Published in final edited form as:
J Neurosci Methods. 2009 May 15; 179(2): 264–270. doi:10.1016/j.jneumeth.2009.02.003.

A novel device to measure power grip forces in squirrel monkeys

Scott D. Bury[1], **Erik J. Plautz**[1,2], **Wen Liu**[1,3], **Barbara M. Quaney**[1,3], **Carl W. Luchies**[1,4], **Rebecca A. Maletsky**[1], and **Randolph J. Nudo**[1,2,3]

1 *Landon Center on Aging, University of Kansas Medical Center, Kansas City, Kansas 66223*

2 *Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, Kansas 66223*

3 *Department of Physical Therapy and Rehabilitation Sciences, University of Kansas Medical Center, Kansas City, Kansas 66223*

4 *Department of Mechanical Engineering, University of Kansas, Lawrence, Kansas 66045*

Abstract

Understanding the neural bases for grip force behaviors in both normal and neurologically impaired animals is imperative prior to improving treatments and therapeutic approaches. The present paper describes a novel device for the assessment of power grip forces in squirrel monkeys. The control of grasping and object manipulation represents a vital aspect of daily living by allowing the performance of a wide variety of complex hand movements. However, following neurological injury such as stroke, these grasping behaviors are often severely affected, resulting in persistent impairments in strength, grip force modulation and kinematic hand control. While there is a significant clinical focus on rehabilitative strategies to address these issues, there exists the need for translational animal models. In the study presented here, we describe a simple grip force device designed for use in non-human primates, which provides detailed quantitative information regarding distal grip force dynamics. Adult squirrel monkeys were trained to exceed a specific grip force threshold, which was rewarded with a food pellet. One of these subjects then received an infarct of the M1 hand representation area. Results suggest that the device provides detailed and reliable information on grip behaviors in healthy monkeys and can detect deficits in grip dynamics in monkeys with cortical lesions (significantly longer release times). Understanding the physiological and neuroanatomical aspects of grasping function following neurological injury may lead to more effective rehabilitative interventions.

Corresponding Author: Randolph J. Nudo, Landon Center on Aging, University of Kansas Medical Center, 3901 Rainbow Blvd/MSN 1005, Kansas City, KS 66160 USA, (913) 588-1247, Fax: (913) 588-1201, email: E-mail: rnudo@kumc.edu.
Scott D. Bury, PhD, Landon Center on Aging, University of Kansas Medical Center, 3901 Rainbow Blvd/MSN 1005, Kansas City, KS 66160 USA
Erik J. Plautz, PhD, Department of Molecular and Integrative Physiology, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160 USA
Wen Liu, PhD, Department of Physical Therapy and Rehabilitation Sciences, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160 USA
Barbara M. Quaney, PhD, Landon Center on Aging, University of Kansas Medical Center, 3901 Rainbow Blvd/MSN 1005, Kansas City, KS 66160 USA
Carl W. Luchies, PhD, Department of Mechanical Engineering, University of Kansas, 3138 Learned Hall, Lawrence, Kansas 66045 USA
Rebecca A. Maletsky, Landon Center on Aging, University of Kansas Medical Center, 3901 Rainbow Blvd/MSN 1005, Kansas City, KS 66160 USA
Randolph J. Nudo, PhD, Landon Center on Aging, University of Kansas Medical Center, 3901 Rainbow Blvd/MSN 1005, Kansas City, KS 66160 USA

Keywords

Grip force; power grip; monkey; stroke; hand; primates

Introduction

The control of grip forces represents a vital and critical component in skilled motor behavior for humans. Grasping behaviors can be broadly classified as either 1) precision grip, typically involving individuated finger movements and finger-thumb opposition, and 2) power grip, typically involving whole-hand flexion of the fingers which may or may not also involve the thumb (Napier, 1956). While the role of the central nervous system in relation to voluntary grip behavior has been studied extensively (Salimi et al., 1999; Ehrsson et al., 2000; Jabre et al., 2000; Lemon et al., 2004; Prabhu et al., 2007) our understanding of how it responds to and recovers from injury or disease is still limited.

Damage or disease affecting central motor structures often results in impairments in manual dexterity. Specific deficits in both precision and power grasping have been associated with a variety of neurological injuries and diseases, including stroke, Parkinson's disease, cerebellar disease, Tourette syndrome and focal hand dystonia. For example, stroke often results in numerous grasping deficits, including inability to modulate grip force, upper and lower limb weakness and spasticity (Hermsdorfer et al., 2004; Nowak and Hermsdorfer, 2005; Quaney et al., 2005). While stroke patients often exhibit an overall reduction in upper limb strength and maximum grip force, especially in the early stages following a stroke, they persistently produce excessive grip forces when manipulating objects (Nowak and Hermsdorfer, 2005; Quaney et al., 2005). This inability to accurately modulate forces often results in difficulties during object manipulation, such as the inability to successfully release objects (Fritz et al., 2005; Voelcker-Rehage and Alberts, 2005).

Animal models play an important role in understanding grasping impairments after such injuries, since precise neurophysiological and neuroanatomical mechanisms can be examined in a well-controlled environment. Previous studies established models of both precision and power grip in primates (Hepp-Reymond and Wiesendanger, 1972), however many of these have not been extensively studied in relation to established lesion models. Thus, there is substantial need for improved methodologies to examine such behaviors in animal models of stroke and other neurological disorders. To examine grasping behavior in a non-human primate model, we have developed a novel grip force measurement device that allows for direct, quantitative assessment of distal power grip force and dynamics in squirrel monkeys. The device is unique in that it provides detailed information on force control. The device itself utilizes a force transducer connected to a computer capable of measuring and recording force data in real time. This simple but unique device selectively measures the grasping forces generated by forearm and intrinsic hand muscles that are directly applied during a grip. It has been constructed in such a way that forces generated by muscles (such as those responsible for elbow, shoulder or torso movements) other than those directly required for distal gripping are minimized. The device is also capable of specifying various reward parameters based upon the detected gripping force, and thus allows the testing of grip force dynamics under a variety of experimental conditions.

The goals of these initial experiments were to 1) establish that the device produces consistent, quantifiable and reliable grip force data to characterize the distal grip forces generated by healthy monkeys, and 2) provide preliminary data on effects of cortical injury, which would furnish baseline values for future studies. Three healthy adult squirrel monkeys were trained to use the device. Data was collected for five days at four different reward thresholds (minimum

force levels required to receive a food reward). Following baseline training, one subject received an infarct of the primary motor cortex (M1) hand representation. The results demonstrate that consistent and reliable data on grip force kinetics and dynamics can be acquired with this device, and provide preliminary evidence for deficits in grasping function produced by cortical injury in M1.

Materials and Methods

Grip Force Device

The grip device consisted of a small force transducer embedded in a bisected aluminum cylinder (Figure 1). In order for the transducer to be activated, the two mating surfaces of the bisected cylinder were required to be pressed together. The mating surfaces were separated by 2 mm of lightweight foam (the added resistance of the foam is accounted for in the calibration of the force sensor). The diameter of the cylinder (10 mm) was designed to easily fit into the palm and fingers of the monkey (length of the manipulandum is 4 cm). Grip force was measured using a Subminiature Honeywell Sensotec Compression Load Cell (Model 13, Honeywell Sensotec Inc., Columbus Ohio) with a 1000 g load range and 0.01 g resolution. The load cell has a full scale ±0.25% non-linearity/hysteresis (max) with 0.5% accuracy, and is temperature compensated (60 °F to 160 °F). The load cell also maintains an infinite resolution, 26 kHz ringing frequency, weighted 1.1 g.

To prevent forces from being imparted on the transducer from sources other than by direct compression of the cylinder, the transducer apparatus was mounted vertically on a universal-joint (U-joint). The load cell was situated in the center of the manipulandum, in such a way that only direct pressure on the load cell would be registered and recorded. Observation of pre- and post-lesion videotapes confirms that the monkeys placed their hands directly over the center of the manipulandum on 98% of trials. That is, the center-line of the hand (between digits 3 and 4) was on the center of the manipulandum (Figure 1). On the remaining 2% of the trials, the hand was placed slightly above the center, with the hand center-line deviating by no more than 3mm. That is, the center-line of the hand was always within the limits of the mounting screws connecting the two halves of the manipulandum on all trials. Based on calibration testing with applied forces ranging from 100–500g, recorded force was attenuated by approximately 3% for forces applied 3mm above the center line and 12% for forces applied 3mm below the center line. Thus, the recorded forces accurately reflected the applied forces, and deviated by no more than 3% on no more than 2% of the trials.

In addition, the manipulandum was mounted to a plate that could slide in a direction perpendicular (i.e., horizontal) to the device. Thus, pulling, pushing or twisting the manipulandum using shoulder or elbow movements did not impart any measurable force on the transducer itself, effectively isolating the distal grip force. In the current design, it is possible that the monkeys could slide the manipulandum to a stationary position at the edge of the rail, thereby allowing forces exerted from shoulder retraction to be recorded. However, this was not observed in any of the monkeys.

Force signals were digitized via an analog-to-digital converter mounted in a laptop computer. The signal was recorded continuously at a sampling rate of 200 Hz, and stored for later, offline analysis. The computer also monitored applied grip force and provided immediate feedback in the form of a food reward (45 mg food pellets, Bioserve, Frenchtown, NJ). Reward parameters were programmable, and included a) a reward threshold, defined as the minimum force required to activate delivery of a food pellet, and b) a return threshold, defined as the lower force limit required for additional pellets to be awarded. The return threshold ensured that the subject produced discrete grip events and prevented multiple rewards within a single grip event. When the force signal exceeded the reward threshold, a TTL signal was sent to a

mechanical food pellet dispenser, which delivered a single pellet into a small bin accessible by the monkey. Prior to experimentation, calibration of the device was confirmed using known weights applied to the manipulandum.

Grip Force Measurement

Subjects—Three adult squirrel monkeys (*Saimiri* spp.; 600 to 800 g), two males and one female, were used in the present study. The monkeys are identified as subjects MK1 through MK3 in the results section that follows. Monkeys were allowed food and water *ad libitum*, except during the initial acclimation period and the day prior to testing days. It should be noted that while many clinical and mechanistic studies focus on deficits in precision grip, squirrel monkeys do not possess this grip as part of their normal behavioral repertoire, but instead exhibit power grips almost exclusively (Fragaszy, 1983; Costello, 1988). This does not impact the present study directly, since it specifically focuses on power grips, behaviors that are quite relevant for translation to human motor behavior as they represent a critical component of forelimb dexterity. All procedures were approved by the University of Kansas Medical Center's Institutional Animal Care and Use Committee.

Acclimation Training—The subjects were acclimated to the testing device by clamping the device onto the front of the home cage for four to five hours on each of two consecutive days immediately prior to testing. During the subsequent shaping period, the monkeys were kept on a restricted diet during training days (five days per week) and then allowed food *ab libitum* the remainder of the time. Acclimation sessions consisted of allowing the monkey free access to the grip device with either limb for 30 min. The reward threshold was initially set at 30 g, a low, easily attainable force for most monkeys. The reward threshold was set so that as soon as the threshold was achieved the pellet was dispensed (with an approximately 1 s delay for the pellet dispenser to respond to the signal). The monkeys were initially encouraged to contact the device by attaching food pellets to the manipulandum with double-sided adhesive tape. Acclimation sessions were videotaped to aid in determining hand preference. The percentage of limb use was calculated for the first three shaping sessions. All three subjects displayed a >75% preference for one limb for the task. Once the subject was consistently gripping the device and receiving reward pellets (at least 60 pellets within 15 min), acclimation training ceased and grip force testing was initiated on the following training day.

Grip Force Testing—Monkeys were tested twice per week for a total of five sessions. Each session consisted of testing at one of four different reward thresholds: 50 g, 100 g, 150 g and 200 g. The order of the reward thresholds was randomized for each session. The duration of each testing session was the time required to obtain 20 pellets or 10 min, whichever came first. Hand usage was restricted to the preferred hand by a Plexiglas barrier placed in front of the manipulandum (Figure 1). It should be noted that no attempt was made to shape or restrict the monkeys to perform a particular gripping strategy for reward acquisition.

Data Analysis—The digitized output from the force transducer acquired during each session was processed offline (i.e., after the testing session) using a laboratory-made program in Matlab, (Mathworks Inc., Lowell, MA). A session was defined as testing at one reward threshold, for 20 successful grips (those that exceeded the reward threshold) or 10 min, whichever, came first. The data processing program was used to calculate the following variables: peak (maximum) grip force per session, maximum force deviation (difference between peak force and force reward threshold), grip time (time from grip onset to peak force), release time (time from peak force until return to baseline), grip rate (maximum force divided by grip time), and release rate (maximum force divided by release time). Within each grip episode (time period when the subject was actively gripping or making contact with the manipulandum), separate grip events were analyzed individually. A grip event was defined as

any action that resulted in a recorded force greater than 15 g, and then returned to a minimum of 10 g.

Procedures for cortical injury

In one monkey (MK1), a surgical procedure was conducted to physiologically identify, and then create an ischemic lesion in, the M1 hand area. Under sterile conditions and after induction of isoflurane anesthesia, a craniectomy was made over the area of interest. The dura was removed, and a small plastic cylinder was fitted over the craniotomy, and filled with warm, sterile silicone oil. Isoflurane was withdrawn and ketamine administered intravenously until the animal was stabilized. Supplemental doses of ketamine were administered throughout the remainder of the experiment as needed to maintain a stable level of anesthesia (15 mg/kg/hr). Valium (0.01 mg/kg/hr) was used to reduce excessive muscle tone. Heart rate, respiration rate, expired CO_2, saturated O_2, and temperature were maintained within normal physiological limits throughout the experiment. Core temperature was maintained with a homeothermic blanket system. Lactated Ringer's solution with 3% dextrose was be infused at the rate of 10 cc/kg/hr.

Using a video frame-grabber, a magnified digital image of the cortical surface vasculature was obtained. A glass micropipette filled with 3.5M NaCl was introduced on a fine grid pattern, placed with reference to the surface vasculature, then advanced perpendicular to the cortical surface to a depth of 1700–1800μm, corresponding to cortical layer V (thresholds for evoking movements are minimal at this depth). Motor fields were defined by determining muscles or movements excited by intracortical microstimulation (ICMS) using near-threshold and suprathreshold electrical stimulation (less than 30μA). These procedures are now widely used for mapping the functional topography of motor cortex and have been in use in our laboratory for over 20 years (e.g. Nudo, 1992). The spatial resolution of the ICMS map (i.e., the interpenetration distance) over the area targeted for the lesion was 500μm, adequate for defining the functional boundaries. The intracortical stimulus consisted of an ICMS train burst, a 40 msec current train of 200μsec monophasic cathodal pulses delivered at 350Hz from an electrically isolated, charge-balanced stimulation circuit. At each site, current was gradually increased from zero until a response is just visible in at least 50% of the train bursts. After two observers agreed on the movement activated at threshold, it was recorded.

The ICMS data from the individual sites were used to define the boundary of the M1 hand area (sites whose stimulation evoked movements of digits, wrist and forearm, but excluding elbow and shoulder). An ischemic infarct was made over the entire hand representation by bipolar electrocoagulation of the vascular bed (Jenkins and Merzenich, 1987; Nudo et al., 1996).

The subject was allowed to recover for one week following surgery. Testing session protocols were the same as pre-lesion protocols, and carried out twice per week for two months.

Statistical Analysis—For statistical comparisons, data from the final two pre-lesion testing sessions for each monkey were pooled for each reward threshold, since adaptation to task requirements was likely to be minimal in later test sessions. Four task measures (peak force, force deviation, grip rate, and release rate) were compared across the four reward thresholds using one-way repeated-measures ANOVA and a post-hoc test for linear trends (Prism, version 4, GraphPad Software, Inc., San Diego, CA). Comparisons between monkeys were done using one-way ANOVA and Bonferroni multiple comparison post-hoc test. Regression and correlation techniques were used to compare data between individual trials. Pre-infarct versus post-infarct data from one monkey was compared over time using one-way ANOVA and Dunnett's multiple comparison post-hoc test. Alpha level was 0.05 for all testing.

Results

Behavioral Performance

All three monkeys were able to perform the required gripping task consistently in a relatively short period of time (average shaping time = four days). Once acclimation training was complete, grip force testing sessions were short, with all subjects typically completing all four thresholds in 10–15 min. All monkeys adopted an exclusive preference for one forelimb on the gripping task (right for MK1 and MK2, left for MK3).

Figure 2 shows representative grip force profiles from the three subjects for each of the tested reward thresholds. While all subjects showed similar grip event force characteristics, such as applied force and force over time profiles, differing strategies in performing the task were observed. Specifically, MK1 employed multiple, rapid grips in a single gripping episode, often receiving two to five pellet rewards in quick succession. In comparison, both MK2 and MK3 tended to perform one to two grips per episode.

Grip Forces

Figure 3A shows the mean peak forces generated by each of the three subjects at each reward threshold over the final two testing sessions. For the group, mean (±S.D.) peak forces were 177.7±32.8 g, 192.4±32.3 g, 224.1±27.8 g, and 232.6±14.8 g for the 50 g, 100 g, 150 g, and 200 g thresholds, respectively. There was a significant effect of reward threshold on peak force ($F=5.16$, $p=0.042$), with post-hoc testing indicating that peak grip force increased as a function of increasing reward threshold ($R^2=0.47$, $p=0.009$). Conversely, the mean (±S.D.) force deviations at each ascending (i.e., 50 g to 200 g) threshold were 127.7±32.8 g, 92.4±32.3 g, 74.1±27.8 g, and 32.6±14.8 g, indicating that the monkeys exceeded the reward threshold by smaller amounts as the threshold increased (Figure 3B). These differences in force deviation were significant ($F=12.0$, $p=0.006$), with a significant inverse relationship between reward threshold and force deviation ($R^2=.68$, $p=0.001$).

All subjects consistently produced more force than required by the reward threshold to receive rewards. However, there was no consistent within-session accommodation of grip forces to the reward threshold; that is, supra-threshold grip forces did not approach the reward threshold as the testing session progressed. For each of the final two testing sessions in each monkey and at each threshold, correlation analyses were used to assess any relationship between peak force produced and the grip event sequence within the test session for each threshold. Three of the 24 correlations examined were significant (MK2, 50 g, day 2, $R^2=0.45$, $p=0.018$; MK2, 200 g, day 1, $R^2=0.31$, $p=0.025$; MK3, 100 g, day 2, $R^2=0.32$, $p=0.009$), and all were negatively correlated, indicating smaller peak forces over time. This relatively few number of significant outcomes suggests that subjects were not routinely optimizing force production around the reward threshold on a trial-to-trial basis. Nevertheless, the mean peak force results described earlier suggest that the monkeys were able to detect the session-to-session shift in the required reward threshold and adjust their subsequent grip forces appropriately. The maximum recorded grip force recorded during all sessions was 642.2 g, indicating the range of the device was adequate under these test conditions.

Grip and Release Rates

Mean grip rates and mean release rates for each subject at each reward threshold during the final two testing sessions are illustrated in Figure 4A and 4B respectively. Group means (±S.D.) for grip rates were 995.4±581.9 g/s, 945.1±393.6 g/s, 1252.0±578.1 g/s, and 1169.0±555.6 g/s for the ascending (50 g to 200 g) thresholds. There was a significant effect of threshold on grip rate ($F=4.98$, $p=0.046$), but this effect was only weakly related to the linear increase in reward threshold ($R^2=0.04$, $p=0.029$). For release rates, the group means (±S.D.) were 829.2

±488.2 g/s, 822.3±237.6 g/s, 1038.0±267.2 g/s, and 929.9±228.2 g/s for the ascending thresholds. There was no significant effect of threshold on release rate ($F=1.41$, $p=0.330$).

Inter-subject performance differences

There were notable differences in peak force, grip rate, and release rate between MK1 versus MK2 and MK3. Pooled across all reward thresholds, peak force for MK1 (185.3±86.3 g) was significantly lower than MK2 (212.4±86.1 g) and MK3 (227.3±110.9 g) (one-way ANOVA, $F=11.2$, $p<0.0001$). Grip rate for MK1 (1688.9±951.8 g/s) was significantly faster than MK2 (729.0±377.5 g/s) and MK3 (868.2±467.3 g/s) ($F=99.2$, $p<0.0001$) and release rate was significantly faster for MK1 (1246.9±1181.5 g/s) compared to MK2 (667.6±460.6 g/s) and MK3 (826.6±645.5 g/s) ($F=20.3$, $p<0.0001$). For all three measures, MK1 was different from MK2 and MK3, while the latter two monkeys were equivalent (Bonferroni post-hoc tests). These differences may reflect the different task strategies exhibited by MK1 (multiple grip events per grip episode) versus MK2 and MK3 (single grip events per grip episode).

Relationship between peak force and grip/release rates

Since mean grip and release rates were poorly related to increasing reward threshold, both rates were compared to peak force applied on individual trials (Figure 5). It is clear from these plots that grip rate and release rate were at least partially modulated by the amount of force applied during each trial. Linear regression analysis indicated significant relationships for MK1 grip rate ($F=40.2$, $p<0.0001$, $R^2=0.11$), MK2 grip rate ($F=119.0$, $p<0.0001$, $R^2=0.50$), MK2 release rate ($F=38.9$, $p<0.0001$, $R^2=0.25$), MK3 grip rate ($F=71.4$, $p<0.0001$, $R^2=0.33$) and MK3 release rate ($F=115.8$, $p<0.0001$, $R^2=.45$). There was no linear relationship found for MK1 release rate, although this is likely due to the bimodal distribution of the data. Superimposed scatterplots of force vs. rate for the four reward thresholds indicated there was considerable overlap in the range of forces and rates produced (not shown).

Effects of M1 Lesion on Grip Behavior

To assess the utility of the grip device for evaluating changes in grip behavior after brain injury, MK1 received an ischemic infarct in M1 (see Methods) and was subsequently tested on the grip device twice/week for eight weeks after the injury. Preliminary analysis of these results are presented here, focusing on the 50 g reward threshold (Figure 6). After infarct, MK1 was able to perform the grip force task, but exhibited altered grip force profiles, most notably with respect to force rates. Grip rate decreased from 1649.0±990.5 g/s (pre-infarct) to 868.5±627.1 g/s during the first week post-infarct, a nearly two-fold reduction. For pre-infarct performance through week 8 post-infarct, one-way ANOVA revealed a significant main effect of time ($F=8.87$, $p<0.0001$) and post-hoc testing indicated a significant reduction in grip rate at week 1 through week 7 post-infarct compared to pre-infarct ($p<0.05$, Dunnett's multiple comparison test). The average grip rate from week 1 to week 7 post-infarct was 894.2g/s, a 46% reduction. Similarly, release rate decreased from 1444.0±1532.0 g/s (pre-infarct) to 290.8±237.4 g/s at week 1 post-infarct, a nearly five-fold reduction. Statistical testing revealed a significant main effect of time ($F=11.5$, $p<0.0001$) and Dunnett's post-hoc test revealed significant decreases in release rate for each week from week 1 to week 8 post-infarct versus the pre-infarct time period ($p<0.05$). Average weekly release rate over the 8-week post-infarct was 497.1 g/s, a 66% reduction.

Peak force was also affected following M1 infarct, but to a lesser degree than grip or release rates. Peak force decreased from 170.1±74.4 g (pre-infarct) to 140.5±92.3 g at week 1 post-infarct. Statistical testing revealed a significant main effect of time ($F=6.29$, $p<0.0001$), but post-hoc testing indicated that peak force was significantly reduced only from week 3 to week 7 post-infarct, with an average peak force of 117.0 during these five weeks (a 31% reduction).

Discussion

These results describe behavioral data obtained in squirrel monkeys using a device capable of measuring and characterizing temporal aspects and magnitudes of distal power grip forces. The device is relatively simple to construct and implement, the monkeys can be acclimated and trained in a short time and the data interpretation is straight-forward. One of the unique features of the device is that the manipulandum slides and pivots, allowing the isolated testing of distal power grip force without the need for extensive behavioral training. While it is not possible to completely rule out the contribution of more proximal musculature, grip forces derived from these muscles are substantially minimized,

The device is capable of accurately measuring grip forces to within 0.01 gram, and resolve grip and release times to 1 msec. The subjects learned to use the device within a few days and performance was reliable and consistent within trials and between testing days. Consistently, higher reward thresholds produced higher mean peak forces. While all the subjects consistently applied more force than necessary to receive the reward, these force deviations diminished as the reward thresholds increased. This suggests that these thresholds were more demanding and may have approached the subjects' maximum sustainable grip force. Maximum grip force was not specifically determined in these initial studies, as it will require different training and testing protocols. Given the clinical importance of this functional measure, determining maximum grip force will be a priority in future studies. In addition, the reward algorithm could be modified to require that the applied force remain within a more limited range for a predetermined time period before the reward pellet is triggered. This would allow assessment of the ability of the monkeys to accurately modulate grip forces, in addition to the assessment of the generation of peak grip forces as demonstrated here.

While the behavioral data following an M1 lesion is still preliminary, it provides compelling evidence that damage to motor cortex impairs grasping behaviors in squirrel monkeys. While the lesion produced in the study was small and focal in comparison to a typical clinical stroke, it nevertheless produced significant, measurable impairments in power grip function, including weakness and, most notably, decreased grip and release rates. In addition, these impairments are similar to those observed in human stroke survivors (Hermsdorfer et al., 2004), most notably changes in applied grip forces as well as changes in power grip kinematics and kinetics.

As mentioned in the methods sections, off-center grips produced slightly attenuated force measurements. While this has not been an issue for the current studies, it is plausible that different training or lesion techniques could dramatically alter gripping strategies in the monkeys. Improved designs for the manipulandum are currently being developed, including the use of a metal sleeve at the bottom of the manipulandum to further guide hand placement, as well as a manipulandum that uses at least two sensors located near the edges.

These preliminary results suggest that this device may have utility for studying the effects of neurological disease and injury on grasping behaviors. Animal models provide an invaluable means to bridge basic and clinical research, as well as provide a means to test effects of pharmacological and behavioral interventions on muscle power and control. Preclinical testing of behavioral endpoints is often conducted in rodent models using somewhat generalized measures of basic sensorimotor control (using the Roto-Rod©) or cognitive ability (using the Morris water maze). While tests that assess more specific impairments are also common (Montoya staircase test, reach training, upright postural support test), they require substantial training of the investigator to achieve reliability and avoid subjectivity, and are relatively laborious as sessions must be videotaped and analyzed post-hoc. Even these tests do not provide quantitative information regarding force control, the specific aspect of musculature control that is probably most relevant for generalization to humans.

Previous tests used to quantify motor performance in primates, such as manual dexterity tasks to train stereotypical reach and retrieval patterns (Plautz et al., 2000; Pizzimenti et al., 2007) also require relatively minimal training to develop novel, skilled use of the hand. These tasks are well-suited to assessment of reaching kinematics and functional success in obtaining food objects. The present device provides a valuable addition to these assessment tools, as it measures an innate motor ability, namely power grip, a behavior monkeys employ extensively in daily home cage activity. Because of this, the subject is only required to learn the relationship between grasping the manipulandum at a minimum force threshold and the delivery of a food reward, resulting in brief acquisition periods. Further, the device provides detailed information about grip force kinetics and kinematics. The relative ease of the testing paradigm along with detailed data on both strength and grip generation dynamics suggests that this device could provide an excellent compliment to established tests of forelimb function in primates.

Acknowledgments

The authors would like thanks Dr. Scott Barbay and Dr. Shawn Frost for their assistance and advice regarding these experiments, Robert Cross for his assistance in animal care, and the personnel of the Landon Center on Aging Human Performance Laboratory for technical assistance. Supported by National Institutes of Health grants NS030853 (RJN), HD02528 (NICHD center grant) and the Landon Center on Aging.

References

Costello, MaFDM. Prehension in *Cebus* and *Saimiri*, I. Grip type and hand preference. Am J Primmatol 1988;15:235–245.

Ehrsson HH, Fagergren A, Jonsson T, Westling G, Johansson RS, Forssberg H. Cortical activity in precision- versus power-grip tasks: an fMRI study. J Neurophysiol 2000;83:528–536. [PubMed: 10634893]

Fragaszy DM. Preliminary quantitative studies of prehension in squirrel monkeys (Saimiri sciureus). Brain Behav Evol 1983;23:81–92. [PubMed: 6667371]

Fritz SL, Light KE, Patterson TS, Behrman AL, Davis SB. Active finger extension predicts outcomes after constraint-induced movement therapy for individuals with hemiparesis after stroke. Stroke 2005;36:1172–1177. [PubMed: 15890987]

Hepp-Reymond MC, Wiesendanger M. Unilateral pyramidotomy in monkeys: effect on force and speed of a conditioned precision grip. Brain Res 1972;36:117–131. [PubMed: 4621473]

Hermsdorfer J, Hagl E, Nowak DA. Deficits of anticipatory grip force control after damage to peripheral and central sensorimotor systems. Hum Mov Sci 2004;23:643–662. [PubMed: 15589626]

Jabre JF, Hallett M, Lemon R, Kernell D. Recent developments in our understanding of motor control, corticomotoneuronal connections and the activation of motoneurons and motoneuronal pools. Suppl Clin Neurophysiol 2000;53:171–177. [PubMed: 12740992]

Jenkins WM, Merzenich MM. Reorganization of neocortical representations after brain injury: a neurophysiological model of the bases of recovery from stroke. Prog Brain Res 1987;71:249–266. [PubMed: 3588947]

Lemon RN, Kirkwood PA, Maier MA, Nakajima K, Nathan P. Direct and indirect pathways for corticospinal control of upper limb motoneurons in the primate. Prog Brain Res 2004;143:263–279. [PubMed: 14653171]

Napier JR. The prehensile movements of the human hand. J Bone Joint Surg Br 1956;38-B:902–913. [PubMed: 13376678]

Nowak DA, Hermsdorfer J. Grip force behavior during object manipulation in neurological disorders: toward an objective evaluation of manual performance deficits. Mov Disord 2005;20:11–25. [PubMed: 15455447]

Nudo RJ, Milliken GW, Jenkins WM, Merzenich MM. Use-dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys. J Neurosci 1996;16:785–807. [PubMed: 8551360]

Pizzimenti MA, Darling WG, Rotella DL, McNeal DW, Herrick JL, Ge J, Stilwell-Morecraft KS, Morecraft RJ. Measurement of reaching kinematics and prehensile dexterity in nonhuman primates. J Neurophysiol 2007;98:1015–1029. [PubMed: 17553948]

Plautz EJ, Milliken GW, Nudo RJ. Effects of repetitive motor training on movement representations in adult squirrel monkeys: role of use versus learning. Neurobiol Learn Mem 2000;74:27–55. [PubMed: 10873519]

Prabhu G, Lemon R, Haggard P. On-line control of grasping actions: object-specific motor facilitation requires sustained visual input. J Neurosci 2007;27:12651–12654. [PubMed: 18003844]

Quaney BM, Perera S, Maletsky R, Luchies CW, Nudo RJ. Impaired grip force modulation in the ipsilesional hand after unilateral middle cerebral artery stroke. Neurorehabil Neural Repair 2005;19:338–349. [PubMed: 16263966]

Salimi I, Brochier T, Smith AM. Neuronal activity in somatosensory cortex of monkeys using a precision grip. I. Receptive fields and discharge patterns. J Neurophysiol 1999;81:825–834. [PubMed: 10036283]

Voelcker-Rehage C, Alberts JL. Age-related changes in grasping force modulation. Exp Brain Res 2005;166:61–70. [PubMed: 16096780]

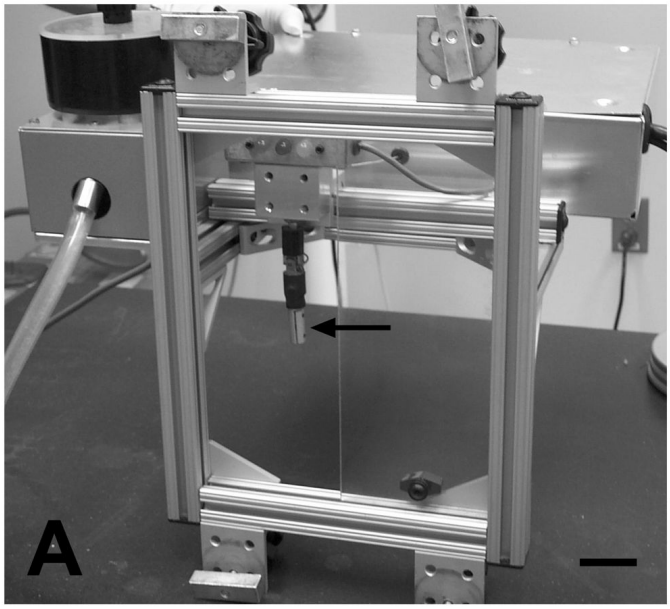

Figure 1.
(A) Photograph of the grip device. Arrow indicates the manipulandum (grip sensor). Scale bar = 5cm. (B) Close up photograph of grip manipulandum, arrow indicates placement of force sensor within the cylinder. (C) Drawing of a squirrel monkey using the device.

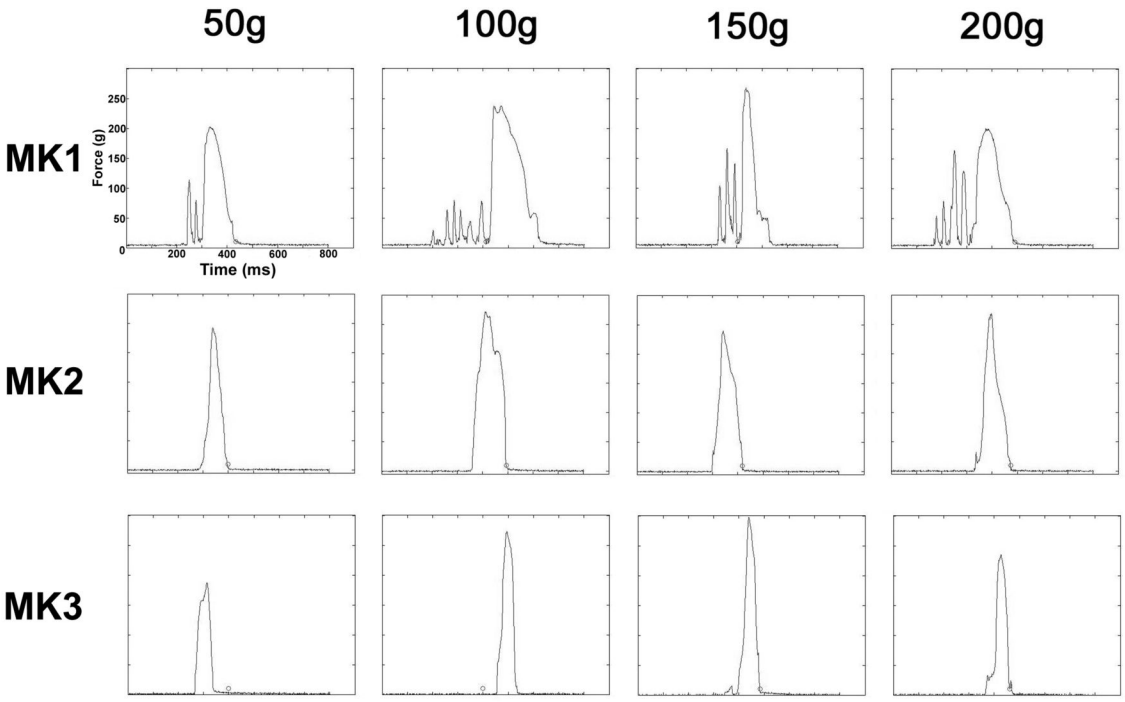

Figure 2.

Representative grip force profiles for all three subjects, for all tested reward thresholds. Note MK1's profile reflects its particular gripping strategy of rapid, multiple flexion grip events, while both MK2 and MK3 tended to perform single flexion grips. X-axis is time in ms (0–900ms), Y-axis is force in grams (0–300g).

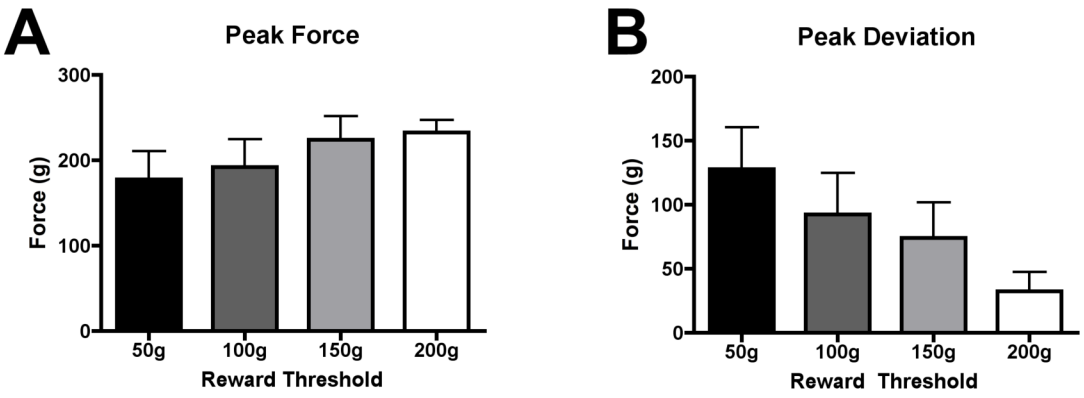

Figure 3.

Mean maximum grip force (A) and mean peak force deviation from reward threshold (B) for each subject across reward thresholds. All subjects increased grip forces with higher reward thresholds. All subjects also tended to exert forces greater than the required threshold (B), although the amount of this force deviation significantly decreased as reward threshold increased.

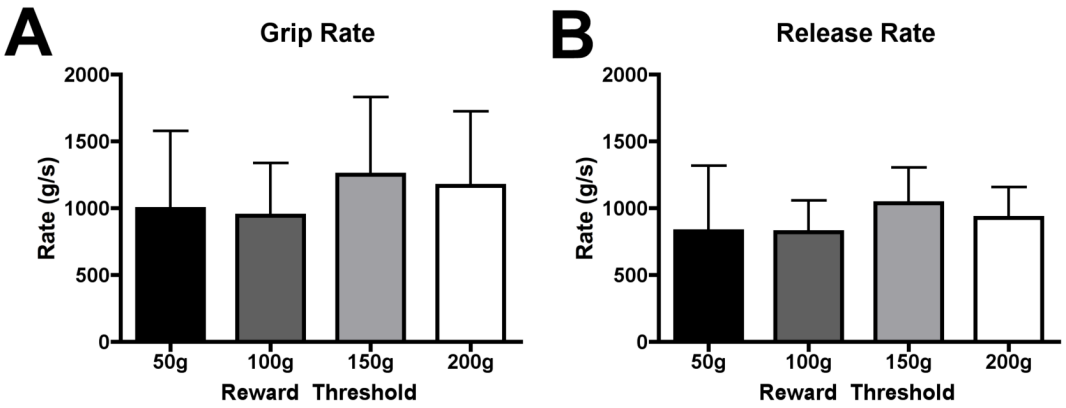

Figure 4.
Mean grip (A) and release rates (B) for all subjects across all reward thresholds. Reward thresholds did not appear to affect either grip or release rates. Data are means ± S.D

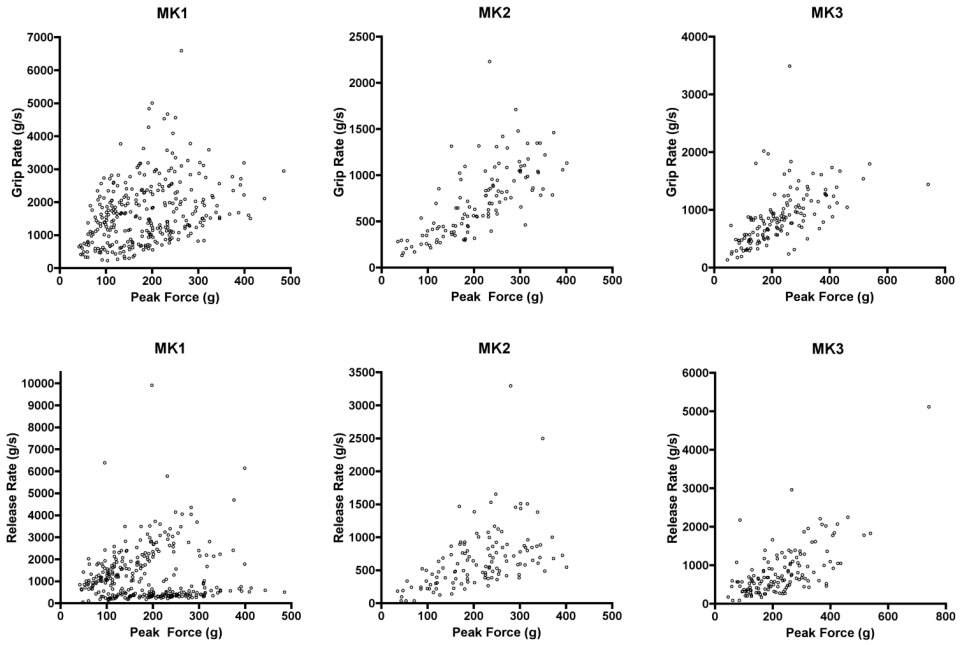

Figure 5.

Peak force versus grip rate (top panels) or release rate (bottom panels) for all three monkeys (all trials from all thresholds plotted). Note that MK1 appears to have two "bands" in both the grip and release scatterplots, perhaps consistent with his behavioral strategy differences compared to MK2 and MK3. Data are means ± S.D.

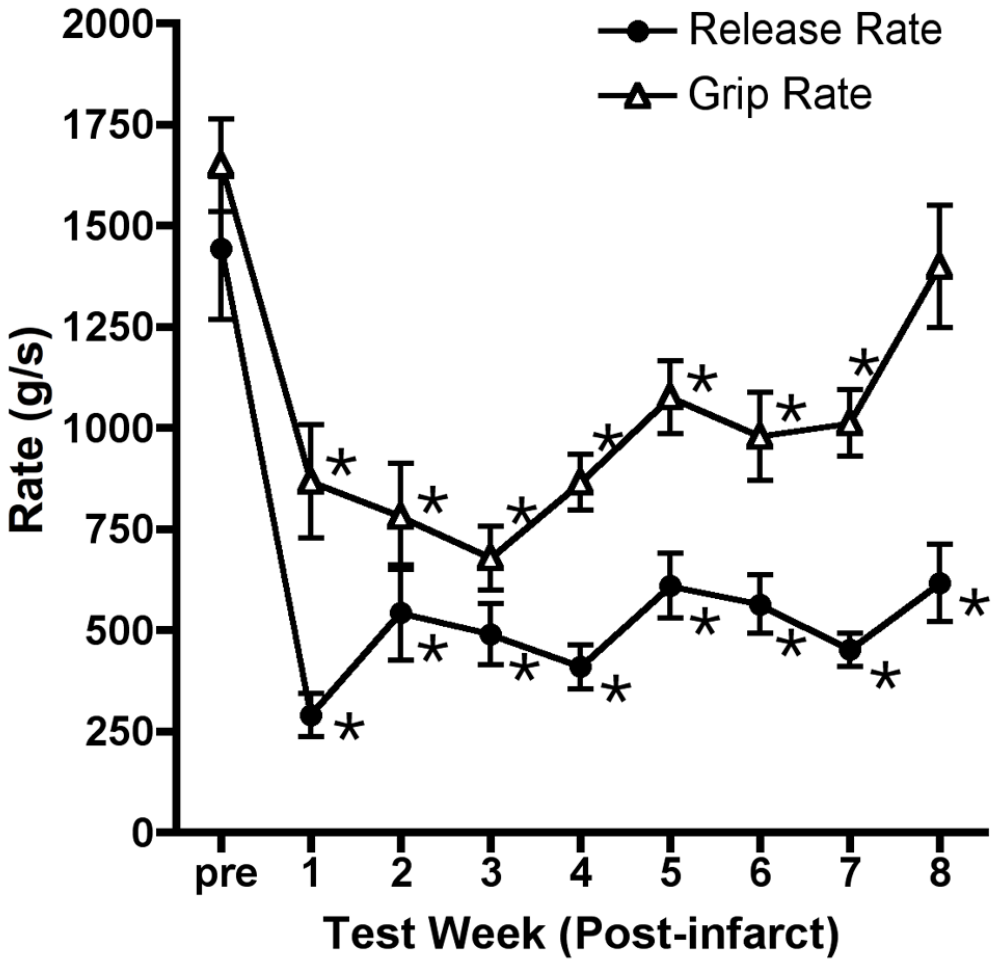

Figure 6.
Grip and release rates for MK1 for 8 weeks after a ischemic infarct in M1. Cortical infarct produced a marked reduction of both grip and release rate, although both rates exhibited gradual recovery over time. Asterisk indicates significant reduction ($p<0.05$) vs. pre-infarct performance. Data are means ± S.E.M