1. Introduction

There are over 2.5 million cases of spinal cord injury (SCI) worldwide, with over 250,000 patients in the United States alone [1]. SCI remains a global issue and although incidence rates vary between countries, studies indicate a trend of increasing prevalence in recent decades [2]. SCI does not have a comprehensive cure, leads to a significant decline in the patient’s quality of life, and factors such as the costs of treatments, rehabilitation, and medical expenses place a heavy financial burden on the impacted patients and their families [1, 3]. Due to the injury, the descending signal pathways carrying voluntary command signals from the brain lose their connections with the spinal cord circuitry below the level of the injury and result in the loss of movement and function. Neural prosthetics, when introduced into activities of a patient’s day-to-day life, can restore select movements either through the implementation of a robotic limb or using the individual’s own limbs through functional electrical stimulation (FES) [4–15]. Current neuroprosthetics research has mainly focused on the use of cortical signals as input to brain–machine interfaces (BMIs) for control of artificial limbs [6, 14, 15], computer cursors [11, 13], and muscles through FES [4, 5, 10].

Most BMIs have utilized signals from relevant cortical sites involved in motor planning and movement.
generate including the primary motor, premotor, and parietal areas of the cortex [16–34]. It is understood, however, that cortical signals undergo further processing prior to their use in muscle activation [35, 36]. Spinal neurons consolidate descending motor information from cortical and subcortical structures and convert them into specific motor commands suitable for causing muscle movements; this integration of information at the level of the spinal cord is mediated by an extensive network of interneurons and propriospinal neurons [37]. Among these spinal networks, studies have found neurons in the high cervical levels contain motor commands for forelimb reaching movements, where the interneurons and the propriospinal neurons at the C3–C4 level mediate forelimb target reaching, grasping, and precision grip [38–41]. The C3–C4 neurons not only mediate target reaching but also update the descending motor commands from the cortex for trajectory updating and deceleration in case of environmental perturbations [42, 43]. The presence of such converging information, its relationship to forelimb movement generation, and the presence of inhibitory input from segmental interneurons that allows for feedback from musculature [38–44] makes the C3–C4 cervical spinal cord an interesting target for neural interfacing studies. These studies provide the rationale for using the spinal cord as a point of convergence for recording motor signals from supraspinal structures that can potentially be used as control signals in a neuroprosthetic approach.

The feasibility for such an approach to access signals from the spinal cord requires proof-of-concept evaluation in various animal models such as rodents and nonhuman primates (NHP) such as those shown for cortically driven BMIs [15, 23, 32, 45–46]. In this study, we used a smaller non-human primate (NHP) model, the common marmoset (Callithrix jacchus), that is increasingly being used in neuroscience research [47–49]. Marmosets provide a good step between rodent and larger NHP models for behavioral neuroscience studies due to their small size, ease of handling, cognitive abilities, and similarities to other primate motor systems [48–51]. The goal of this study is to discuss detailed methods that are necessary to create a spinal cord neural interface in common marmosets. We discuss our experience in working with this animal model, which includes behavioral training and performing chronic recordings from awake behaving animals. We also discuss in detail the microelectrode array specifications and design modifications suited for interfacing with the spinal cord and surgical techniques for microelectrode placement in the marmoset spinal cord.

2. Methods and results

Five adult male marmosets were used in this study. Table 1 includes a summary of all the animals used in the study, their recording duration post-surgery, and the cause of recording failure. All animal care, surgical, and research procedures were performed in accordance with the National Research Council Guide for the Care and Use of Laboratory Animals and were approved by the University of Miami Institutional Animal Care and Use Committee (IACUC).

2.1. Electrode arrays

Figure 1 shows the schematics of the microelectrode array used in the study and its intended implant location relative to the spinal cord tissue (figures 1(A)–(C)). Platinum–iridium (Pt–Ir) floating microelectrode arrays (FMA, MicroProbes for Life Science, Gaithersburg, MD) were used (figures 1(D) and (E)). FMAs were either 13 channel (1D) or 32 channel (1E), made up of three or four rows of electrodes with 250 μm separation and consisted of a 4–5 cm cable from the array to the connector. A silicone sheath was used for reinforcing the wire from the connector to the array (1E). All MEAs were sterilized using ethylene oxide (EtO) gas in a gas sterilizer prior to surgery.

2.2. Surgical procedure

2.2.1. Animal preparation and physiological vital measurements.

All surgical procedures were performed in a dedicated surgical suite under sterile conditions. Animals were fasted for up to 12 h prior to surgery to minimize the risk of pulmonary aspiration during the administration of anesthesia. The animals were anesthetized with ketamine (intramuscular, 10−50 mg kg⁻¹) and aseptically prepped for surgery. Upon shaving the surgical site (head and the back), the animals were maintained under deep anesthesia using isoflurane (0.5%–4%) and oxygen (1–2 l min⁻¹) delivered through a nose cone attached to the stereotaxic apparatus. Their vital measurements, which included rectal temperature, heart rate, electrocardiogram (ECG), and peripheral capillary oxygen saturation (SpO2) were continuously monitored. Additionally, blood glucose was periodically monitored during the surgical procedure.

2.2.2. Skull preparation for headstage assembly.

The animals were positioned with appropriate ear and bite bars on a standard stereotaxic frame (Kopf Instruments, Tujunga, CA) for small animals. Eye lube was applied on the eyes. The animals were then draped with sterile drapes and the head and upper back were cleaned with multiple scrubs of iodine and isopropyl alcohol. A dorsal midline incision was made on the skull and the periosteum was removed to expose the skull surface. Appropriate drill bits corresponding to the size of the anchoring screws were used to manually drill holes on the skull. Care was taken to ensure that the holes did not extend beyond the skull into the cranial space. Four to six screws (00–90 gauge) were then manually inserted into the predetermined location.
locations (figure 2(A(i)). These screws were used as an anchor for the array connector. The FMA connector was then fixed on the skull using dental acrylic.

2.2.3. Laminectomy.
Following screw placement and fixing the connector on the skull, the bony protrusion of the spinous process at the second cervical vertebrae C2 was identified on the animal’s back as this spinous process is palpable over the skin. A midline incision was made from the base of the skull to the thoracic vertebrae and the skin was retracted to expose the back muscles. A pair of blunt-tipped scissors were used to separate the muscles under the incision site to expose the cervical vertebrae C2–C7. Subsequently, a laminectomy was performed at the C3–C4 level of the spinal cord ipsilateral to the dominant arm. Figure 2(A(i)) shows the laminectomy at the C3–C4 level. In the first animal, two screws, similar to the skull screws, were drilled in the C2 and C5 vertebra, with the assumption that these screws will stabilize the spinal cord where the FMA would eventually be implanted. We did not observe any advantage associated with placing the screws on the vertebrae and therefore, chose not to place screws on the vertebrae in the other animals. This also reduced the overall surgical time and the

| Animal | Behavior (reaching task) | ~# of trials/training session | FMA type (recording depths of 1.3–1.5 mm from dorsal surface) | Recording duration post-surgery (months) | Failure mode |
|--------|-------------------------|-------------------------------|-------------------------------------------------------------|---------------------------------------|-------------|
| Cu     | 2-target                | 100                           | 32-channel                                                  | 1.43                                  | Mechanical failure (interconnect cable broke) |
| Mi     | 9-target                | 25                            | 13-channel                                                  | 3.97                                  | Mechanical failure (interconnect cable broke) |
| Ky     | 9-target                | 50                            | 13-channel                                                  | 5.17                                  | Signal degradation                          |
| Ax     | Touch screen            | 200                           | 32-channel                                                  | 4.50                                  | In study                                  |
| Bu     | Touch screen            | 100                           | 32-channel                                                  | 1.67                                  | Mechanical failure (interconnect cable broke) |

Table 1. Summary of behavioral task, training and recording duration, and electrode failure mode.

Figure 1. Floating microelectrode array (FMA) schematics for spinal implant. (A) Electrode location along the rostrocaudal axis on the spinal cord ipsilateral to the dominant forelimb of the animal. (B) Schematic of a 13-channel FMA that was used in two implants. Each FMA (13- or 32-channel array) was connected to either a 16-channel or a 32-channel Omnetics connector using an interconnect cable. A 32-channel array had higher number of electrodes with the same inter-electrode distance of 250 µm. (C) Cross-section of the spinal cord with the desired implant location. (D) 13-channel FMA without the silicone sheath. (E) 32-channel FMA with the silicone sheath that was used to reinforce the interconnect wire.
additional surgical risk associated with drilling screws into the vertebrae. Post-mortem analysis in all animals indicated that the FMA was still anchored in the spinal tissue. We also observed in all animals that there was a layer of fibrous tissue that covered the substrate of the FMA that would stabilize the array in the spinal cord tissue, eliminating the need for anchoring screws on the vertebrae.

### 2.2.4. FMA implantation

Following the laminectomy, the dura was gently lifted with forceps and punctured using a 25-gauge sterile needle bent at approximately 90 degrees. The dura was carefully resected using microscissors to expose the spinal cord. The FMA ceramic substrate was held to a vacuum wand attached to the anterior–posterior and the medial–lateral arms of the stereotaxic arm,

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**Figure 2.** Surgical implantation of microelectrode array in the spinal cord. (A) Skull preparation for headstage assembly, laminectomy, and FMA implantation: (i) laminectomy at C3–C4 was performed to expose the spinal cord and screw locations are shown on the skull that were used to anchor the Omnetics microconnector on the head; (ii) FMA was held using a vacuum wand attached to the stereotactic arm, and stereotactically lowered into the spinal cord tissue; (iii) a 32-channel FMA is shown after it was stereotactically inserted in the cervical C3–C4 level of the spinal cord; (iv) after the FMA was implanted, a strain relief was provided to the interconnect cable. The image also shows the silicone reinforcement on the cable and the location of the connector on the skull with dental acrylic used to fix the connector. (B) Intraoperative electrophysiological recordings: multi-unit activity from a 32-channel FMA that was acquired intraoperatively with manually set threshold levels. (C) Electrophysiological recordings: four channels of broad band activity recorded from the spinal cord, bandpass filtered between 500 Hz to 6 kHz, are shown for day 0 (post-surgery) and at chronic time points on days 35 and 98, respectively.
allowing for accurate positioning of the FMA on one half of the spinal cord in the rostrocaudal axis above the implant location, which corresponded to the laminectomy at the C3–C4 level (figure 2(A(ii))). The MEA was positioned in this manner so that the electrode shanks could span the grey matter along the medial–lateral axis to target the interneuronal and propriospinal circuitry at the C3–C4 level (figure 1(C)). A micropositioner (FHC, VT) was used to lower the array assembly slowly (~1 mm min⁻¹) into the spinal cord to the desired implant location (figure 2(A(iii))). Figure 2(A(iii)) shows a close-up of a 32-channel FMA implanted in the C3–C4 segment of the spinal cord. A small piece of gelfoam soaked in sterile saline was then placed on top of the FMA along with a drop of butyl cyanoacrylate (Vetbond, WPI, FL), and a suture at a distant location relative to the implant was placed on the interconnect wire of the FMA to allow for strain relief. The muscles of the back were closed in layers using size 5.0 absorbable sutures, and the skin of the back was closed using size 4.0 absorbable sutures. On the skull, more acrylic was applied in layers around the FMA connector (figure 2(A(iv))) to encase it securely. Care was taken to avoid putting any dental acrylic where the interconnect wire exited the microconnector, allowing the wire assembly to remain flexible when the animals made head movements.

2.2.5. Intraoperative and chronic electrophysiological recordings.

Electrophysiological recordings were performed concurrently with FMA insertion into the spinal cord. Spinal cord signals were recorded at 24 414 Hz sampling rate and bandpass filtered between 500 to 6000 Hz using a real-time data acquisition system (RZ2, TDT, FL) while inserting the FMA through the spinal cord tissue. Online spike sorting based on manually set thresholds and box sorts were used to isolate spiking activity. Figure 2(B) shows an example of multi-unit activity from the spinal cord obtained intraoperatively after the FMA was inserted into the cord at the target location. Intraoperative electrophysiological recording was useful in guiding the eventual placement of the array at the desired location and depth. Figure 2(C) shows examples of four channels of broad band activity (bandpass filtered between 500 Hz to 6 kHz) from the spinal cord on day 0 (day of implant) and at two chronic time points (day 35 and day 98).

2.3. Post-operative recovery and care

Post-operative care entailed monitoring of cardiac stability, glucose, and temperature. Animals generally were awake within 15–30 min after anesthesia removal. They were returned to their home cages once they regained consciousness and regained sufficient mobility. Animals were monitored daily for neurological markers such as nystagmus, alertness, grip and limb strength, gait, and climbing ability. Further, special attention was given to the animals’ diet, hydration, and solid waste excretion in the days post-surgery. During this time, they were more frequently offered treats, rice milk, and a nutrition drink (Ensure, Abbott Labs, USA) to aid recovery. After surgery, implanted animals were single housed to prevent other animals from interfering with the surgical wound. Cephalexin (20 mg kg⁻¹ orally twice daily for 5 d) and buprenorphine (0.001–0.015 mg kg⁻¹ IM twice daily for 3 d) were administered as an oral antibiotic and an analgesic, respectively.

Post-surgery, animals were monitored for signs of pain and distress such as lethargy, over-grooming or scratching excessively, self-mutilation, shaking, reluctance to eat, drink, or swallow, abnormal or hunched posture, guarding, urinary, stool consistency, and signs of dehydration. Animals were also monitored for neurological indications such as abnormal posture of head and neck, nystagmus, abnormal gait, paralysis, forelimb movements and range of motion, grip strength, and climbing capability, as a result of electrode placement in the spinal cord tissue. Neurological deficits in the forelimbs can occur due to the placement of the microelectrode array in the spinal tissue that control forelimb movements. Post-surgery, though animals tended to favor the use of their contralateral arm for reaching and grasping, they used all four limbs for weight bearing and climbing. Grip strength was reduced in the ipsilateral arm post-operatively, but all animals recovered within 2–3 weeks following surgery. At these time points, their grip strength improved, and they tended to use both limbs in daily activities.

Marmosets are arboreal animals and spend a significant amount of time on top of the cage and climbing around. In our experience, microelectrode implantation did not cause paralysis in the limbs of any of the implanted animals. There were also no behavioral changes in the animals. We used micro computed tomography (micro-CT) images to evaluate if there was any indication of loss of spinal tissue and compression of the spinal cord as a result of the implant and the microelectrode array substrate. Micro-CT was performed after the animals were euthanized and the spinal cord harboring the electrode was dissected out. Figure 3(A) shows a brightfield image of an intact marmoset spinal cord with no implant at the C3–C4 level. Figure 3(B) is a micro-CT image with the microelectrode implant in the spinal cord. The dense tissue around the array is the spinal tissue. Clearer, higher resolution images could not be obtained because of the low resolution of the scanner, contrast issues between the tissue and highly reflective metal electrodes, and the small size of the tissue being imaged. However, it can be observed that the microelectrode array did not appear to cause a loss of tissue around the electrode tips and the array also did not compress the spinal cord tissue at the dorsal surface where it penetrated the tis-
Figure 3. Post-mortem micro-CT imaging. (A) Brightfield image of an intact marmoset spinal cord with no implant at the C3–C4 level; (B) micro-CT image with the microelectrode implant in the spinal cord; (C) micro-CT image overlaid on the brightfield image of an unimplanted cord to show the location of the electrode tips relative to the spinal cord.

Figure 4. Behavioral task and training times: (A) animal with the nine-target door device in front of them (not to scale); (B) sequence of the events of the task with timeline; (C) individual times taken (in weeks) for five animals to reach behavioral milestones; (D) mean and standard deviation of five animals trained for each behavioral milestone; (E) approximate duration (minutes) for which each animal performed during a behavioral session.

2.4. Behavioral task
Animals were not food or water deprived for behavioral training. Prior to training for any of the behavioral tasks, animals received basic scoop and chair training. Subsequently, the animals were trained to complete reaches for one of three types of tasks: a nine-target reaching task (figure 4(A)), two-target robot task and a touch screen task. For the nine-target reaching task, the sequence of the trial is shown in figure 4(B) with the experimental timeline. During each session, the animal sat in front of the custom-made behavioral device with the door closed. Each trial was initiated by the experimenter, with the animal placing his hand on an infrared sensor (touchpad) for a random hold period (700–1200 ms). After the random hold period, an audio cue (‘Go Tone’) was presented simultaneously with the door opening, revealing a treat at one of the nine targets. The animals had to reach, grasp,
and retrieve the food accurately within 2s before the door was closed again. For the two-target robot task, the timing and trial information was the same. However, instead of reaching to a treat, the animal reached to a sensor indicated by a light either on the left or right and successfully captured targets resulted in robot movement and a treat [46]. In the touchscreen task, a target appeared on the screen and the animal was required to trigger the target within a 2s period. Animals were considered to be trained for a particular task if they were able to perform the task with at least 80% accuracy. Table 1 summarizes the approximate number of trials each animal performed during each session, the recording duration post-surgery, and the cause of the recording failure. Table 1 also gives the trials per session once the animal was fully trained. Figure 4(C) shows the training time it took for each animal to reach different behavioral milestones before surgery. The average duration for all animals is shown in figures 4(C) and (D), and the approximate time that each animal spent on the behavioral chair performing the task during each session is shown in figure 4(E). In general, once the animals had kinematic tracking markers and the surgical procedure had been completed, the average number of trials per session for all animals reduced to about 20–60 trials.

We defined each of the milestones during the behavioral training as the following, in the order they were introduced to the animals.

2.4.1. Scoop training.
Animals were transferred between the home cage and the experimental chair using a custom-made scoop [48], and were considered trained when they were comfortable with getting into the scoop within five minutes. Four of the five animals were scoop trained in 5–6 d while the last animal took approximately two weeks (figure 4(C)).

2.4.2. Chair training.
An animal was considered chair trained if the animal was comfortable sitting in the chair and was not agitated or vocalizing for at least 15 min. All five animals were chair trained in 1–2 weeks.

2.4.3. Free reach.
Animals were considered trained for free reaching when they learned to reach for food treats with their hands instead of reaching with their mouth or tongue. Once calm in a seated position in the chair, the animals learned to reach freely in less than a week.

2.4.4. Touchpad training.
Trials were time aligned with the use of an infrared sensor attached to a touchpad. The animals were ‘touchpad trained’ when they successfully kept their hand on the touchpad for the random hold period. This part of the training took the longest time where some animals were able to learn faster than others (~1.5–5.7 weeks).

2.4.5. Reaching task.
Animals were considered trained for the reaching tasks when they willingly reached to all required target locations to receive food rewards. All animals learned this within two weeks.

2.5. Kinematics acquisition
Forelimb kinematics during the reaching tasks were acquired using two different systems. One system consisted of four infrared cameras (Innovision Systems, Columbiaville, MI) positioned around the animal to capture forelimb movements sampled at 60 Hz. Two spherical infrared sensors were attached to Velcro and placed on the animal’s forelimb at the forearm and wrist to track the forelimb kinematics. Kinematic information was streamed at 60 frames per second to the MaxPRO software (Innovision Systems, Columbiaville, MI). The frames were tracked offline following the recording sessions and 3D trajectory data from each marker was exported into MATLAB for further analysis. The second system was a 3D tracking system by Trakstar (Ascension technologies, Shelburne, VT) sampled at 1017 Hz. It consisted of a sensor attached to the animal’s hand and a magnetic field generated by a DC magnetic field transmitter. Figure 5(A) shows example trajectories (x, y and z directions) from two animals during the reaching movement. Each subplot is an average of five reaching trials towards one target. Figure 5(A(i)) uses the MaxPRO system. Figure 5(A(ii)) shows the data acquired with the Trakstar system from a different animal. Depending on the task, some animals did not have kinematics tracking, only end point information instead. Figures 5(A(i) and (ii)) show different x, y and z directions, which are unique to the system the data is recorded from. Figure 5(B) shows the 3D trajectories for individual reaching trials in two animals. Figure 5(B(i)) illustrates 3D trajectories in four directions and Figure 5(B(ii)) illustrates trajectories in two directions. In each instance, movement started at the touchpad, reached one of the visible targets, and ended at the mouth.

2.6. Spinal cord recordings
Neural signals were recorded at 24 414 Hz sampling rate and 24-bits of resolution using a real-time data acquisition system (RZ2, TDT, FL) and a custom-made software program (RPvdsEx, TDT, FL). A band-pass filter (500–6000 Hz) was used to record neural activity. Multi-unit activity was acquired with manually set threshold levels, and waveforms were discriminated online by amplitude and shape using box-sorting methods. Figure 6(A) shows histograms from two channels each of multi-unit activity from two animals which were sorted online during the experiment. Time zero indicates the movement onset. The time
histograms show an increase in neural activity (figure 6(A(i))), which coincides with movement in the $y$ direction for animal Ky (figure 5(A(i))). Similarly, figure 6(A(ii)) shows an increase in neural activity during movement in animal Ax. While the time histograms in figure 6(A) show the isolated threshold crossings from individual channels that modulated with the reaching task, figure 6(B) illustrates band-pass filtered, rectified-averaged neural signals from all 32 channels from two animals during a reaching trial. The envelope of the rectified-averaged signal (black trace) shows an increase in activity following movement onset and then once again following 0.5 s during the retrieval phase. Baseline activity prior to reach onset was different between trials and across channels, and an increase in activity in the broadband signals before movement onset can be attributed to the animal moving their forelimb to the touchpad and the muscle force that is needed to hold the forelimb until the next cue. The large amplitude artifact observed in these traces is due to the chewing of food treats.

3. Discussion

Previously, spinal cord recordings have been reported in larger macaque model [35–37, 52, 53] but not in marmosets, a species which is being increasingly used in neuroscience studies as a smaller NHP model. Recordings from the spinal cord can provide an additional area within the motor system, other than the motor cortex, where volitional motor signals can be recorded. However, recording from the spinal cord poses several technical challenges compared to recording from the cortex. Further, accessing these recording sites in a smaller primate model also presents additional challenges. In this work, we discuss the methods and challenges for chronic recording of spinal cord activity using microelectrode arrays in awake, behaving marmosets, which can be useful for research labs interested in this animal model. We also describe the behavioral task, surgical procedure, and present examples of electrophysiological recordings post-implant.

The spinal cord tissue has a small cross-sectional area, and the cord undergoes large amounts of movement during daily activities. Therefore, the choice of array design is significant to maintaining viable recordings. Penetrating FMAs were chosen over flexible surface electrode arrays based on the deeper anatomical location of neurons involved in motor processing in the spinal cord [54, 55]. In the first few implants ($n = 2$), we used a lower channel count FMA that consisted of 13 recording channels. This choice was based on the assumption that an array of smaller dimensions
with limited electrodes (1.6 mm × 1.95 mm) would cause less trauma to the spinal cord tissue than a larger array. However, this smaller footprint array could only span one segment of the spinal cord. Therefore, in subsequent animals, we decided to use a 32-channel FMA which was larger than the 13-channel FMA. We used an FMA where the array footprint (1.6 mm × 2.8 mm) was slightly larger, had a higher number of electrodes, and a geometry that could span most of the C3 and C4 segments as well as access most of the grey matter in one half of the spinal cord in the mediolateral direction. In each array design (13- or 32-channel), we used three different electrode lengths (1.3 mm, 1.4 mm, and 1.5 mm, see figure 1(B)) in order to target a majority of neurons within the laminae VII–IX. Extra precautions were taken during the laminectomy and opening of the dura so as to not damage the spinal cord. The dura is significantly thinner than at the cortex and the entire procedure was performed carefully under a surgical microscope to prevent damage to the cord surface. Using an array with tapered tips, such as those used in this study, is also recommended as it aids penetration into the spinal tissue. All animals were monitored carefully post-surgery for several days, and post-operative neurologic deficits were not observed in any of the animals that were implanted with either of the FMA type.

The spinal cord is subjected to a variety of torques during daily activities and thus provides additional challenges during the implantation and securing of a chronic penetrating FMA. We chose a floating electrode array because it can move with the cord, minimizing the relative movement between the two structures compared to a fixed array type. We also placed multiple loops within the interconnect wire so that the array is subjected to minimum strain due to the interconnect wire cable. This also prevents the interconnect wire from pulling the array out of the spinal tissue. A majority of the electrode array failures in these implants was due to the interconnect wire breaking at the location where it exits the connector fixed to the skull. Earlier array design (figure 1(D)) shows an example where there is no reinforcement on the interconnect wire. Due to the array failures resulting from this wire breaking, later array designs added silicone tubing (figure 1(E)) or additional silicone layers (figure 2(A(iv))), incorporated by the manufacturer, on the interconnect cable. We are currently using this array design for the spinal implants because the added reinforcement provided by the silicone minimizes the possibility of wire breakage. Further, the placement of the connector on the skull is also important to minimize wire breakage. In earlier implants, the connector was placed closer to the interaural line. However, the wire between the connector and the array broke in most of those implants. In more recent cases, we moved the connector posterior to the interaural line.
which puts less stress on the wire between the connector and the array, minimizing wire breakage.

Representative electrophysiological recordings provide evidence that chronic recordings can be performed using FMAs implanted in the spinal cord of awake behaving marmosets. All recordings were performed with respect to a reference electrode, which was a slightly longer electrode shank (1.8 mm) on the FMA compared to the recording electrodes. A separate Pt wire tied to a skull screw was used as the ground. In the first animal, where we drilled two screws on the spinal vertebrae, we used one of the screws for grounding the array. However, we did not observe any significant difference in the noise floor level between using a ground screw on the skull or the vertebrae. There is also a higher risk of damaging the spinal cord with screws on the vertebrae. Therefore, we continued to use the skull screw as ground for all subsequent animals. Recordings in awake, behaving animals suggested an increase in neural activity in the spinal cord that was coincident with forelimb movement.

Chronic recordings, such as those shown in figure 2(C), suggested an increase in noise floor at chronic time points, however, field potential and multi-unit activity was still discernible at these time points. The study showed that the feasibility of recording spinal cord signals and using marmosets in behavioral neuroscience studies as a smaller NHP due to their small size and similarities to other primate motor systems. While interconnect cable breakage was the most common recording failure mechanism, use of flexible recording arrays and careful attention to the choice of array and cable design, connector placement, and handling of the wire bundle, may result in better recording outcomes chronically.

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Conflict of interest

The authors declare no competing financial interests.

ORCID iDs

Abhishek Prasad  
https://orcid.org/0000-0001-9586-9400

References

[1] National Spinal Cord Injury Statistical Center 2018 Facts and Figures at a Glance (Birmingham, AL: University of Alabama)
[2] Furlan J C et al 2013 Global incidence and prevalence of traumatic spinal cord injury J. Neurosurg. 80 456–64
[3] De Vivo M J 1997 Causes and costs of spinal cord injury in the United States Spinal Cord 35 809–13
[4] Aijboye A B et al 2017 Restoration of reaching and grasping movements through brain-controlled muscle stimulation in a person with tetraplegia: a proof-of-concept demonstration Lancet 389 1821–30
[5] Bofuton C E et al 2016 Restoring cortical control of functional movement in a human with quadriplegia Nature 533 247
[6] Hochberg L R et al 2006 Neural ensemble control of prosthetic devices by a human with tetraplegia Nature 442 164–71
[7] Moritz C T, Perlmutter S I and Fetz E E 2008 Direct control of paralysed muscles by cortical neurons Nature 456 639–42
[8] Santhanam G et al 2006 A high-performance brain–computer interface Nature 442 195–8
[9] Schwartz A B et al 2003 Brain-controlled interfaces: movement restoration with neural prosthetics Neuron 52 205–20
[10] Gant K et al 2018 EEG-controlled functional electrical stimulation for hand opening and closing in chronic complete cervical spinal cord injury Biomed. Phys. Eng. Express 4 066005
[11] Schalk G et al 2008 Two-dimensional movement control using electrocorticographic signals in humans J. Neuroeng. Rehabil. 5 75
[12] Collinger J L et al 2013 High-performance neuroprosthetic control by an individual with tetraplegia Lancet 381 557–64
[13] Simeral J D et al 2011 Neural control of cursor trajectory and click by a human with tetraplegia 1000 d after implant of an intracortical microelectrode array J. Neuroeng. Rehabil. 8 205027
[14] Hochberg L R et al 2012 Reach and grasp by people with tetraplegia using a neurally controlled robotic arm Nature 485 372–5
[15] Taylor D M, Tillery S I and Schwartz A B 2002 Direct cortical control of 3D neuroprosthetic devices Science 296 1829–32
[16] Afflalo T et al 2015 Decoding motor imagery from the posterior parietal cortex of a tetraplegic human Science 348 906–10
[17] Batista A P et al 2007 Reference frames for reach planning in macaque dorsal premotor cortex J. Neurophysiol. 98 966–83
[18] Cisek P and Kalaska J F 2002 Simultaneous encoding of multiple potential reach directions in dorsal premotor cortex J. Neurophysiol. 87 1149–54
[19] Cisek P and Kalaska J F 2005 Neural correlates of reaching decisions in dorsal premotor cortex: specification of multiple direction choices and final selection of action Neuron 45 801–14
[20] Cui H and Andersen R A 2007 Posterior parietal cortex encodes autonomously selected motor plans Neuron 56 552–9
[21] Desmurget M et al 1999 Role of the posterior parietal cortex in updating reaching movements to a visual target Nat. Neurosci. 2 563–7
[22] Donoghue J P et al 1998 Neural discharge and local field potential oscillations in primate motor cortex during voluntary movements J. Neurophysiol. 79 159–73
[23] Georgopoulos A P et al 1982 On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex J. Neurosci. 2 1527–37
[24] Georgopoulos A P, Kettner R E and Schwartz A B 1988 Primate motor cortex and free arm movements to visual targets in three-dimensional space. III. Positional gradients and population coding of movement direction from various movement origins J. Neurosci. 8 2928–37
[25] Kertzman C J et al 1997 The role of posterior parietal cortex in visually guided reaching movements in humans Exp. Brain Res. 114 170–83
[26] Kettner R E, Schwartz A B and Georgopoulos A P 1988 Primate motor cortex and free arm movements to visual targets in three-dimensional space. III. Positional gradients and population coding of movement direction from various movement origins J. Neurosci. 8 2993–47
[27] Mirabella G, Pani P and Ferraina S 2011 Neural correlates of cognitive control of reaching movements in the dorsal premotor cortex of the macaque monkey J. Neurophysiol. 106 1454–66
[28] Pesaran B, Nelson M J and Andersen R A 2003 Dorsal premotor neurons encode the relative position of the hand, eye, and goal during reach planning Neuron 51 125–34
[29] Rubino D, Robbins K A and Hatsopoulos N G 2006 Propagating waves mediate information transfer in the motor cortex Nat. Neurosci. 9 1549–57
J. Neural Eng. 17 (2020) 016031

Scherberger H, Jarvis M R and Andersen R A 2002 Cortical local field potential encodes movement intentions in the posterior parietal cortex Neuron 46 347–54

Schwartz A B, Kettner R E and Georgopoulos A P 1988 Primate motor cortex and free arm movements to visual targets in three-dimensional space. I. Relations between single cell discharge and direction of movement J. Neurosci. 8 2913–27

Snyder L H, Batista A P and Andersen R A 1997 Coding of intention in the posterior parietal cortex Nature 386 167–70

Takahashi K et al 2017 Encoding of both reaching and grasping kinematics in dorsal and ventral premotor cortices J. Neurosci. 37 1733–46

Truccolo W et al 2008 Primary motor cortex tuning to intended movement kinematics in humans with tetraplegia J. Neurosci. 28 1163–78

Yanai Y et al 2008 Coordinate transformation is first completed downstream of primary motor cortex J. Neurosci. 28 1728–32

Zinger N et al 2013 Functional organization of information flow in the corticospinal pathway J. Neurosci. 33 1190–7

Shalit U et al 2012 Descending systems translate transient cortical commands into a sustained muscle activation signal Cereb. Cortex 22 1904–14

Isa T, Kinoshita M and Nishimura Y 2013 Role of direct versus indirect pathways from the motor cortex to spinal motoneurons in the control of hand dexterity Frontiers Neurol. 4 191

Alstermark B et al 2011 Motor command for precision grip in the macaque monkey can be mediated by spinal interneurons J. Neurophysiol. 106 122–6

Issa T et al 2007 Direct and indirect cortico–motoneuronal pathways and control of hand/arm movements Physiology 22 145–52

Pauvert V, Pierrot-Deseilligny E and Rothwell J 1998 Role of spinal premotoneurons in mediating corticospinal input to forearm motoneurons in man J. Physiol. 508 301–12

Ifft M and Lundberg A 1978 Collateral connections to the lateral reticular nucleus from cervical propriospinal neurones projecting to forelimb motoneurones in the cat Neurosci. Lett. 7 167–72

Alstermark B and Ekeroth C F 2013 The lateral reticular nucleus: a precerebellar centre providing the cerebellum with overview and integration of motor functions at systems level. A new hypothesis J. Physiol. 591 5453–8

Alstermark B et al 1981 Integration in descending motor pathways controlling the forelimb in the cat Exp. Brain Res. 42 282–98

Carmenta J M et al 2003 Learning to control a brain–machine interface for reaching and grasping by primates PLoS Biol. 1 E42

Pohlmeyer E A et al 2014 Using reinforcement learning to provide stable brain–machine interface control despite neural input reorganization PLoS One 9 e87253

MacDougall M et al 2016 Optogenetic manipulation of neural circuits in awake marmosets J. Neurophysiol. 116 1286–94

Prins N W et al 2017 Common marmoset (Callithrix jacchus) as a primate model for behavioral neuroscience studies J. Neurosci. Methods 284 35–46

Walker J, MacLean J and Hatsopoulos N G 2017 The marmoset as a model system for studying voluntary motor control Dev. Neurobiol. 77 273–85

Burmak J K et al 2008 Anatomical and physiological definition of the motor cortex of the marmoset monkey J. Comp. Neurol. 506 860–76

Chaplin T A et al 2013 A conserved pattern of differential expansion of cortical areas in simian primates J. Neurosci. 33 15120–5

Prut Y and Perlmutter S J 2003 Firing properties of spinal interneurons during voluntary movement. I. State-dependent regularity of firing J. Neurosci. 23 9600–10

Prut Y and Perlmutter S J 2003 Firing properties of spinal interneurons during voluntary movement. II. Interactions between spinal neurons J. Neurosci. 23 9611–9

Alstermark B, Johannisson T and Lundberg A 1986 The inhibitory feedback pathway from the forelimb to C3–C4 propriospinal neurones investigated with natural stimulation Neurosci. Res. 3 451–6

Riddle C N and Baker S N 2010 Convergence of pyramidal and medial brain stem descending pathways onto macaque cervical spinal interneurons J. Neurophysiol. 103 2821–32