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A Method for Assessing Recovery of Fine Motor Function of the Hand in a Rhesus Monkey Model of Cortical Injury: An Adaptation of the Fugl-Meyer Scale and Eshkol-Wachman Movement Notation.

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Abstract

Motor dysfunction of the upper extremity can result from stroke, cortical injury and neurological diseases and causes significant disruption of activities of daily living. While some spontaneous recovery in terms of compensatory movements does occur after injury to cortical motor areas, full recovery is rare. The distinction between complete recovery and compensatory recovery is important as the development of compensatory movements in the upper extremity may not translate into full functional use in human patients. However, current animal models of stroke do not distinguish full recovery from compensatory recovery. We have developed a Non-Human Primate Grasp Assessment Scale (GRAS) to quantify the precise recovery of composite movement, individual digit action, and finger-thumb pinch in our rhesus monkey model of cortical injury. To date, we have applied this GRAS scale to assess the recovery of fine motor function of the hand in young control and cell-therapy treated monkeys with cortical injury confined to the hand representation in the dominant primary motor cortex. We have demonstrated that with this scale we can detect and quantify significant impairments in fine motor function of the hand, the development of compensatory function during recovery and finally a return to full fine motor function of the hand in monkeys treated with a cell therapy.

Keywords

Grasp Function; Recovery; Motor Function; Rhesus Monkey

Introduction:

Motor dysfunction of the upper extremity, especially the hand, can result from stroke, cortical injury and neurological diseases and causes significant disruption of activities of

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daily living. While some spontaneous recovery does occur after injury to cortical motor areas controlling the hand and digits, full recovery of digit function is rare. Further, the spontaneous recovery that does occur is compensatory in nature and not a complete return to pre-injury fine motor function (Hylin et al. 2017). The distinction between complete and compensatory recovery is important for assessing new treatments for stroke and cortical injury as the development of compensatory movements falls short of full functional use and hence limits normal activities of daily living (Levin et al. 2009; Lum et al. 2009). Therefore, the assessment of the efficacy of new therapies to enhance innate recovery mechanisms and produce a more complete recovery of function needs to involve an assessment scale that can differentiate between compensatory and complete recovery in an animal model with fine motor function similar to humans.

Rodent models of cortical injury are a common model used to assess recovery of motor function. However, rodents do not have precise fine motor function of individual digits which can be mapped and quantified making it difficult to fully assess the effectiveness of treatments in rodents. Alternatively, we have developed a rhesus monkey model of cortical injury that creates a focal cortical lesion limited to the hand representation of primary motor cortex (M1) and results in significant unilateral impairment of the hand and digits. With this model, we have also developed our Non-Human Primate Grasp Assessment Scale (GRAS) to detect and quantify significant impairments in fine motor function of the hand and to evaluate recovery of function of individual digits and precise finger-thumb pinch used by monkeys to retrieval of food morsels (Moore et al, 2012:2013). We developed the GRAS based on the principles of the human occupational therapy Eshkol-Wachman Movement Notation (Carr et al. 1985; Whishaw et al. 2002) and the Fugl-Meyer Motor Assessment scale (Fugl-Meyer, Jaasko, et al. 1975; Fugl-Meyer, Jääskö, et al. 1975) which are both widely used in human clinical populations to assess recovery of motor function.

The Fugl-Meyer Assessment (FMA) scale is a performance-based impairment index designed to assess motor function, balance, sensation and joint function in individuals who have experienced a stroke or cortical injury (Fugl-Meyer, Jaasko, et al. 1975; Fugl-Meyer, Jääskö, et al. 1975; Duncan et al. 1983; Gladstone et al. 2002; Sullivan et al. 2011). The FMA measures five domains (motor, sensory, balance, range of motion, joint pain) on an ordinal scale (0 (severe impairment) – 2 (no impairment)) to produce an overall index of impairment. For our GRAS scale, we adapted from the FMA the measures for the motor domain that quantify voluntary limb movement of the upper extremity (FMA - 33 items; score range, 0 – 66). Specifically, we adapted the sections of the scale that focused on the hand, including finger mass flexion, finger mass extension and maturity of grasp pattern. See Sullivan et al, 2011 for review of the FMA.

The Eshkol-Wachman Movement Notation (EWMN) was developed in the 1950s in Israel by Noa Eshkol and Avraham Wachman as a system to record body movement. The system does not depend on a certain movement style but rather produces an analysis of the spatial and temporal parameters of a movement and the position of body segments relative to other body segments during movement. Our GRAS scale, uses EWMN principles of assessing changes in the relationship between individual segments of the body. For example, in one portion of our scale, we assess the specific relationship of the first digit to the plane of the

palm of the hand. A similar system has also been successfully used in movement studies with macaques (Ottenheimer Carrier et al. 2015).

To date, we have applied our GRAS scale to assess the recovery of fine motor function of the hand in untreated young and young cell-therapy treated monkeys with cortical injury to the hand representation in the dominant primary motor cortex. Specifically, we have demonstrated the sensitivity of the scale to detect and quantify significant impairments in fine motor function of the hand and digits, the development of compensatory function during recovery in untreated monkeys and finally a return to a pre-injury pattern of fine motor function of the digits in monkeys treated with a cell therapy. Here we show that this scale can be used in monkey models of cortical injury and stroke to determine if new therapeutics facilitate full recovery of function, rather than compensatory function. Specifically, we describe, in detail, the methodology for applying this scale for future studies and provide an example of the application of the scale using data from our previously published study.

Materials and Methods:

Subjects:

The data presented in this paper were originally published in Moore et al, 2013 and is being presented here to demonstrate the application of our scale. The subjects were eight behaviorally naive, young male rhesus monkeys (Macaca mulatta) (Table 1). Four monkeys received a cell therapy and four age-matched monkeys received a vehicle control. All of the monkeys were obtained from national primate research facilities or private vendors and had known birth dates and complete health records. Before entering the study, they received medical examinations that included serum chemistry, hematology, urine analysis and fecal analysis. In addition, all monkeys underwent magnetic resonance imaging to ensure there was no occult neurological damage. Results of the medical exams and MRIs revealed that all monkeys were healthy at the time of the study. While on study, monkeys were individually housed in the Animal Science Center (ASC) of Boston University Medical Campus in colony rooms where they were in constant auditory and visual range of other monkeys. The ASC is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) and all animal procedures were conducted in accordance with the guidelines of the National Institutes of Health and the Institute of Laboratory Animal Resources *Guide for the Care and Use of Laboratory Animals* and were approved by the Boston University Institutional Animal Care and Use Committee. Diet consisted of Purina Monkey Chow (Purina Mills Inc, St. Louis, MO), 12–15 biscuits per day, supplemented by fruit and vegetables with feeding taking place once per day, immediately following behavioral testing. During testing, small, visible food reward (M&M's, Mars, Inc) were used as rewards. Water was available *ad libitum*. The monkeys were housed under a 12-hour light/dark cycle with cycle changes occurring in a graded fashion over the course of an hour.

Pre-operative Training on Fine Motor Function Testing:

As described in detail previously (Moore et al. 2010; Moore et al. 2012; Moore et al. 2013), monkeys were trained on tests of fine motor function of the hand using a testing apparatus that controls, quantifies and video records responses from each hand (Figure 1). Using this

apparatus, the monkeys were trained on the Hand Dexterity Task (HDT) for a total of 15 days (Monday, Wednesday and Friday each week for 5 weeks). The HDT requires precise control of the digits, particularly apposition of the thumb and index finger, to retrieve a small, visible food reward (M&M's, Mars, Inc) from two different size round wells in a Plexiglas tray. Food rewards (M&M's, Mars, Inc) were round and approximately 1cm in diameter. Both wells were 1 cm deep. The large well was 25 mm wide and the small well was 18 mm wide. Time to retrieve the food reward was recorded by a timer that was activated by photocells located in the openings on each side of the apparatus (Figure 1). The timer starts when the monkey put a hand through one of the openings, triggering the photocells to start the timer. The timer stops when the monkey removed his hand. The response time to retrieve was recorded and an experimenter recorded whether or not the reward was successfully retrieved. Each test day consisted of 16 trials for each of the two well sizes and for each hand resulting in a total of 32 trials for each hand. The order of trials for each hand and well followed a pseudorandom balanced sequence to eliminate any order effects. Monkeys were given 30 seconds to complete a trial. If they would not complete a trial in 30 sec, the trial was terminated and the monkey was given one additional opportunity to complete that trial. After a second failed attempt, a non-response was recorded, the monkey's difficulties were noted in the study record and the next trial was initiated.

Hand Preference:

At the completion of pre-training on the HDT, free choice trials with both sides of the apparatus baited and accessible are administered to determine which hand is "preferred" for this task. This assessment is also compared with the pre-operative acquisition rates for each hand. Based on this assessment, the cortical injury was targeted to the hand representation of the hemisphere controlling the preferred hand for this task. This helps to ensure that monkeys are motivated to use the impaired hand during post-operative testing.

Electrophysiological Mapping of the Hand Representation in Motor Cortex:

As described in detail in Moore et al, 2010; 2012 and 2013, to create reproducible cortical injury and motor deficits, a craniotomy was made over the central sulcus and the dura was incised to expose the precental sulcus and primary motor cortex. A calibrated photograph of the precental gyrus was then taken and printed. The precentral gyrus was then systematically explored using electrical stimulation delivered through a small monopolar silver ball electrode placed gently on the surface of the pia to evoke movements. During each stimulation, a trained observer noted muscle movements (e.g. distinct movement or twitches of muscle) in specific areas of the digits, hand, forearm or arm, both visually and by palpation. The intensity of the motor response in the hand and digits was graded on a scale of 1 to 5 (barely visible to maximal). Specific stimulation sites with the highest motor response were marked on the calibrated photograph creating a cortical surface map of the hand area that was used to guide placement of the lesion.

Placement of Selective Cortical Injury:

Using the map described above, cortical injury was induced by making a small incision in the pia at the dorsal limit of the mapped representation. A small glass pipette was then inserted under the pia and used to bluntly transect the small penetrating arterioles as they

enter the underlying cortex. Since the hand representation is known to extend down the rostral bank of the central sulcus, the sulcus was then opened down to the fundus along the length of the gyral hand representation by microdissection with a small glass pipette and a blunt periosteal elevator, taking care to leave the somatosensory areas on the caudal bank intact. The pia was then dissected with the glass pipette down to the fundus of the sulcus. This pial dissection of penetrating vessels removes the blood supply to the cortex of the hand representation, inducing degeneration of the gray matter but without physically damaging the underlying white matter. After the lesion was made and any bleeding stopped, the dura was closed, the bone flap was sutured back in place.

Cell Therapy Administration:

To demonstrate the use of this scale with non-human primates, we present data here from a previous study that investigated the potential restorative ability of the investigational cell drug product, CNTO 0007 (Therapy developed by Advanced Technologies and Regenerative Medicine (ATRM); Moore et al, 2013), that contains human umbilical tissue-derived cells (hUTC) in a proprietary thaw and inject formulation called CSCV4. Intravenous administration of CNTO 0007 was completed between 23 and 24 hours following surgery at a concentration of 10M cells / ml and a rate of 0.5ml per minute using a syringe pump to deliver a total dose 10M cells / kg. Vehicle was administered at the same volume and rate (Moore et al. 2013).

Post-operative Testing:

Post-operative testing on the HDT began two weeks after surgery, was conducted on Monday, Wednesday and Friday of each week (32 trials per day), and continued for 12 weeks. Seventy percent of the trials required the use of the **impaired** hand, while 30% were given to the hand controlled by the undamaged hemisphere. The 30% of trials given to the unimpaired hand allow sufficient rewards to be obtained to maintain motivation and sufficient data to demonstrate that effects are not due to generalized changes in motivation or motor function. Each animal was given 30 seconds to complete a trial as in pre-operative training. The forced use of the impaired hand on 70% of the trials is similar in nature to constraint-induced therapy used in human rehabilitation which forces use of the impaired limb(s) (Corbetta et al. 2015; Souza et al. 2015; Kwakkel et al. 2016).

Grasp Pattern Assessment:

All study personnel were blinded to the treatment status for each of the subjects. An initial review of video recordings revealed that compensatory grasp patterns were not effective in the small well, resulting in failure to retrieve the food reward. Therefore, since the goal of the GRAS scale is to distinguish between compensatory grasp and a return to pre-injury grasps patterns, only trials using the large well were used for rating grasp.

Performance on the HDT during pre-operative training and post-operative testing was video recorded with fixed placement cameras (Logitech Pro 9000 Webcam with 2-Megapixel Optical Resolution, Logitech, Newark, CA) fixed directly over the area of the apparatus where each hand retrieved the food reward. The cameras were positioned so that the entirety of each hand could be observed during each trial. Each camera was connected to a MacBook

laptop (Apple, Inc, Cupertino, CA) where the daily videos were saved to the hard drive as well as to an external hard drive.

Pre-operative Performance:

Using QuickTime Player all videos were analyzed by a trained research technician. Starting with day 1 of pre-operative training, each trial for the dominant hand was observed using the slow-motion feature of QuickTime, and for each trial evidence of each of the following were recorded:

1. mass versus isolated digit action
2. amount of thumb opposition observed
3. isolated use of specific digits during the precise pinch grasp

Once the identical grasp pattern was observed for three consecutive trials on a single day, the final trial for that day was analyzed to determine if the same grasp pattern was used. If the grasp pattern on the final trial matched the three consecutive trials, then trials from the next day were analyzed in the same fashion until the identical grasp pattern was observed for 3 consecutive trials over 3 consecutive days. This was then designated as the pre-operative grasp pattern and used as the reference for post-operative grasp recovery.

Post-operative Performance:

Starting with day 1 of the post-operative HDT trials (14 days after the lesion), each trial for the dominant (impaired) hand was analyzed using the slow-motion feature of QuickTime. For each trial, details of each element of the grasp pattern were recorded, including:

1. amount of metacarpophalangeal movement in the dominant hand
2. involvement of the thumb in the grasp
3. use of digits in isolation when obtaining the reward
4. evidence of compensatory grasp patterns (e.g. any grasp that involved the use of multiple digits working together in a “scooping” action) or a return to pre-operative grasp.

As with the pre-operative trials, once 3 consecutive trials with the same grasp pattern were observed, with or without successful reward retrieval, the technician then analyzed the final trial of that testing day. If the final trial was dissimilar to the previous trials analyzed, the technician continued analysis of the remaining trials of that testing day before beginning to analyze trials in the next day. If the grasp pattern on the final trial did match the grasp pattern of the three consecutive trials, then the technician moved to the next testing day and then began analyzing trials on that day until three consecutive trials with the same grasp pattern was again achieved. This pattern was continued for trials throughout the entire post-operative period. A summary of measures listed above for each testing day analyzed was recorded. These summaries were then used to assign a grasp rating for each trial (see next section).

Grasp Assessment Scale:

Using the summaries described above and the corresponding video recordings of testing, the Occupational Therapist then reviewed all data points for each subject to assign a rating for each trial using the GRAS (Table 2) and an overall score was assigned for each testing day. When a subject demonstrated elements of various rating levels on the scale within a single testing date, the lowest scale rating was used for that day. See figure 2 for photographs of grasp patterns that are representative of several scores in the scale.

Results

Post-operative Grasp Assessment:

Figure 3 shows the mean rating on the GRAS each week for individual monkeys in the vehicle control and cell treated groups. Based on this data, the mean number of post-operative days required to reach asymptotic levels of grasp on the large well in HDT with the impaired hand was determined for all monkeys. Asymptotic levels of performance were defined as a grasp assessment score that returned to pre-operative levels (score of 8; functional pinch between thumb and 1 individual digit) for 2 consecutive days. If an animal did not return to pre-operative levels of grasp (score of 8), then the first 2 consecutive days at their highest rating were used as asymptotic performance. In addition, the mean grasp assessment rating across the post-operative period for the HDT and the final grasp rating for each monkey were also calculated and compared between groups.

As shown in Moore et al, 2013, a Student's t-test was used to compare the mean number of post-operative days required to reach asymptotic levels of grasp for the impaired hand between vehicle and cell treated monkeys. This analysis revealed a significant difference between groups on ($t=2.708$, $df=6$, $p\leq0.01$) with treated monkeys showing superior recovery of grasp pattern. (Figure 4)

A Mann Whitney U test revealed a significant difference between groups for the mean grasp rating across the post-operative period. ($U=16$, $p\leq0.01$) (Figure 5). Finally, a Mann Whitney U test revealed a significant difference between groups for the final grasp rating achieved during the post-operative period. ($U=2$, $p\leq0.04$) (Table 2). Taken together, these results demonstrate that monkeys that received a cell therapy following cortical injury, demonstrated a more complete recovery and return to pre-operative grasp pattern. This is further supported by final grasp rating – all 4 monkeys treated with the cell therapy returned to pre-operative grasp patterns while only one untreated monkey reached pre-operative grasp patterns. It is important to note that on the GRAS scale, only monkeys that demonstrated a complete return to pre-operative grasp with no evidence of compensatory pinch action receive a score of 8. The vehicle control monkeys that achieved a rating of 7.5 still showed evidence of compensatory grasp on a subset of trials.

Discussion

Summary:

We have developed a non-human primate Grasp Assessment Scale that allows us to quantify the recovery of grasp function following cortical injury and most importantly, to differentiate compensatory recovery from complete recovery. Using this scale, we have demonstrated that untreated young monkeys show evidence of recovery of function of the hand and digits but did not demonstrate a return to pre-injury grasp patterns (e.g. finger-thumb pinch action) which is considered a complete level of recovery. Instead, they developed compensatory grasp actions that involved use of multiple digits to "scoop" the food reward into the palm of the hand. While this did achieve the goal of retrieving the food reward on our motor task, this type of compensatory grasp, which is often observed in human stroke patients, does not translate into effective fine motor function of the digits that is required for successful completion of activities of daily living. However, in contrast, monkeys that received a cell therapy following cortical injury, did return to pre-injury grasp patterns (e.g. finger-thumb pinch action) demonstrating a complete recovery of function.

Definition of Grasp:

An early study of human grasp was conducted by Napier (NAPIER 1956) that categorized grasp into either power (large areas of contact between object and surface of palm and fingers) and precision (object held with the tips of the fingers and thumb) grasps. This classification was further developed by Cutkosky (Cutkosky 1989) in which grasps were further defined based on the function to be performed and the size and shape of the object to be grasped. Human grasp have also been extensively studied by Jeannerod (Jeannerod 1984) who distinguished between reaching and grasping functions based on velocity, grip size and the size of object to be grasped. Building on this work, researchers at Yale University, Otto Bock Health Care and the KTH Royal Institute of Technology, Stockholm recently developed a taxonomy to describe types of human grasp and the properties of each grasp type (Feix et al. 2016). They define human grasp as "every static hand posture with which an object can be held securely with one hand" and in their review of literature identified 33 grasp types. They arranged these 33 grasp types into a taxonomy based on 1) the need for power or precision in grasp, 2) the directions that the hand can apply force (palm, pad or side opposition), and 3) the functional unit of fingers working together (e.g. called the virtual finger) and finally 4) the position of the thumb during a grasp. Their classification also takes into consideration the size and shape of the object being grasp and has a secondary level of classification for more precise descriptions of grasp patterns. Based on their taxonomy, the grasp we are measuring in our monkeys is the "palmar pinch" which is a precision grasp that involves single finger opposition to the pad of the thumb and abduction of the thumb (Feix et al. 2016). This type of grasp is highly prevalent in humans and represents a high level of precision in fine motor function and therefore recovery after damage to this type of grasp would represent significant recovery of function following cortical injury.

While human grasp parameters have been extensively studied and several taxonomies of grasp patterns have been proposed, there have been limited investigations of grasp patterns

in monkeys (Roy et al. 2000; Castellanos et al. 2015). However, one study conducted using rhesus monkeys measured kinematics of reaching and grasping and compared their findings to human grasp taxonomies (Roy et al. 2000). They distinguished reaching (the transport of the hand to the vicinity of the object to be retrieved) from grasping (the hand configuration to ensure accurate prehension) in humans. Then they examined the kinematics of unconstrained reaching and grasping in two monkeys and demonstrated that grasp patterns in the monkey were highly similar to human grasp patterns. They concluded that monkey grasp functions can serve as a valuable model for investigating motor function of the hand in humans (Roy et al. 2000). This provides support that our model for assessing fine motor function of the hand following cortical injury in the rhesus monkey with various treatments will be translatable to human studies.

Fine Motor Functions Assessed by the Grasp Assessment Scale:

Similar to the studies described above, our Grasp Assessment Scale measures several components of grasp which can be assessed in the intact hand (e.g. pre-operative baseline performance) and then in the impaired hand (eg. post-operative recovery of function). First, our scale measures whether an attempt to use the impaired hand occurs during a trial. Second, if a response is attempted measures the degree of flexion and extension of the digits as a group as well as the degree of flexion in the metacarpophalangeal (MP) joint. Third, it documents for each trial whether the digits move together in a mass action or if there is individual digit movement and how close this comes to complete recovery. Fourth, movement of the thumb is also documented for each trial along with notation of the presence of a functional pinch. Finally, the presence or absence of compensatory movements (i.e. typically the use of one or more fingers to scoop the object into the palm of the hand) is determined. As described in the Methods section, these parameters are determined for individual trials on consecutive days of testing their composite enables determination of the level of recovery.

Comparison with Similar Scale:

Pizzimenti et al, 2007, used a similar task to our HDT and also video recorded the performance of monkeys completing the task. They analyzed the performance of each monkey based on six criteria: 1) reach duration (time from cage to pellet or board), 2) manipulation duration (time from initial pellet contact until pellet is acquired or attempt is abandoned); 3) number of “contacts” (defined as 1 + the number of times contact between the digit and pellet is broken during manipulation); 4) accuracy (distance from index finger to pellet at time of contact with the board); 5) grip aperture (distance between the fingertip and thumb tip at time of contact with the board); and 6) whether the trial was a success (pellet acquired and lifted from the board), failure (pellet not acquired), or no attempt was made to retrieve the pellet. These measures were used to determine the extent of recovery (Pizzimenti et al. 2007). Our model, with the use of the GRAS, builds on this work and expands it to include the ability to distinguish between compensatory action and complete recovery, which is critical for assessing the efficacy of new therapeutics in human stroke patients.

Non-human Primate versus Rodent Models of Cortical Injury:

The majority of studies investigating treatments for stroke and cortical injury use rodents. However, since rodents do not have the same degree of individual digit functionality as monkeys and humans, the full extent of fine motor recovery cannot be easily quantified. Further, while a large number of therapeutic agents that have been tested in these rodent models do show efficacy, the positive effects have not translated to humans. Of 1,206 neuroprotective treatments collated in 2006, none have made it to a successful clinical trial (O'Collins et al. 2006). The basis for this difference is likely in part a difference in the underlying biology between rodents and humans and suggests that the response to injury in the rodent may be different than that in the primate. Our NHP model of cortical injury is a well-controlled and minimally variable model that has been tested and validated in our laboratory and used to assess various therapeutic agents (Moore et al. 2012; Moore et al. 2013; Moore et al. 2016). Results have consistently found that focal injury to the hand representation of motor cortex produces a well-characterized deficit in fine motor function, which is very similar to that seen in human stroke patients. Similar to the human condition, fine motor function in the monkey following injury does recover to some degree without treatment but largely as the result of functional compensation (Moore et al. 2012). However, monkeys in our model that have been treated with a cell therapy do demonstrate, as quantified with our GRAS scale, a more complete, full recovery that should be the endpoint for recovery that investigations of future therapeutics strive to reach.

Conclusions:

We have demonstrated that our Grasp Assessment Scale can quantify recovery of fine motor function of the hand and distinguish between compensatory recovery and full recovery of function in the non-human primate model of cortical injury. This model and the use of the GRAS scale are highly translatable and can be utilized to determine the efficacy of new therapeutic agents to produce a more complete level of recovery of function following cortical injury.

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Abbreviations:

NHP	Non-human Primate
GRAS	Grasp Assessment Scale
M1	Primary Motor Cortex
FMA	Fugl-Meyer Assessment
EWMN	Eshkol-Wachman Movement Notation
HDT	Hand Dexterity Task

hUTC	human umbilical tissue-derived cells

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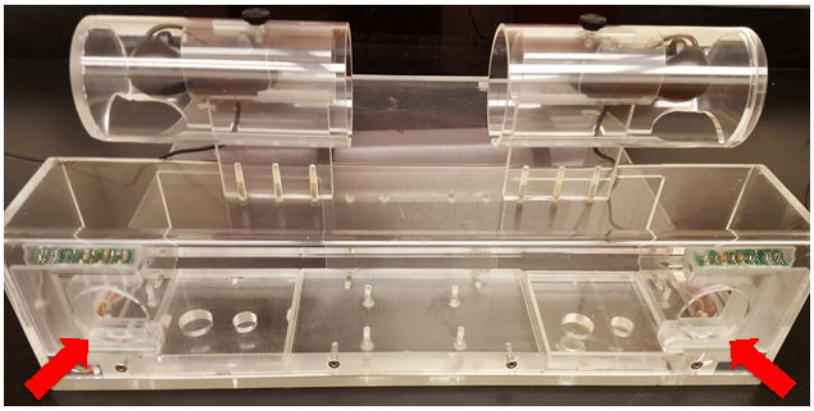

Figure 1.

A photograph of the plexiglass testing apparatus used to administer the Hand Dexterity Task (HDT). The red arrows indicate the right and left openings that the monkey must put the appropriate hand through in order to retrieve the food reward from the wells in each tray.

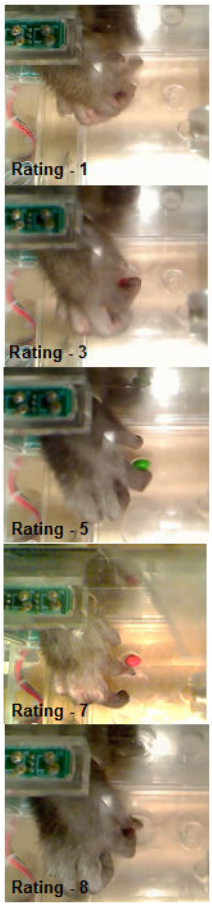

Figure 2.
Representative images of grasp patterns that represent various rating stages in the Grasp Assessment Scale.

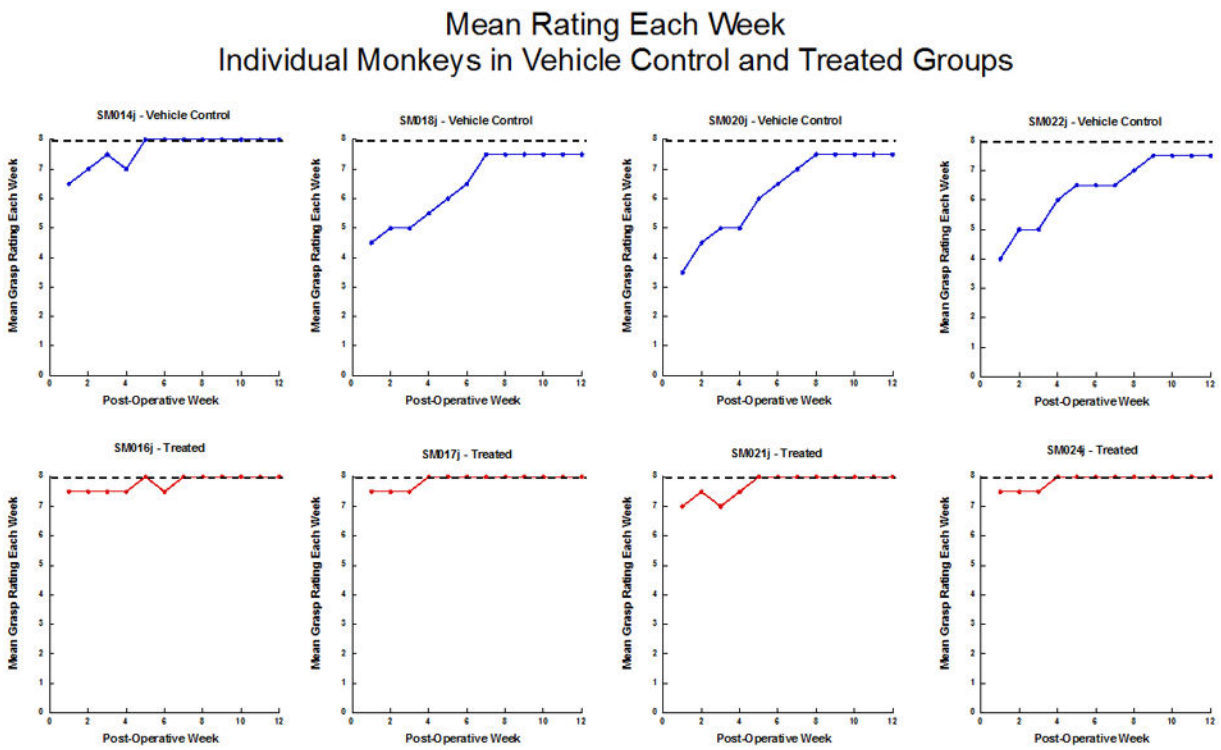

Figure 3.
Graphs showing the mean grasp rating each week for individual monkeys in each group.

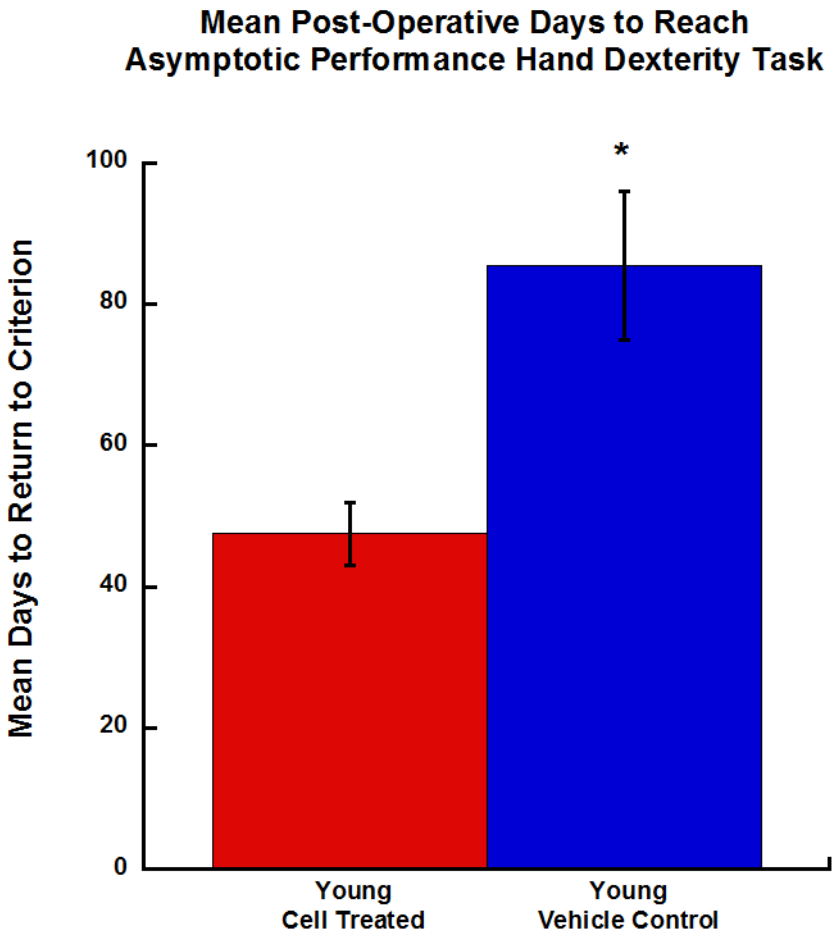

Figure 4.

This graph shows the mean number of post-operative days to reach asymptotic performance on the Hand Dexterity Task using the Grasp Assessment Scale for monkeys that received a cell therapy or vehicle control. $p \leq 0.01$, Errors bars = Standard Error

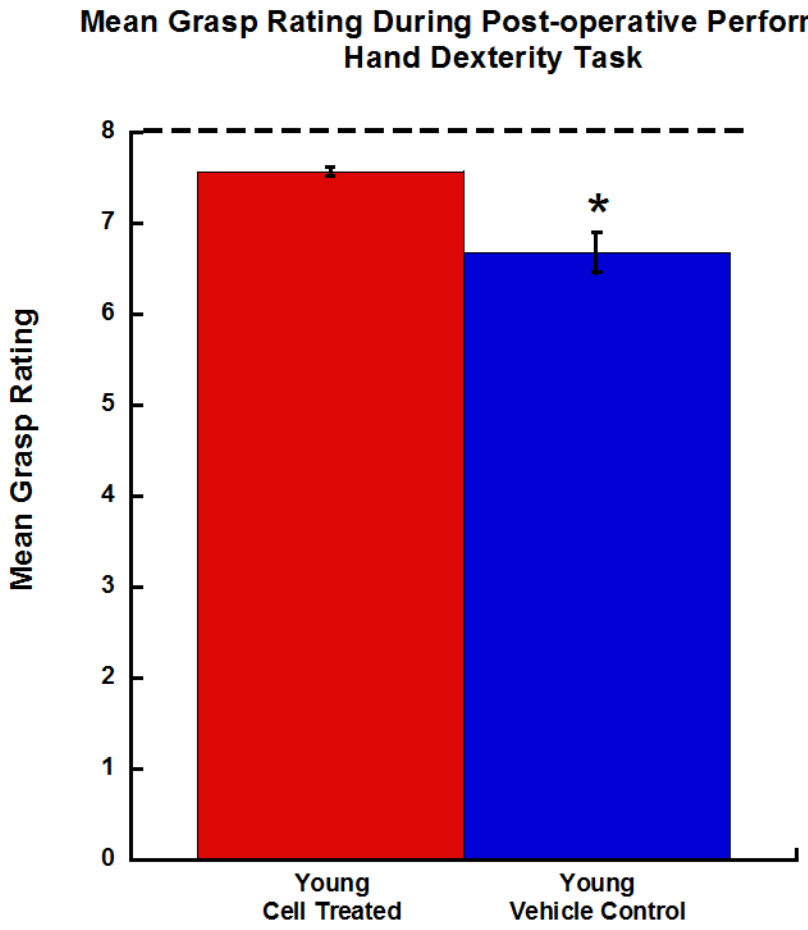

Figure 5.

This graph shows the mean grasp rating across the post-operative period on the Hand Dexterity Task using the Grasp Assessment Scale for monkeys that received a cell therapy or vehicle control. $p \leq 0.01$, Errors bars = Standard Error

Table 1

Information about each monkey described in this study and individual data on the Grasp Assessment Scale. The mean number of days to reach an asymptote rating on the GRAS scale, mean grasp rating on the GRAS across the entire post-operative period and the final grasp rating on the GRAS are listed for each monkey.

Monkey	Group	Sex	Age at Death	Mean # of Days to Reach Asymptote	Mean Grasp Rating Across Post-operative Period	Final Grasp Assessment Rating
SM016j	Young, Cell Therapy	M	7.58	56.00	7.62	8.00
SM017j	Young, Cell Therapy	M	6.00	35.00	7.57	8.00
SM021j	Young, Cell Therapy	M	8.92	51.00	7.42	8.00
SM024j	Young, Cell Therapy	M	9.58	48.00	7.65	8.00
			Mean	**47.50**	**7.57**	**8.00**
			SD	**8.96**	**0.10**	**0.00**
			SE	**4.48**	**0.05**	**0.00**
SM014j	Young, No Treatment	M	5.92	54.00	7.33	8.00
SM018j	Young, No Treatment	M	6.92	96.00	6.54	7.50
SM020j	Young, No Treatment	M	6.67	96.00	6.42	7.50
SM022j	Young, No Treatment	M	8.08	96.00	6.42	7.50
			Mean	**85.50**	**6.68**	**7.63**
			SD	**21.00**	**0.44**	**0.25**
			SE	**10.50**	**0.22**	**0.13**

Table 2

Grasp Assessment Scale

0	Complete absence of active finger movement and makes no attempt to use impaired hand to test.
1.0	Attempts to use impaired hand/digits to retrieve food reward No flexion and extension of digits either singly or as a group. Unsuccessful at retrieving any food rewards.
2.0	Attempts to retrieve Flexion and extension of digits as a group Less than 15 degrees of digit MP flexion No evidence of the purposeful “scooping” of reward. No movement of thumb towards palm No evidence of isolated digit movement Unsuccessful at retrieving any food rewards
3.0	Attempts to retrieve Flexion and extension of digits as a group Less than 15 degrees of digit MP flexion Development of compensatory “scooping” movement of reward toward palm No movement of thumb towards palm Multiple fingers and mass action of digits No functional pinch present Successful retrieval of food reward on at least 10% of trials.
3.5	Attempts to retrieve Flexion and extension of digits as a group Less than 15 degrees of digit MP flexion Development of compensatory “scooping” movement of reward toward palm No movement of thumb towards palm Multiple fingers and mass action of digits No functional pinch present Successful retrieval of food reward on at least 25% of trials
4.0	Attempts to retrieve Flexion and extension of digits as a group Greater than 15 degrees of digit MP flexion Purposeful compensatory “scooping” movement of reward toward palm No movement of thumb towards palm Multiple fingers and mass action of digits No functional pinch present Successful retrieval of food reward on at least 25% of trials.
4.5	Attempts to retrieve Flexion and extension of digits as a group Greater than 15 degrees of digit MP flexion Purposeful compensatory “scooping” movement of reward toward palm Movement of thumb observed during testing session Multiple fingers and mass action of digits No functional pinch present
5.0	Attempts to retrieve Flexion and extension of digits as a group Greater than 15 degrees of digit MP flexion. Purposeful compensatory “scooping” movement of reward toward palm Movement of thumb towards palm with a web space no greater than one digit width. Thumb does not reach opposition. Multiple fingers and mass action of digits No functional pinch present Successful retrieval of food reward on at least 50% of trials
5.5	Attempts to retrieve Flexion and extension of digits as a group Greater than 15 degrees of digit MP flexion Purposeful compensatory “scooping” movement of reward toward palm Multiple fingers and mass action of digits Thumb in opposition. No functional pinch present Successful retrieval of food reward on at least 50% of trials
6.0	Attempts to retrieve Reaches with all digits in extension Evidence of isolated individual finger movement (least 10% of trials per day) Purposeful compensatory “scooping” movement of reward toward palm

	Mass movement of digits still predominates Thumb in opposition No functional pinch present Successful retrieval of food reward on at least 75% of trials
6.5	Attempts to retrieve Reaches with all digits in extension Evidence of isolated individual digit movement (25% of trials per day) Purposeful compensatory “scooping” movement of reward toward palm Mass movement of digits still predominates. Thumb in opposition No functional pinch present Successful retrieval of food reward on at least 75% of trials
7.0	Attempts to retrieve Reaches with all digits in extension Evidence of isolated individual digit movement (50 % of trials per day) Purposeful compensatory “scooping” movement of reward toward palm becoming less predominant. Isolated movement of digits predominates Thumb in opposition Functional pinch present in < 25% of trials Successful retrieval of food reward on 100% of trials.
7.5	Attempts to retrieve Reaches with all digits in extension Evidence of isolated individual finger movement (> than 50 % of trials) Purposeful compensatory “scooping” movement of reward toward palm less than 25% of trials Isolated movement of digits predominates Thumb in opposition Functional pinch present in < 25% of trials Successful retrieval of food reward on 100% of trials.
8.0	Attempts to retrieve Pre-operative movement pattern of all digits and hand is observed No evidence of compensatory “scooping” movements Isolated movement of digits predominates Thumb in opposition Functional pinch present in all trials