SYDNEY '97
XVI World Congress of Otorhinolaryngology Head and Neck Surgery

Sydney, Australia
2-7 March 1997

The effect of pulsatile intracochlear electrical stimulation on intracellularly recorded cochlear nucleus neurons

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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 neurones 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 50 ms. At rates 400 Hz and below in all neurones tested a deterministic response was seen to this longer duration pulsatile stimulation. With increasing rate of stimulation the response become 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 uses. Recent developments in sound processing has suggested that high rate stimulation of the cochlea way 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[1]. 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 tympany stimulating electrode array was inserted into the cochlea 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 cell 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 halve 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 (Fig. 2). At rates greater than 1200 Hz stimulation, however, neurons responded with a stochastic firing pattern with regularly spaced spikes of similar amplitude at a rate lower than that of the stimulus (100-200 Hz). This firing pattern is similar to that seen in neurons classified as chopper in response to acoustic stimulation. In one cell stimulated up to 4000 Hz, this neural chopping behaviour became more prominent with increasing rate. The response of this cell changed from deterministic firing at low rates of stimulation to a more stochastic response pattern at high stimulus rates (Fig. 3). This is reflected in the interspike interval

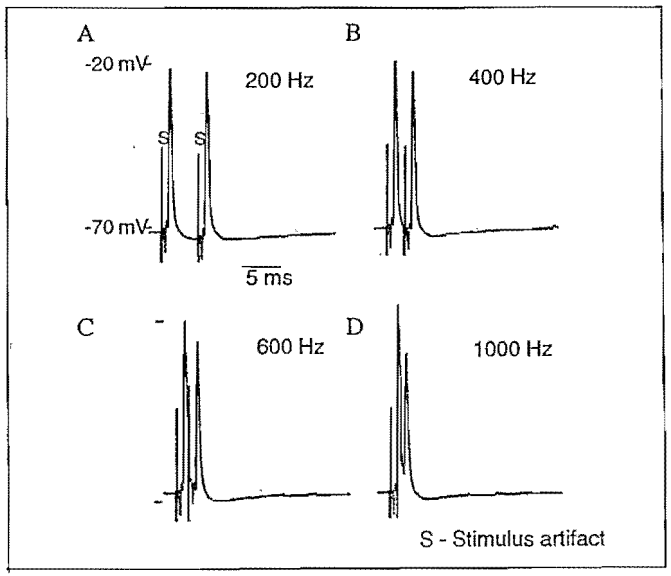

Figure 1. (A-D) These neurones elicited spikes which were able to follow twin pulse stimulation tested up to 1000 Hz at just above spike threshold. Stimulation at 1.3 mA. "S" indicated stimulus artifact.

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.

Table 1: Effect of 50 ms pulsatile electrical stimulation on neural response. + and - 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.

	Frequency of Stimulation (Hz)									
Neurone	*200*	*400*	*600*	*800*	*1000*	*1200*	*1500*	*2000*	*3000*	*4000*
218-002	+d	+d								
218-003	-d	-d	-s	-s	-s					
218-006	ncd	-d	-s	-s	-s					
223-003	ncd	+d	+s	+s	+s	ch	ch	ch	ch	ch
224-003	ncd									
224-004	+d	+d								
242-019	+d	+d								
243-004	-d	-d								
251-001	ncd	-d								
251-002	+d									
251-004	ncd	+d	+s							
251-005	ncd	+d								
251-006	-d	-d	-s	-s	-s		ch		ch	
253-001	ncd	-d	-s	-s	-s					

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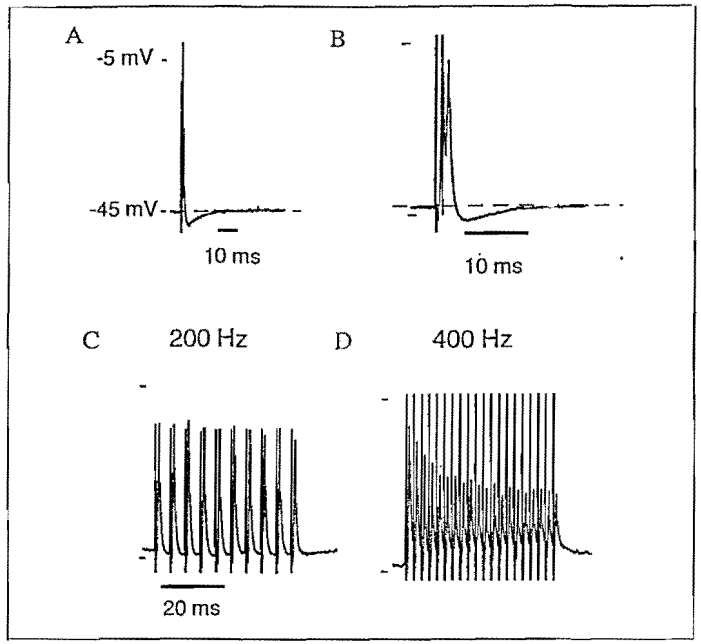

Figure 2. Response of an AVCN neurone to intracochlear electrical stimulation. (A) Response to electrical stimulation (1.4 mA) showing long lasting hyperpolarisation following spike response. (B) This neurone was able to fire successive pulses in response to twin pulse electrical stimulation. (C) In 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[2]. 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

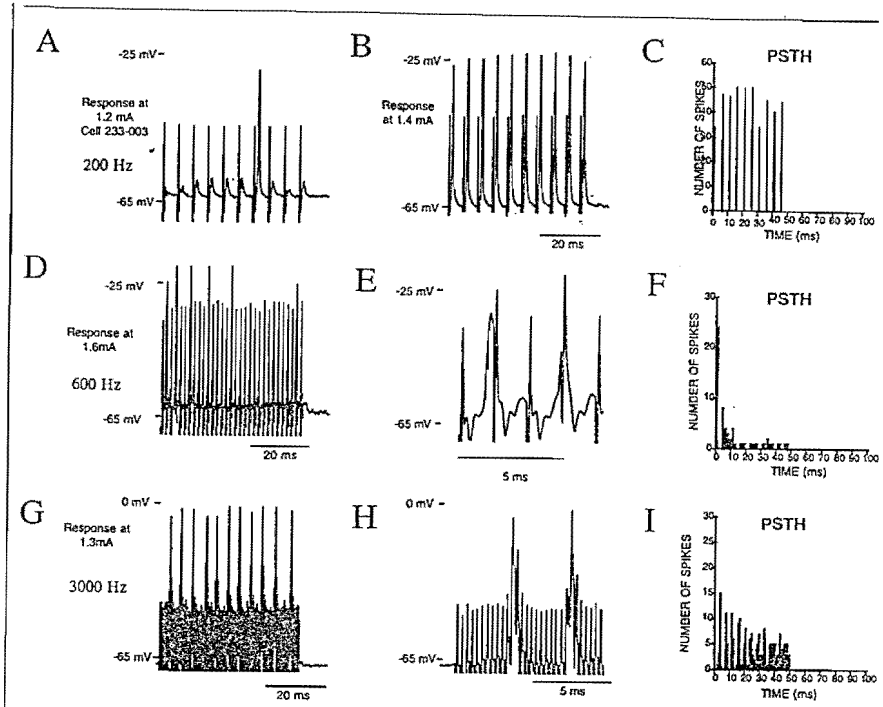

Figure 3. Anteroventral cochlear nucleus cell (identified bushy cell) response to pulsatile electrical stimulation. (A-C) 200 Hz intracochlear electrical stimulation. (A) Response at spike threshold (1.2 mA). EPSP response are evident to each pulse with the amplitude of the EPSPs increasing during the 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.

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.

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Title:
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Date:
1997

Citation:
Paolini, A., & Clark, G. M. (1997). The effect of pulsatile intracochlear electrical stimulation on intracellularly recorded cochlear nucleus neurons. In Cochlear Implants: XVI World Congress of Otohinolaryngology Head and Neck Surgery, Sydney, N.S.W.

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