To analyse how the discharge pattern of units in the AVCN change throughout the stimulus duration, responses were sampled at specific times throughout the 50ms electrical stimulus burst. These times correspond to 0, 10, 20, 30 and 40ms post stimulus onset. The responses to the first 2 pulses at each time window were sampled. With the exception of 2 units exhibiting 100% entrainment in response to all stimulus rates across all time windows, entrainment declines with higher stimulus rates, particularly at later times in the stimulus duration. This is illustrated in the plot of entrainment in figure 1A. A similar decline has been reported by Javel (1987) for auditory nerve fibres were it was argued, adaptation of the fibres accounted for this decrease. Such a decline in entrainment, AVCN unit responses would suggest a loss of stimulus encoded temporal information.

Irrespective of unit CF, the degree of phase-locking evoked by the electrical stimuli was high. An analysis of VST at specific time windows throughout the stimulus duration showed the two units with 100% entrainment for all stimulus rates at each stimulus time window also showed maximum VST across the same stimulus conditions. Interestingly for some other units, precise synchrony was attained in response to all stimulus rates irrespective of a decline seen in their response entrainment while others showed a marked decrease in VST throughout the stimulus over increasing pulse rates (Figure 1B). These data suggest that although some AVCN units are able to phase-lock to high rate pulsatile electrical stimuli, the level of response at higher pulse rates may not be adequate to code these rates correlating with the psychophysical studies (Eddington et al., 1978; McKay, 1994) showing pitch perception to decline with rates of electrical stimulation exceeding 300-400pps. Encoding of temporal frequency for electric and acoustic stimuli in the auditory system may therefore be dependent on the adequate response of a population of units.

REFERENCES


Moxon, C.E., Neural and mechanical responses to electric stimulation of the cat's inner ear. Doctoral Dissertation, University of Melbourne, 1991


SUMMARY

The anterior division of the ventral cochlear nucleus (AVCN) is the first relay station of the auditory pathway. We examined responses of neurons in the AVCN to intracochlear electrical stimulation using in vivo intracellular recordings. Twin pulse stimulation results indicated that these neurons evoke action potentials which are able to follow pulsatile stimulation at high rates. This ability to respond to each pulse along the stimulus train diminished when stimulus duration was increased to 50ms. At rates of 400 Hz and below in all neurons tested a deterministic response was seen to this longer duration pulsatile stimulation. With increasing rate of stimulation the response became more stochastic with apparent loss of encoding ability. These results have implications in the clinical application of cochlear implants operating at high stimulus rates.

INTRODUCTION

Development of speech processing strategies have been crucial for increasing speech recognition in cochlear implant users. Recent developments in sound processing has suggested that high rate stimulation of the cochlea above the stimulus rate equal to the fundamental frequency of voice (up to 200 pulses per second) can improve speech perception. Recently there has been interest in speech processing strategies using high pulse rate stimulation up to 1000 pulses per second to improve speech perception. The use of such high stimulus pulse rates may, however, place considerable metabolic stress on the auditory nerve, which
could have detrimental effects on sound processing. Currently little is known
about the physiological or psychophysical responses to variations of the time
intervals between pulses and their relative amplitudes. This knowledge could lead
to a new generation of speech processing strategies. In this investigation we are
examining physiological responses of neurons in the anteroventral cochlear nucleus
(AVCN) to electrical stimulation using the Melbourne/Cochlear scala tympani
banded electrode array. Using intracellular electrophysiological techniques we
hope to gain an insight into the physiological mechanisms underlying neuronal
responses in the AVCN to electrical stimulation and what effect high rate
stimulation might have on these mechanisms. As the AVCN is the first brain
region which receives information about sound, the understanding of the effects of
neural response to high rate stimulation of the cochlea in this area is essential if we
wish to determine its possible benefits on auditory processing in cochlear implant
users.

MATERIALS AND METHODS

All experiments were performed on male hooded rats anaesthetised with
intraperitoneal urethane in water (1.3g/Kg) and breathing spontaneously. A
modified version of the Melbourne/Cochlear scala tympani stimulating electrode
array was inserted into the cochleae through the round window. Intracellular
recording electrodes for the AVCN were visually after cerebellum aspiration.

Microelectrodes were filled with 1M potassium acetate (70-80 MΩ). Upon
impalement, the cochlea was stimulated with charged balanced bi-phasic
constant current pulses delivered at 100 μs per phase, 0-2.5 mA intensity. Two
stimulus paradigms were investigated to determine the synchrony and the
effectiveness in eliciting neural responses: (1) pulse pairs with varying interpulse
intervals; and (2) a 50 ms burst of stimulation delivered at constant rates with
varying amplitudes.

RESULTS

Spike responses were elicited by both stimulus pulses in all cells tested (n=16)
up to 1000 Hz on paradigm one (Fig. 1; Fig. 2). Testing on paradigm two (n=14
see table 1 for summary) showed that at stimulus rates below 600 Hz neuronal
firing occurred on presentation of each pulse during the stimulus train
(deterministic firing). In half the cells recorded, at rates 400 Hz and greater,
baseline resting potential became more negative during the stimulus. This
hyperpolarising response persisted up to 60 ms post stimulation. At higher rates
(600 Hz and above) this deterministic response was no longer seen with neurons
responding stochastically. In response to higher stimulus rates, between 400 to
1000 Hz, most neurons responded with progressively smaller action potential
amplitudes to pulses along the stimulus train. This drop in action potential
amplitude was more prevalent with increasing strength of stimulation. At rates greater than 1500 Hz stimulation produced a chopper response in this
neurone (Fig. 3). This was also seen in another neurone stimulated up to 3000 Hz.

Table 1: Effect of 50 ms pulsatile electrical stimulation on neural response.
+ signs indicate a more positive or more negative membrane potential respectively;
nc, no change in membrane potential; d, deterministic response; s, stochastic
response; ch, chopper like activity.

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Figure 1. (A-D) These neurones elicited spikes which were able to follow twin
pulse stimulation tested up to 1000 Hz at just above spike threshold. Stimulation
at 1.3 mA. "S" indicated stimulus artifact.

histogram shown in Fig. 3 F compared to that for lower stimulus rates (Fig. 3 C).
At rates greater than 1500 Hz stimulation produced a chopper response in this
neurone (Fig. 3). This was also seen in another neurone stimulated up to 3000 Hz.

Figure 2. Intracellular recordings of action potentials (A) and membrane
potential (B) following electrical stimulation of the cochlea.
Figure 2. Response of an AVCN neurone to intracochlear electrical stimulation. (A) Response to electrical stimulation (1.4 mA) showing long lasting hyperpolarisation following spike response. (B) This neurone was able to fire successive pulses in response to twin pulse electrical stimulation. (C) In response to 200 Hz electrical stimulation over 50 ms this neurone responded in a deterministic manner. Resting potential did not change during this period. (D) In response to 400 Hz stimulation over 50 ms spike amplitude decreased with resting potential increasing. Dashed line indicate resting membrane potential.

DISCUSSION

Results from this investigation suggest that stimulation at rates greater than 1200 Hz results in a loss of neurone encoding ability. At rates above 1000 Hz, the response became chopper like with evenly spaced action potentials possibly as a result of auditory nerve fatigue. Electrical stimulation at high rates has been shown to cause a reduction in the excitability of auditory nerve fibres. This reduction in excitability may alter the response of AVCN neurones to stimulation with the chopper like response a result of less frequent auditory nerve firing. In addition, prolonged stimulation also produced a change in resting membrane potential and action potential amplitude. The decrease in action potential amplitude at rates higher than 200 Hz may be attributed to ionic imbalances, such as sodium depletion. The prolonged underlying depolarisation and hyperpolarising response during stimulation may also depend on neural mechanisms which require further in vitro investigation.

In conclusion, pulsatile stimulation results suggest that AVCN neurons are able to follow high frequency stimulation for short periods. The long duration pulsatile stimulation results suggest that stimulation above 600 Hz and below 1200 Hz produces a loss in encoding ability. Above 1200 Hz stimulation, the rate encoded, however, is effectively lower. The encoding ability of these neurons may have implications in the clinical application of cochlear implants where new speech-processing strategies have tended to operate at higher stimulus rates.

Figure 3. Anteroventral cochlear nucleus cell (identified bushy cell) response to pulsatile electrical stimulation. (A-C) 200 Hz intracochlear electrical stimulation. (A) Response at spike threshold (1.2 mA). EPSP response are evident to each pulse with the amplitude of the EPSPs increasing during the 50 ms of stimulation until spike generation (seen rising above stimulus artifact). (B) Response at above spike threshold showing spike response to each pulse. resting potential remained constant throughout the 50 ms of stimulation. (C) Peri-stimulus time histogram (PSTH) of 50 trials at 1.4 mA stimulation showing deterministic pattern of firing corresponding to the number of stimulus pulses delivered. (D-F) 600 Hz intracochlear electrical stimulation. Spike response (seen above artifact at 1.6 mA) occur early and progressively decrease during the stimulus period. Resting membrane potential is also elevated returning to normal after cessation of electrical stimulation. (E) Expanded trace showing the initial action potential. Artifact did not obscure the intracellular response. (F) PSTH of 50 trials at 600 Hz electrical stimulation. The progressive decline in firing is evident. The response to stimulation is also less deterministic and more stochastic. Although not shown similar responses were observed at stimulus frequencies of 1000 and 1500. (G-I) 3000 Hz intracochlear electrical stimulation. (G) At stimulus frequencies above 2000 Hz a chopping response was evident. Spikes can be seen riding above artifact (H). (I) This chopping response is shown in the PSTH.
REFERENCES


SUMMARY

Mathematical models are a useful means of investigating pertinent features of complex auditory system. These features may be deduced from psychophysical experiments utilising animal and engineering studies. Historically, models of response to electrical stimulation have ignored activity which has been recorded in physiological studies. However, these models have been unable to accurately predict psychophysical phenomena. In this study, a random activity of the AN is presented, and psychophysical performance. These results indeed an important part of the response to stimulation.
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Author/s:
Paolini, Antonio, G.; Clark, Graeme M.

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