2019 IEEE 16th International Conference on Rehabilitation Robotics (ICORR)
Toronto, Canada, June 24-28, 2019

A Robotic Platform for 3D Forelimb Rehabilitation with Rats

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Abstract— **In an attempt to promote greater functional recovery after spinal cord injury, researchers have begun exploring combinatorial treatments, such as robotic rehabilitation combined with stem cell transplantation. Since these treatment methods are in their nascent stages, rodent models have been proposed for initial investigations. Robots have been built for locomotion rehabilitation and planar forelimb reach and grasp assessment with rodents; however, a robotic platform suitable for three-dimensional movement rehabilitation of the rodent forelimb has not yet been developed. In this paper, a novel three degree of freedom robotic manipulator for automated forelimb rehabilitation combined with stem cell transplantation after cervical spinal cord injury with rats is proposed. The robot interfaces with a rat in an end-effector manner, measuring and interacting with the forelimb in the 3D Cartesian space. In this work, we trained two rats through behavioral shaping to actively interact with the device during two robot control modes. This work provides preliminary investigations into the feasibility of 3D forelimb rehabilitation with rats, which could be translated as a paradigm for combinatorial treatments after spinal cord injury in a controlled manner.**

I. Introduction

More than 200,000 individuals with spinal cord injury (SCI) live with chronic paralysis in the United States alone [1]. Rehabilitation and exercise training is a non-invasive therapy that has shown to increase functional recovery of the hind limbs in experimental animal models [2]–[4] and human SCI patients [5]–[7]. Possible mechanisms of rehabilitation/training-mediated recoveries could be a combination of cellular, molecular, and trophic effects induced within the central nervous system (CNS) as evidenced in animal models [3], [8]. Indeed, previous studies with rat models demonstrated exercise-dependent enhancement of neurotrophin production and secretion [9], [10], which may promote neuronal survival and plasticity as well as axonal sprouting and regeneration. Exercise also increases the expression of genes regulating the regeneration capacity of neurons [11] to enhance the axonal sprouting and/or regeneration in rat models [12], [13]. Rehabilitation may also contribute to the reorganization of neuronal circuitry and to improvements in synaptic function and behavior [14].

Studies with SCI rats have primarily focused on the effects of rehabilitation in the recovery of hind/lower-limb movement and coordination; however, many SCI patients exhibit injury at the cervical level, which adversely affects hand function. Regaining hand function is a priority of SCI patients [15] since even partial recovery of hand function could significantly increase quality of life. Skilled food reaching is commonly used as task-specific training for reaching function after cervical SCI in rodent models. When combined with other treatments, such as PTEN knockdown [16], skilled food reaching training can enhance the plasticity of the CNS and recovery of reaching function. This training though is labor intensive and can yield results with significant day-to-day and animal-to-animal variability. Additionally, this training may promote recovery in reaching and grasping, but not in forelimb locomotion [17].

In studies with humans, robotic rehabilitation has become an ubiquitous approach for training motor function after neurological impairments, such as SCI [18]. Rehabilitation robots have been used in human rehabilitation for high-intensity training, and to gain insight into movement kinematics and kinetics, which are useful for assessing functional recovery [19], [20]. Robots are well-suited for such rehabilitation since they are programmable, accurate, repeatable and can perform rehabilitation without tire. Rehabilitation with these robots [19], [21] has resulted in increased functional gains for the patient, albeit modest. In an attempt to elucidate the impacts of robotic rehabilitation on neurological impairment, robotic devices have recently been created for rodents [22], [23]. Currently, only one multi-dimensional forelimb device has been proposed, and it is limited to support planar reaching movements in rat models [23]. This device was designed to leverage the skilled food reach training, while also having the capability to augment or assist motion in the horizontal two-dimensional plane including forearm rotation.

With the motivation of providing a robotic rehabilitation platform to study combinatorial treatments in a rat SCI model, we have developed a proof-of-concept device that can perform 3D forelimb rehabilitation tasks with rats (see Fig. 1). We hypothesize that training 3D motions compared to 2D ones will provide a more functional training, an important component in task-specific rehabilitation. To evaluate the efficacy of such training, we performed behavioral shaping with two rats in an effort to provide rat-initiated training with the robot during two control modes.

This work was supported in part by Mission Connect, a project of the TIRR Foundation, through the Dr. Eugene Alford Endowed Fund for Robotics, by the Rice University IBB Hamilton Innovation Award, and by the National Science Foundation Graduate Research Fellowship Program under Grant No. 1450681.

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II. Prototype Forelimb Rehabilitation Device

By developing a robotic rehabilitation platform for functional forelimb training in a rat model, we can investigate combinatorial treatments, such as robotic rehabilitation and stem cell transplantation, in a controlled manner. Investigating the forelimb as opposed to the hind limb, we expect to encounter more challenges as hind limb approaches to rodent rehabilitation are already well-established [22], but the forelimb, i.e., hand, is equally important and must be addressed [15], [23]. To achieve functional forelimb training in a rat model, we have developed a low-cost and lightweight prototype of a robotic manipulator that can measure and interact with the forelimb in 3D (see Fig. 1).

A. Kinematic Structure

To achieve measurement and interaction with a rat forelimb, we pursued a design that could accommodate 3D motion as opposed to the 2D motion with rotation demonstrated by the ETH Pattus device [23]. Pursuing 3D motion creates additional challenges, as gravity becomes a factor in the design and requires an additional actuator. Creating a design for interaction with a rat requires limiting the moving mass of the device for backdrivability, while still being able to produce modest force output. To accomplish this, we elected to pursue an end effector based design, using a parallel structure which locates the motors on a stationary base.

We chose to pursue a 3 revolute-prismatic-spherical (RPS) kinematic structure to achieve 3D measurement and interaction. As opposed to using the 3RPS design for an exoskeleton interface, as done for human-robot interaction [24]–[26], we used the architecture for an end effector interface (see Fig. 2). This is accomplished by incorporating an additional Cartesian link, which includes a grip mount for rat-robot interaction, from the wrist ring (see Fig. 1). This transfers the measurement and control platform from the wrist ring to the end effector through an additional transformation matrix. In this way, 3D position at the interaction point can be measured and controlled. In the following paragraph, the necessary transforms to evaluate the rat's 3D position and to control the interaction point are described.

The necessary formulations to find the forward and inverse kinematics as well as the Jacobian from the base frame to the wrist frame of a 3RPS manipulator have been described in previous works [24], [26]. With the additional Cartesian link in this work, the following transforms are necessary to convert base or wrist frame measurements to the end effector. We define the Cartesian link length by the vector $\mathbf{h} = [h_x \ h_y \ h_z]^T$. The wrist frame coordinates are defined as $\mathbf{x_w} = [z_c \ \alpha \ \beta]^T$ where z_c is the linear translation of the wrist platform from the base frame, and α and β are two Euler angles describing the rotation of the wrist frame with respect to the base frame. To convert from wrist frame coordinates to end effector coordinates requires multiplying the rotation matrix describing the Euler angle rotations with the Cartesian link vector $\mathbf{R_{WE}} = \mathbf{R}_{\alpha\beta}\mathbf{h}$ while accounting for the translation of z_c. The end effector coordinate, $\mathbf{X_e}$ where the subscript e denotes the end effector frame, is thus given by

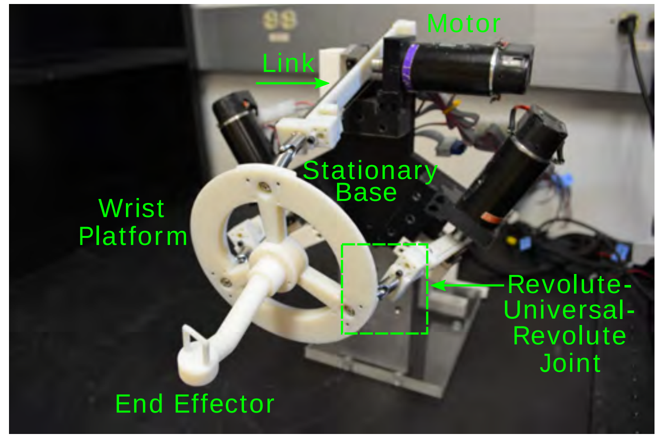

Fig. 1. Prototype robotic device for 3D forelimb training with a rat model.

$$\mathbf{X_e} = \begin{bmatrix} x_e \\ y_e \\ z_e \end{bmatrix} = \begin{bmatrix} h_x c(\beta) + h_z s(\beta) \\ h_x s(\alpha) s(\beta) - h_z c(\beta) s(\alpha) \\ z_c + h_z c(\alpha) c(\beta) - h_x c(\alpha) s(\beta) \end{bmatrix} \quad (1)$$

where the *sin* and *cos* functions have been abbreviated (e.g., $c(\beta) = cos(\beta)$). Note that in equation (1) since the variables x_c, y_c, and γ are small relative to $\mathbf{x_w}$, they have been neglected. As a result, the velocity at the end effector is simply $\dot{\mathbf{X}}_\mathbf{e} = \frac{d}{dt}\mathbf{X_e}$. The last robot transform of interest for our work is the transform to convert from end effector forces to wrist frame forces and torques. This is accomplished through the force/moment transform which yields

$$\mathbf{F_w} = \begin{bmatrix} F_{z_c} \\ \tau_\alpha \\ \tau_\beta \end{bmatrix} = \begin{bmatrix} f_{z,e} \\ -f_{y,e} h_z \\ f_{x,e} h_z - f_{z,e} h_x \end{bmatrix} \quad (2)$$

where the subscript w denotes the wrist frame.

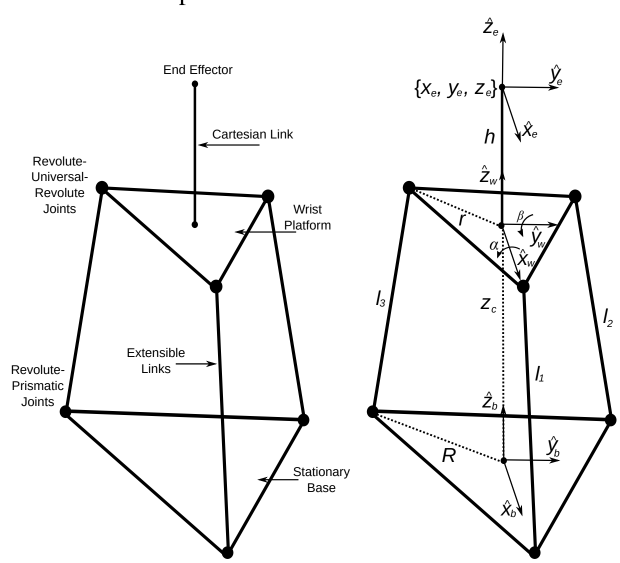

Fig. 2. Parallel 3RPS kinematic architecture of the robot for 3D forelimb training with a rat.

TABLE I

STRUCTURAL PARAMETERS AND DEVICE SPECIFICATIONS

R [mm]	r [mm]	$z_{c,min}$ [mm]	h_x [mm]	h_z [mm]	Mass Moving Parts [g]	Workspace [mm^3]	Force Output [N]
88.9	59.7	118.6	16.5	105.4	350	53x50x50	>2.5

B. Structural Parameters

To define the 3RPS kinematic structure, the base ring radius R, wrist ring radius r, minimum platform height $z_{c,min}$, and the Cartesian link $\mathbf{h}$ needed to be determined. The primary objective in choosing the structural parameters was to achieve the desired workspace and force requirements. Leveraging the findings of [23] and our own preliminary evaluations, we determined that the device should achieve a workspace volume of 50x50x50 mm^3 with a force output capability of 2.5 N in any $\hat{\mathbf{X}}_\mathbf{e}$ direction within the workspace. Additionally, we set a requirement that the interaction point on the Cartesian link be sufficiently far from the wrist ring for comfort of the rat. Finally, a constraint was placed on the design to limit the wrist ring angles α and β to reduce the joint motion required by the universal joints.

Determining r, R, and $z_{c,min}$ is a trade-off that affects the required motor torque and the amount of translation required by the linear links. Decreasing r results in less torque required by the motors, but correspondingly more travel by the linear links, both with an inverse relationship. Increasing $z_{c,min}$ has the effect of increasing the travel required, but also results in less motor torque needed. Considering these trade-offs, the chosen parameters and resulting device specifications are presented in Table I. The objectives for the workspace and force output were accomplished with a necessary link travel of < 90 mm, and required motor torque of < 10 N·mm.

C. Components

Nearly all structural components were 3D printed using plastic composites to create a low-cost and lightweight prototype. The motors selected to achieve the desired motor torque output, were the Maxon RE 35 (273759) with an Avago HEDL 5540 encoder (500 cnt/rev) which led to a resolution of 0.0167 mm in the joint space. Finally, all cables were routed with cable sleeves to adhere to the "Standards for Sanitation" approved by the Animal Welfare Committee (AWC) from the University of Texas Health Science Center at Houston (UTHSC-H). All animal care, training and testing were undertaken in strict accordance with procedures approved by the AWC at UTHSC-H.

D. Control

Control of the device was performed through a real-time software implementation using a Matlab-Simulink model communicating with Quanser's Q8 USB board at a 1 KHz loop rate. For estimating 3D rat motion, the robot recorded joint motion which was then translated to end effector coordinates through the forward kinematics. Joint velocity was computed through the device Jacobian between the base frame and wrist frame and then using the formulation for $\dot{\mathbf{X}}_\mathbf{e}$ described previously. To improve transparency during assessment, simple gravity and Coulomb friction compensation were implemented.

III. RAT-ROBOT INTERACTION

To evaluate the possibility of using the prototype robotic device for rehabilitation with a rat model after SCI, we trained two able-bodied rats to actively interact with the robot. The rats were trained through behavioral shaping using a custom-designed enclosure and grip interface to ensure the rats felt secure, as well as to replicate the robot's end effector (see Fig. 3). As a result of behavioral shaping, trained rats would reach, and occasionally push as desired, the training handle (see Fig. 4). At the conclusion of behavioral shaping, training and evaluation with the robot consisted of three sessions on three separate days lasting 3 hr total.

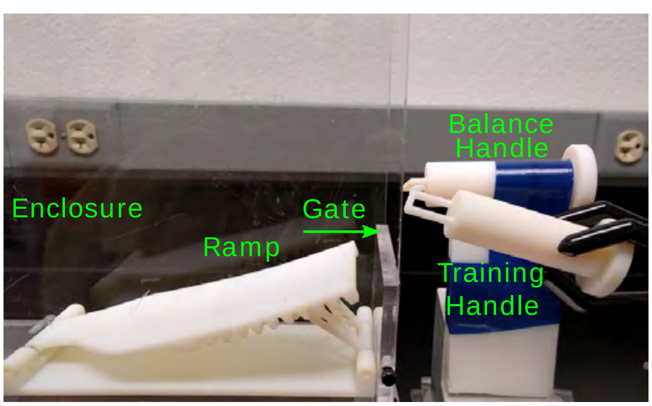

Fig. 3. Enclosure with a ramp as well as handles for grip and support during behavioral shaping.

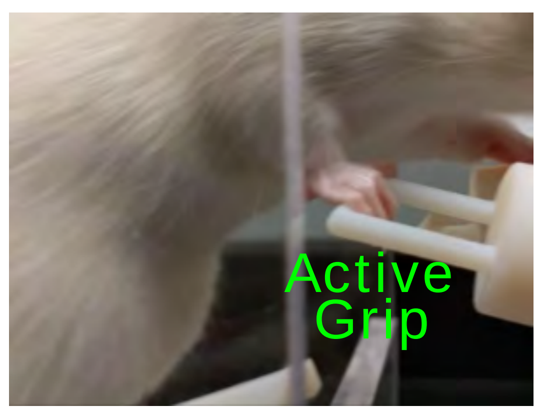

Fig. 4. The results of behavioral shaping: a trained rat reaches to the handle on command.

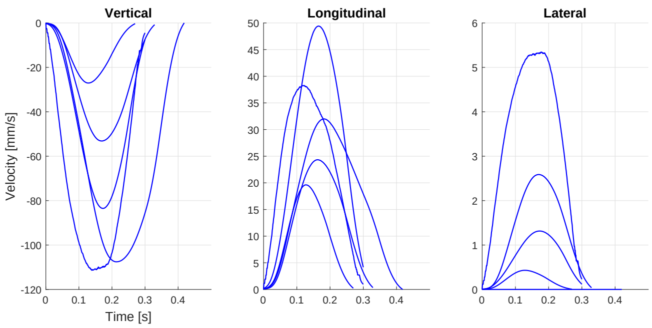

Fig. 5. Five reach and push movements collected during rat-robot interaction. The movements resemble the smooth bell-shaped point-to-point movements found during experiments with human-participants [27].

A. Behavioral Shaping

Two female heterozygous athymic nude rats were trained using clicker-training [28] and positive reinforcement methods, which have both been used successfully in a variety of species. Additionally, clicker-training provided immediate feedback and allowed for expedited behavioral shaping [29]. We define clicker-training as a positive reinforcement technique that uses a hand held manual clicking device and high-value reward treats given after the desired behavior is performed. In this context, rats were trained initially to associate a click with a treat given immediately following the sound. This conditioned association of click to treat reward is defined as the bridging stimulus.

To train the animals to use the device, we used behavioral shaping which we define as successive reinforcements given as the animal progressively performs small parts of a behavior until the animal is accurately performing the target behavior. We define target behavior as the final successful action (i.e. handle pull, handle push, and handle hold) used to grip the Cartesian link's handle. For example, to use the handle the rat was rewarded first for approaching the handle, then a nose touch of the handle, then a paw touch, then a paw grip, and so on until the desired behavior was reached.

Rats were obtained and handled regularly starting at 14 days old. After being weaned at 21 days, rats were introduced to reward treats in the home enclosure for 3 days. Next, a bridging stimulus was shaped using a training clicker as an auditory stimulus combined with high-reward treats. Rats were individually trained in 10 minute sessions, 3 sessions a day, for 5 days during week 1. Rats underwent behavioral shaping and acquisition 5-7 times daily for 5-10 minutes each time 5 days a week for weeks 2-4. At the end of each training session, the target behavior was reached consistently. Target behaviors included coming on command, entering/staying/exiting the enclosure on command, and interacting with the handle by gripping, holding, pulling, and pushing. After one month of training, successful performance was achieved for 1) Active Training: reaching and grasping the handle in a reach-push-pull motion and 2) Passive Training: continuously holding the handle during motion. Although some attempts were inconsistent, the successful performances outweighed failed interactions.

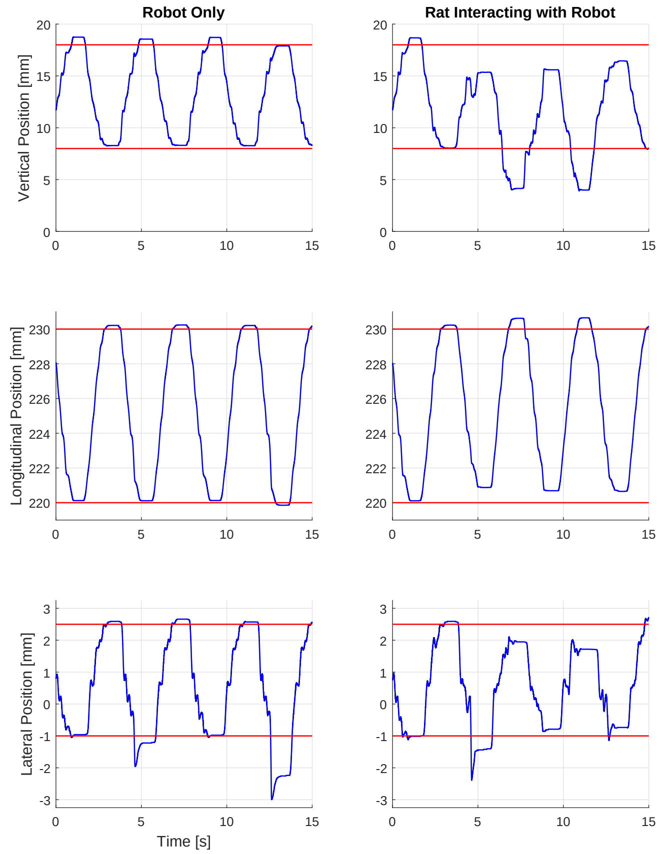

Fig. 6. Experimental evaluation comparing 3D robot end effector position measurements between (left) robot only and (right) rat-robot interaction. Using soft control gains enables distinguishing between the two conditions.

B. Rat-Robot Interaction

After behavioral shaping was completed, the robot was introduced for the first time to the rats. The rats were encouraged, using the previously described clicker training, to interact with the robot in two ways: rat active reach and push (robot passive, similar to Active Training for the rats) and rat initiated reach and hold on the moving robot (robot active, similar to Passive Training for the rats). These interactions were covered over the course of three sessions on three separate days. The first session lasted 1 hr, the second session (the following day) lasted 0.5 hr, and the last session (two days after the second session) lasted 1.5 hr. Session dates and duration were determined on-line based on perceived rat comfort and engagement. Similarly, a given rat underwent training until the rat was perceived to be not engaging with the training, and then the rat who was resting was switched to the training. In the following results, the engagement was not recorded as a function of which rat was undergoing training.

C. Active Training: Rat-Initiated Movements

Over the approximately 3 hr of training sessions, approximately 2 hr were spent on reach and push movements testing (day 1: 25 min, day 2: 30 min, day 3: 65 min). Over these sessions, approximately 17 reach and push movements were collected. Of these 17 collected movements, 5 were representative of able-bodied point-to-point movements (see Fig. 5) as observed in human experiments [27]. Note that some movements were not recorded, as data was not recorded continuously due to the exploratory nature of the testing, but the maximum bound likely did not exceed twice the collected movements. This yields an approximate engagement of 8-16 movements/hr of encouraged rat-initiated reach and push movements.

D. Passive Training: Robot-Initiated Movements

In the second evaluation mode, the robot was position controlled with soft PD control gains and a rat was encouraged to interact with the robot, ideally to reach and hold on. This mode was tested for approximately 1 hr during the three sessions (day 1: 25 min, day 2: 0 min, day 3: 35 min). Using soft gains allows for evaluating rat interaction (see Fig. 6). During these tests, 75 s of data was recorded with the rat holding the grip. Again, not all data was recorded, but the likely upper bound was 150 s of interaction. This yields and approximate engagement percentage of 2-4%.

IV. Discussion and Conclusions

In this work we have developed a robotic rehabilitation platform for functional forelimb training in a rat model. To achieve measurement and interaction with a rat forelimb, we pursued a design that could accommodate 3D motion as opposed to the 2D motion currently possible in prior work [23]. The prototype robot was designed with a parallel kinematic architecture to house the DC motors on a stationary platform, while also enabling 3D interaction and measurement. The robot interface was modified compared to exoskeletons using the same kinematic structure for human-robot interaction [24]–[26], with the robot interacting with the rat in an end-effector manner, measuring and interacting with the forelimb in the 3D Cartesian space.

To test interactions with this device, we used an active-based interaction approach to facilitate rat-robot interaction. We trained two able-bodied rats with one month of behavioral shaping without the robot to familiarize the rat with reaching and pushing or grasping the handle on the end effector of the robot. To test our robotic rehabilitation platform concept, we performed three sessions on three separate days totaling 3 hours of interaction with the rats and the robot. During these sessions, we both trained the rats to interact with the robot, and evaluated interactions when the rat was comfortable. From these three sessions, we report the first 3D kinematic measurements of a rat performing a reach and push motion (active training). We also measured the rat interacting with the robot which was commanded to move in the 3D space (passive training). From the evaluations, we found that it was possible to perform robotic assessment and training through active rat engagement.

With reference to reach and push movements (Fig. 5), the rat's movements resulted in smooth, bell-shaped curves similar to human point-to-point movements. Additionally, in the rehabilitation training condition reach and hold, the rat's interaction could be detected since the robot was commanded to move using soft control gains (Fig. 6). As such, this detection could be used as a measure of engagement in a more automated setting. Additionally, this mode might be useful in the future for regaining movement for a rat with limited movement capabilities. Despite the passive nature of the training once holding the robot's handle, the training still encourages active participation through the rat's initiation to reach and hold the handle. During our preliminary testing though, rat engagement with the robot was very low. During reach and push training, we estimated 8-16 movements/hr over 2 hr of training and testing. During reach and hold training, rat-robot interaction was estimated to be 75-150 s in 1 hr of training and testing. In the future the efficiency of this training would need to be improved for this method to be a viable option. Additionally, the behavioral shaping required intense human directed training which would need to be reduced or automated.

The estimates of rat engagement during these sessions do not account for time spent changing robot parameters, modifying the experimental setup, and allowing rest time for the rats. The rats were given time to rest since we did not force the rats to participate in training, and instead chose which rat to interact with the robot depending on how comfortable and engaged the rat was with the interactions. Additionally, we did not collect data continuously to ensure only appropriate trials would be analyzed due to the exploratory nature of the training sessions. Finally, engagement was also hindered since the noise from the motor current controller, the Advanced Motion Controls AB15A100, occasionally seemed to cause some apprehension for the rats. More time to interact with the robot before these sessions, especially with the robot powered off or alternatively placing the motors in a sound proof box, might increase rat-robot engagement during active-based training.

Regarding the robot prototype, the device provided adequate range of motion and force output for the preliminary tests. Although these parameters might be improved, we found them suitable for our initial investigations. Future efforts though should aim to increase the transparency of the device. The transparency could be increased by using smaller motors with less damping and inertia than the Maxon RE 35 motors used in this work, although this would come at the cost of force output. Similarly, reducing the size of the links and using lighter linear rails could aid in reducing the inertia of the device. These improvements are important since only smooth reach and push movements were collected while performing simply gravity and Coulomb friction compensation. With the motors not on, while some movements were collected, the device was difficult for the rat to backdrive resulting in more of a full-body push down then a reach and push movement. This resulted in jerky movements which are not representative of able-bodied point-to-point movements.

Related to the rat-robot interface, a main focus of the collaborative effort was on the best means of interfacing the rat with the robot. Early attempts focused on a soft glove which connected the rat and robot rigidly. In this way, once the two were connected, as in previous work which placed rats in a harness for treadmill walking, the established connection could not be broken easily. This soft connection between the rat and robot was found to be non-trivial for the forelimb, and could use further investigation to arrive at the best interface. As a result, this passive interaction was abandoned in favor of active engagement, which also could be more positive for rehabilitation, in which the rat would be trained through behavioral shaping to interact with the robot.

In this work we have presented the preliminary development and testing of a novel robotic rehabilitation platform for 3D forelimb training with a rat. Future investigations will improve the rat-robot interface, as well as provide reach and grasp assessment in 3D with a more transparent device. Additionally, although we found behavioral shaping to be time-intensive and a limiting factor, we still found positive takeaways from the preliminary research. To increase the amount of interaction of the rat with the robot during training and evaluation, a more iterative process between behavioral training without the robot followed by sessions with the robot might increase the number of movements collected during active training or the duration of reach and hold during passive training. A rehabilitation paradigm using these two interaction modes might facilitate investigating combinatorial treatments that offer the possibility to increase functional gains after SCI.

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