Chronic multi-channel neural recording in feline sensorimotor cortex

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Abstract

Our previous work has demonstrated the ability to reliably evoke cortical activity in S1 using primary afferent microstimulation (PAMS) in an acute setting [1]. Early success has been encouraging but there remain many unanswered questions that would benefit from longer-term studies. This paper describes ongoing efforts to transition to a chronic implant animal model for long-term cortical recording with PAMS.

Keywords: *somatosensory feedback, dorsal root ganglion*

Introduction

Even the most advanced prosthetic will remain at best an extracorporeal tool without an intuitive mechanism of somatosensory feedback. There are many potential avenues for delivering artificial feedback [2,3]. Our lab is focusing on primary afferent microstimulation in the dorsal root ganglion (DRG), which are compact structures that provide convenient access to a heterogeneous population of sensory fibers and associated cell bodies.

Microstimulation delivered via penetrating microelectrodes in the DRG can recruit a wide range of fiber types including muscle and cutaneous afferents [4] providing the basis for artificially driving multimodal sensory feedback**.** However, it is not known how the spatial and temporal patterns of microstimulation pulses should be controlled to encode clear and functional sensations of touch and proprioception. Even less clear is how to determine if a given stimulus is effective in delivering the intended information. Indeed, quantifying sensory experiences is generally considered to be a difficult problem, even when dealing with human subjects that can provide a verbal report. This problem is arguably intractable when dealing with animal models.

Rather than attempting to quantify the conscious sensory experiences, our approach is to measure ensemble activity in a population of neurons in primary somatosensory (S1) cortex. Our approach is motivated by the pioneering studies of Mountcastle and colleagues, which showed that the spike discharge activity of neurons in S1 provides a robust neural representation of the physical qualities (e.g. vibration frequency, location) of a sensory stimulus [5]. Romo and colleagues extended these findings to show that S1 neural activity provides a neural basis for perceptual discrimination; firing rates of individual S1 neurons covaried reliably with behavioral performance in a vibrotactile frequency discrimination task, revealing a striking parallel between psychometric and neurometric discrimination functions [6]. In the present study, we are relying on the coding properties of S1 neurons to reveal how conveyed information is modified by various features of the spatiotemporal patterns of PAMS. Thus, S1 neuronal activity provides a direct and objective measure of the effects of stimulation.

Our initial experiments were performed in anesthetized cats during acute experiments [1]. Results from these experiments demonstrated that varying patterns of PAMS evoke discriminable responses in S1 cortex. However, performing these experiments acutely poses several changes that may be overcome by transitioning to a chronic implant model. First, the number of well isolated cortical units generally peaks several weeks after surgery [7].

Performing an acute experiment requires that staff must operate for multiple days with limited sleep increasing the potential for mistakes. Time limitations preclude detailed analysis between trials that might inform the ongoing procedure. Evoked sensory responses are very much anesthesia dependent and switching drugs is typically not an option in a terminal surgery. Finally, acute experiments preclude the possibility of gathering any behavioral data collected during DRG stimulation.

Methods

Chronic cortical recording studies were performed in a cat both while awake and while under anesthesia. Protocols were approved by the University of Pittsburgh IACUC. Isoflurane (1-2%) was used to anesthetize the cat during a craniotomy performed in a sterile surgical field. A 96-channel penetrating electrode array (Utah MEA, Blackrock Microsystems) was implanted in the hindlimb area of S1 cortex (post-cruciate gyrus) with lead wires routed under the skin to a Cereport connector. Both reference wires were placed epidurally and during recording sessions were shorted using external jumpers. The animal was monitored for several days post-surgery and recording experiments began 5 days after surgery.

Initial recordings were performed with the animal anesthetized using either isoflurane or medetomidine to evaluate the quality of recordings under each. A gross channel identification procedure was performed using isolated movements of individual joints or skin palpation. Transcutaneous electrical stimulation was applied to several locations on both limbs as well. Signals were captured at 25 kHz using an RZ2 system (TDT).

Prior to cortical implantation surgery the cat was trained daily to maintain quiet stance and to walk on a split belt treadmill (Bertec). After a post-surgery recovery period, training continued with routine recording sessions on alternate days.

During walking, ground reaction forces were recorded and digitized at 1 kHz from force plates located beneath each belt of the treadmill. Motion capture data and video was recorded at 100 Hz from 12 cameras (OptiTrack, NaturalPoint). A multichannel recording system (Grapevine, Ripple) system was used to capture

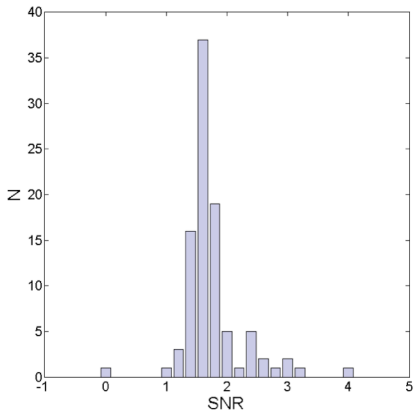

Fig. 1: Distribution of cortical channel SNRs 3 weeks post implant.

neural spiking data at 30 kHz. Spike events were created from thresholded waveforms and sorted into isolated units (Offline Sorter, Plexon).

Results

Coarse unit identification was performed using a variety of methods, but transcutaneous stimulation under medetomidine proved to be the most informative. Of all 96 channels 21 responded to forelimb (elbow) stimulation, 12 responded to hindlimb (knee), and 7 responded to both (t-test; $p < .01$). Hindlimb channels were located medially and forelimb laterally in rough agreement with the expected somatotopic organization of the post-cruciate gyrus [8].

Early results from treadmill walking (Fig. 2) have validated successful array implantation and high quality unit recordings were captured on multiple channels. On average each channel recorded 1.4 +/- 0.6 units. Phasic activity roughly aligned with walking was present on a subset of channels. Further development of motion capture system interoperability is required to establish accurate step timing to

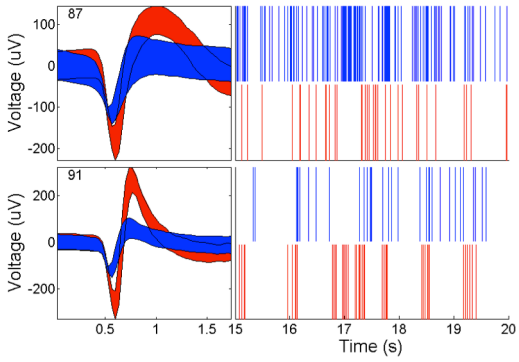

Fig. 2: Phasic unit activity during locomotion.

average responses during walking.

Previous experiments had used isoflurane during PAMS. There was more spontaneous activity while the cat was under medetomidine (Fig 3A) than during isoflurane (Fig 3B). Further analysis remains to determine the extent of projection differences and changes in the dynamic properties of individual neurons between the two anesthetics.

Discussion

Initial recording sessions have demonstrated the success of our first attempt at chronically implanting an electrode array in S1 cortex. The next step is to perform a second implant surgery to chronically implant microelectrode arrays in lumbar DRG for continuing the microstimulation experiments. Several stimulation protocols will be used to test the efficacy of PAMS. A suitable chronic DRG recording and stimulation methodology is also being developed, similar to [9]. Randomly chosen single DRG electrode channels will be stimulated using several amplitudes and frequencies. Pairings of electrode channels will be selected to evaluate potential interactions. Models of sensory encoding using many electrodes will be tested for their ability to deliver meaningful information to somatosensory cortex.

Longitudinal studies of DRG microstimulation are needed to determine the viability of the DRG as a viable substrate for future neural prosthetics. These studies will allow testing of DRG stimulation model stability across many days.

Fig. 3: Spontaneous activity while the cat lay on its side under medetomidine (A) and 2% isoflurane (B). Shown is unsorted data from the raw signal being filtered from 300 – 3000 Hz using a 2nd order filter and thresholded at -40 µV.

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