Examination of Perceptual Generalizations Elicited by Intracortical Microstimulation of Adult Rat Auditory Cortex

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INTRODUCTION

Chronically implanted neural electrodes offer the potential for direct two way communication between machines and the brain. The brain-machine interface offers exciting possibilities to replace lost neural function, or augment current nervous system abilities. Specifically, external sources directly influencing neural tissue can be hypothesized to direct and manipulate local neuronal processing to invoke artificial sensory stimulation. Previously, the communication pathway from machine to brain via electrical stimulation has been only loosely explored (Brindley et al. 1968, Ronner et al. 1983, Dobelle et al. 1974). A promising communication type, intra-cortical microstimulation (ICMS), has been shown to introduce a "virtual" signal that subjects use in the processing of sensory information (Groh et al. 1997, Romo et al. 2000). Further studies exploring the properties of the stimulus are required to establish the brain machine interface as a viable communication protocol between organism and the external environment (Otto et.al. 2001, Rousche et.al. 2001). The objective of this study is to test the hypotheses that electrical activation of similar neural circuits as natural auditory stimuli will invoke similar perceptions and predictable behavior.

METHODS/RESULTS

Multi-channel brain-machine interface implantation

Adult Sprague-Dawley rats were chronically implanted in auditory cortex of the left hemisphere with arrays of microelectrodes as described in a previous publication (Williams et.al 1999). Electrode arrays consisted of two rows of eight, 50µm diameter, polyimide coated tungsten microwires. Electrode spacing in a given row, and between rows was approximately 250 µm. The multi-channel chronic brain-machine interface was used in two modes. Neural activity was recorded to determine auditory receptive fields. The same electrodes were also used to electrically stimulate local neuronal populations (ICMS) in a controlled behavioral environment. The ICMS stimulus consisted of cathodic first, charge-balanced, biphasic square-wave pulse train (150 Hz ; 100 msec on; 400 msec off) lasting 2.5 sec. A return current pathway was provided via a cranial bone screw.

ICMS Intensity Generalization

After initial pure tone detection training, four implanted rats were trained to **detect the presence or absence** of ICMS of a single electrode in auditory cortex (90 uA current level). In subsequent session, "probe" stimuli were randomly inserted on approximately 25% of the trials during the experimental sessions to test the subject's perceptual stimulus generalization. Probe stimuli were delivered at one of five intermediate ICMS intensities (72, 54, 36, or 18 uA). Behavioral responses were monitored to determine response preference to each probe value. Daily behavioral sessions consisted of 150 reinforced trials, resulting in approximately 40 probe trials. Figure 1 displays averaged psychometric function curves showing behavioral response probability to graded ICMS of 8 different electrodes in each of 4 different subjects. Error bars indicate the standard deviation of the measurement. Behavioral threshold, or the point of subjective equality (PSE), for these subjects ranged from 31.52 to 50.60 uA.

ICMS Generalization to Auditory Stimuli

Four other implanted rats were first trained to ***discriminate*** between 1 kHz and 16 kHz auditory stimuli (five 100 msec tone bursts, 400 msec intertone burst). Frequency generalization was determined by

delivering unreinforced auditory probe trials of intermediate frequencies. Figure 2 AA (Auditory task – Auditory probe) shows auditory typical generalization curves. The intermediate frequency stimuli were then replaced by ICMS probe trials of a single row in the microwire array. Row 1 probe stimuli consisted of ICMS on electrodes: 1, 3, 5, and 7, while row 2 probe stimuli consisted of ICMS of electrodes: 9, 11, 13, 15. Figure 2 AI (Auditory task – ICMS probe) shows that animals generalized the ICMS stimuli according to the spatial location of the implanted electrodes in the auditory tuning gradient as determined below.

Electrode location within auditory cortex was verified by recording local field potential (LFP) activity on each stimulated electrode. Animals were anesthetized, and auditory pure tone bursts (100 msec on, 900 msec off) were presented at 40, 70 and 90 dB from 1 kHz to 25 kHz. LFP activity was windowed using a Hanning window, and a fourier transform was performed. Data from 10 Hz – 200 Hz was averaged, normalized and a best frequency for each electrode was calculated from a weighted average of the frequencies that responded with greater than 80% of the maximum power for that channel. Calculated best frequencies were averaged across the four intensity presentations, and tuning gradients were estimated based on the best exponential fit on each row.

ICMS Generalization

The same discrimination trained rats were then switched from an auditory discrimination paradigm, to an ICMS discrimination paradigm. For this experiment animals were retrained to discriminate the perceptions resulting from ICMS of two distant electrodes (each at the opposite ends of a single row separated by approximately 1.75 mm). Subjects were then tested for ICMS generalization: remaining single electrodes in the same row were individually stimulated during probe trials. Animals again generalized response preference according to position of the implanted ICMS electrode within the row. Figure 3 displays averaged results.

DISCUSSION

Animals implanted with a multichannel brain-machine neural interface responded in a predictable and reliable manner to ICMS of auditory cortex under controlled behavioral conditions. For single electrode ICMS *detection*, both intra-subject and inter-subject variability were very low, (mean PSE was ~40 µA. with a standard deviation of ~8 µA.) The dynamic range or the current intensity range that elicited measurable behavior was ~50 µA. This suggests that single electrode ICMS may induce a rich continuum of perceptual experience.

Perceptual *discrimination* of ICMS sensations was also achieved using a 2-electrode stimulus paradigm. It was found that the recording properties (LFP) of each stimulation electrode provided an effective measure of the sensation induced by ICMS of that electrode. Despite inherent variability across subjects in the location of the arrays within auditory cortex, inter-subject results are strikingly similar. Of note is the observation that electrodes spaced as little 250 µm. apart induced different behaviors. This result is an important initial finding regarding the number of independent channels that may be available for information transfer into the cortex through ICMS.

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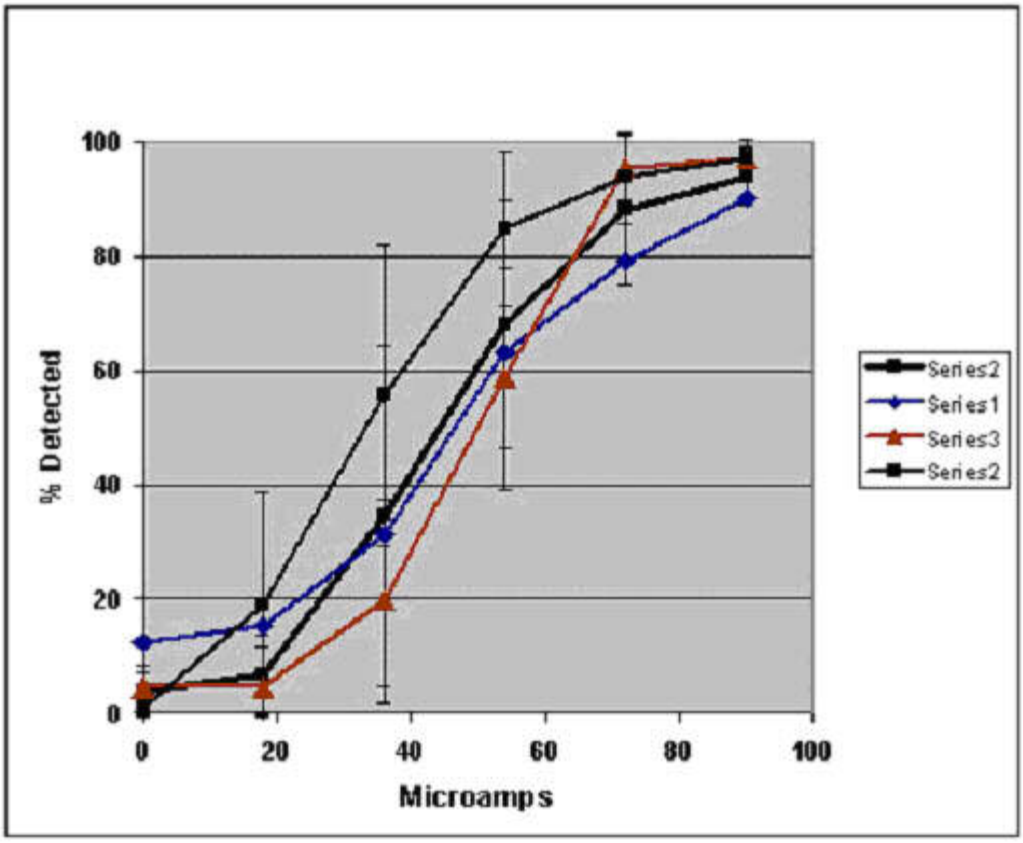

Figure 1. ICMS intensity generalization gradients. Each curve represents the averaged behavioral responses at the corresponding ICMS intensity from eight different electrodes in the array. Error bars indicate the standard deviation of the measurements.

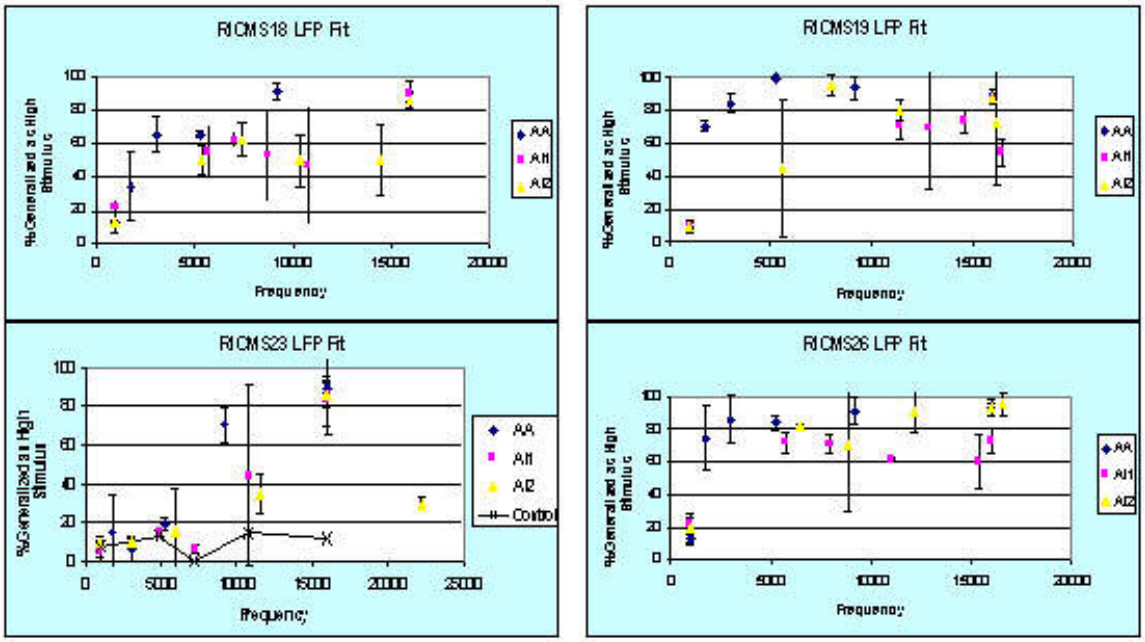

Figure 2. A-A and A-I results from four subjects. For each subject, averaged behavioral results from several sessions are shown. The A-A data indicates the subjects perceptual generalization to actual auditory stimulation. The A-I data is behavioral responses due to ICMS of single electrodes plotted vs. the calculated best frequency of the electrode as determined from auditory induced local field potentials. A-I1 refers to row 1 of the electrode array, and A-I2, row 2. The control experiment on RICMS23 was conducted in a similar protocol as the other experiments, except the stimulus isolator was turned off, insuring no ICMS current to the subject.

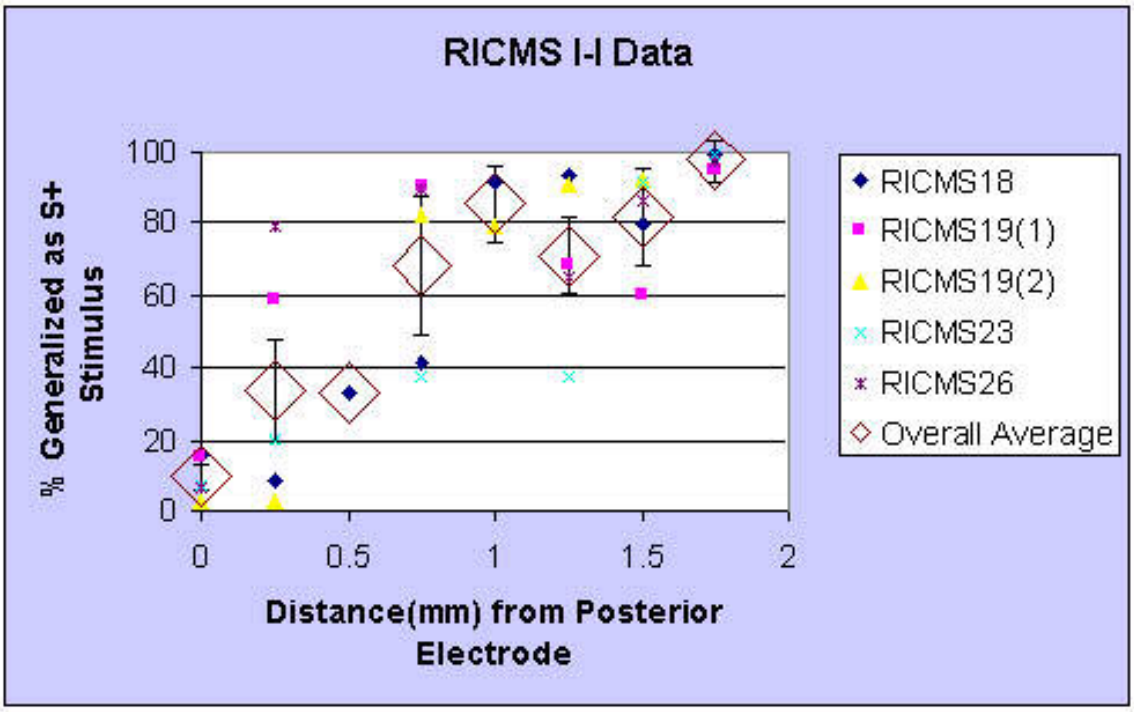

Figure 3. Averaged I-I data from four subjects. Each data type reflects an average of 2-3 sessions on a single row. Subjects were reinforced for behavior on the electrodes at position 0 and 1.75 mm. for left (S^-) and right (S^+) responses respectively. The diamond data set reflect the overall average from the five experimental session types. As the stimulus progresses across the cortex in a linear fashion, the perceptual gradient induced is nearly monotonically increasing.