Utilizing neuromuscular force recording as a novel proxy for functional assessments of brain or peripheral nerve stimulation in a mouse model

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Introduction

Mice are excellent model organisms to study human diseases as a handful of genetic tools are available to manipulate their genome to simulate most human diseases. Since the mice genome is similar to that of humans (only less than 10 among approximately 4,000 genes studied are different), mice can be used as a tool to study molecular pathogenesis and develop novel therapeutic interventions. Although mouse models have been used in developing brain and peripheral nerve stimulation modalities, functional assessments are very difficult to carry out due to the size of the animal. Artifacts generated through any intervention often contaminate recordings of evoked electromyogram (EMG), a common index used to quantify the results of brain or peripheral nerve stimulation in human experiments. This is because the small size of a mouse enables stimulation signals to travel easily from target sites to EMG electrodes (Fig. 1).

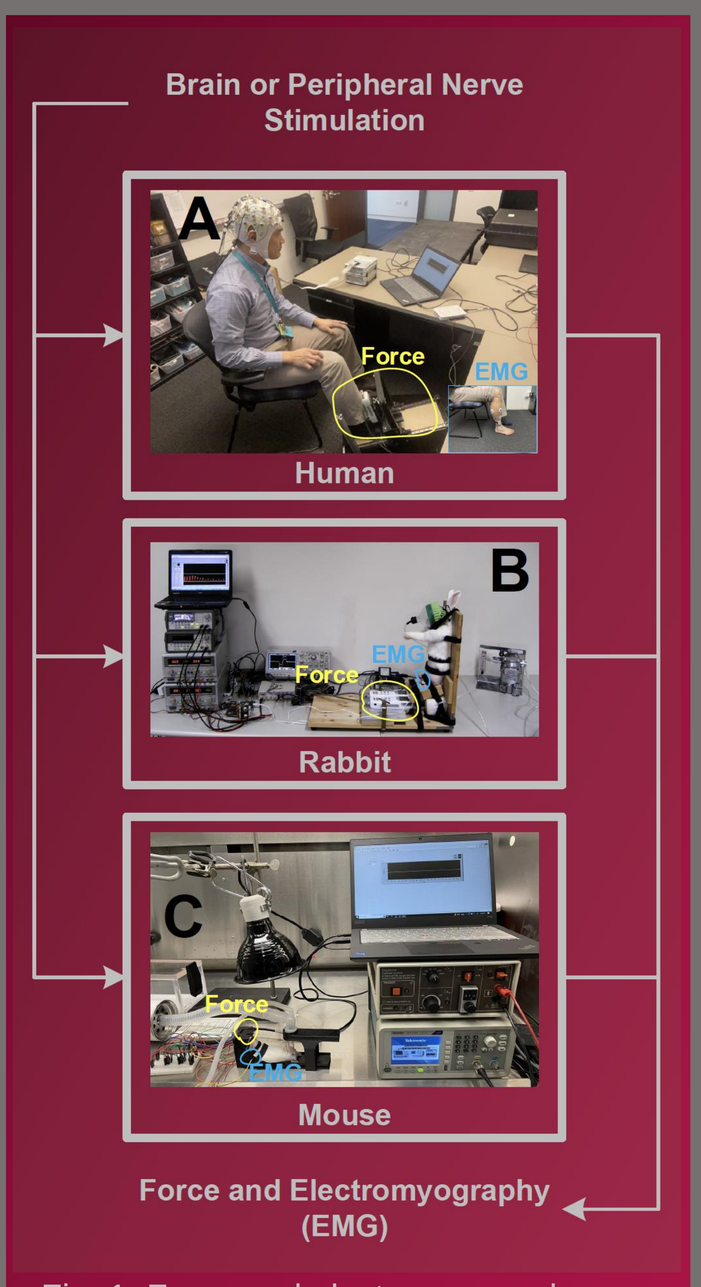

Fig. 1. Force and electromyography (EMG) measurements of (A) human, (B) rabbit, and (C) mouse.

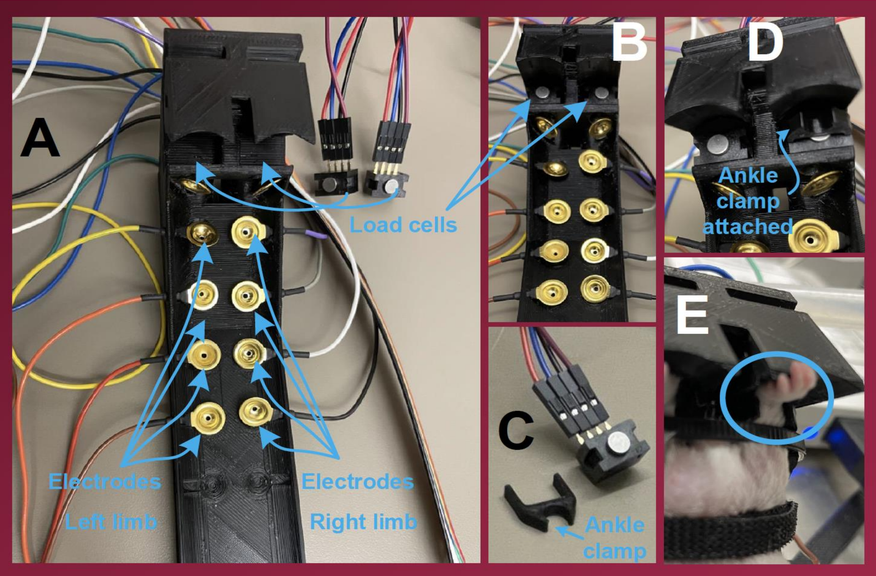

Fig. 2. 3D printed fixation frame and adapter design. (A) Electrodes for electrical stimulation and electromyography (EMG) data acquisition, brain stimulation electrodes will be secured via a 3D printed helmet. Load cell are connected to instrumentation amplifiers. (B) Load cell integrated in the frame. (C) Ankle clamp designed to secure the mouse ankle to the load cell actuator. (D) Attached ankle clamp. (E) Mouse's right ankle secured to the clamp.

Methodology

To eliminate this issue, we designed a 3D printable fixation frame (Fig. 2) that integrates a pair of miniaturized load cells or force sensors (FSG005WNPB, Honeywell) and instrumentation amplifiers (INA128, Texas Instruments), allowing us to quantitatively measure the change of stimulation induced force of selected muscle groups and myotome of a mouse *in vivo* during a stimulation session.

Challenges and Future Plans

We encountered several challenges during the process of the apparatus design (Fig. 4). This included issues that involve force consistency, bilateral comparisons for nerve regeneration experiments, electrode placement, and convenience for applying gaseous anesthetics. However, we believe that studies using this mouse model will provide pilot results for planning future clinical trials that involve brain and peripheral nerve stimulation.

Results

By analyzing recordings from mechanical force instead of from electrical signals, i.e., EMG, corticospinal and peripheral contributions of electrical or magnetic stimulation can be accurately measured after appropriate procedures are being applied to a restrained mouse under anesthesia (Fig. 3).

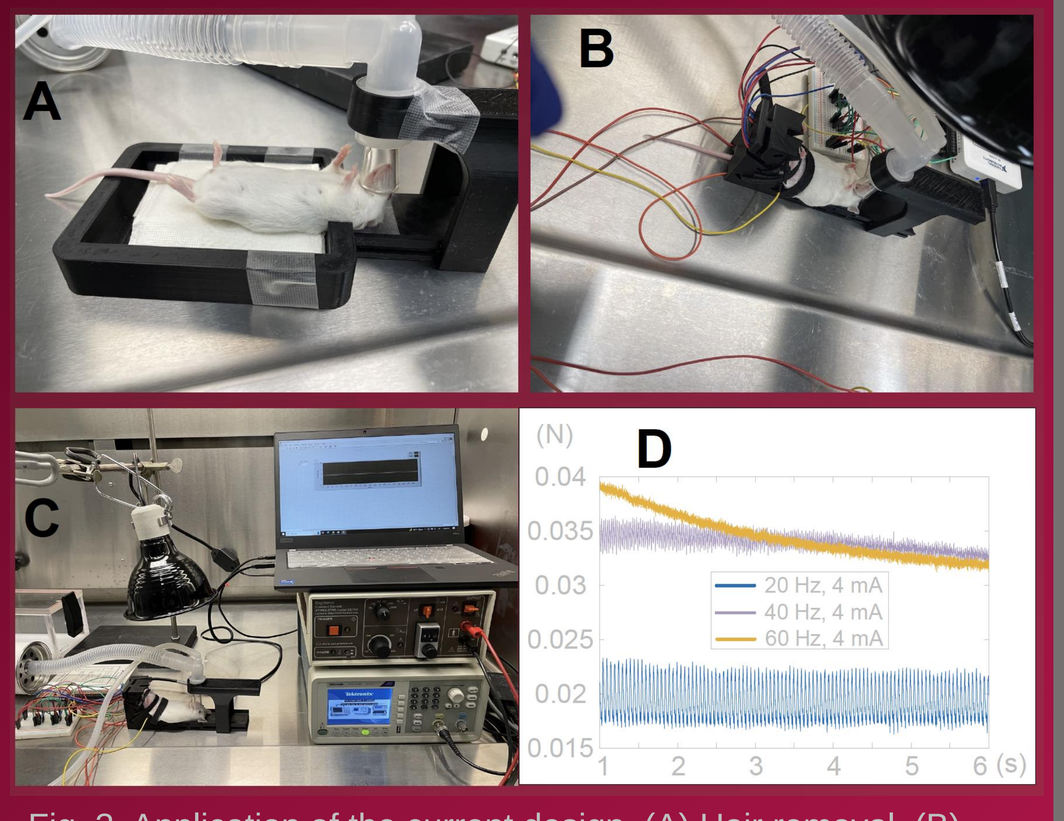

Fig. 3. Application of the current design. (A) Hair removal. (B) Applying the electrodes and securing the mouse ankle to the load cell. (C) Providing electrical stimulation trains and collecting data. (D) Hamstring force data collected at different stimulation rates.

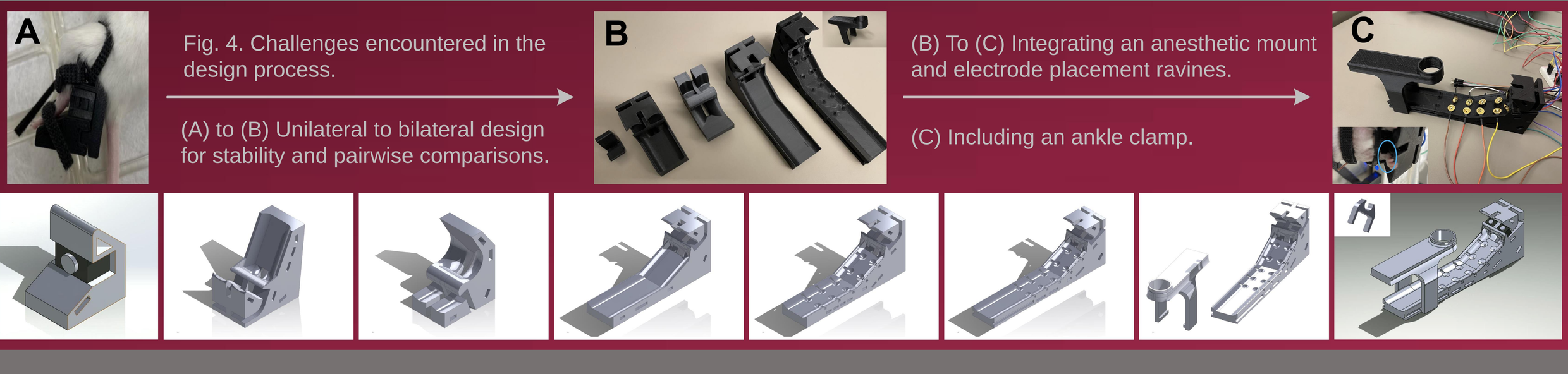

Fig. 4. Challenges encountered in the design process.

(A) to (B) Unilateral to bilateral design for stability and pairwise comparisons.

(B) To (C) Integrating an anesthetic mount and electrode placement ravines.

(C) Including an ankle clamp.