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A Novel Experimental System for Investigation of Cortical Activities Related to Lower Limb Movements

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Abstract—*We report the development of a novel experimental system for investigation of potential correlation between cortical neuronal signals and lower limb movement with targeted application towards cortical controlled neuroprosthesis. The system consists of a specially designed chair and a virtual reality based task environment. We designed a training paradigm for non-human primates to perform whole leg full extension and retraction task that simulates standing and sitting. With the special chair, the 'stand up' and 'sit down' can be performed with the head fixed, which is required for steady and especially acute cortical recordings. In this experimental environment we can simultaneously record leg kinematics during simulated stand up and stepping, ground reaction forces, leg muscle activities and neuronal activities in different cortical areas through either microdriveable electrodes or chronically implanted arrays. With this system and other state-of-the-art techniques, and combined with computational tools that we are developing, we aim to identify neural activity patterns that correlate with muscle activity and/or kinematics associated with leg movement during standing and stepping activities under naïve and well trained conditions.*

Keywords—*Lower limb movements, cortical neural recording, standing and stepping control, neuroprostheses.*

I. INTRODUCTION

How brain controls our behavior is one of the most intriguing and investigated questions in neuroscience research. With the development of advanced imaging, sensor technology and computational power, it becomes feasible to explore the secrets of the inner brain function. For example, cortical single unit recording technology and multiple electrode recording technology have being broadly used to investigate the relationship between the firing pattern of cortical neurons and the animal's motor performance (1-5). Using these methods, significant progress has been achieved in the study of the brain areas directly controlling limb movement in rats and monkeys (6-10). These pioneering research studies provide hopes and promises for the development of neuroprostheses for spinal cord/brain injured patients or people suffering from many neural degenerative diseases.

Current techniques also put certain limitations on certain behavioral experiment. For example, microdrivable electrode recording technology requires the limitation of movement of the subject's head. It is the deficiency of this technology that limits its utility and using range (11). Quite a few of current research achievements in this area are focused on the upper limb movements. For lower limb movements, there are very few reports (12). In this investigation, we want to demonstrate the pattern changes in cortical neuronal activities during standing, sitting, and stepping during recovery from spinal cord injury. The results from this study should be important for the development of neuroprostheses.

One major issue is to design a new experimental apparatus allowing the animal to perform sitting and standing movement with head position relatively fixed with respect to the recording electrodes. Another issue is to develop an animated behavior task with different visual cues to instruct the animal's standing and sitting movement. We report the design of these systems in this paper. With the developed system we can start to investigate the correlation of cortical signals with lower limb movement. By knowing how cortical neurons modulate their activities to initiate and control the standing and sitting movement we may eventually be able to develop cortically controlled neuroprosthetics system for spinal cord injury patients.

Currently, there are more than 200,000 people who are suffering from the tragically debilitating consequences of spinal cord injuries in US alone. The significance in searching for effective means of helping these people to regain ability to stand and walk is obvious. Our research will also contribute to understanding the fundamental principles of neural control of lower limb movement.

II. METHODOLOGY

To identify the cortical areas related to lower limb movements, a microdrive recording system (Thomas Recording system, Germany) will be used first. Then chronically implanted electrodes will also be applied and muscle activities will be recorded simultaneously. The Institutional Animal Care and Use Committee approved the behavioral paradigm, surgical procedures and general animal care.

(1) The Specially designed monkey chair:

For acute recording, the current technology requires that the subject's head needs to be fixed so that the relative position of the head and micro-drivable electrode arrays remains constant and can maintain a stable connection for recording. Before a wireless unit becomes available, this requirement will continue to get stable quality recording, either very rigid for micro-drivable electrodes or loosely for chronically implanted electrode arrays (11). Therefore, the challenge in our experiment is to develop apparatus and experimental paradigm to accommodate standing and sitting while the head is relatively immotile with respect to the recording setup. To

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reach the requirement of unit spike recording, we designed a new chair for the experiment (Fig. 1).

The chair was made of stainless steel and acrylic plastic, equipped with a protection plate adjustable to the size of the subject. One of the novel parts of this chair is that it was equipped with a movable pedal. While the head and body are restrained in the chair, the subject can still perform standing and sitting movement, via pushing down the pedal with adjustable weight. The pedal is connected to the chair with two inner-set Axletrees, which make it possible to move up and down easily with negligible friction. When the subject wants to stand up, he instead pushes the pedal down to achieve the upright standing posture. When the subject intends to sit down and releases the pushing force, the pedal is pulled up by the counter weight through the sliding axles, which are set on the back part of the chair.

(2) The Virtual Sit-Stand-Sit Task:

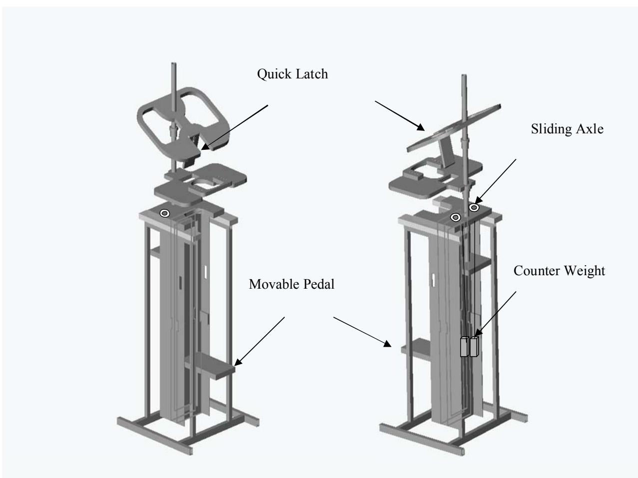

Fig. 1. A new designed monkey chair. One of the favorite parts of this chair is that it can be used to fix the monkey's head during it performs a sit-stand-sit task. This is required by cortical recording, either very rigid for micro-drivable electrodes or loosely for chronically implanted electrodes.

In the preliminary training stage, the subject was habituated to head fixation, without cortical signals recording. The subject performed the sitting and standing task in a virtual reality environment. A LED marker placed at the ankle was represented as a red ball in the animation environment (Fig. 2). Each trial is preceded by an inter-trial reset interval (varied randomly between 5 to 10 seconds) when the screen is illuminated with bright blank scene to prevent dark adaptation since the room is in low light condition. A trial is commenced with appearance of a green box representing the starting position (Center On). The subject was required to move his ankle position to match the green box (Center hit) for 100 msec. After that, another green ball (Target) was displayed on the top of the monitor (Target on). The subject was required to push down the pedal to match the ankle cursor with target position. Once the ankle cursor left the box, the box turned back to green (Center release). The subject was trained to fully extend his legs to hit the green ball (target) for 100 msec and the counterweight matches the body weight to simulate the standing. A reward was provided and the target ball turned into red (Target hit). Then, the subject was required to retract both legs back to the starting position. The cursor left the target ball (Target release) and the target ball turned back to green. When animal fully retracted both legs, the cursor hit the center box again, and the box turned into red (Center hit again). After another 100 msec, both of the center box and the target ball disappeared indicating the end of a trial. The subject received his second reward (Center and Target off). The process entered into another inter-trial interval period. For this experiment, we expected to record kinematics from the legs through the whole sit-stand-sit task.

(3) The Experimental Setup

For many years, people used to investigate the activity of brain by examining the firing patterns of single neurons one at a time while the animal performed well trained tasks. In our

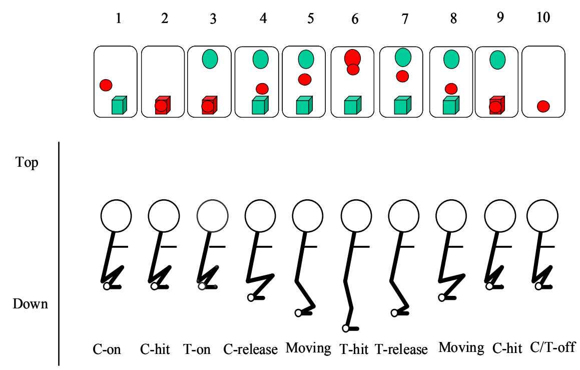

Fig. 2. Behavioral procedures of the *sit-stand-sit task*. 1). Center on period: At the beginning stage, the subject sits on the chair. A red ball (a cursor representing the location of the animal's right ankle) shows in the virtual reality environment. A green box (center) shows in the bottom of the monitor. 2). Center hit period: The subject is required to move his leg so as to let the cursor overlap with the green box (center). When the cursor overlaps with the green box, the box will turn red. 3). Target on period: 100ms Later, another green (Target) shows on the top of the monitor. 4). Center release period: the subject is required to push down the pedal of the chair so that it can stand up. The cursor leaves the box and the box turns back to green. 5). Moving up period. 6). Target hit period: When the subject fully stands up, the cursor hits the green ball (target), and the target ball turns into red. After 100 ms successful hitting, the subject will receive its first reward. 7). Target release period: the subject is required to sit down. The cursor leaves the target ball and goes down toward the center box. The target ball turns back to green when the cursor leaves it. 8). Moving down period. 9). Center hit again period: when then animal fully sits down, the cursor hit the center box again, and the box turns into red. 10). Center and target off period: 100ms later, both of the center box and the target ball disappear, and the subject receives its second reward. The process enters into an inter-trial interval period (5-10 seconds).

primary experiment, animals will be implanted with microelectrode arrays into the motor and somatosensory cortices after demonstrating satisfactory performance under virtual reality environments. The goal of this investigation is to examine the details of cortical control of lower limb movement in normal and neural impaired conditions.

Compared to research on upper limb tasks, the cerebral cortical areas related to lower limbs are much smaller, and the neurons are located much deeper. Theoretically and technologically, it is also very difficult to detect the neuronal activities related to lower limb movement. Therefore, we choose to perform acute rather than chronic recording system first in the primary experiment. The Uwe Thomas microelectrode system is currently smallest and most lightweight electrode positioning and recording system (13-16). Its microelectrode manipulator can drive up to 5 quartz platinum/tungsten electrodes independently in steps of 1µm, and the travel distance of each microelectrode is about 15mm. This kind of long travel distance is just required in investigation of lower limb related recording.

In this study, we also want to understand the dynamics and the kinematics of leg movements. So, we adopt some other advanced technologies, including virtual reality, intra-muscular EMG and ongoing force testing (Fig.3).

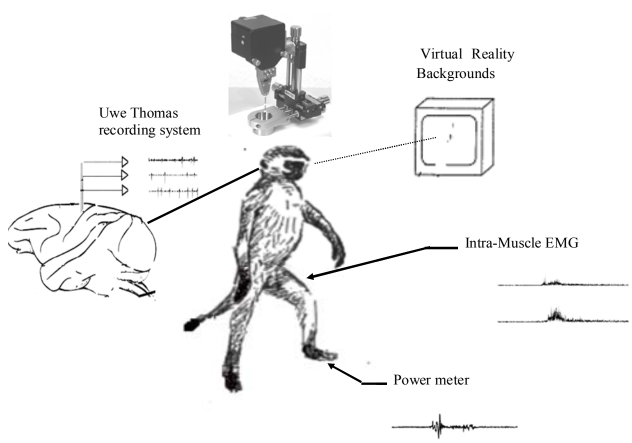

Fig.3. Experimental setup. Several state-of-the-art technologies will be combined for recording various signals simultaneously, including multiple single-unit spike recording, online force measurement and intra-muscular EMG monitoring.

III. RESULTS

We trained one subject in the preparatory experiment. It took one week for the subject to get used to the chair, and another two weeks to head fixation. Then, the animal was required to perform the sit-stand-sit task. After three weeks' practice, the subject was able to perform the task corresponding to the visual cues displayed on the virtual reality monitor.

Fig. 4. showed the latest performance records from 5 consecutive days. We may consider the total number of center hits as the total number of trails, and the successful rate as the total number of center hits divided by the number of target hits. The average number of trials the subject performed in a daily session was 203.8 ± 27.81(mean ± SD), and the successful rate was 98.3 ± 1.03%. All of the successful rates were above 96% for the consecutive 5 days'.

We used not to consider the times of center on as the total trials, for it is very difficult to keep a subject concentrate on a given task exclusively for any significant length of time. However, the successful rate was 91.0± 3.0 % in this preparatory experiment, and all of the successful rates were above 85% for the 5 consecutive days'.

These results showed that the newly designed system is a useful tool for studying animal standing and sitting while allowing acute cortical recording.

	Events					
	Center on	Center hit	Target on	Target hit	Back-to-center	Center off
Session 1	265	250	250	248	248	248
Session 2	197	182	182	180	180	180
Session 3	249	218	218	211	211	211
Session 4	187	172	172	171	171	171
Session 5	205	197	197	192	192	192

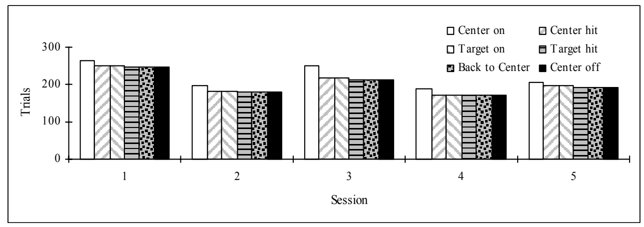

Fig. 4. The performance records of one monkey for the consecutive 5 days' experiments.

IV. DISCUSSION

The goal of this preliminary experiment is to establish a nonhuman primate model to delineate the subdivisions of M1 and somatosensory cortex related to lower limb movements, to describe the details of topographic order in the different areas of the brain, and to discover how these representations are interconnected (17).

Two general approaches were adopted in training primates. One is real physical task of standing and sitting while recording cortical signals, which will generate data for analysis of correlation between patterns of cortical neuronal activity and motor behaviors of initiation and termination of standing and sitting. The other is closed-loop biofeedback training in a virtual reality environment, which takes advantage of the flexibility or modulation of cortical neurons' fires patterns (18).

It is a challenge to directly record the neuronal activities when the primates perform a real natural standing and sitting motor task. One reason is that neuronal recording nowadays requires the fixation of the animal's head relative to the recording device, while standing and sitting behaviors are coupled with the movements of the head vertically. To address this issue, we designed a new experimental chair, which is carefully delineated above. We have trained one subject to perform a sit-stand-sit task, the results show that it is a useful tool for studying animal standing and sitting.

Another challenge to directly record the neuronal activities related to lower limb motor tasks comes from physiology itself. Compared to upper limb, the cerebral cortical areas related to lower limbs are much smaller, and the neurons are located much deeper. To our knowledge, it is quite difficult to locate the exact functional areas related to lower limb movements. We choose Uwe Thomas microelectrode system for our cortical recording. This system is not only small and light, but also has a travel distances up to 15mm for each electrode. Using this system, we can easily solve this theoretical and technological problem (13-16).

We also want to get some ideas for other two fundamental issues. First, what kinematical and dynamic variables are exactly encoded by the activities of the brain? For instance, the endpoint trajectory, the total movement time, and the curvature of the trajectories are all valid kinematical variables. Likewise, both of the total force exerted for standing and the EMG are valid dynamic variables. Second, how are these variables processed in the brain? We will investigate how the activity of neurons in M1 and somatosensory areas reflects the kinematics and dynamics of leg movements. Both of the issues remain open (19-21).

V.CONCLUSSION

In this paper, we present a novel system and methodology for investigation of cortical control of lower limb movement, which is effective to record cortical signal patterns during standing and sitting movements in monkeys. We believe that the new system will be beneficial to enhancing our understanding of cortical control of lower limbs, thereby contributing to the development of neuroprostheses for spinal cord injured patients.

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