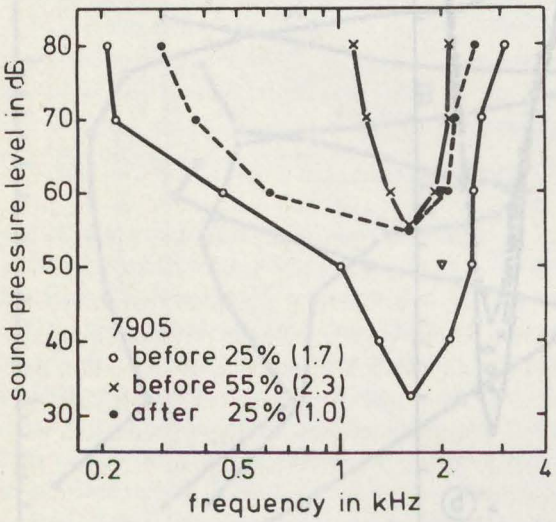

Fig. 15. Effect of masking criterion and noise trauma on APTCs. The masking criteria before the trauma are 25 and 55%. After inducement of the trauma tuning curves are wider than the curves before the trauma, irrespective of the masking criterion. Numbers in parentheses show Q_{10} values.

4.3. Model of mechanisms underlying APTCs

Now we will discuss the present results with the help of a qualitative model, taking into consideration that the AP is built up from discharges of fibers in a certain CF range. In this model we assume that:

(a) the shape of the curve (firing-rate pattern) giving the firing rate for fibers with different CF evoked by a stimulus tone with fixed frequency is independent of stimulus SPL;
(b) firing rate is proportional to stimulus SPL (no saturation);
(c) discharges of fibers excited by the test-tone each contribute the same amount to the AP amplitude;
(d) the decrease of a fiber's probability of firing during the onset of a test tone due to a preceding masker is proportional to the firing rate produced by that masker and is independent of the probability of firing itself (additivity).

Furthermore, for convenience in modelling, the firing-rate pattern produced by a single-tone stimulus is approximated by an asymmetric triangle whose apical side is steeper than its basal side. These assumptions lead to the following explanation of processes underlying the APTC (Fig. 16). Presenting a single-tone stimulus to the ear causes fibers to fire at a rate which depends upon the excitation produced at the place on the basilar membrane innervated by that fiber. Fig. 16a shows the firing-rate pattern of a single-tone masker (cross-hatched triangle plus open triangle). This figure also shows the reduction pattern (open triangle), i.e., the extent to which the masker, at the onset of the test-tone, reduces the firing-rate for fibers with differing CFs. Note that the decrease is proportional to the firing-rate produced by the masker. Figs. 16b–f show the firing-rate pattern of one test tone (hatched triangle) and reduction patterns (open triangles) due to several maskers for which we obtain a decrease in firing rate by a fixed amount. A constant decrease of firing rate means in Fig. 16 that the areas where firing-rate pattern and reduction pattern overlap (lightly hatched areas) have equal sizes. The firing-rate patterns of maskers producing these particular reduction patterns are not shown.

In contrast to the left-hand side of the figure which gives firing rate as a function of CF the right-hand side represents SPL as a function of CF. Firing rate and SPL differ by a constant of proportionality (assumption b). On the analogy of firing-rate patterns we can construct so-called excitation patterns. Therefore, firing rates produced by a stimulus are converted into SPLs of single-tone stimuli at a fiber's CF that would produce the same rate. Fig. 16g represents the excitation pattern of the single-tone masker which has a firing-rate pattern shown in Fig. 16a.

The dashed line shown in Fig. 6h represents, as a function of masker frequency, the SPLs of the maskers that produce reduction patterns overlapping the test-tone firing-rate pattern by a fixed amount. The SPLs of the maskers which produce the reduction patterns shown in Figs. 16b–f are indicated by corresponding characters in Fig. 16h. By definition, the dashed line forms an APTC because a constant overlap of reduction pattern and firing-rate pattern means (in the model) a fixed AP amplitude decrease. The modelled APTC has the following characteristics:

(1) the low (high)-frequency slope of the APTC is equal to the basal (apical) slope of the masker excitation pattern. Note that the population of fibers excited by maskers along the two slopes of the APTC do not completely overlap (the lightly hatched

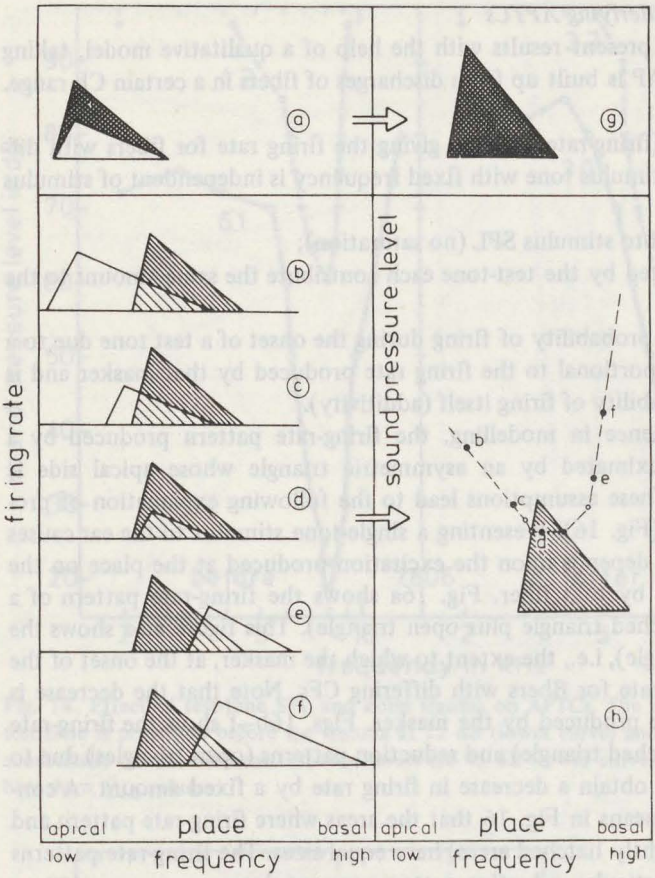

Fig. 16. Schematic representation of the construction of APTCs. (a) The crosswise-hatched triangle represents the firing-rate as a function of CF of a fiber, produced by a sinusoidal masker (firing-rate pattern). The open triangle represents the amount of reduction of the firing-rate produced by a tone following this masker (reduction pattern). (b–f) Examples of reduction patterns of maskers reducing by a fixed amount the firing rate produced by the test tone. Firing-rate patterns of the maskers are not plotted. The parallel-hatched triangles represent the firing-rate patterns of the test tone. Areas of the light-hatched triangles are constant, showing the fixed masking criterion. (g) The conversion of the firing-rate pattern into the SPL of sinusoidal stimuli at the fiber's CF which produce the same firing-rate (excitation pattern). (h) The hatched triangle is the excitation pattern of the test tone. The dashed lines represent the set of those maskers reducing by a fixed amount the firing rate produced by the test tone. The dots represent frequency and intensity of those maskers of which the reduction pattern is shown in Fig. 16b–f.

areas in Figs. 16b and c versus those in e and f). The two branches of psycho-physical tuning curves also seem to be determined by detection in different frequency regions [16].

(2) The APTC has a flat tip. This reflects that maskers within a range of frequencies produce reduction patterns falling completely within the test-tone firing-rate pattern

(Fig. 16d) and these maskers meet the masking criterion at constant SPL. This means that the width of this tip depends upon the width of the test-tone firing-rate pattern (excitation pattern) and also upon masking criterion. To show the relation between the width of the test-tone excitation pattern and the set of maskers fulfilling the masking criterion, the excitation pattern of the test tone is plotted in Fig. 16g.

4.4. Predictions of the model

The present model predicts the effects of test-tone filtering and test-tone SPL on APTCs. No filtering and high test-tone SPL lead to wider excitation patterns than those resulting from filtered and low-SPL test tones. Hence, no filtering and high test-tone SPL produce wider APTCs. According to the model, low- and high-frequency slopes of APTCs are not affected by filtering and test-tone SPL.

Fig. 7 showed that increasing the masking criterion resulted in decreasing width of the APTC. This is also in agreement with the model because the range of masker frequencies for which the larger reduction patterns fall completely within the test-tone firing-rate pattern decreases whereas the slopes of the APTC remain equally steep.

The model gives no explanation for low values of the low-frequency slopes of APTCs in comparison with single-fiber FTCs (Fig. 9). Therefore, we will discuss the assumptions made to construct the APTC.

4.5. Discussion of the assumptions made in the model

Assumption a. From single-fiber studies [23,24] we know that the shape of the curves representing firing rate produced by single-tone stimuli as a function of stimulus frequency (response areas) changes if stimulus levels of more than 30 dB above the threshold of the fibers are used for mid-range or high-CF fibers. The low-frequency slope becomes shallower and the high-frequency slope remains constant or becomes steeper if stimulus level increases. For low-frequency fibers (less than 1 kHz) the opposite is true (high-frequency slope shallower and low-frequency slope constant or steeper). Response areas can be converted into firing-rate patterns and also into excitation patterns. A shallower low-frequency slope of a response area means a shallower basal slope of the excitation pattern. Fig. 17 shows that shallower basal slopes of masker excitation patterns for higher masker levels result in shallower APTC low-frequency slopes. This is not a property peculiar to APTCs: low-frequency slopes of single-fiber FTCs also reflect the level dependence of response areas. Hence, this cannot explain the low values of the low-frequency slopes of APTCs in comparison with low-frequency slopes of FTCs.

Assumption b. A fiber's firing rate is not completely proportional to stimulus SPL. Above a certain level the firing rate saturates. In the forward-masking paradigm the saturated firing rate determines the maximum amount by which the firing rate produced by the test tone decreases because the decrease in firing rate is proportional to the firing rate produced by the preceding masker. Saturation plays no role in APTCs if test-tone SPL is chosen such that the SPL of the masker at test-tone frequency, fulfilling the masking criterion, does not give saturation.

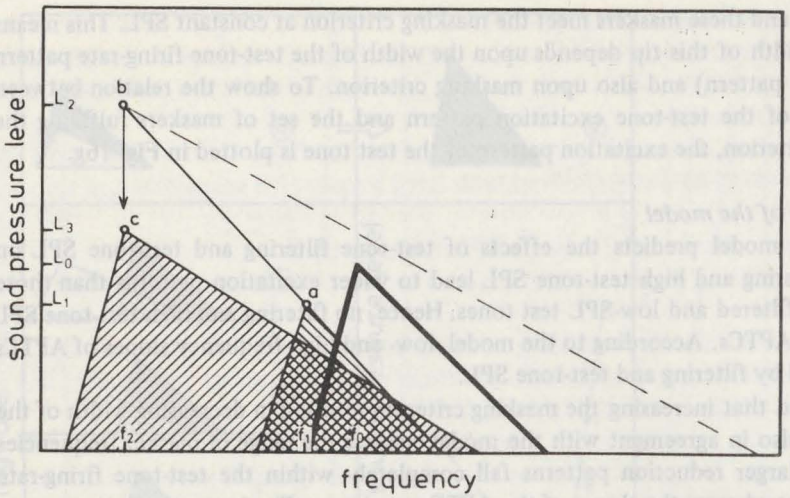

Fig. 17. Schematic representation of the effect of SPL-dependent excitation patterns on the APTC. Excitation patterns are represented by triangles. The open triangle represents the excitation pattern produced by a test tone (f_0, L_0). Masker (f_1, L_1) reduces the firing rate produced by the test tone (f_0, L_0) by a certain amount. If the slopes of the excitation patterns are independent of masker SPL, a masker with frequency f_2 should be presented at level L_2 to obtain an amount of firing rate reduction equal to that produced by masker (f_1, L_1). Because the high-frequency slope of the excitation pattern decreases for increasing stimulus SPL, a masker (f_2, L_3) is required to obtain the desired reduction in firing rate. Note that masker (f_1, L_1) partially excites fibers with other CFs than masker (f_2, L_3) does.

Assumption c. Fig. 17 shows that shallower basal slopes of masker excitation patterns for higher masker levels implies that more high-CF fibers and fewer low-CF fibers are excited by those maskers fulfilling the masking criterion.

More apically, increasing cochlear travel-times result in more time spread in the contributions to the AP. Therefore, it is expected that, for wide-band stimuli such as clicks, basal generators contribute significantly more to the AP amplitude than apical ones. In case of single-tone stimuli we do not expect that the effect of dominance of basal generators is large enough to explain the differences in low-frequency slopes of single-fiber FTCs and APTCs because the CF range covered by the test tone is estimated to be only half an octave.

Assumption d. The firing rate produced by a test tone decreases in proportion to the firing rate produced by the preceding masker if test-tone frequency is equal to the CF of the fiber and the masker frequency is equal to [26] or different from the CF [13]. Proportionality is also verified for fibers which have CFs not equal to the test-tone frequency and maskers at CF [1]. It is as yet unknown whether or not the results reported for firing rate also hold for probability of firing during test-tone onset.

For the normal ear we conclude that the dependence of APTC width on test-tone level, test-tone filtering and masking criterion can be explained by means of the present model. This model is also in agreement with the data showing that APTC slopes are

independent of these parameters. Furthermore, the tip shift of the APTC as shown in Figs. 10 and 11 can be explained. However, the model gives no explanation for the small low-frequency slope values of low-frequency APTCs in comparison with slope values of single-fiber FTCs.

4.6. APTCs in the acoustically traumatized ear

Figs. 12 and 13 show that in the acoustically traumatized ear, APTCs in the region of increased thresholds are wider than in the normal ear if test-tone SPL is chosen such that the amplitude of the unmasked AP is about 10 μV. At least part of this widening is due to shallower low- and high-frequency slopes (defined between 5 and 25 dB above the tip). Furthermore, we found that the tip segment of APTCs shifted more to higher SPLs than the tails did. These effects of excessive noise stimulation on APTCs are also observed in single fibers in the acoustically traumatized ear [19,21]. In using APTC width as a measure of frequency selectivity there is the problem that APTC width depends upon the width of the test-tone excitation pattern. After excessive noise stimulation the test-tone excitation pattern might be wider than in the normal ear. Furthermore, differences in APTC width before and after inducement of a trauma may be due to different test-tone SPLs. Fig. 14 showed that widening of APTCs is not simply an SPL effect because APTCs obtained with equal test-tone SPLs before and after inducement of a noise trauma also show wider APTCs after inducement of the trauma. From the present results we conclude that it is preferable to use slope values instead of Q_{10} values, in order to compare APTCs for normal and acoustically traumatized ears. However, it must be emphasized that tips of tuning curves sometimes shift considerably. In that case it might be impossible to find reliable values for the low-frequency slopes.

5. CONCLUSIONS

APTCs obtained by means of a forward-masking technique using low test-tone SPLs, filtered test tones, and a 25% N_1 reduction criterion show smaller Q_{10} values than eighth-nerve fiber tuning curves.

Low-frequency slopes of APTCs are shallower for low-frequency test tones and equal or perhaps steeper for high-frequency test tones in comparison with low-frequency slopes of FTCs.

Filtered test tones give rise to narrower APTCs than non-filtered ones whereas filter slopes of more than 96 dB/oct give no further improvement.

Increasing test-tone SPL results in decreasing Q_{10} values of APTCs.

Q_{10} values of APTCs increase with an increasing masking criterion, but do not reach Q_{10} values found for FTCs.

Effects of test-tone SPL, test-tone filtering, and masking criterion on APTC width can be explained by assuming that fibers with CFs not equal to the test-tone frequency are excited by the test tone and contribute to the AP.

After excessive broad-band noise exposure APTCs are wider than in the normal ear.

This widening is not simply an SPL effect, because APTCs measured at equal SPL before and after inducement of the trauma also show higher Q_{10} values in the normal ear.

To obtain APTCs with tips at a high SPL a high test-tone SPL or a high masking criterion can be used. These methods are not equivalent.

ACKNOWLEDGEMENTS

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CHAPTER VI

RESPONSES FROM AVCN UNITS IN THE CAT BEFORE AND AFTER INDUCEMENT OF AN ACUTE NOISE TRAUMA

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Responses from AVCN units in the cat before and after inducement of an acute noise trauma

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Acoustically evoked responses of single units in the anteroventral part of the cochlear nucleus (AVCN) in the cat were studied together with compound eighth-nerve action potentials (AP). Halfway through the experiments the cats were exposed for half an hour to pink noise at 105 dB SPL, producing an average threshold shift of 30 dB (maximum 50 dB) in the 2–6 kHz region. The effect of the noise exposure was studied in two ways. On the one hand we compared the results for one population of units measured before the noise exposure with those found for another population measured afterwards. On the other hand we compared the results before and after the noise exposure for one unit that could be kept under observation during the noise exposure. After the noise exposure spontaneous activity and phase-locking of the responses of the units to the stimulus waveform were not significantly different from the pre-exposure findings. Response latency tended to increase. Therefore, the decrease of latency found for APs must be due to a shift to higher frequencies of the population of units contributing to the AP. The sharply tuned tip segments of tuning curves shift to higher levels whereas the low-frequency tails remain at about the same level. Q_{10} decreases by at most 50%, which was also found for AP tuning curves. Response spectra for clicks and noise (reverse correlation function) did not show a significant decrease of frequency selectivity. Units with CF < 3 kHz may show a shift of CF to a lower frequency by 10–20%. After inducement of the noise trauma the sharply tuned tip segment of a tuning curve may not be found and CF may be assigned to a local minimum in the low-frequency tail of the tuning curve.

Key words: anteroventral cochlear nucleus; noise-induced hearing loss; response latency; tuning curves; reverse correlation function.

1. Introduction

The aim of the present study was to investigate how neural responses to acoustic stimuli are affected by noise trauma. Our special interest was frequency selectivity in traumatized ears as compared with frequency selectivity for normal ears. This interest was aroused by the notion that the reduction in speech discrimination against ambient noise which is found for people with sensorineural hearing loss might be explained by reduced frequency selectivity [25,29,30,40].

We chose to record responses from single units in the anteroventral part of the cochlear nucleus (AVCN) of the cat although in most related studies eighth-nerve fibers are chosen [8,9,11,14,15,26,32,38]. The advantage of eighth-nerve fiber studies is that the fibers are easily accessible, that they represent the first stage in the

auditory neural pathway and that they constitute quite a homogeneous population with regard to their responses. A disadvantage, however, is that recording time for these fibers is limited. Units in the AVCN, on the contrary, can be maintained under observation for many hours. Since responses from AVCN units as compared with those from other parts of the auditory pathway are closest to responses from eighth-nerve fibers [35] and since our experimental design required long observation times for a single unit we chose to record from the AVCN.

Long observation times were required for two reasons. First, we intended to collect a number of measures for each unit, i.e. (a) timing of the neural discharges with respect to the stimulus waveform (phase-locking), (b) latency between stimulus and response and (c) frequency selectivity using sine-wave, click and noise stimuli. Second, we wanted to have the time to record from the same unit before and after inducement of the trauma in order to establish clearly the effects of the trauma.

The second point is an important aspect of the present study. Without the pre- and post-inducement data for the same unit we would only have a comparison of data for one population of units before inducement of the trauma with data for another population of units measured afterwards. This comparison gives results of limited significance because of high inter-unit variability in the responses. Moreover, it may be improper to compare results before and after inducement of the trauma for units with the same characteristic frequency (CF). Recently, Robertson and Johnstone [33] showed that the CF of spiral ganglion cells in kanamycin-treated guinea pigs was lower than the CF of ganglion cells located at the same place along the normal cochlea. Thus, while better alternatives are not available, CF may not be a unique indicator of the fiber and of the place along the basilar membrane it innervates. The number of units recorded from both before and after inducement of the trauma is, of course, limited to only one per experiment (if we are successful) since the noise trauma can be induced only once during the experiment.

The trauma was induced by exposing the cat's ear to broadband noise at 105.3 dB SPL for half an hour. Broadband noise was chosen in order to induce threshold shifts across a large range of CFs. This increased the chance of finding units in the affected region since we have only limited control of the CF of units encountered during penetration of the AVCN. The noise exposure was restricted to half an hour in order to minimize the chance of losing the unit during or after the exposure. A disadvantage of only half an hour of exposure is that it produces a threshold shift which varies considerably from one animal to another [21,22,27]. Therefore, we always included in our experiments measurements of the compound action potential of the eighth nerve (AP) so that, for each cat, single-unit data could be considered with respect to AP thresholds. In previous papers [21,22] we showed that the type of noise exposure chosen here produces threshold shifts with little recovery during the experiment.

Before and after inducement of the acute noise trauma we studied frequency selectivity with three types of stimuli: *sinusoids, clicks* and *noise*. Different stimuli were used because sound encoding in the cochlea is not a linear, time-invariant process. Therefore, measures of frequency selectivity may depend on spectral and temporal aspects of the stimulus.

Sinusoids were used to measure frequency selectivity in two common ways: (1) *response areas* (neural firing rate as a function of stimulus frequency at constant stimulus level) and (2) *tuning curves* (stimulus level as a function of stimulus frequency for constant neural firing rate). In addition to firing rate we measured phase-locking of the neural discharges to the sinusoidal stimulus [2,24,34,35].

Using *clicks*, frequency selectivity of the cochlea is revealed in the timing of the neural discharges up to the limit of phase-locking at about 4 kHz. Post-stimulus-time histograms (PSTH) or period histograms (where the period is the interclick interval) show the impulse response of the cochlear filter from which frequency selectivity can be calculated.

For *noise* we used the reverse correlation technique (revcor) to determine frequency selectivity [4–7,10]. This technique is also based on phase-locking of the neural discharges to the effective stimulus. Correlating the neural discharges with the white noise stimulus produces the impulse response of the cochlear filter.

In addition to frequency selectivity we also studied the latency between stimulus and response. In a previous paper [21] we reported latency differences for APs after the same noise exposure. We suggested that these differences might be due to a change in the population of fibers contributing to the AP and not to a change in latency for individual fibers. This will be checked in the present study by measuring the latency for the impulse responses obtained with click and noise stimuli and by calculating the latency from the phase versus frequency curves obtained from phase-locked responses to the sinusoidal stimuli.

2. Materials and Methods

2.1. Preparation

14 healthy adult cats were anesthetized with sodium pentobarbital (Nembutal). After an initial i.m. injection of atropine sulfate (0.5 mg) and an i.p. injection of Nembutal (45 mg/kg), supplementary doses of Nembutal were administered i.v. to maintain the animal at a surgical level of anesthesia during the experiment. In addition, every 8 h an intramuscular injection of atropine sulfate (0.5 mg) was given. All cats were tracheostomized. Rectal temperature was maintained at approximately 38°C by means of a thermostatically controlled heating blanket. Arterial blood pressure, heart rate, and percentage of carbon dioxide in expired air were monitored. Eighth-nerve action potentials, as they occur in the vicinity of the round-window membrane (silverball electrode, opened bulla), were recorded in order to check the state of the animal. AP experiments on acute noise traumata were reported in previous papers [21,22].

2.2. Approach to the anteroventral cochlear nucleus

The surgical approach to the cochlear nucleus was through the posterior and middle fossa. Part of the cerebral cortex with underlying white matter was aspirated and a portion of bony tentorium was excised. Cerebellum overlying the dorsal part of the cochlear nucleus was removed to enable the cochlear complex to be seen. We tried to leave intact a few cerebellar folia overlying the anteroventral cochlear

nucleus to protect it from damage. This method is the same as described previously by Rose et al. [35]. An indium electrode with a gold and platinum tip, about 5–7 μm in diameter, was used for recording extra-cellular potentials. The electrode was mounted in a hydraulic drive attached to a step motor (Frederick Haer & Co.). The hydraulic drive was placed on a plastic chamber cemented to the skull of the cat. After each experiment the electrode tracks were verified histologically. All neurons considered in this paper are believed to have been located in the AVCN. The recording site was ipsilateral to the stimulated ear.

2.3. Stimulus generation

Experiments were performed in a room especially constructed for acoustic insulation and electric shielding. Stimulus generation and response storage were fully controlled by a computer (PDP 11-10). Stimuli were delivered through an electrodynamic transducer (Beyer DT 48) connected to the cat's external meatus (resected pinna). The transducer was calibrated by measuring sound pressure level and phase of sine-wave stimuli with a probe tube microphone in close proximity (2–3 mm) to the tympanic membrane. The calibration signals covered the frequency range from 40 Hz to 20 kHz in steps of 40 Hz. Sound pressure level (SPL) and phase data (both specified at the tympanic membrane) were stored in the computer and were used to calculate the electrical stimuli required to produce the desired acoustic stimuli at the tympanic membrane (for more details see [21]).

The three types of stimuli (sinusoids, clicks and noise) were generated as follows:

- *Sinusoids* were stored in a revolving memory consisting of 256 samples with 12 bits resolution each.
- *Clicks* were synthesized from 63 successive harmonics with equal amplitude and cosine phase at the tympanic membrane. The harmonics were spaced at frequency intervals equal to 1/15th of the CF of the neuron under study. Thus, the interclick interval corresponded to 15 cycles of the CF. The level of the clicks is given in terms of the SPL of the individual harmonics (not the peak level). The waveform required to produce the click at the tympanic membrane (depending upon CF) was also stored in a revolving memory (256 samples, 12 bits).
- In principle we could synthesize the *noise* signal also in such a way that a gaussian 'white' noise arrives at the tympanic membrane. However, this requires a long revolving memory which we did not have at our disposal. Instead, we simply used a pseudorandom noise generator (HP 8057A, 5 s period of noise pattern). The output of this noise generator was fed through parallel 1/3-octave filters in order to equalize, as much as possible, the frequency-dependent transfer from transducer to tympanic membrane. After the single-unit measurements we corrected the reverse correlation functions for the remaining spectral irregularities in the noise at the tympanic membrane. The noise levels are specified in terms of click levels. Equal levels for noise and clicks mean equal output levels for a 1/3-octave filter centered at or near the CF of the neuron under study while click levels are specified in terms of the level of a single frequency component of the click train. With this definition of noise level we expect about equally effective stimulation of a neuron by clicks and noise at the same specified level.

2.4. Data processing

For each unit we recorded the firing rate of spontaneous and driven discharges and the timing of the discharges with respect to the stimulus. For *sinusoidal* stimuli and *clicks*, driven discharges were processed into period histograms. Systematically, one period histogram was determined for the stimulus itself and the second one for the stimulus with inverted polarity. The second histogram was subtracted from the first to obtain a compound period histogram [19]. If spontaneous activity is present in both period histograms this activity is reduced in the compound histogram. If period histograms reflect the half-wave rectified effective stimulating waveform [2], compound period histograms reflect the full-wave effective stimulating waveform.

For *noise* stimuli the reverse correlation function was obtained by averaging the stimulus waveform segments (256 samples, 20 kHz sampling rate) immediately preceding the neural discharges. Averaging was performed on-line. However, at high discharge rates, some waveform segments had to be skipped from the averaging procedure as a consequence of limited calculation speed. This skipping may result in a systematic error [41]. Therefore, timing of the discharges with respect to the period of the pseudorandom noise sequence was stored for complete off-line computations.

2.5. Measure of phase-locking

To express in a single value the amount of phase-locking (synchronization) between stimulus and discharges, we first calculated the vector sum, VS, from period histograms obtained for sinusoidal stimuli using the formula

$$\mathrm{VS} = \left\{ \left[\sum_{i=1}^{N} b_i \cdot \cos(2\pi i/N) \right]^2 + \left[\sum_{i=1}^{N} b_i \cdot \sin(2\pi i/N) \right]^2 \right\}^{1/2}$$

where b_i = number of discharges in bin i, and N = total number of bins.

The synchronization index, SI, is then given by

$$\mathrm{SI} = \mathrm{VS} / \sum_{i=1}^{N} b_i$$

which is the vector sum divided by the total number of discharges. For compound period histograms b_i represents the difference of two values for stimuli of opposite polarity and the total number of discharges will exceed $\Sigma\, b_i$. In this case the vector sum should be divided by the total number of discharges. Absence of synchronization implies SI = 0, modulation of the discharge rate according to the half-wave rectified sinusoidal stimulus implies SI = $\pi/4$ (indicated by horizontal dashed lines in the figures presenting the results), and all discharges concentrated at a single phase value of the sinusoidal stimulus implies SI = 1.

2.6. Two measures of response latency

The general term *response latency* will be used for two measures of latency, namely (1) for sinusoidal stimuli the *weighted average group delay* and (2) for noise and click stimuli the *center of gravity* of the impulse response. For linear systems these two measures are equivalent [20].

The weighted average group delay, τ_w, is calculated from the phase shift, as revealed by the period histograms, between stimulus and response as a function of stimulus frequency. The phase shifts are weighted according to the discharge rate:

$$\tau_\omega = \sum_{i=k}^{N} A^2(\omega_i) \frac{\Delta\phi_i}{\Delta\omega} / \sum_{i=k}^{N} A^2(\omega_i)$$

where ω_i = angular frequency incremented stepwise, $A(\omega_i)$ = amplitude of ω_i in compound period histogram, $\Delta\omega$ = frequency step size, $\Delta\phi_i$ = phase shift for one frequency step at ω_i, and k, N = lower and upper limit of ω_i for which unit shows phase locking, i.e. for which $A(\omega_i)$ exceeds noise in histograms.

The center of gravity of the impulse response, τ_g, is calculated from the revcor function for noise stimuli or from the compound period histogram for click stimuli according to:

$$\tau_g = \sum_{i=1}^{N} t_i \cdot h^2(t_i) / \sum_{i=1}^{N} h^2(t_i)$$

where t_i = time since stimulus onset, $h(t_i)$ = impulse response, and N = upper limit of t_i for which $h(t_i) \neq 0$.

2.7. Inducement of acute noise trauma

In order to generate traumatizing noise well defined at the tympanic membrane, we synthesized the noise. The noise was constructed from 127 harmonics spaced at 160 Hz intervals starting at 160 Hz. The SPL of the first harmonic was 98 dB and the levels of the higher harmonics were lower according to a -3 dB/oct slope (constant intensity per octave). The total SPL was 105.3 dB. The phase relation among the 127 harmonics was chosen such that the noise as a function of time had as small a crest factor (peak factor) as possible [39]. The waveform of the electrical signal necessary to produce the noise at the tympanic membrane was stored in a revolving memory (12 bit, 256 samples). Cats were exposed for 30 min to this 'pink' noise, halfway through the experiments. This noise could not be used to measure the revcor functions because it is not sufficiently random.

3. Results

3.1. Single unit thresholds and spontaneous firing rates

For the 14 cats used in this research Fig. 1a shows the thresholds of 75 units as a function of CF. In addition, Fig. 1a shows the average AP-threshold for these 14 cats. The AP-thresholds differed somewhat from cat to cat; the standard deviation across the 14 cats is 6.0 dB. The standard deviation of the thresholds of the units is 9.3 dB when they are expressed relative to the average AP-threshold at their CF. Expressing the thresholds of the units relative to the AP-thresholds for each cat individually does not result in a significant decrease in this standard deviation; in fact we find a nonsignificant ($P > 0.05$) increase to 9.9 dB. Thus, the inter-cat differences in AP-threshold are not reflected in the scatter of the unit threshold data.

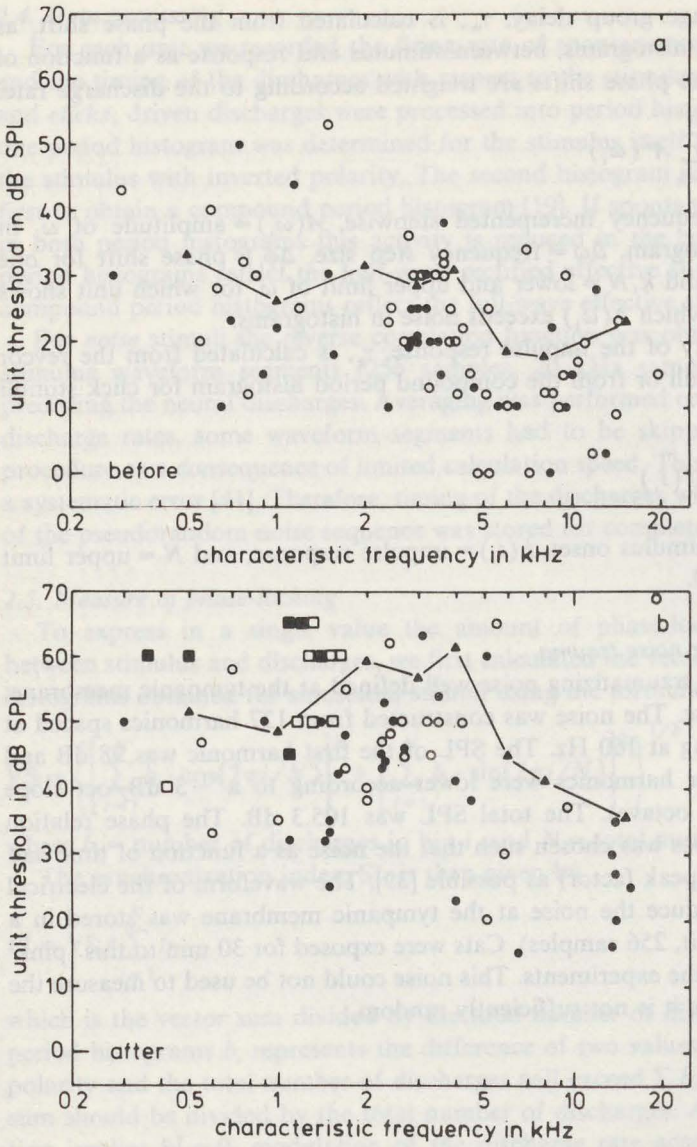

Fig. 1. Thresholds of AVCN-units before (a) and after (b) the noise exposure as a function of CF. Open symbols represent units with spontaneous activity ≤ 10 spikes/s, filled symbols units with spontaneous activity > 10 spikes/s. Triangles connected by solid lines represent the average AP-threshold; criterion 2.5 μV. The squares in Fig. 1b represent units to which probably an incorrect (too low) CF was assigned.

The open symbols in Fig. 1a represent units with spontaneous firing up to 10 spikes/s, the filled symbols spontaneous firing in excess of 10 spikes/s. The data do not show a correlation between spontaneous firing rate and threshold. For eighth-nerve fibers Liberman and Kiang [26] did find a correlation; high spontaneous firing

rate correlated with low threshold. The thresholds of our AVCN units are on the average 6 dB lower than the AP-threshold whereas the thresholds of the highly spontaneously active nerve fibers are 10–15 dB lower than our AP-thresholds based on a 2.5 μV criterion [21].

The results collected after inducement of the noise trauma are presented in Fig. 1b (9 cats, 65 units). After the noise exposure the average AP-threshold has increased by 18 dB at 500 Hz, by about 28 dB in the mid-frequency range and by 12 dB at 15 kHz. The increased AP-threshold showed little recovery (≤ 5 dB) during the experiments [21]. The standard deviation of the AP-thresholds across cats has increased to 11.6 dB after the noise exposure. The standard deviation of the thresholds of the units relative to the average AP-thresholds has increased to 15.3 dB. Again, expressing the thresholds of the units relative to the AP-thresholds for each cat individually does not result in a significant decrease in the standard deviation of these thresholds (14.2 dB, $P > 0.05$) in spite of the large spread in AP-thresholds. Also, open and filled symbols show that there is still no correlation between spontaneous firing rate and threshold of the units after inducement of the noise trauma.

The squares in Fig. 1b represent units to which probably an incorrect CF was assigned. The CF was probably assigned to a local minimum in the low-frequency tail of units which lost the sharply tuned segment of their tuning curve after the noise exposure. This implies a shift in the squares of Fig. 1b to higher thresholds and higher CF. We shall discuss this problem in more detail in section 3.3.3.

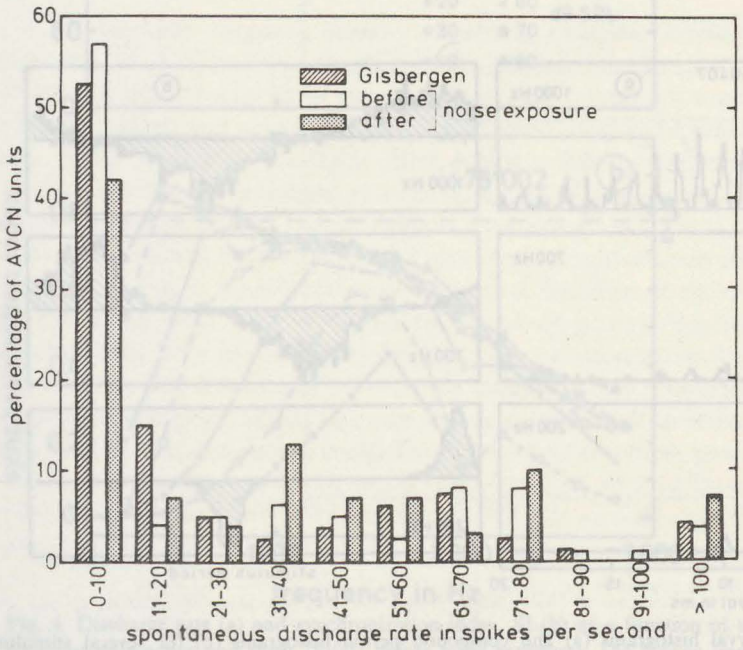

Fig. 2. Distribution of AVCN units according to their spontaneous discharge rate. Data taken from van Gisbergen [18] are for normal ears.

Fig. 2 shows the distribution of the units according to their spontaneous discharge rate. Our distribution before the noise exposure does not differ from the one reported by van Gisbergen [18] for AVCN units. Also, there is no apparent difference between our distributions before and after the noise exposure. For 7 out of 8 units that we were able to keep under observation during the noise exposure the spontaneous discharge rate remained fairly constant whereas the thresholds of the units had increased after the noise exposure. The eighth (non-spontaneously active) unit became spontaneously active. Liberman and Kiang [26] and Alder [1] found both higher and lower spontaneous rates in acoustically traumatized ears.

3.2. Phase-locked responses

3.2.1. Synchronization index. Fig. 3a shows interspike-interval histograms for sinusoidal stimuli of several frequencies at 80 dB SPL and Fig. 3b shows, for the same stimuli, compound period histograms. The interspike-interval histograms show that discharges of AVCN neurons may occur, like those of eighth-nerve fibers, at intervals which group around integral multiples of the period of the stimulus [35]. The compound period histograms, obtained by subtracting the period histograms found for stimuli of opposite polarity (section 2.4), show the relation between stimulus and discharge probability in more detail. At 1000 Hz the compound period histogram reflects roughly the stimulus waveform. This is in agreement with Rose et al. [35] who emphasized that the discharge probability follows the stimulus waveform. However, at lower stimulus frequencies the compound period histograms of Fig. 3b are more peaked than is the stimulus waveform. The discharges are restricted

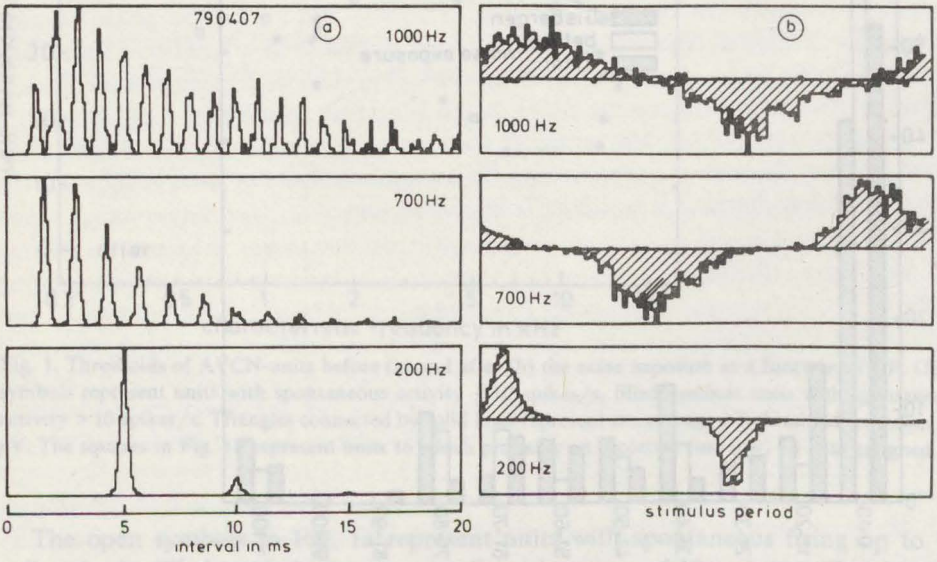

Fig. 3. Interspike interval histograms (a) and compound period histograms (b) for several stimulus frequencies at 80 dB SPL (unit 790407 before noise exposure). At low stimulus frequencies this unit shows a probability of discharge more peaked than the sinusoidal waveform which implies SI > $\pi/4$.

to the peaks; the empty bins between the peaks of the compound period histogram reflect the absence of discharges rather than being due to equal discharges for the stimuli of opposite polarity cancelling out after subtraction. This implies that at low frequencies the synchronization index SI will exceed a value of $\pi/4$ (section 2.5). Lavine et al. [24] and Anderson [3] reported similar results for neurons of the cochlear nucleus complex and the auditory nerve, respectively.

Fig. 4b shows SI as a function of frequency for another, spontaneously active, unit together with the discharge rate as a function of frequency in Fig. 4a. At low stimulus levels discharge probability of the spontaneously active unit will be determined by the stimulus to a limited extent only. There is still considerable firing during the least-effective half-cycle of the stimulus and, consequently, SI is low. At these low levels the effect of the stimulus is not apparent in the discharge rate (Fig.

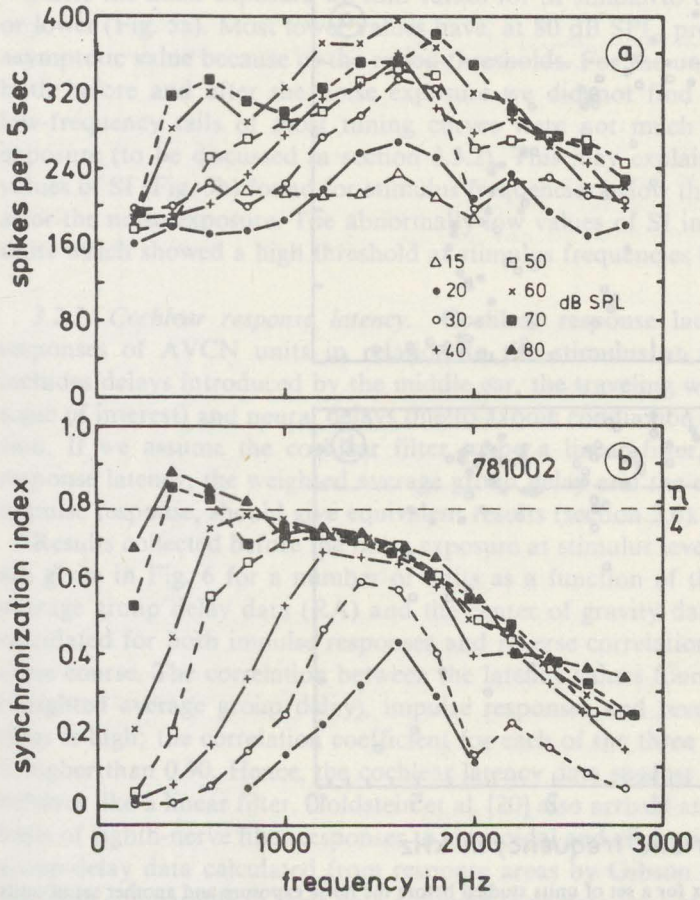

Fig. 4. Discharge rate (a) and synchronization index, SI (b) as a function of stimulus frequency for a spontaneously active unit (unit 781002 before noise exposure). The broken line indicates SI = $\pi/4$, the value of SI found if the discharge probability of a unit follows a half-wave rectified version of the sinusoidal stimulus.

4a), while it is apparent in SI (Fig. 4b). For spontaneously active units, neural tuning at low stimulus levels is better reflected in SI than in the discharge rate.

Increasing stimulus level, SI reaches a maximum value which depends on stimulus frequency. The asymptotic value of SI increases with decreasing stimulus frequency. The highest asymptotic value of SI is found at a frequency below CF. In most of our AVCN neurons SI reaches its asymptotic value at a stimulus level well below the level at which the neuron's discharge rate saturates. This was also reported by Evans [13] for eighth-nerve fibers in the cat.

For a number of units and tones at the CF Fig. 5a shows SI at 80 dB SPL. Since SI reaches its asymptotic value at a relatively low level, the SI values at 80 dB SPL generally represent aymptotic values. In addition to the asymptotic SI values at CF,

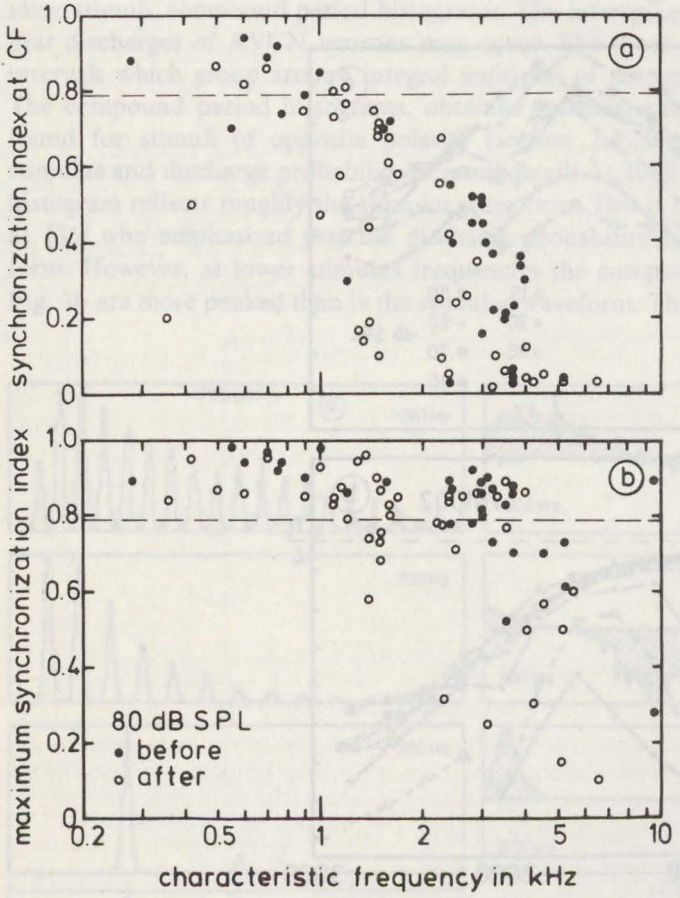

Fig. 5. Synchronization index for a set of units studied before the noise exposure and another set of units studied after the noise exposure as a function of their CF at a stimulus level of 80 dB SPL. (a) Stimulus frequency at CF; (b) stimulus frequency below CF at a value showing maximum SI. The broken line indicates SI = $\pi/4$, discharge probability following the half-wave rectified version of the sinusoidal stimulus.

Fig. 5b shows the highest values of SI that are found for stimulus frequencies lower than CF and at 80 dB SPL. SI is plotted in Fig. 5b as a function of the CF of the unit. The stimulus frequencies for which maximum SI was found ranged between 200 and 1200 Hz if CF > 2 kHz, between 100 and 800 Hz if 1 < CF < 2 kHz and between 100 Hz and CF if CF < 1 kHz. Fig. 5a shows a decrease of SI with increasing stimulus frequency (at CF) with complete loss of synchrony at about 5 kHz. Fig. 5b shows that this loss of synchrony is due to the stimulus frequency and not to the CF of the unit. Units with high CF that still respond to low-frequency stimuli may show high values of SI, e.g. SI = 0.9 for a unit with CF = 9.5 kHz in Fig. 5b where the stimulus frequency was about 500 Hz. These results are in agreement with a model by Anderson [3] in which he explains the decrease in SI with increasing stimulus frequency on the basis of time jitter in the travel times of action potentials of the eighth nerve. The time jitter in his model is independent of CF.

After the noise exposure we find values for SI similar to the pre-exposure values or lower (Fig. 5a). Most lower values have, at 80 dB SPL, probably not reached the asymptotic value because of the raised thresholds. For the units that we could study both before and after the noise exposure we did not find a decrease in SI. The low-frequency tails of most tuning curves were not much affected by the noise exposure (to be discussed in section 3.3.2). This may explain why most maximum values of SI (Fig. 5b) found for stimulus frequencies below the CF are about normal after the noise exposure. The abnormally low values of SI in Fig. 5b are found for units which showed a high threshold at stimulus frequencies below 1.5 kHz.

3.2.2. Cochlear response latency. Cochlear response latency is measured for responses of AVCN units in relation to the stimulus at the eardrum. Thus, it includes delays introduced by the middle ear, the traveling wave in the cochlea (the topic of interest) and neural delays due to axonic conduction and synaptic transmission. If we assume the cochlear filter to be a linear filter, the two measures of response latency, the weighted average group delay and the center of gravity of the impulse response, should give equivalent results (section 2.6).

Results collected before the noise exposure at stimulus levels of about 40 dB SPL are given in Fig. 6 for a number of units as a function of their CF. The weighted average group delay data (RA) and the center of gravity data (impulse), the latter calculated for both impulse responses and reverse correlation functions, follow the same course. The correlation between the latency values found from response areas (weighted average group delay), impulse responses and reversed correlation functions is high; the correlation coefficient for each of the three pairwise combinations is higher than 0.90. Hence, the cochlear latency data suggest that the cochlear filter behaves like a linear filter. Goldstein et al. [20] also arrived at this conclusion on the basis of eighth-nerve fiber responses to sinusoidal and click stimuli. Fig. 6 also shows group-delay data calculated from response areas by Gibson et al. [17]. Our results are quite comparable to their data although their data are not weighted according to the firing rate. We subtracted 0.3 ms from their data since they include a delay between transducer and eardrum.

Response latencies collected after the noise exposure at about 65 dB SPL are also

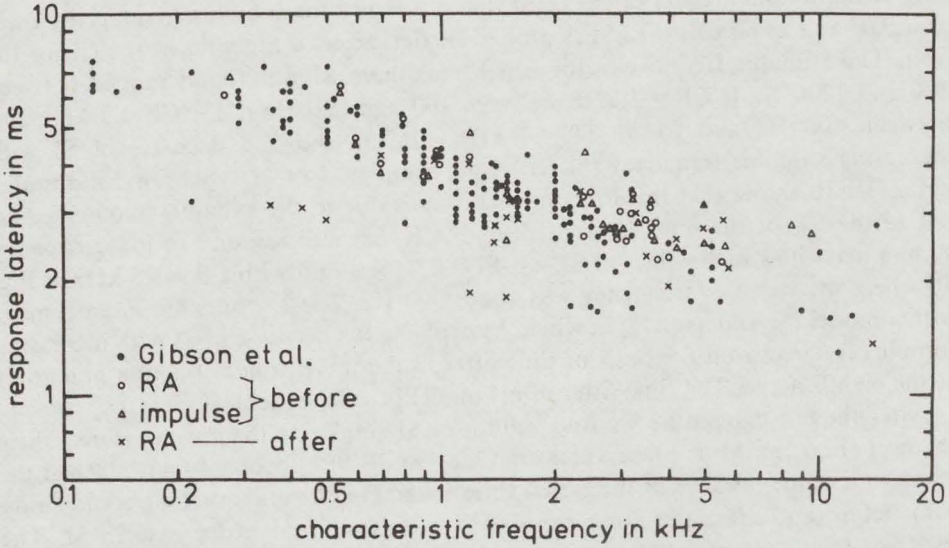

Fig. 6. Response latency values for a number of AVCN units as a function of their CF before and after inducement of the noise trauma. *RA*: weighted average group delays calculated from phase versus frequency shifts for sinusoidal stimuli; *impulse*: center of gravity of compound period histograms for impulse responses and of reverse correlation functions for noise stimuli. The data from Gibson et al. [17], added for reference, are reduced by 0.3 ms since their data include a delay between transducer and eardrum whereas our data do not.

given in Fig. 6. These data are restricted to weighted average group delays (RA). They are not critically dependent on stimulus level. Except for a few units (to be discussed later), the latency values in Fig. 6 lie within the normal, pre-exposure, range. Hence, if there is an effect of the noise exposure, it is small in comparison with the range of latency values found pre-exposure for different units with about the same CF. We may also compare the pre- and post-exposure latency values at the same SPL. Fig. 7 shows that the latency might decrease by about 10% if the pre-exposure stimulus level is raised from 40 to 65 dB SPL. This is only a small decrease (amounting to no more than about 0.5 ms) which, judging from the variability in the data of Fig. 6, would not result in a significant difference between the pre- and post-exposure latency values measured at the same level of 65 dB SPL. Yet, for the units that we kept under observation during the noise exposure we did find, after the noise exposure, an increase in latency up to 0.6 ms comparing the latency values pre- and post-exposure at the same SPL.

A few units in Fig. 6 show post-exposure latency values significantly smaller than the pre-exposure values. Smaller latency values may be regarded as indicative of deteriorated tuning (increased bandwidth) after the noise exposure (sections 3.3.2 and 3.3.3). However, these smaller latency values are not necessarily an effect of noise exposure on latency. In section 3.3.3 we shall show that the CFs assigned to, for example, the three low-latency units with $0.3 < CF < 0.5$ kHz in Fig. 6 studied after the noise exposure are too low. In the absence of pre-exposure data the CFs for these units are assigned to local minima in the low-frequency tails of their tuning

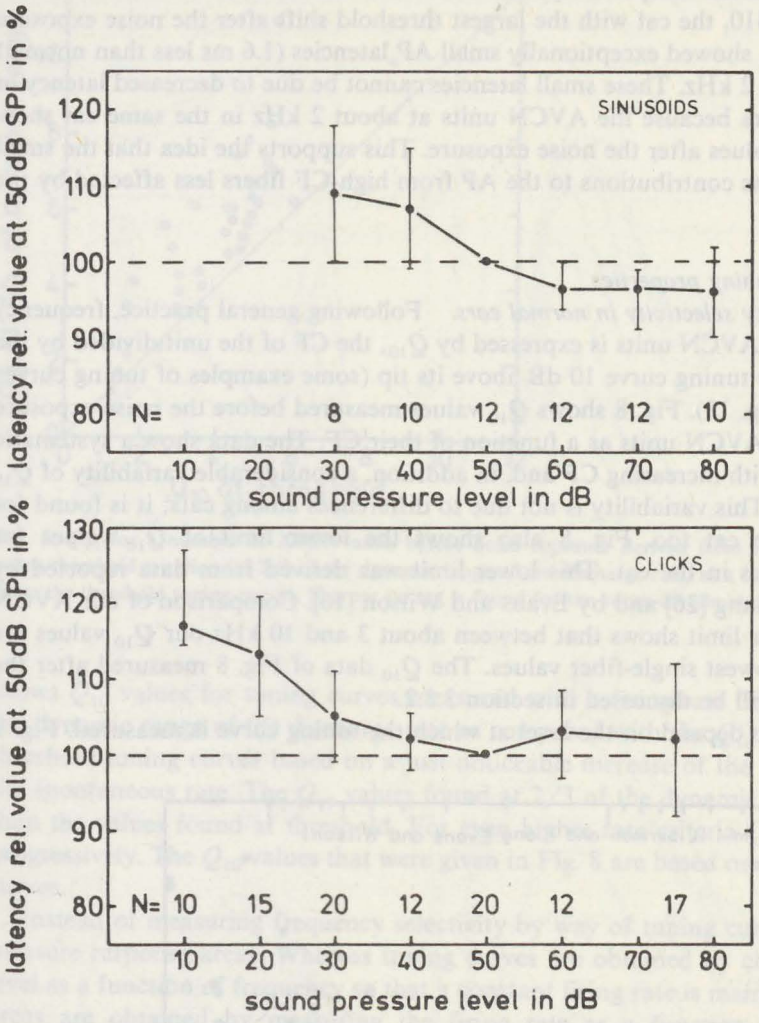

Fig. 7. Effect of stimulus level on response latency for sinusoidal stimuli (weighted average group delay) and for clicks (center of gravity of the impulse response). The value of the latency at 50 dB SPL is set at 100%. Dots represent the median values, bars the quartiles. Note that the data are not based on a constant number of units across stimulus levels.

curves which completely lost their sharply tuned tip segments. The estimated true CF for each of these units (the cochlear frequency region innervated by these units) is about 2.4 kHz. For this CF the latency values found are perfectly normal.

In a previous paper [21] we reported equal or increased latencies for the compound eighth-nerve action potential (AP) after inducement of a noise trauma as compared to the values found at the same SPL before inducement of the trauma. Pre- and post-exposure latencies measured at the pre- and post-exposure thresholds were about equal in most cases. In some cases, however, we found, like for the

present AVCN data, exceptionally small AP latencies at or near threshold. For example, CAT 7810, the cat with the largest threshold shift after the noise exposure (50 dB at 5 kHz), showed exceptionally small AP latencies (1.6 ms less than normal) for tone bursts at 2 kHz. These small latencies cannot be due to decreased latency in 2 kHz nerve fibers because the AVCN units at about 2 kHz in the same cat show normal latency values after the noise exposure. This supports the idea that the small AP latency reflects contributions to the AP from high-CF fibers less affected by the noise exposure.

3.3. Single unit tuning properties

3.3.1. Frequency selectivity in normal ears. Following general practice, frequency selectivity of our AVCN units is expressed by Q_{10}, the CF of the unit divided by the bandwidth of the tuning curve 10 dB above its tip (some examples of tuning curves can be seen in Fig. 13). Fig. 8 shows Q_{10} values measured before the noise exposure for a number of AVCN units as a function of their CF. The data show a systematic increase of Q_{10} with increasing CF and, in addition, a considerable variability of Q_{10} at the same CF. This variability is not due to differences among cats; it is found for units in a single cat too. Fig. 8 also shows the lower limit of Q_{10} values for eighth-nerve fibers in the cat. This lower limit was derived from data reported by Liberman and Kiang [26] and by Evans and Wilson [16]. Comparison of our AVCN data to this lower limit shows that between about 3 and 10 kHz our Q_{10} values are lower than the lowest single-fiber values. The Q_{10} data of Fig. 8 measured after the noise exposure will be discussed in section 3.3.2.

Q_{10} appears to depend on the level at which the tuning curve is measured. Fig. 9

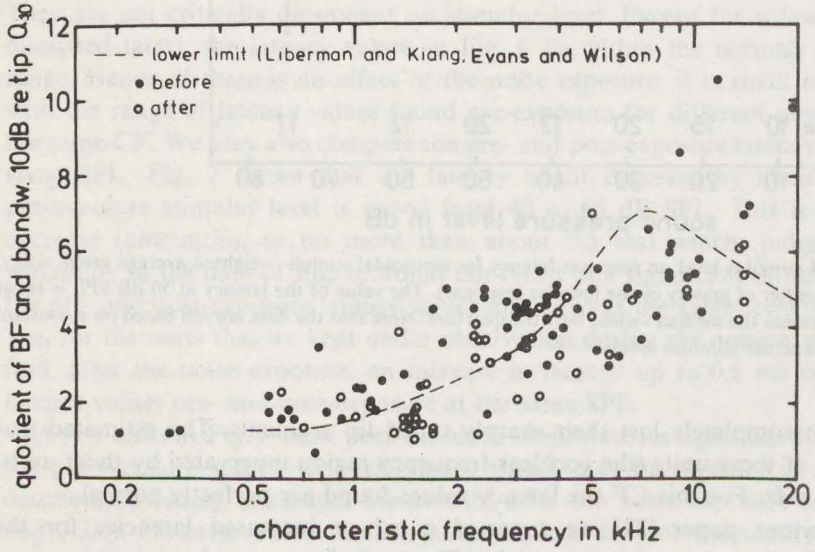

Fig. 8. Q_{10} for one set of AVCN units measured before noise exposure and another set measured after exposure as a function of the CF of the units. The broken curve represents the lower limit of Q_{10} found for eighth-nerve fibers in the cat by Liberman and Kiang [26] and by Evans and Wilson [16].

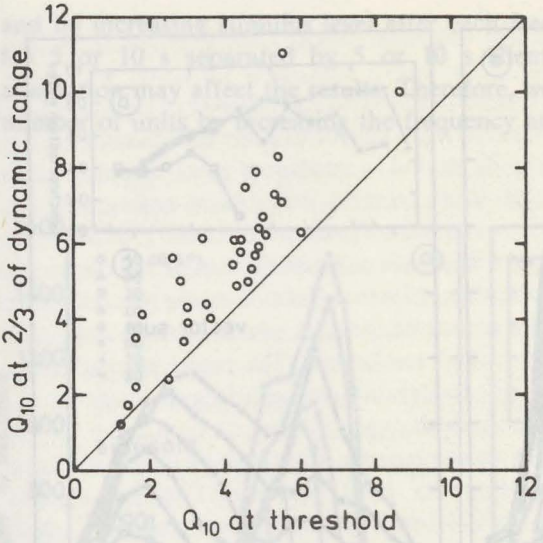

Fig. 9. Q_{10} for a number of AVCN units before noise exposure derived from tuning curves using a supra-threshold criterion (at 2/3 of the dynamic range of the discharge rate) as a function of Q_{10} derived from the threshold tuning curves. Sharper tuning is found for the supra-threshold curves.

shows Q_{10} values for tuning curves measured with a firing-rate criterion at 2/3 of the dynamic range of the discharge rate as compared with the Q_{10} values found for threshold tuning curves based on a just-noticeable increase of the firing rate above the spontaneous rate. The Q_{10} values found at 2/3 of the dynamic range are higher than the values found at threshold. For even higher rate criteria Q_{10} may decrease progressively. The Q_{10} values that were given in Fig. 8 are based on threshold tuning curves.

Instead of measuring frequency selectivity by way of tuning curves we may also measure response areas. Whereas tuning curves are obtained by changing stimulus level as a function of frequency so that a constant firing rate is maintained, response areas are obtained by measuring the firing rate as a function of frequency at constant stimulus level. From a stimulus point of view measurements of response areas are closer to measurements with click or noise stimuli since all frequency components of click and noise stimuli are at equal level.

Fig. 10 shows response areas at several stimulus levels for a unit with CF = 3.9 kHz and Fig. 11 for a unit with CF = 0.55 kHz. The course of the response areas in Fig. 10 is typical for medium and high-CF units. With increasing stimulus level the high-frequency skirt of the response areas hardly shifts whereas the low-frequency skirt shifts toward lower frequencies. The opposite is true for the low-frequency unit in Fig. 11. Here the low-frequency skirt hardly shifts whereas the high-frequency skirt shifts to higher frequencies. This is a typical result for low-frequency units (see also Rose et al. [35]).

We usually measure response areas by stepwise *de*creasing the stimulus frequency

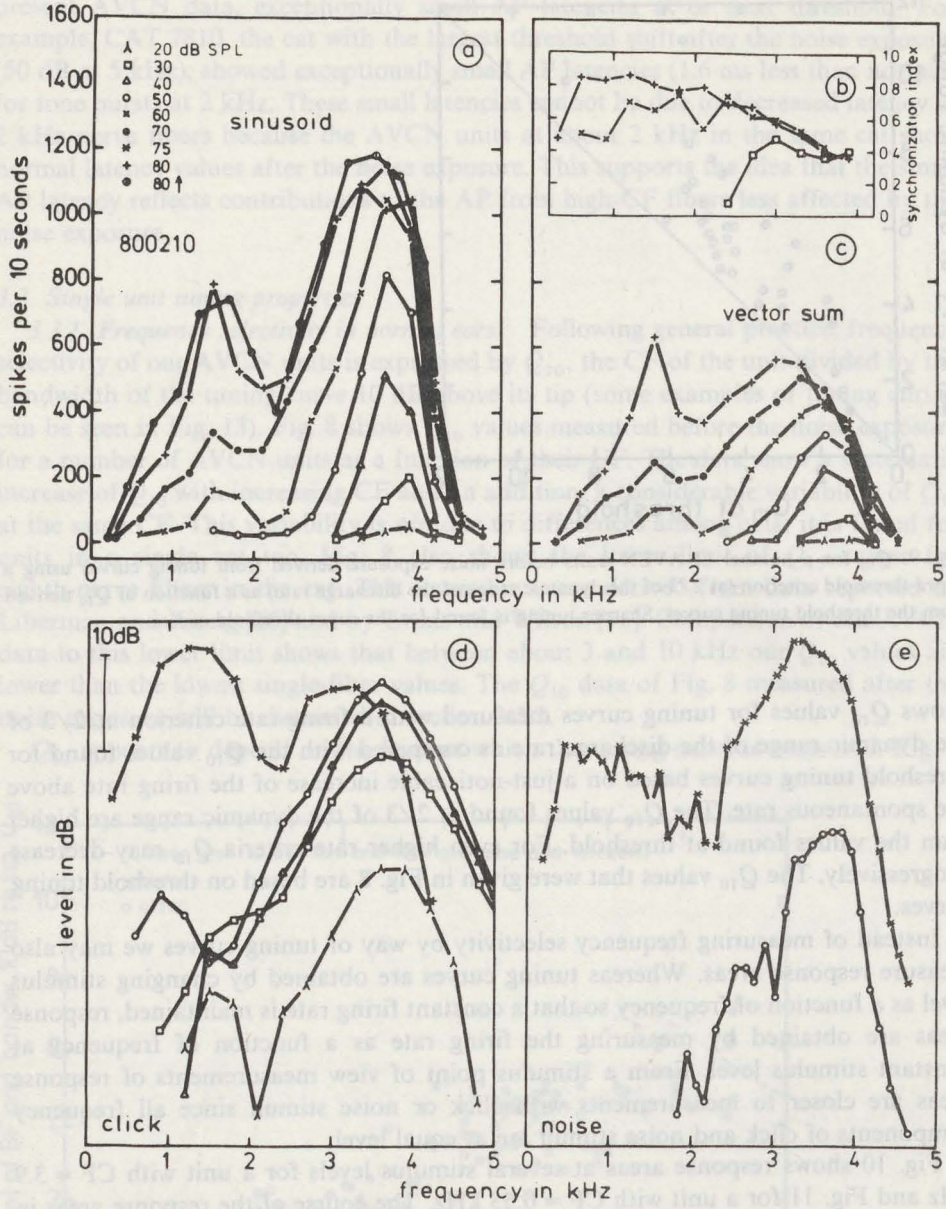

Fig. 10. Tuning properties of AVCN units before noise exposure measured in several ways. (a) Normal response areas, number of spikes evoked by a sinusoidal stimulus 10 s in duration; (b) synchronization index for sinusoidal stimuli as a function of stimulus frequency; (c) vector sum, response area weighted by the synchronization index, for sinusoidal stimuli; (d) response spectra obtained by Fourier transformation of compound period histograms found for click stimuli; and (e) response spectra obtained by Fourier transformation of reverse correlation functions found for noise stimuli. In panel a two curves are given for 80 dB SPL; data indicated by + were collected with decreasing stimulus frequency, data indicated by ⊕ with increasing frequency.

and by increasing stimulus level after each frequency sweep. Stimuli are presented for 5 or 10 s separated by 5 or 10 s silent intervals. At high stimulus levels adaptation may affect the results. Therefore, we also measured response areas for a number of units by *in*creasing the frequency at a stimulus level of 80 dB SPL. The

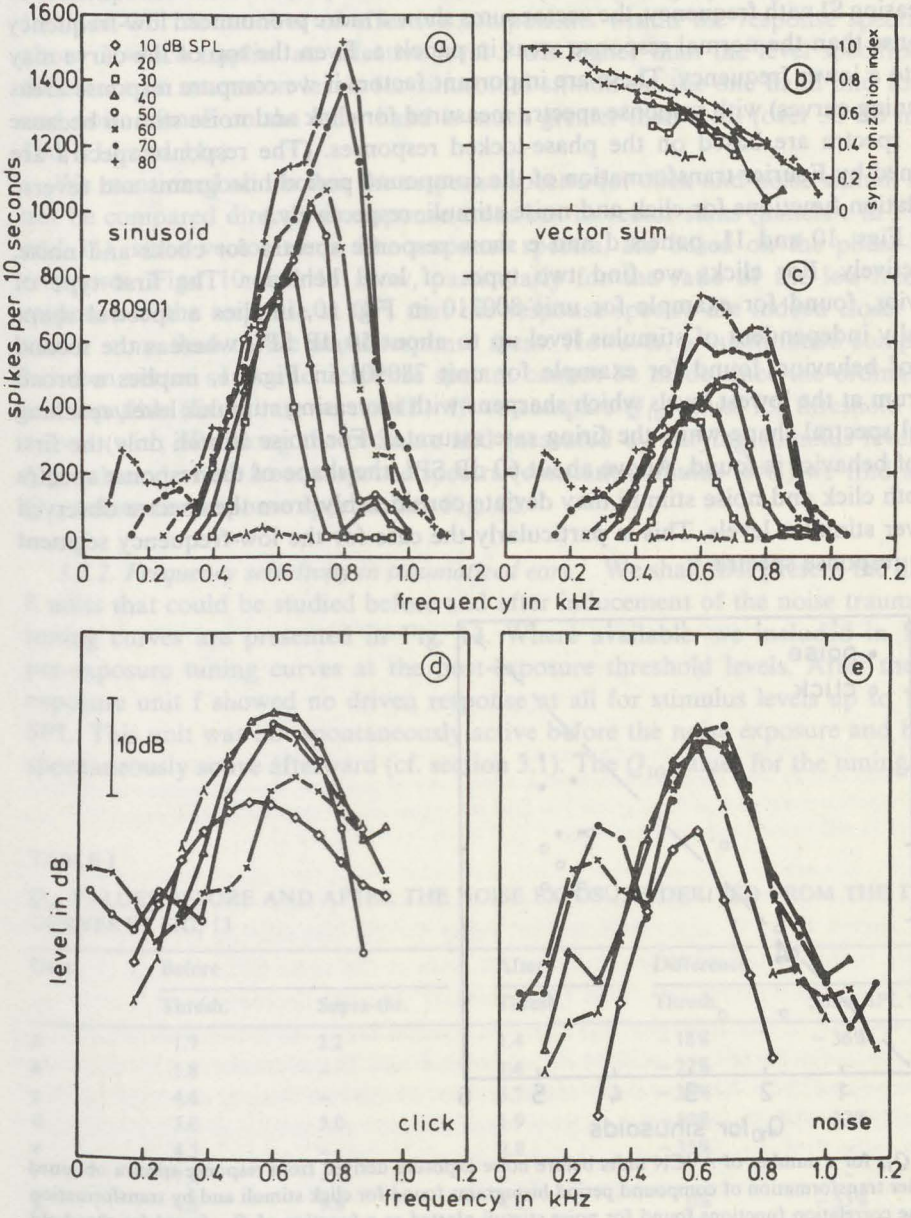

Fig. 11. As Fig. 10 for a low-frequency unit before noise exposure.

effect of adaptation on the shape of the response area at 80 dB SPL is small (Fig. 10).

Response areas present the firing rate irrespective of the amount of phase locking. In the previous section we saw that the synchronization index (SI) decreases with increasing stimulus frequency. Figs. 10 and 11, panels c, give response areas weighted according to the SI (vector sums, section 2.5). As a consequence of decreasing SI with frequency, the vector sums show a more pronounced low-frequency response than the normal response areas in panels a. Even the top of the curve may shift to a lower frequency. These are important factors if we compare response areas (or tuning curves) with response spectra measured for click and noise stimuli because these spectra are based on the phase-locked responses. (The response spectra are obtained by Fourier transformation of the compound period histograms and reverse correlation functions for click and noise stimuli, respectively.)

In Figs. 10 and 11, panels d and e show response spectra for clicks and noise, respectively. For clicks we find two types of level behavior. The first type of behavior, found for example for unit 800210 in Fig. 10, implies a spectral shape virtually independent of stimulus level up to about 50 dB SPL whereas the second type of behavior, found for example for unit 780901 in Fig. 11, implies a broad spectrum at the lowest levels which sharpens with increasing stimulus level, reaching a final spectral shape while the firing rate saturates. For noise stimuli only the first type of behavior is found. Above about 60 dB SPL the shape of the response spectra for both click and noise stimuli may deviate considerably from the spectra observed at lower stimulus levels. This is particularly the case for the low-frequency segment of the response spectra.

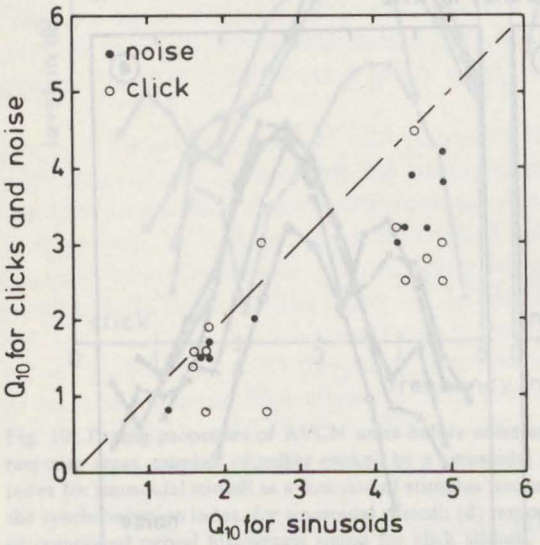

Fig. 12. Q_{10} for a number of AVCN units before noise exposure derived from response spectra obtained by Fourier transformation of compound period histograms found for click stimuli and by transformation of reverse correlation functions found for noise stimuli plotted as a function of Q_{10} found for threshold tuning curves measured with sinusoidal stimuli. Tuning curves for sinusoidal stimuli show sharper tuning.

The firing rate for clicks and noise often saturates at lower levels than the saturation levels for sinusoidal stimuli (Figs. 10d, 11d and 11e). This is also true if we take into account that the effective stimulus level of the click and noise stimuli is higher than the levels specified in Figs. 10 and 11. The specified level is the level of only one frequency component of the click while the noise level is specified in relation to the click level (section 2.3). With a frequency spacing for the clicks of 1/15 of CF the number of effective components within the response spectrum is about 3 which implies an effective level 5 dB higher than the level specified. The difference in saturation levels for sinusoidal stimuli on the one hand and for click and noise stimuli on the other hand is much greater than 5 dB (over 30 dB in Figs. 10d, 11d and 11e).

We mentioned above that the response spectra for click and noise stimuli should not be compared directly to response areas but to vector sums (panels c in Figs. 10 and 11), since vector sums, like response spectra, are based on the phase-locked responses. Figs. 10 and 11 show, particularly for the ratio of the low-frequency response to the response at CF, that the response spectra are indeed closer to the vector sums than to the usual response areas. However, a quantitative comparison between vector sums and response spectra cannot be made since the ordinates are incompatible (firing rate versus dB). If we compare Q_{10} values for threshold tuning curves (with dBs along the ordinate and measured by varying stimulus level) with Q_{10} values derived from response spectra (constant stimulus level) we find smaller Q_{10} values for response spectra; see Fig. 12.

3.3.2. Frequency selectivity in traumatized ears. We shall first present the data for 8 units that could be studied before and after inducement of the noise trauma. The tuning curves are presented in Fig. 13. Where available, we included in Fig. 13 pre-exposure tuning curves at the post-exposure threshold levels. After the noise exposure unit f showed no driven response at all for stimulus levels up to 100 dB SPL. This unit was not spontaneously active before the noise exposure and became spontaneously active afterward (cf. section 3.1). The Q_{10} values for the tuning curves

TABLE I

Q_{10} VALUES BEFORE AND AFTER THE NOISE EXPOSURE DERIVED FROM THE TUNING CURVES IN FIG. 13

Unit	Before		After	Difference	
	Thresh.	Supra-thr.	Thresh.	Thresh.	Same SPL
a	1.7	2.2	1.4	−18%	−36%
b	1.8	–	1.4	−22%	–
c	4.6	–	3.7	−20%	–
d	3.0	3.0	1.9	−37%	−37%
e	4.3	–	2.8	−35%	–
f	7.4	–	–	–	–
g	4.6	9.8	4.6	0%	−53%
h	10.5	–	6.5	−39%	–

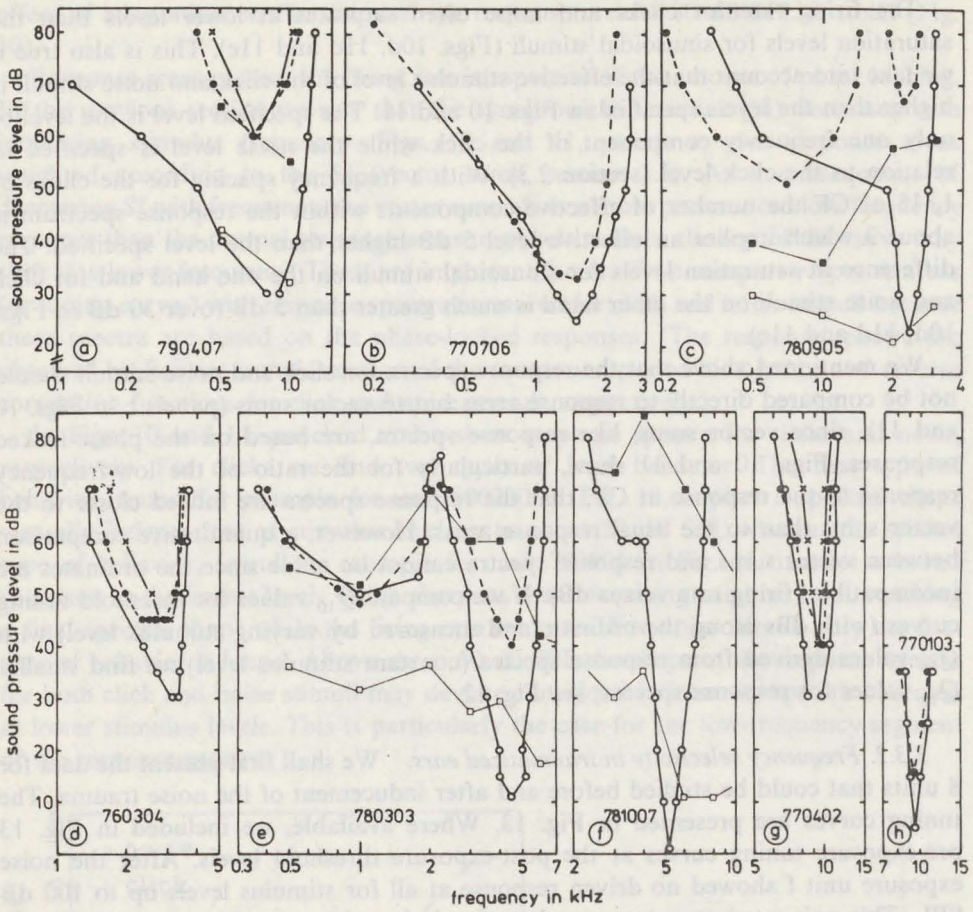

Fig. 13. Pre- and post-exposure tuning curves for eight units that we could maintain during the noise exposure indicated by solid lines and broken lines, respectively. If available, pre-exposure tuning curves at the post-exposure thresholds are also given. Pre- and post-exposure AP thresholds are included for units numbered 78 and higher in the first two digits.

in Fig. 13 are given in Table I. Since Q_{10} tends to be greater for supra-threshold tuning curves (Fig. 9; also reflected in Table I) the decrease in Q_{10} after noise exposure is more marked if we compare the data at the same SPL than at the pre- and post-exposure thresholds. This shows clearly that the decrease in Q_{10} after the noise exposure is not a level effect. In this limited set of data we did not find a correlation between the increase in AP threshold and the decrease in Q_{10} after the noise exposure. For AP threshold shifts up to 35 dB we find a decrease in Q_{10} between 0 and 40% comparing tuning curves at the pre- and post-exposure thresholds and a decrease of about 40% comparing at the same SPL.

Fig. 14 presents for unit a (unit 790407) the response spectra for clicks and noise before and after the excessive noise exposure. The response spectra for clicks are of the second type with broad spectra at the lowest levels (see previous section). The

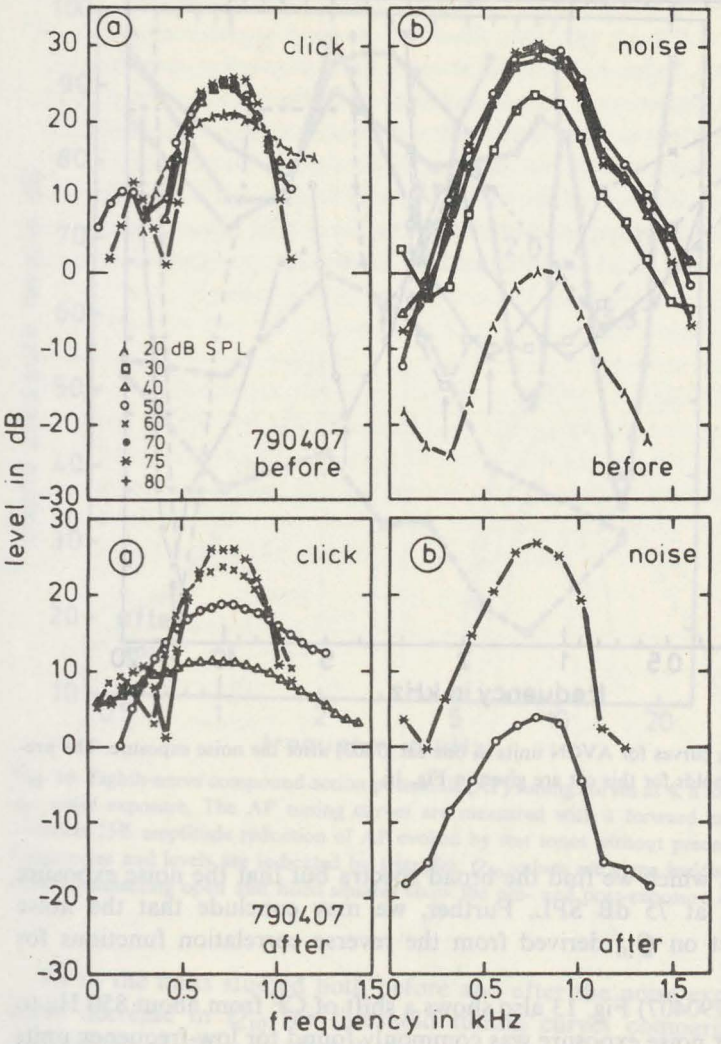

Fig. 14. Response spectra for unit 790407 before and after the noise exposure. The response spectra for click stimuli (a) are obtained by Fourier transformation of compound period histograms and for noise stimuli (b) by Fourier transformation of the reverse correlation functions.

Q_{10} values found before the excessive noise exposure for clicks increase with stimulus level from less than 1.0 at 20 dB SPL, 1.5 at 40 or 50 dB SPL up to 1.7 at 75 dB SPL while the Q_{10} values for the noise stimulus are steady at 1.3. The Q_{10} values found for sinusoids (tuning curves in Fig. 13) were 1.7 to 2.2 (Table I). After the noise exposure Q_{10} values for clicks ranged from less than 0.9 at 50 dB SPL, 1.4 at 60 dB SPL up to 1.7 at 75 dB SPL, while Q_{10} values for the noise stimulus were about equal to the pre-exposure values of 1.3. For clicks we may conclude that the increase in threshold after the excessive noise exposure is reflected in the pre- and

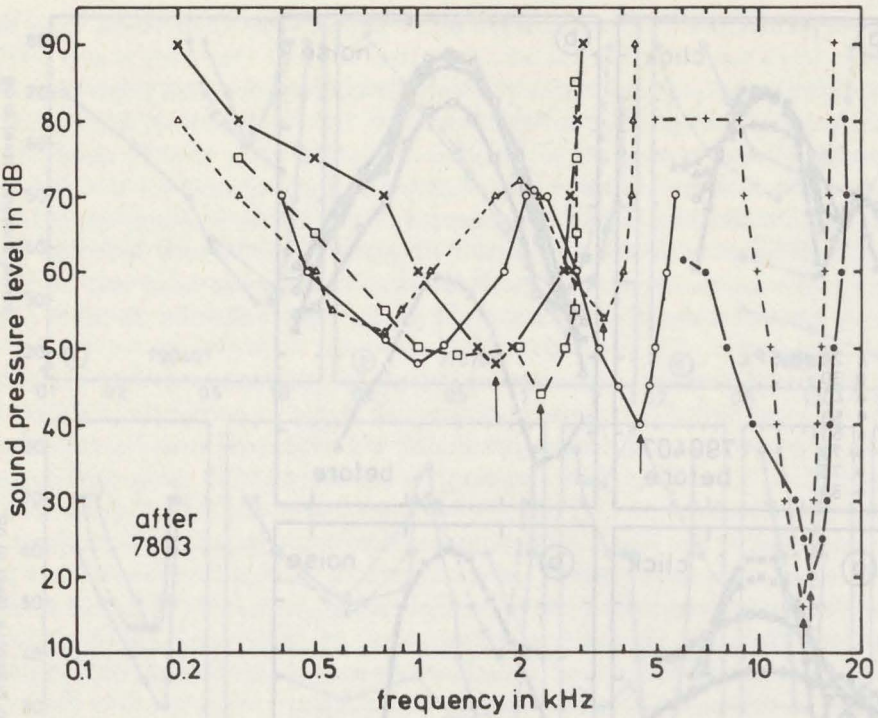

Fig. 15. Six threshold tuning curves for AVCN units in one cat (7803) after the noise exposure. The pre- and post-exposure AP thresholds for this cat are given in Fig. 16.

post-exposure levels at which we find the broad spectra but that the noise exposure has no effect on Q_{10} at 75 dB SPL. Further, we may conclude that the noise exposure has no effect on Q_{10} derived from the reverse correlation functions for noise stimuli.

For the same unit (790407) Fig. 13 also shows a shift of CF from about 850 Hz to 700 Hz. This shift after noise exposure was commonly found for low-frequency units up to about 3 kHz but was not found for units with higher CF. The shift of CF for unit 790407 is not reflected in the response spectra of Fig. 14.

Fig. 15 shows six tuning curves collected for one cat (7803) after the noise exposure. In addition, Fig. 16 shows three post-exposure AP tuning curves and pre- and post-exposure AP thresholds for the same cat (for more details see our previous publication on AP tuning curves [22]). The shapes of the single-unit tuning curves (Fig. 15) in the frequency region most affected by the noise exposure (2–8 kHz, Fig. 16) are quite distorted. The tips of the tuning curves are elevated whereas the low-frequency tails are at about the pre-exposure level. Local minima in the low-frequency tail may occur at lower levels than the level of the elevated tip. The high-frequency tuning curves in the region not affected by the noise exposure show a near normal shape. These effects are also present in the AP tuning curves of Fig. 16.

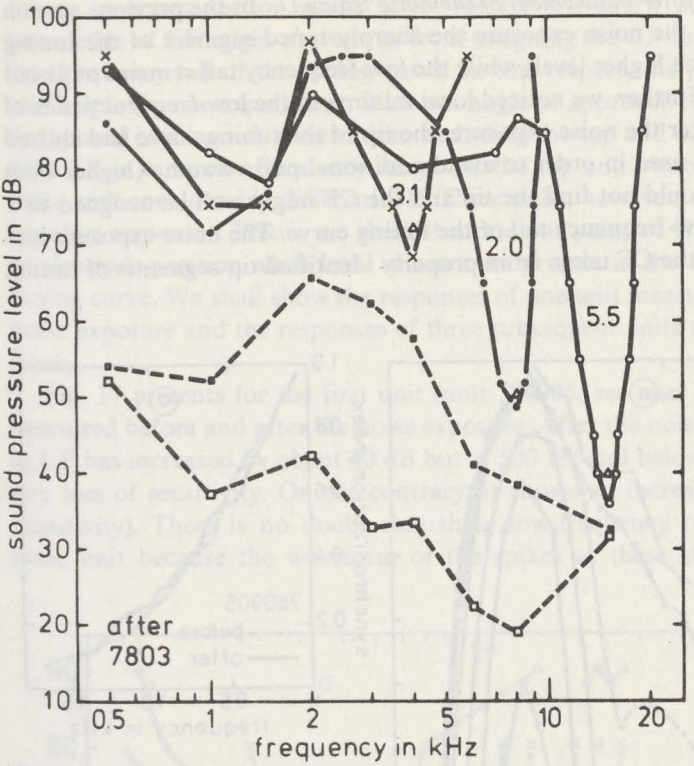

Fig. 16. Eighth-nerve compound action potentials (AP) tuning curves at 4, 8 and 15 kHz for cat 7803 after the noise exposure. The AP tuning curves are measured with a forward masking technique; masking criterion 25% amplitude reduction of AP evoked by test tones without preceding masker [21]. Test tone frequencies and levels are indicated by triangles, Q_{10} values are given inside the tuning curves. Dashed curves connecting open and filled squares show the pre- and post-exposure AP thresholds, respectively.

As in the units studied both before and after the noise exposure, we also found some decrease in Q_{10} for threshold tuning curves comparing the data for one population of units studied before the noise exposure with those for another population studied afterwards. The data were already presented in Fig. 8. Comparing the Q_{10} values in half-octave intervals we found significant differences (t-test, $P < 0.05$) in the frequency regions 1.4–4 and 11.3–16 kHz. In these regions average Q_{10} for half-octave intervals decreased by 19–54%. For the limited population of units from which we obtained response spectra for click and noise stimuli after the excessive noise exposure we did not find a significant effect of the noise exposure on Q_{10}. This is in line with the results of Fig. 14.

A cluster of seven units with post-exposure CF of about 1.5 kHz in Fig. 8 was excluded from the Q_{10} comparison given above because we have indications based on latency (section 3.2.2) and electrode position that the CF of about 1.5 kHz was assigned to local minima in the low-frequency tails of the post-exposure tuning curves while their tips were not found. This will be discussed in the next section.

3.3.3. CF assignment after inducement of the noise trauma. In the previous section we have seen that after the noise exposure the sharply tuned segment of the tuning curve might shift to much higher levels while the low-frequency tail remains at about the pre-exposure level. Further, we noticed local minima in the low-frequency tails of the tuning curves. If, after the noise exposure, the tip of the tuning curve had shifted to levels higher than we used in order to avoid additional noise trauma (higher than 80 or 90 dB SPL), we would not find the tip and the CF might well be assigned to a local minimum in the low-frequency tail of the tuning curve. The noise exposure had only a limited effect on the CF taken from properly identified tip segments of tuning

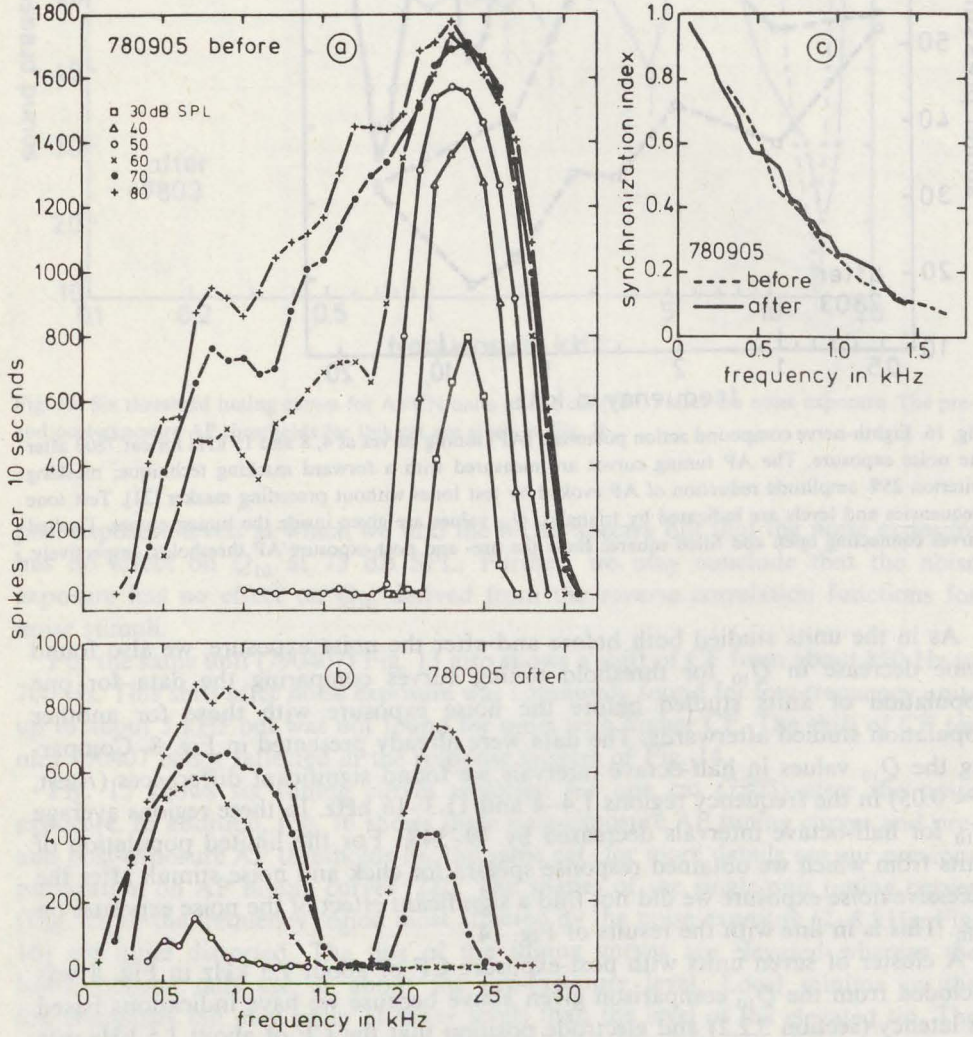

Fig. 17. Response areas for unit 780905 before the noise exposure (a) and afterwards (b). Panel c shows the pre- and post-exposure synchronization index as a function of stimulus frequency.

curves (previous section, some effect for CF < 3 kHz). Therefore, some advance knowledge of CF might prevent us from assigning the CF to a local minimum in the low-frequency tail of the tuning curve. In this respect, the position of the electrode was helpful in our experiment. With our angle of approach to the AVCN we find for unexposed cats in each penetration, excluding the top and bottom of the track, units with CF in a narrow frequency range. At the top and bottom of the tracks we find units with considerably different CF. These units, however, are distinguished by fast negative responses. Below, we shall illustrate our point of CF assignment in relation to electrode position when local minima are present in the low-frequency tail of the tuning curve. We shall show the responses of one unit measured before and after the noise exposure and the responses of three subsequent units along the same electrode track.

Fig. 17 presents for the first unit (unit 780905, see also Fig. 13c) response areas measured before and after the noise exposure. After the noise exposure the threshold at CF has increased by about 40 dB but at 500 Hz and below the unit does not show any loss of sensitivity. On the contrary, it shows an increase of firing rate (hypersensitivity). There is no doubt that these low-frequency responses stem from the same unit because the waveform of the spikes at these stimulus frequencies was

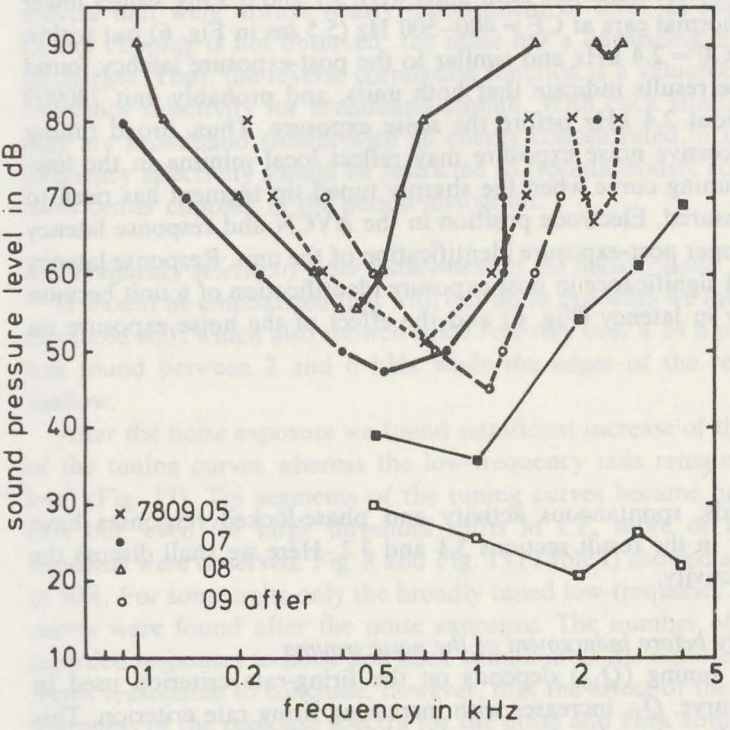

Fig. 18. Tuning curves for four units in the same electrode track after the noise exposure. Note the responses at about 2.4 kHz, probably the pre-exposure CF for all units. Open and filled squares present the pre- and post-exposure AP thresholds, respectively.

identical to the one found for higher stimulus frequencies. At 50 dB SPL Fig. 17b shows no response after the noise exposure for a stimulus at CF while a response is found at about 700 Hz. Thus, the level of the post-exposure tuning curve at 700 Hz will be lower than the level at CF. This, and the hypersensitivity for the low frequencies, can be seen in Fig. 13c. Fig. 17 and Fig. 13c also show a slight downward shift in apparent CF from 2.4 to 2.2 kHz. No click response and reverse correlation functions were obtained for this unit because SI at CF is very low (Fig. 17c). The noise exposure had no effect on SI. From the phase shift between responses evoked by low-frequency stimuli at 100 Hz intervals we calculated a response latency that increased from 2.7 ms pre-exposure to 3.3 ms post-exposure (both values determined at 70 dB SPL).

Upon further advance of the electrode we found units 780907, 780908 and 780909. Fig. 18 shows minima in the tuning curves at 400, 500 and 1000 Hz, respectively. However, at 80 dB SPL we found some response localized at about 2.4 kHz (the pre-exposure CF of unit 780905) for unit 780907 and, increasing stimulus level up to 90 dB SPL, we found some response localized in the 2.4 kHz region for the next unit. Both units showed good phase-locking for low stimulus frequencies and some phase-locking in the 2.4 kHz region. Response spectra for both units derived from reverse correlation functions showed secondary peaks at about 2.4 kHz. Response latencies calculated for both units were 3.1 and 3.3 ms, values lower than those found for normal ears at CF = 400–500 Hz (5.5 ms in Fig. 6) but within the normal range for CF = 2.4 kHz and similar to the post-exposure latency found for unit 780905. These results indicate that both units, and probably unit 780909 too, were tuned to about 2.4 kHz before the noise exposure. Thus, broad tuning curves found after excessive noise exposure may reflect local minima in the low-frequency tail of the tuning curve when the sharply tuned tip segment has risen to levels above those measured. Electrode position in the AVCN and response latency may be helpful in a proper post-exposure identification of the unit. Response latency is, of course, of limited significance in post-exposure identification of a unit because of the large variability in latency (Fig. 6) and the effect of the noise exposure on latency.

4. Discussion

Single-unit thresholds, spontaneous activity and phase-locked responses have been discussed already in the result sections 3.1 and 3.2. Here we shall discuss the data on frequency selectivity.

4.1. Frequency selectivity before inducement of the noise trauma

Fig. 9 showed that tuning (Q_{10}) depends on the firing-rate criterion used in measuring the tuning curve. Q_{10} increases with increasing firing rate criterion. This corresponds to the finding that the slope of the function between firing rate and stimulus level depends on stimulus frequency [37]. In Fig. 8 we found, in the frequency region 3–10 kHz, Q_{10} values for AVCN neurons lower than the lowest

values reported for eighth-nerve fibers. The dependence of Q_{10} on rate criterion does not explain this difference because for both AVCN neurons and eighth-nerve fibers the Q_{10} values are based on threshold tuning curves. Also, the low Q_{10} values probably do not reflect pre-exposure cochlear damage because the AP thresholds before inducement of the trauma are normal for all cats presented in this paper (see also [21]). Of course, normal AP thresholds are not complete proof of normal functioning of the cochlea. We think that the tuning curves for AVCN neurons may be broader than those for eighth-nerve fibers because two or three eighth-nerve fibers terminate on one AVCN neuron [28,31]. If the activity of these fibers is summed one may expect to find broader tuning curves. This may show up particularly in the frequency region above 3 kHz where Q_{10} for eighth-nerve fibers is high.

For a number of units we found broad response spectra for clicks at low stimulus levels. Inspecting the compound period histograms found for these units we noticed that they show center clipping. (Center clipping, i.e. responses restricted to the peaks of the effective stimulus waveform, can be seen in Fig. 3b, 200 Hz.) The very high SI values found for these units at low stimulus frequencies also point in this direction. Center clipping suggests a threshold type of spike generating mechanism. The other units (mostly spontaneously active) showed narrow tuning at low stimulus levels. This may imply a randomly fluctuating threshold. Reverse correlation functions gave spectra that were always nearly independent of level, at least up to 60 dB SPL. Center clipping is not observed; the noise has a linearizing effect on the pattern of discharges. Thus, the reverse correlation function is a valuable tool to determine the frequency selectivity for broadband stimuli. With click stimuli, interesting because they are broadband stimuli with all energy concentrated in time, determination of frequency selectivity should be restricted to (spontaneously active) units that do not show center clipping in the period histogram.

4.2. Frequency selectivity after inducement of the noise trauma

It should be emphasized that with our noise exposure we induced only a moderate threshold shift which also showed some recovery over a 24 h period. The highest loss was found between 2 and 6 kHz while the edges of the region of the loss were shallow.

After the noise exposure we found significant increase of the threshold at the tips of the tuning curves whereas the low-frequency tails remained at about the same level (Fig. 13). Tip segments of the tuning curves became broader than in normal ears but, even for large threshold shifts at CF, more or less sharply tuned tip segments were observed. Fig. 8 and Fig. 13 (Table I) showed a decrease of Q_{10} by up to 50%. For some units only the broadly tuned low-frequency segments of the tuning curves were found after the noise exposure. The number of units from which we recorded responses to noise and click stimuli after the noise exposure was limited. It seems reasonable to conclude, however, that the effect of the noise exposure on the sharpness of the response spectra for the noise and click stimuli (derived by Fourier transformation of the reverse correlation functions and the compound period histograms, respectively) is smaller than the effect on the sharpness of tuning curves. Other papers on the effect of excessive noise stimulation on the sharpness of tuning

curves [1,8,26,38] also mention broader tip segments and relatively unaffected low-frequency tails. Liberman and Kiang [26] also observed tuning curves with a low-frequency tail below the threshold at CF while the tip at CF was still more or less sharply tuned. They stated that this type of tuning curve was most prominent for units with CF in the high-frequency region of the loss. We observed this type of tuning curve also for units with CF at the low-frequency border of the loss (Fig. 13).

For units with CF $\leq$ 3 kHz our broadband noise exposure resulted in a small shift of CF to lower frequencies (about 10–20%). Cody and Johnstone [8] also found, after excessive exposure to sinusoidal stimuli which produced a moderate threshold shift, that the tip of their tuning curves had shifted to lower frequencies and higher levels. For longer exposure durations, producing larger threshold shifts, the tip disappeared in the low-frequency tail. We did not observe this large effect. The edge on the low-frequency side of the region of the loss may be steeper for their losses produced by sinusoidal stimuli than for our losses produced by pink noise. The asymmetry of their loss with respect to the response areas of units at the low-frequency edge of the loss region may account for their large shifts of the tip to lower frequencies.

There are a number of neurophysiological studies indicating that tuning of eighth-nerve fibers deteriorates for a variety of cochlear damage. The damage may be due to, for example, ototoxic drugs [9,14,15,23,33], hypoxia [11] and perilymph removal from scala tympani [32]. For kanamycin-induced damage there is discrepancy in the results reported in the literature. In chinchillas Dallos and Harris [9] observed only an upward shift of the sharply tuned segment whereas Evans and Harrison [14] found much broader tuning curves in kanamycin-treated guinea pigs than in normal ones. Our results are similar in appearance to those of Dallos and Harris (sharp tips at the low-frequency edge of the loss). However, we also found a moderate decrease of frequency selectivity in our tips which they did not report. Dallos and Harris may not have been able to observe a modest loss of frequency selectivity in their tip segments because they did not have, as a reference, the frequency selectivity of the tip segment for the same unit before drug administration. As we have seen in Fig. 8, comparison of Q_{10} values for different populations of units before and after cochlear damage is limited by the large variability in Q_{10}. The broad tuning curves reported by Evans and Harrison might reflect, for a number of units, low-frequency tails of the tuning curves. The threshold shifts reported by them are larger than those found by us while even for our limited threshold shifts confusion of tip and tuned low-frequency tail is possible (Fig. 18). In such cases electrode position and response latency were helpful in our study to assign the proper CF to a unit after inducement of the noise trauma.

In a number of psychophysical studies on frequency selectivity for people suffering from sensorineural hearing loss, broader tuning curves are brought forward to explain reduced speech discrimination against ambient noise. It seems to us that reduced selectivity at the tip is less detrimental to speech perception than the shift of the tip segment to higher levels while the low-frequency tail remains at the same level. The reduced distance between tip and tail suggests increase of masking by low-frequency noise while low-frequency tails below the tip segment imply a distortion in frequency coding.

5. Conclusions

Exposure of cat ears for half an hour to pink noise at 105 dB SPL produced an average threshold shift of 20 dB at 0.5 kHz, 30 dB at 2.6 kHz and 15 dB at 16 kHz. The maximum threshold shift found was about 50 dB.

For AVCN units we do not find a correlation between the spontaneous activity and the threshold of a unit. After inducement of the noise trauma no significant change in spontaneous activity was found for these units.

The degree of phase locking of responses of AVCN units to the stimulus (the synchronization index, SI) is primarily a function of stimulus frequency, not of the characteristic frequency (CF) of the unit. SI was not significantly affected by inducement of the noise trauma.

Response latency for AVCN units tends to increase after inducement of the noise trauma. Therefore, decrease of the latency of compound eighth-nerve action potentials (AP) after inducement of the noise trauma cannot be due to a decrease of latency for single units but it must be due to a shift to higher frequencies of the population of units contributing to the AP.

After inducement of the noise trauma the sharply tuned tip segments of tuning curves shift to higher levels whereas the low-frequency tails remain at about the same level. Q_{10} decreases by at most 50%, which was also found for AP tuning curves. Units with CF < 3 kHz may show a shift of CF to a lower frequency by 10–20%.

Response spectra derived by Fourier transformation from compound period histograms for click stimuli and from reverse correlation functions for noise stimuli do not show a significant decrease in frequency selectivity after inducement of the noise trauma. However, data on this point were limited.

After inducement of the noise trauma the sharply tuned tip segment of a tuning curve may not be found (at safe stimulus levels) and CF may be assigned to a local minimum in the low-frequency tail of the tuning curve. Electrode position in the AVCN and response latency may be helpful in assigning the proper CF to a unit after inducement of the noise trauma.

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SUMMARY

This thesis consists of a collection of papers on auditory frequency selectivity in the cat before and after inducement of an acute noise trauma.

The present research was inspired by recent findings from psycho-acoustic studies, indicating that sensorineural hearing loss may be associated, not only with reduced sensitivity (upward shift of the threshold for sounds), but also with reduced discrimination of suprathreshold sounds.

Auditory frequency selectivity was measured in two ways:

a) by recording from single units in the anteroventral part of the cochlear nucleus (AVCN), and
b) by recording compound eighth-nerve action potentials (AP) with an electrode placed in the vicinity of the round-window membrane.

The first approach is commonly accepted for studying aspects of frequency selectivity at a peripheral stage in the auditory pathway. However, the complex and invasive character of the recording technique makes it unsuited for clinical practice. The second approach has already proven its clinical importance in providing gross measures of cochlear function. Its disadvantage, however, is that the AP reflects synchronous activity of a group of eighth-nerve fibers. Hence, it tends to be less suited for studying detailed aspects of frequency selectivity of the ear.

In addition to auditory frequency selectivity we also studied auditory functions which are, directly or indirectly, connected with frequency selectivity namely: absolute threshold and synchronisation between stimulus waveform and neural activity.

This synchronisation is, among other measures, used to calculate cochlear response latency.

In order to be able to study neural activity in the same animal both before and after inducement of the trauma, cats were exposed to broadband noise at about 105 dB SPL (equal intensity per octave) for half an hour halfway through the experiments. This exposure resulted in a long-term temporary threshold shift which remained fairly steady during the experiments.

The main results, given below, are ranked in the order of presentation in Chapters II to VI of this thesis:

1. single-unit frequency tuning curves are broader after inducement of the trauma. AP frequency tuning curves can be measured with a forward masking technique. These AP tuning curves are broader than single-unit tuning curves, but an effect of the noise trauma on the width of the tuning curve can be measured. Neither the AP latency data nor the response latency calculated from single unit data suggest that a decrease in the sharpness of tuning found after inducement of the noise trauma is accompanied by a decrease of cochlear response latency;

2. in the traumatized ear response latency is a good indicator of a unit's characteristic frequency;

3. curves representing AP threshold as a function of test-tone frequency have a shape similar to behavioral and single-fiber threshold curves. After inducement of the trauma the greatest threshold shift is found between 2 and 6 kHz. AP latency values at threshold before and after inducement of the trauma are not significantly different. For a minority of responses after inducement of the trauma lower latencies at threshold are found;

4. potentials and limitations of AP tuning curves (APTC) in providing us with a measure of frequency selectivity are studied.

Width of APTCs is dependent upon test-tone sound pressure level and masking criterion. This can be explained by assuming that APs are formed by discharges of fibers with somewhat different characteristic frequencies. APTCs are wider in traumatized ears than in normal ears. This widening is not simply an effect of sound pressure level, but for a significant part due to the noise trauma;

5. results for one population of units measured before the noise exposure were compared with those found for another population measured afterwards. In addition, results for single units that could be kept under observation during the noise exposure were compared before and after inducement of the trauma. The comparisons show that the sharply-tuned tip segments of tuning curves shift to higher levels whereas the low-frequency tails remain at about the same level. The tip of the tuning curves are broader after inducement of the trauma than before. Response spectra for clicks and noise did not show a significant decrease of frequency selectivity. After inducement of the noise trauma the sharply-tuned tip segment of the tuning curve may not be found and the characteristic frequency may be assigned erroneously to a local minimum in the low-frequency tail of the tuning curve.

SAMENVATTING

In dit proefschrift wordt een systematisch onderzoek naar het frekwentie-oplossend vermogen van zowel het normale- als het beschadigde gehoororgaan van de kat beschreven. De volgende observaties waren de aanleiding tot dit onderzoek.

Wanneer mensen geconfronteerd worden met slechthorenden, zullen ze meestal hun stem verheffen. Dit is gebaseerd op de ervaring dat bij slechthorenden de drempel voor de waarneming van geluid verhoogd is. Bij het hoortoestel wordt dit verlies in gevoeligheid gecompenseerd door het ontvangen signaal (frekwentie-afhankelijk) te versterken. Veel slechthorenden, vooral degenen die lijden aan een gehoorverlies dat zijn oorsprong vindt in het slakkehuis (cochleair verlies), klagen echter dat wanneer het geluid wel hard genoeg is, ze gehandicapt zijn in het spraakverstaan wanneer er omgevingslawaai aanwezig is (verkeerslawaai, meerdere sprekers in dezelfde ruimte, etc.). Dit duidt erop dat, naast een drempelverhoging, ook het onderscheidingsvermogen voor geluid dat de drempel overschrijdt verminderd is. De oorzaak van het afgenomen vermogen om spraak van storend lawaai te onderscheiden kan zijn, dat de frekwentie-selectieve filters van het gehoororgaan in het beschadigde orgaan breder zijn dan in het normale. Deze veronderstelling hebben we nader onderzocht. De resultaten van dit onderzoek staan in dit proefschrift beschreven.

Daar bovengenoemde klachten meestal optreden wanneer het gehoorverlies in het slakkehuis (cochlea) is gelegen, is het zinvol de overdrachtskarakteristiek van de cochleaire filters te bepalen.

Immers, in de cochlea vindt de omzetting van geluid naar zenuwaktiviteit plaats met als belangrijk element van dit proces het scheiden van de frekwentiecomponenten van het geluid. Daarom moet de zenuwaktiviteit aan de uitgang van de cochlea, opgewekt door een goed gedefinieerde geluidsstimulus, gemeten worden. Mogelijkheden voor het meten van zenuwaktiviteit aan de uitgang van de cochlea (de gehoorzenuw) zijn, het registreren van:

a) extracellulaire potentialen van afzonderlijke zenuwvezels

b) synchrone responsies van groepen zenuwvezels.

ad a) Aan afzonderlijke vezels kan gemeten worden door microelektroden te plaatsen in de gehoorzenuw. Hiervoor moet men zich operatief een weg banen door schedel en hersenen. Het belang van metingen aan afzonderlijke vezels is, dat de meeste van deze vezels verbonden zijn met slechts één haarcel, zodat per cochleair gebied resultaten kunnen worden verzameld.

ad b) Synchrone responsies van een groep zenuwvezels (samengestelde aktiepotentialen, AP) kunnen worden gemeten met een electrode in de buurt van het ronde venster. Hiervoor hoeft men, bij mensen, slechts een gaatje in het trommelvlies te maken. Dit betekent, dat registraties van samengestelde aktiepotentialen klinisch mogelijk zijn (Elektrocochleografie, ECoG). Samengestelde aktiepotentialen zijn minder geschikt om gedetailleerde informatie omtrent de frekwentieselectiviteit van de cochlea aan te onttrekken omdat ze afkomstig zijn van een groep zenuwvezels die een relatief groot cochleair gebied innerveren.

We achtten het methodologisch noodzakelijk in hetzelfde proefdier te meten voor- en na het aanbrengen van een gehoorverlies.

Deze eis heeft zowel de plaats van de electrode als de wijze waarop het gehoorverlies werd aangebracht sterk beïnvloed. We hadden echter de volgende reden. Zonder registraties voor en na het aanbrengen van het gehoorverlies in hetzelfde proefdier kan alleen een vergelijking gemaakt worden tussen de registraties van één populatie zenuwvezels voor het aanbrengen van het gehoorverlies en van een andere populatie, in een andere kat, erna. Deze vergelijking geeft resultaten van een beperkte waarde vanwege de verschillen tussen responsies van normale vezels onderling. Bovendien zijn er aanwijzingen, dat de stimulusfrekwentie waarvoor een vezel de laagste excitatiedrempel heeft (de karakteristieke frekwentie, CF) kan veranderen ten gevolge van het aanbrengen van het gehoorverlies. Bij het normale gehoororgaan correspondeert de karakteristieke frekwentie met een beperkt cochleair gebied. Vergelijken we nu de responsies van vezels met dezelfde karakteristieke frekwentie voor en na het aanbrengen van het trauma dan kan dit misleidend zijn omdat deze vezels verschillende gebieden in de cochlea zouden kunnen innerveren. Om nu aan één vezel zowel voor als na het aanbrengen van het gehoorverlies te kunnen meten, is het noodzakelijk dat de elektrode gedurende enkele uren kontakt houdt met dezelfde vezel. Dit is voor vezels in de gehoorzenuw zelden het geval. Daarentegen kan er van neuronen in het antero-ventrale gedeelte van de cochleaire nucleus (AVCN), het volgende station in de auditieve zenuwbaan, langdurig worden geregistreerd. Bovendien lijken AVCN responsies, in vergelijking met andere delen van de auditieve keten, het meest op responsies van de vezels in de gehoorzenuw. Daarom is er gekozen voor het registreren van extracellulaire potentialen van afzonderlijke neuronen in de AVCN in plaats van vezels in de gehoorzenuw.

De manier waarop het gehoorverlies moet worden aangebracht wordt ook beïnvloed door de eis aan één vezel te kunnen meten voor en na het aanbrengen van het verlies. Het trauma moet vanwege deze eis tijdens het experiment snel kunnen worden aangebracht. Als middel is daarom gekozen voor het aanbrengen van een acuut lawaaitrauma. De proefdieren werden halverwege het experiment gedurende dertig minuten blootgesteld aan breedbandig lawaai met een konstante geluiddruk per oktaaf van 98 deciBel (dB). De totale geluiddruk was 105.3 dB. De drempelverhoging zoals veroorzaakt door dit type lawaai (gemiddeld 30 dB tussen 2 en 6 kHz) is ongeveer konstant tijdens het experiment, maar vertoont een grote variatie tussen de proefdieren onderling.

Om de experimenten in een breder kader te kunnen plaatsen, zijn naast de frekwentieselektiviteit ook auditieve funkties gemeten die direkt of indirekt kunnen samenhangen met de frekwentieselektiviteit, te weten: de absolute drempel en de synchronisatie van aktiepotentialen met de golfvorm van de stimulus. Deze synchronisatie is van belang bij de bepaling van de responsietijd, het tijdinterval tussen de stimulus aan het trommelvlies en de responsie van het neuron.

De belangrijkste vragen die aan deze studie ten grondslag liggen kunnen nu als volgt worden geformuleerd:

1. wat zijn de effekten van een acuut lawaaitrauma op de frekwentieselektiviteit zoals deze is af te leiden uit de perifere neurale codering van geluid in afzonderlijke neuronen in de AVCN van de kat?

2. hoe hangen de resultaten verkregen voor afzonderlijke neuronen samen met die verkregen met de voor de klinische praktijk belangrijke methode van het registreren van samengestelde aktiepotentialen?

3. wat zijn de effekten van een acuut lawaaitrauma op absolute drempel en responsietijden voor zowel afzonderlijke neuronen in de AVCN als voor samengestelde aktiepotentialen?

Hieronder zijn enige van de belangrijkste resultaten samengevat.

1. Frekwentieselektiviteit in AVCN neuronen

Frekwentieselektiviteit in AVCN neuronen werd gemeten voor en na het aanbrengen van het acute lawaaitrauma met behulp van drie stimulus typen: sinusoiden, kliks en ruis. Verschillende stimuli werden gebruikt omdat de codering van het geluid in de cochlea niet een lineair en tijdsonafhankelijk proces is. Daarom kan de gevonden frekwentieselektiviteit afhangen van èn spektrale èn temporele aspekten van de stimulus.

1.1 Sinusoiden

Sinusoiden werden toegepast om de frekwentieselektiviteit op twee uit de literatuur bekende manieren te meten:

a) responsiegebieden (neurale vuurfrekwentie als funktie van de stimulusfrekwentie gemeten op een konstant stimulus niveau) en

b) afstemkrommen (stimulusniveau als funktie van de stimulusfrekwentie waarbij een gelijke neurale vuurfrekwentie wordt gevonden).

In het normale oor werd waargenomen dat de toppen van de afstemkrommen van AVCN neuronen in het algemeen iets breder waren dan de toppen van de afstemkrommen van de zenuwvezels in de gehoorzenuw zoals vermeld in de literatuur. De frekwentieselektiviteit werd uitgedrukt in Q_{10} waarden die gedefinieerd zijn als het quotient van de karakteristieke frekwentie en de bandbreedte 10 dB boven de top. Na lawaaiexpositie werd de veronderstelde verbreding van afstemkrommen waargenomen.

De afname van de Q_{10} waarden van deze krommen liep voor sommige neuronen op tot 50%. De drempel aan de top van de afstemkrommen was verhoogd, terwijl het laagfrekwente gedeelte van de afstemkrommen minder verhoging vertoonde. Wanneer de punt van de afstemkromme hoger is komen te liggen dan de laagfrekwente "staart" is het mogelijk dat een lokaal minimum in de laagfrekwente staart wordt aangezien voor de karakteristieke frekwentie.
Het lijkt ons toe dat een afgenomen selektiviteit aan de top minder nadelig is voor spraakperceptie dan het verschuiven van het top segment naar hogere niveaus terwijl het laagfrekwente gedeelte van de afstemkrommen ongeveer op hetzelfde niveau blijft liggen. De afgenomen afstand tussen "top" en "staart" betekent voor de perceptie een toename van de maskering door laagfrekwent lawaai. Bovendien veroorzaken de laagfrekwente gedeelten, die een lagere drempel hebben dan de top, een verstoring van de frekwentiekodering.

1.2 Kliks

Wanneer we gebruik maken van kliks kan de frekwentie-selektiviteit van de cochlea worden afgeleid uit de tijd-verdeling van de aktiepotentialen zolang stimulus en responsie synchronisatie vertonen (ongeveer tot 4 kHz). Tengevolge van deze synchronisatie weerspiegelen post-stimulus-tijdhistogrammen (PSTH) of samengestelde PSTH, waarin als periode het interklik interval wordt genomen, de impulsresponsie van het cochleaire filter. Fourier transformatie van het samengestelde PSTH levert het cochleaire filter.

In het normale oor werden voor één groep neuronen spektra van de klikresponsies gevonden waarbij de breedte niet van het geluiddrukniveau afhing, terwijl voor een andere groep neuronen juist een grote niveau-afhankelijk-heid bestond. Bij deze laatste groep neuronen vertoonden de samengestelde periodehistogrammen duidelijk "center

clipping". Dit suggereert, dat het aktiepotentiaal-genererend-mechanisme een drempelmechanisme is. Ook het feit, dat voor lage stimulusfrekwenties en neuronen met een karakteristieke frekwentie tot 10 kHz de synchronisatieindices groter kunnen zijn dan $\pi/4$ (de waarde voor sinusvormig periodehistogram) wijst op een drempelmechanisme. Center clipping manifesteert zich in bredere spektra. Mede omdat center clipping relatief minder invloed heeft op de aktiepotentiaal-generatie bij hogere geluiddruk niveaus, is de breedte van de spektra van klikresponsies niveau-afhankelijk. Deze afhankelijkheid is voor de spektra van klikresponsies groter dan voor de afstemkrommen. Na de lawaaiexpositie was de drempel aan de top verhoogd, de breedte van de spektra van de klikresponsies was echter niet significant afgenomen. Hierbij moet worden opgemerkt dat de populatie neuronen waarvoor deze spektra gemeten zijn nogal klein was.

1.3 Ruis

Voor ruis gebruikten we de uit de literatuur bekende techniek van Reverse Correlation (REVCOR) om frekwentieselektiviteit te bepalen. Deze techniek is ook gebaseerd op synchronisatie tussen neurale aktiviteit en effektieve stimulus. In dit geval wordt de impulsresponsie van het cochleaire filter verkregen door het correleren van neurale responsies met de "witte" ruis stimulus. Fourier transformatie van een revcorfunktie levert een revcorspektrum. In het normale oor hadden de revcorspectra ongeveer dezelfde vorm als de afstemkrommen. Er konden echter geen laagfrekwente staarten worden waargenomen omdat de dynamiek van de revcorspektra niet groot genoeg was (30 à 40 dB). Revcorspektra vertoonden nauwelijks niveau-afhankelijkheid. Revcorspektra vertoonden, evenals spektra van klikresponsies, geen signifikante afname van Q_{10} na lawaai expositie. Ook hier was echter de onderzochte populatie klein.

2. Frekwentieselektiviteit voor samengestelde aktiepotentialen

Voor samengestelde aktiepotentialen (AP) opgewekt door een testtoon, worden afstemkrommen verkregen met behulp van een voorwaartse maskeringstechniek. De afstemkrommen worden gedefinieerd als het geluiddrukniveau van de maskeerder als funktie van de maskeerfrekwentie waarbij de amplitude van de AP met een gelijke faktor wordt gereduceerd. De hypothese die aan deze techniek ten grondslag ligt luidt: de maskering van een testtoon is evenredig aan de excitatie veroorzaakt door de aan de testtoon voorafgaande maskeerder. Deze voorwaartse maskeertechniek wordt in de psychofysica veelvuldig gebruikt om interaktie tussen maskeerder en testtoon te vermijden.

In het normale oor vertoonden de AP afstemkrommen essentieel kleinere Q_{10} waarden dan de afzonderlijke neuronen. Dit is inherent aan het karakter van de samengestelde aktiepotentiaal: synchrone responsies van een groep zenuwvezels met karakteristieke frekwenties in de buurt van de testtoon frekwentie. Na de lawaaiexpositie is de drempel aan de top van de AP-afstemkromme verhoogd. Ook hier is de drempelverhoging aan de top groter dan aan het laagfrekwente gedeelte van de kromme. De Q_{10} waarden van de AP-afstemkrommen zijn na de lawaaiexpositie, net als de Q_{10} waarden van de afzonderlijke neuronen tot 50% kleiner dan ervoor. Dit betekent, dat de AP-afstemkrommen een goede monitor zijn van de perifere neurale frekwentieselektiviteit.

3. Drempel en responsietijden voor neuronen en samengestelde aktiepotentialen

De drempel (2.5μV) van samengestelde aktiepotentialen voor

testtonen ligt in het normale oor ongeveer 7 dB hoger dan de gemiddelde drempel van AVCN neuronen. Na lawaai-expositie is dit verschil nog maar 1 dB, zodat de drempel-verschuiving, zoals deze afgeleid kan worden uit APs, de drempelverschuiving van AVCN neuronen onderschat.

In het normale oor zijn responsietijden van neuronen in de AVCN een funktie van de karakteristieke frekwentie; de responsietijd neemt af met toenemende CF. Na lawaai-expositie blijken de responsietijden weinig veranderd te zijn, indien we ze vergelijken op gelijk relatief (t.o.v. drempel) geluiddrukniveau. Hierdoor kan de respon-sietijd als indicator gebruikt worden bij het toekennen van een CF wanneer het na lawaaiexpositie niet duidelijk is of we met een top danwel met een lokaal minimum van het laagfrekwente gedeelte van een afstemkromme te maken hebben. Ook de responsietijden van samengestelde aktiepotentialen (tijdverschil tussen aanzet van testtoon en top van de AP) zijn na lawaaiexpositie ongeveer evengroot als ervoor, indien we vergelijken op gelijk relatief (t.o.v. drempel) geluiddrukniveau.

Aangezien de frekwentiefilters na lawaaiexpositie breder zijn dan ervoor zou men, indien het cochleaire filter zich lineair zou gedragen, na lawaaiexpositie kleinere responsietijden verwachten dan ervoor. Voor samengestelde aktiepotentialen worden soms na lawaai-expositie, bij bepaalde stimulus-frekwenties, veel kleinere responsietijden gemeten dan in het normale oor. In dezelfde experimenten hebben we echter waar-genomen, dat de responsietijden van neuronen in de AVCN met karakteristieke frekwenties overeenkomstig deze stimulus-frekwenties ongeveer normale responsie-tijden vertonen. Dit suggereert, dat de AP in deze gevallen is opgebouwd uit responsies afkomstig van een ander cochleair gebied (hogere frekwenties).

Bij AP responsies op testtonen moet dus ook gelet worden op de bijbehorende responsietijd, omdat een niet met de stimulus-frekwentie overeenkomende responsietijd kan duiden op responsies van een ander gebied die tot een verkeerde interpretatie van de AP-afstemkromme kunnen leiden.

CURRICULUM VITAE

Evert van Heusden werd op 30 december 1949 geboren te Hengelo (O.). Na het doorlopen van de HBS-B begon hij in 1968 met de studie in de elektrotechniek aan de Technische Hogeschool Twente. Het baccalaureaats-examen behaalde hij in 1972, waarna in 1975 het doctoraalexamen volgde. De doctoraalstage liep hij aan de Universidad del Valle te Cali (Colombia). Het afstudeerwerk verrichtte hij bij de afdeling hersenonderzoek van het Medisch Fysisch Instituut TNO. Van 1975 tot 1980 was hij wetenschappelijk medewerker bij de afdeling audiologie van het Instituut voor Zintuigfysiologie TNO. In deze periode was hij in dienst van resp. TNO, Ministerie van Defensie en de Nederlandse Organisatie voor Zuiver Wetenschappelijk Onderzoek ZWO. In 1977 begon hij het in dit proefschrift beschreven onderzoek. Sinds 1980 werkt hij op de ontwerpafdeling van de Hollandse Signaal Apparaten B.V. te Hengelo.

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STELLINGEN

1. Na het aanbrengen van een acuut lawaaitrauma is de bandbreedte van de frekwentieselektieve filters van het gehoororgaan vaak breder dan ervoor. (Dit proefschrift).

2. Na lawaaiexpositie is de drempel aan de punt van afstemkrommen van neuronen in de AVCN in het algemeen meer verhoogd dan aan het laagfrekwente gedeelte van deze krommen. (Dit proefschrift).

3. De responsietijd van een neuron in de AVCN kan na lawaaiexpositie beter als indicator gebruikt worden van het gebied dat geïnnerveerd wordt door dit neuron dan de karakteristieke frekwentie. (Dit proefschrift).

4. Afstemkrommen van samengestelde aktiepotentialen, die geregistreerd kunnen worden in de buurt van het ronde venster van de cochlea, vormen een betrouwbare monitor van de perifere neurale frekwentieselektiviteit voor en na het aanbrengen van een acuut lawaaitrauma, mits de responsietijd van deze samengestelde aktiepotentialen, opgewekt door een testtoon, normaal is. (Dit proefschrift).

5. Men moet waken voor het wekken van te hoge verwachtingen van het nut van 'stereo' hoortoestellen, omdat ook deze hoortoestellen niet kunnen compenseren voor een abnormale vorm van de frekwentieselektieve filters.

6. De fase methode voor het afleiden van responsietijden van AVCN neuronen kan met succes worden toegepast voor het bepalen van afstanden met behulp van een passieve sonar.

7. Het eenvoudige scenario voor 'software' ontwikkeling, waarbij er een strikte scheiding bestaat tussen specificatie, ontwerp en implementatie, is in het bijzonder voor grote systemen slechts van theoretisch belang.

8. Mathematische modellen van interacties tussen populaties neuronen kunnen een belangrijke rol spelen bij het in duidelijke termen vastleggen van sterke en zwakke punten in onze experimentele kennis van het klinisch elektroencefalogram.

F.H. Lopes da Silva, A. van Rotterdam, P. Bats, E. van Heusden and W. Burr (1976): Perspectives in Brain Research, 281-308.

9. Het vooroordeel dat 'Montessori-vrijheid' leidt tot wanorde, vloeit voort uit de veronderstelling dat vrijheid impliceert dat er geen regels zijn.

10. De hoeveelheid vuil die door spelende kinderen rondom speelplaatsen in woonwijken wordt achtergelaten, stemt pessimistisch over de opvoeding met betrekking tot het milieu.

11. Een instituut dat fysiologie in zijn naam draagt behoort tenminste één fysioloog in dienst te hebben.

12. Het is eenvoudiger over principes te praten dan er naar te handelen.

Stellingen behorende bij het proefschrift:

AUDITORY FREQUENCY SELECTIVITY IN PERIPHERAL NEURONS

E. van Heusden Utrecht, 7-12-1983