The Marmoset as a Model System for Studying Voluntary Motor Control

Jeff Walker,[1] Jason MacLean,[1,2] Nicholas G. Hatsopoulos[1,3]

[1] Committee on Computational Neuroscience, University of Chicago, Chicago, Illinois, 60637

[2] Department of Neurobiology, University of Chicago, Chicago, Illinois, 60637

[3] Department of Organismal Biology and Anatomy, University of Chicago, Chicago, Illinois, 60637

Received 4 July 2016; revised 6 October 2016; accepted 7 October 2016

ABSTRACT: **The common marmoset has recently gained interest as an animal model for systems and behavioral neuroscience. This is due in part to the advent of transgenic marmosets, which affords the possibility of combining genetic manipulations with physiological recording and behavioral monitoring to study neural systems. In this review, they will argue that the marmoset provides a unique opportunity to study the neural basis of voluntary motor control from an integrative perspective. First, as an intermediate animal model, the marmoset represents an important bridge in motor system function between other primates, including humans, and rodents. Second, due to the marmoset's small brain size and lissencephalic cortex, novel electrophysiological and optical recording technologies will allow an integrative study of cortical function at multiple spatial scales beyond that afforded by other non-human primate models. Finally, as a primate expressing an ancestral state of corticospinal organization, the marmoset offers the possibility of understanding the integrative function of cortical and spinal interneuron circuitry in isolation of more recent corticomotoneuronal elaborations. If the potential of the marmoset as a model species is to be realized, they will need to learn to work with their natural behavioral repertoire. They have concluded by considering practical aspects of studying motor systems with marmosets.** Develop Neurobiol 77: 273–285, 2017

Keywords: **motor control; marmoset; motor cortex; corticospinal tract; spinal interneuron**

INTRODUCTION

The common marmoset offers an opportunity for an integrative study of motor systems. In this review we will demonstrate three ways in which marmosets provide such an opportunity. First, in terms evolution, marmosets diverged from humans around 33 million years ago (MYA), between that of rats and mice (~96 MYA), and macaque monkeys (~23 MYA), a few of the most widely used model species in the study of motor systems (Nei and Glazko, 2002). As a result, marmosets provide a central point of comparison for understanding principles of motor system organization integrated across species. Second, the marmoset's small size and relatively lissencephalic cerebral cortex allows for recordings of populations of neurons both across multiple cortical areas with multielectrode arrays and within a given area or cortical column by densely sampling populations using optical imaging approaches. The intersection of these neuroanatomical facts and recording capabilities will allow us to interpolate between multiple cortical fields and the scale of a single cortical column to dramatically enhance our understanding of motor cortical function. The third opportunity offered by the marmoset is to enhance our understanding of the integration of descending signals by spinal interneurons,

---

Correspondence to: J. Walker (walkerjd@uchicago.edu).

DOI 10.1002/dneu.22461

as the majority of the marmoset's corticospinal terminations ramify in lamina XII of the spinal cord. Moreover these populations of neurons will become identifiable using genetic tools making the marmoset a unique tool to uncover the principles of corticospinal engagement that provide a foundation for voluntary movement.

Goal directed voluntary movements, such as reaching to grasp, depend on coordination of many areas across frontal and parietal cortex (Kalaska et al., 1997). Only through studying the intracortical communication among these areas as motor behaviors unfold can we hope to gain an integrative understanding of the cortical motor system. Technical challenges often limit the ability to record from populations of individual neurons across many cortical areas in macaques. The marmoset's smaller, smoother brain allows an electrode array, which can only record from a portion of a given area in a macaque, to record from multiple areas in a marmoset. The marmoset's relative lack of sulci makes almost the entirety of the cortical motor system accessible to optical imaging techniques that allow for recordings at sampling densities not previously available in the study of primate cortical motor systems. The combination of these neuroanatomical features and technologies for recording single cell activity at different scales and sampling densities promises an unprecedented capacity to bridge our understanding of the cortical motor system across multiple cortical areas with our understanding of cortical computation as implemented at the scale of an individual cortical column. While exciting, a pure focus on the cortical components of the motor system would neglect fundamental components on which cortical control of movement is built.

The cortical motor system supporting voluntary movement is intimately woven with the subcortical structures like the thalamus (Sherman and Guillery, 2013), basal ganglia (Hoover and Strick, 1999; Miyachi et al., 2006; Akkal et al., 2007), cerebellum (Dum and Strick, 2002; Kelly and Strick, 2003; Akkal et al., 2007; Lu et al., 2007; Bostan et al., 2013; Kipping et al., 2013; Proville et al., 2014) and brain stem nuclei (Kuypers and Lawrence, 1967; Kuypers, 1981; Esposito et al., 2014). Further, without the neural structures of the spinal cord and its descending pathways the brain would have no access to the musculoskeletal system of most of the body and a severely limited capacity to produce motor behaviors. Many of the descending pathways connecting the brain and spinal cord are common to all mammals investigated so far. In addition to the structures comprising the vertebrate plan (the reticular formation, the vestibular nuclei and the interstitial nucleus), the mammalian plan includes descending projections from the following: the nucleus of the descending trigeminal tract, the Raphe complex, the nucleus of the solitary tract, the hypothalamus, the red nucleus and the deep cerebellar nuclei (Nudo and Masterton, 1988). Any satisfying account of the primate motor system will need to be an integrative account that considers how all of these neural and musculoskeletal structures come together to support skillful motor behavior. For a broader discussions of the motor system homologies across species see Lemon and Griffiths (2005) and Nudo and Frost (2007). In what follows, most of our discussion will be about the corticospinal system as these are the most well studied components of the marmoset motor system and probably the areas within which there will be most divergence across mammalian taxa. We will begin with a review of what is known about the organization of the marmoset motor system and finish by suggesting that its eccentricities make the marmoset well suited as a model system for providing a more integrative understanding of the motor system.

MOTOR SKILL AND DEVELOPMENT

To provide context for the organization of the motor system let us briefly introduce the marmoset motor behavioral repertoire. See Schultz-Darken et al., (2016) and Wang et al., (2014) for a more comprehensive account of marmoset motor behavioral development. Marmosets live in multigenerational family groups where care of young is a shared among family members. For their first five weeks of life, newborns are carried on the bodies of family members. As of its first week after birth, a newborn marmoset will be able to grasp, hang, and right itself after being placed on its back (Wang et al., 2014). During the next four weeks of its life, it will begin to climb and cling to vertical posts. By week eight, the newborn marmoset will essentially have acquired all of the motor behaviors of an adult and begin acquiring food on its own. An adult marmoset will spend more than a third of its active hours leaping, climbing and galloping through trees and vines, foraging and visiting gouge holes to feed on tree-exudates that seep out of these holes (Francisco et al., 2014; Abreu et al., 2016). Additionally they will catch diverse small prey with a range of strategies (Schiel et al., 2010). They can move with great speed and agility, and are capable of remarkable acrobatic feats as they range through the canopy. Generally marmosets will rest on all four limbs, but will sit up on their hind limbs when grooming. Their hands are examples of the simplest primate hand (Napier and Napier, 1967). Though capable of adept prehension, they do not have opposable thumbs and lack the capacity for precision grip. Additionally they do not have the capacity for relatively independent finger movements. They are not known to use tools in the wild but have been taught to use tools in the laboratory (Yamazaki et al., 2011). For a more comprehensive treatment of marmoset ecology and behavior see Sussman and Kinzey (1984).

CURRENT AND COMPARATIVE UNDERSTANDING OF THE MARMOSET MOTOR SYSTEM

While a complete description of the marmoset motor system would include a description of those structures that comprise the common mammalian plan for descending control, the majority of the efforts to understand the marmoset motor system have focused on its cortical components. As a result, the discussion that follows will focus on these components. It will proceed from an introduction of the cortical areas giving rise to the corticospinal tract to a description of the organization of that tract in marmoset (Nudo and Masterton, 1990). Beginning in the early 1990s, Krubitzer and colleagues (Krubitzer and Kaas, 1990; Huffman and Krubitzer, 2001a,b) began mapping the organization of the somatosensory cortex of marmoset monkeys. These studies were part of a larger effort to understand the principles guiding cortical field organization. This work has provided the basis for what we know about marmoset somatosensory cortex and its intracortical and thalamic projections. This work suggests that the cortical fields of the marmoset anterior parietal cortex, namely area 3a, 3b, 1, and 2, are homologous with those of macaques. Further, they are both elaborations on a basic mammalian cortical field organization shaped by strong constraints on mammalian nervous system evolution dependent on distributions of transcription factors, gene regulatory networks and early experience of developing organisms (Krubitzer and Seelke, 2012).

Since these initial mappings of the marmoset somatosensory cortex, the topography of the marmoset cortical and thalamic motor systems has been mapped by electrical stimulation and tracer studies (Krubitzer and Kaas, 1990; Huffman and Krubitzer, 2001a,b; Burish et al., 2008; Burman et al., 2008, 2014a, 2015) that have been reviewed by Bakola et al., (2014). These studies have found that the gross organization of the cortical motor system of marmosets (Fig. 1) is similar to that of both macaques and humans. For instance, as with both humans and macaques, marmosets possess an electrically excitable strip of agranular cortex, the primary motor cortex (M1), within which movements of hind limb, torso, upper limb, and face can be elicited by stimulation of the cortex along a medial to lateral progression. Differences across species may however arise at a finer scale. For instance, there is evidence for a more fine-grained structure within the upper limb area of M1 in both macaques (Kwan et al., 1978; Park et al., 2001) and humans (Meier et al., 2008) such that distal representations of the wrist and fingers form a central core surrounded by a representation of the proximal segments of the elbow and shoulder. In contrast, in marmosets, there seems to be no clear proximo-distal organization of the upper limb representation at the scales examined so far.

Marmosets generally show less differentiated cortical fields than macaques and humans. In fact, Burman et al. (2008) suggest that the marmoset provides a model species with the constituents of anthropoid primate cortex in their simplest form. In macaques, rostral and caudal subdivisions of M1 have been described such that the caudal portion situated within the anterior bank of the central sulcus contains a greater density of corticomotoneurons with projections terminating in the motor pools of the cervical spinal cord (Rathelot and Strick, 2009). A rostro-caudal subdivision of M1 has also been suggested on the basis of stronger proprioceptive input to the rostral portion of M1, and stronger cutaneous input to the caudal part of M1 (Strick and Preston, 1982; Picard and Smith, 1992). Additional evidence for a rostro-caudal subdivision of macaque M1 comes from observations of differences in the densities of input from basal ganglia and cerebellum through the ventrolateral thalamic nuclei (Holsapple et al., 1991). Current evidence suggests that corticospinal termination on motoneurons is relatively rare or absent in marmosets (Kondo et al., 2015). So it seems unlikely that there would be great enough variation in the distribution of these characteristics across motor cortex to justify a rostro-caudal differentiation of M1 on such grounds in marmoset.

Within somatosensory cortex (SI) immediately caudal to M1, area 3a receives deep muscle afferent signals conveying proprioceptive information about limb state (Jones and Porter, 1980). Studies have demonstrated projections from area 3a to M1 in macaques (Huerta and Pons, 1990). Recent work done in marmosets has identified significant intracortical projections from 3a to M1 using retrograde tracers (Burman et al., 2014a). Within the cortex of both macaques and humans, area 3a is buried within the

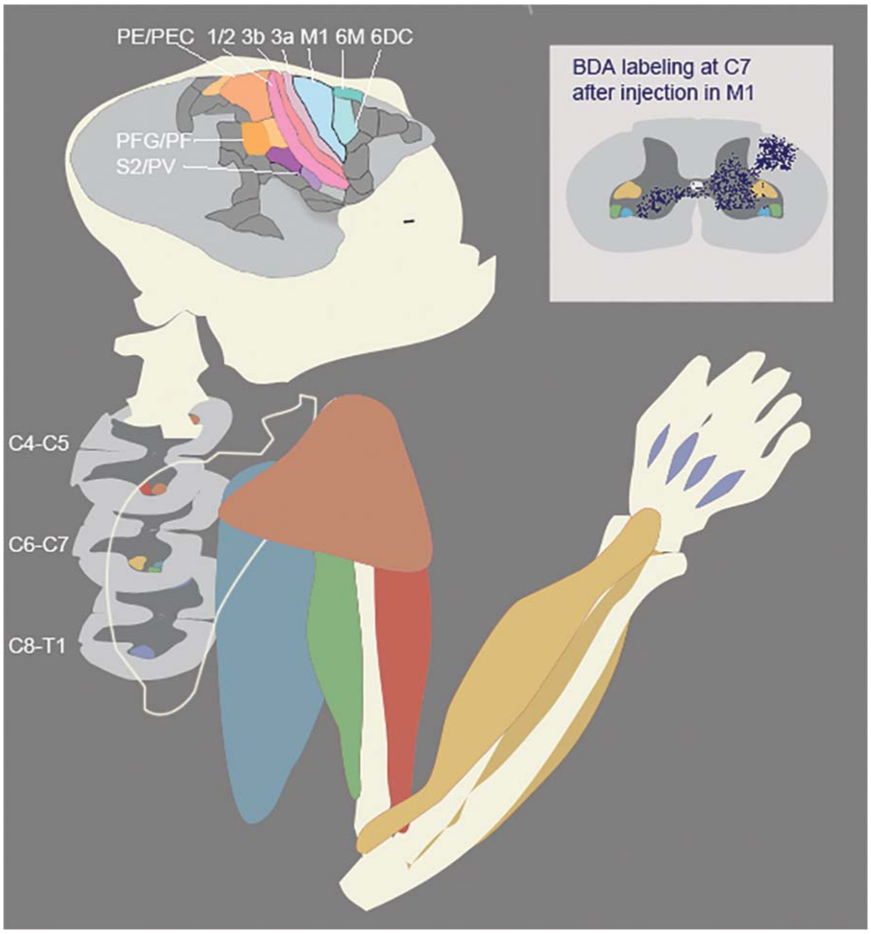

Figure 1 Summary of the current understanding of the corticospinal organization of the marmoset motor system. Colored cortical areas are those that contribute greater than 5% of afferent projections to the upper limb area of primary motor cortex in at least two of the cases investigated by Burman et al., 2014a, b. Dark grey cortical fields represent those areas in which cells projecting to M1 were found in any of the cases described by Burman et al., 2014a, b. Brachial spinal segments illustrated with motor pools colored according to their corresponding upper limb musculature as described by Watson et al. (2015), see text for details. Inset: Illustration of BDA labeling at C7 after injection in M1 as in Kondo et al. (2015). [Color figure can be viewed at wileyonlinelibrary.com]

central sulcus (Krubitzer et al., 2004). This location has made it relatively difficult for investigators to access area 3a with electrophysiological recordings. In contrast, area 3a sits on the cortical surface of the marmoset brain and is accessible to both single and multielectrode recording approaches (Huffman and Krubitzer, 2001a). In fact, the first mapping of the entire somatotopic representation of deep sensory receptors in area 3a of any primate was done in the marmoset due to its lissencephalic cortex (Huffman and Krubitzer, 2001a). Both marmosets and macaques also contain area 3b, caudal to area 3a, that responds to cutaneous stimulation and contains a somatotopic organization of the entire body that mirrors that of both M1 and area 3a (Krubitzer and Kaas, 1990).

The premotor areas of the marmoset have been mapped using cytoarchitectonic characteristics, and the afferent projections to areas 6DC, 6DR, 6Va and 8C have been investigated using tracer injections (Burman et al., 2006, 2014b, 2015; Bakola et al., 2014). Areas 6DC and 6DR both receive afferents from the anterior and lateral ventral complexes of the thalamus, and both receive substantial input from the medial premotor cortex (Burman et al., 2014b). These thalamic connections within the marmoset were found to be largely consistent with those between thalamus and premotor cortex of macaque as described by Matelli et al., (1989). Based on their patterns of connections with other cortical and thalamic areas (Burman et al., 2014b) conclude that there is a strong similarity between dorsal premotor areas 6DC and 6DR with the rostral and caudal subdivisions of dorsal premotor cortex identified in macaques (Barbas and Pandya, 1987).

Some interesting differences do appear within marmoset parietal areas (Bakola et al., 2014). A well-differentiated somatosensory area 2 does not seem to be present in the marmoset. Instead, Paxinos et al., (2012) have defined an area 1/2 in marmosets suggesting that it likely incorporates homologs of both area 1 and area 2 of other primates (Padberg et al., 2007). In macaque and cebus monkeys, a distinct area 2 is present and contains somatotopically-organized sensitivities to both cutaneous and deep muscle stimulation (Padberg et al., 2007). Single and multi-unit recordings in posterior parietal area 5 of macaque monkeys show sensitivity to both cutaneous and deep muscle stimulation of the hand and arm (Padberg et al., 2007) and implicate it in coordinate transformations during reach preparation (Bremner and Andersen, 2014). With its prominent projections to M1 and 6DC, posterior parietal area PE should draw greater interest from investigators of the cortical contributions to motor control, but it is unclear to what extent marmoset area parietal PE and adjacent area PF/PFG might be homologous to macaque posterior parietal area 5 (Bakola et al., 2014; Burman et al., 2014b).

The marmoset spinal cord has all of the features typical of a mammalian spinal cord. Watson et al., (2015) divided the cord both anatomically and functionally based on identifying the lateral motor column and the preganglionic column by staining for cholinergic neurons using acetylcholinesterase histochemistry and acetyltransferase immunohistochemistry. They found their subdivisions based on the distributions of cholinergic neurons to be in accord with subdivisions of mouse and chicken spinal cord-based *Hox* gene expression during development (Dasen et al., 2003). The motor neuron pools of the marmoset spinal cord are arranged in the musculotopic organization characteristic of other primates (Fig. 1) (Watson et al., 2015). Though there is some inter- and intra-specific variation in the extent of the brachial spinal cord, specifically whether it spans from C4 to C8 or C5 to T1, the motor pools are similarly distributed throughout. In the most rostral segments, there are two main motor pools: a ventrolateral pool innervating the deltoids and a dorsolateral pool innervating the biceps. In the more caudal segments of the brachial cord there are four major motor neuron pools: two dorsal groups, one lateral innervating the forearm extensors, and one medial group innervating the forearm flexors; and two ventral groups, one medial innervating the pectoral muscles and one lateral innervating the triceps. In the caudal most segment of the brachial spinal cord, the motor pools come together into a single group of motoneurons innervating the hand. This proximodistal organization of the motor neuron groups in the brachial spinal cord of the marmoset is very similar to that of the macaque monkey (Jenny and Inukai, 1983), cat, rat, and mouse (McHanwell and Watson, 2009) suggesting that the organization of the motor pools is highly conserved across mammals.

Much of what we know about the contributions of motor cortical areas to upper limb movements comes from work with macaques. A great deal of effort over the last half century has been put toward answering the general question of what do cells in motor cortex encode. This work began in the 1960s with the demonstration of a relationship between the activity of cells recorded from M1 in macaques and the force produced during voluntary movements (Evarts, 1968). This work continued in the 1980s with studies in which macaques made two-dimensional reaching movements while single cells were recorded from the motor cortex (Georgopoulos et al., 1986). Motor cortical cells were found to exhibit directional tuning. These cells had higher firing rates when the animals moved their arms in certain directions rather than others and this activity could be well modeled by cosine tuning curves. Subsequent to these initial investigations, this basic result was extended to three dimensional reaching (Georgopoulos et al., 1988), and these functional tuning preferences have been mapped across the motor cortex (Georgopoulos et al., 2007). In addition to force exerted during voluntary movement (Evarts, 1968) and movement direction (Georgopoulos et al., 1986) the activity of motor cortical cells in macaques has been found to correlate to some degree with almost any conceivable movement parameter (Aflalo and Graziano, 2007).

We know next to nothing about the cortical basis of upper limb movements in behaving marmosets. While there has been pioneering neurophysiological studies of the auditory and visual systems of behaving marmosets (Wang et al., 2005; Eliades and Wang, 2008; Roy and Wang, 2012; Mitchell et al., 2014; Mitchell and Leopold, 2015), we have yet to characterize the functional properties of cortical motor areas within the context of actual behavior. Our knowledge of the organization of the motor cortical system contributing to upper limb control has been limited to mapping cortical fields associated with motor control using intracortical microstimulation in anesthetized preparations, tracer injections and cytoarchitectonic characterization (see Bakola et al., 2014 for a review). However, a few studies have assessed motor deficits in stroke or spinal cord injury models (Iwanami et al., 2005; Fujiyoshi et al., 2007).

Looking beyond the cortical components of the motor system, a recent electrophysiological and histological study of the marmoset corticospinal system has shown that the marmoset corticospinal system lacks direct corticomotoneuronal projections to the motor pools in lamina IX of the cervical spinal cord (Fig. 1) (Kondo et al., 2015). These findings were anticipated given the presumed importance of corticomotoneurons for manual dexterity and fractionated finger movements and the lack of such capacities in the marmoset (Bortoff and Strick, 1993; Lemon and Griffiths, 2005). The majority of marmoset corticospinal projections to the cervical spinal cord were found to terminate in intermediate lamina VII (Kondo et al., 2015). Thus the bulk of cortical influence on spinal resources for muscle activation is mediated by spinal interneurons in the intermediate zone. Although some synaptic boutons from corticospinal fibers could be detected in lamina IX, no postsynaptic effects of medullary stimulation were observed at latencies consistent with monosynaptic corticomotoneuronal connections. Marmosets, therefore, force us to explicitly consider the influence of spinal interneurons on motor control.

MOVEMENT CODING ACROSS MULTIPLE SCALES OF MOTOR CORTICAL CIRCUITS

Marmosets offer a number of practical advantages as a non-human primate model species for the study of cortical function. Two advantages often mentioned by authors are that the marmoset brain is mostly lissencephalic and that there have been demonstrations of transgenic animals (Sasaki et al., 2009; Belmonte et al., 2015; Mitchell and Leopold, 2015; Sasaki, 2015). These represent advantages for the study of motor systems as well. The mammalian motor system is distributed throughout the brain and body. Our understanding of the cortical contributions to movement began with single electrode recordings of motor cortical cells. While much was learned about the functional properties of individual neurons during voluntary movements, any movement is certainly the result of coordinated activity across populations of neurons. With the capability to record from many neurons simultaneously has come the capacity to decode movement intention from neural recordings in a clinically useful way (Hochberg et al., 2006, 2012). These abilities, while certainly impressive, obscure the fact that our understanding of motor cortical functioning contains significant gaps.

One gap in our understanding relates to the functional relationships of neural activity within and between cortical areas during ongoing movement. Marmosets offer the potential to build an understanding of how to interpolate the activity of neural populations sparsely sampled across millimeters of cortex using electrophysiological methods with activity sampled more densely on the scale of a single cortical column using calcium imaging approaches (Fig. 2). A second gap is that, based on extracellular recordings, we have little to no access to cell type or identity. This fact severely limits the depth of insight we can gain about a system containing a multitude of cell types. With the combination of its relatively small and lissencephalic cerebral cortex and the prospects for its genetic modification, the marmoset offers the potential to address these gaps in understanding.

The basic organization of the cortical fields are largely conserved across mammals with some species specific adaptations (Krubitzer and Seelke, 2012). However in macaques and humans, central components of the cortical motor system, about (half of M1 and all of 3a) sit within the central sulcus, which makes these areas more difficult to access for neurophysiological recording. As a result, there have been relatively few studies of a significant proportion of M1 and of the entirety of sensory area 3a (see Krubitzer et al., 2004 and Rathelot and Strick, 2009 for two exceptions). The marmoset lacks a central sulcus, and as a result the entirety of these key sensorimotor areas is readily accessible to multielectrode array recordings and optical imaging. Furthermore, the small size of the marmoset brain allows for recording across multiple motor cortical areas at once with a typical multielectrode array. A single well-placed Utah array could potentially record from all of the forelimb area of M1 and from much of the adjacent corresponding upper limb region of sensory area 3a and premotor area 6DC (Fig. 2). Simultaneous recordings covering the entirety of these three areas involved in the cortical coordination of the upper limb is unprecedented and will likely lead to insights into how these three areas function together to support skilled upper limb control. With genetic approaches, it should also be possible to untangle the contributions of direct intracortical communications from intracortical communication via the transthalamic pathway (Sherman and Guillery, 2011). We would predict such contributions to manifest in the

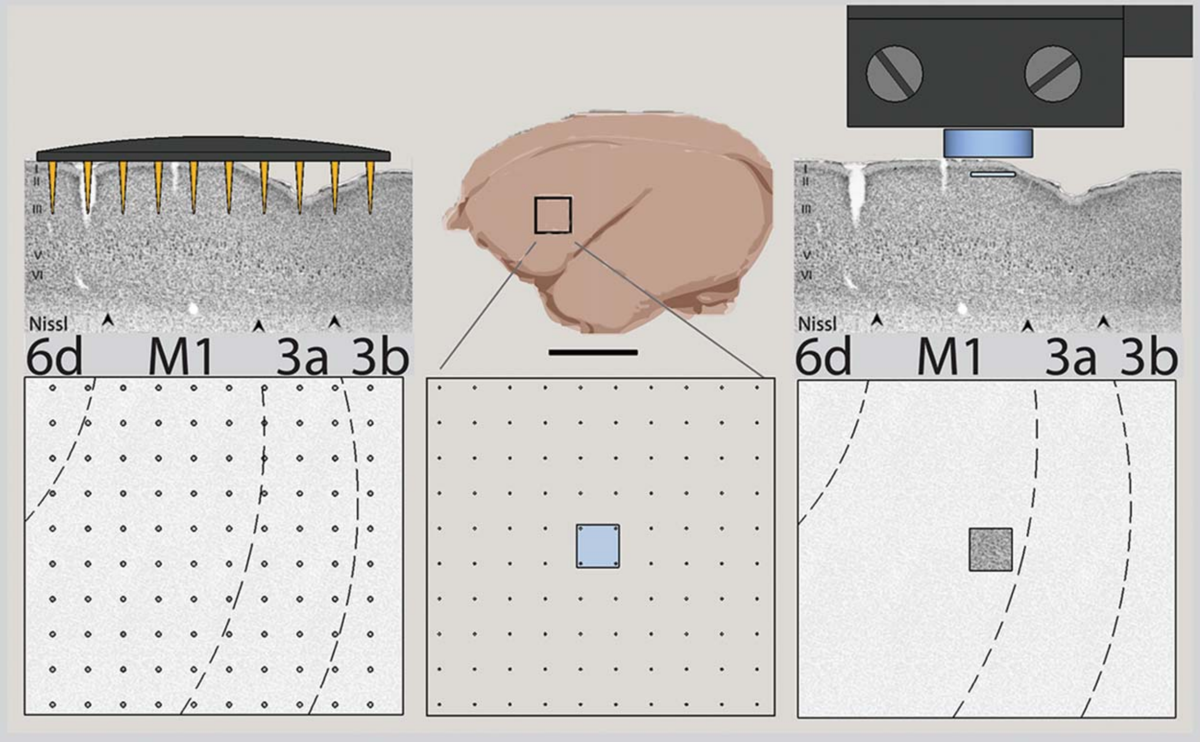

Figure 2 Marmosets offer an opportunity to interpolate across multiple scales of motor cortical functioning (central panels). The marmoset's relatively small and smooth brain will allow multi-electrode arrays (left panels) to sample neural activity across multiple cortical fields central to the cortical contribution to motor control and calcium imaging techniques (right panels) to sample densely within a given region. Sagittal slices through marmoset sensorimotor cortex adapted from (Burish et al., 2008). Scale bar 1 cm for central top panel, 1 mm for all other panels. [Color figure can be viewed at wileyonlinelibrary.com]

distribution of latencies in measures of functional connectivity corresponding to direct cortico-cortical projections and trans-thalamic communication across cortical areas.

As solutions for expressing calcium indicators come online in marmosets, as they have in mice, we will be able to densely sample motor cortical circuits with single cell resolution at the scale of a cortical column (Sadakane et al., 2015). As a result, we will be able to begin bridging two spatial scales at which computations supporting upper limb control unfold: the scale of how multiple areas interact and how computation unfolds within a single cortical column (Fig. 2). Additionally, imaging approaches provide the ability to unambiguously track the same neurons over multiple days (Ziv et al., 2013). These factors come together to provide a unique platform for testing multiscale and longitudinal hypotheses in a non-human primate.

Transgenic approaches in mice have proven powerful tools in many areas of study. Genetic access affords cell type specificity, which extracellular multi-unit recording techniques do not provide. The history of our physiological understanding of motor cortex is one of electrical microstimulation and electrophysiological recording. Much of what we know about the organization of the rest of the motor system was learned by electrically stimulating components of the system and recording downstream effects. There are some examples of functionally identifying cell types, such as corticospinal neurons through antidromic pyramidal tract stimulation and corticomotoneurons via spike-triggered averaging of muscle activity. While these approaches have been used to gain deeper insight into the nature of the cortical motor system (e.g., Merchant et al., 2008; Griffin et al., 2015), it is difficult to build an understanding of the primate motor system that acknowledges the diversity of cell types we know comprise motor cortical circuits. The ability to target specific genetically accessible classes of cortical cells, for either recording or manipulation as now available in mice, would allow for a dissection of the primate motor cortical circuits at a resolution not currently available.

We would ideally be able to develop cell type specific tools for dissecting the organization of local motor cortical circuits giving rise to the corticospinal tract (premotor, primary motor, and sensory areas) and understand their role in the integrating long range inputs from posterior parietal, premotor, and somatosensory areas to produce descending commands to the spinal cord.

TOWARD AN INTEGRATIVE UNDERSTANGING OF CORTICOSPINAL ENGAGMENT

Without a connection to the motor neurons of the spinal cord, the cortical motor system would have no capacity to move the body. Spinal interneurons are the target of the majority of corticospinal terminations even in animals that possess direct projections from cortex to the motor pools (Kuypers, 1981; Yoshino-Saito et al., 2010). We know a great deal about the organization of the corticomotoneuronal component of the corticospinal system (Porter and Lemon, 1993; Griffin et al., 2015). Apart from some very interesting work on the C3-C4 propriospinal system (Alstermark et al., 2007; Alstermark and Isa, 2012; Kinoshita et al., 2012), and some impressive electrophysiological characterizations of segmental interneuron activity (Fetz et al., 2002; Prut and Perlmutter, 2003a,b), we know comparatively little about the role of spinal interneurons in mediating corticospinal influence on motoneurons (Harel et al., 2008; Miri et al., 2013).

Knowledge of the developmental origins of most spinal interneurons is growing and has allowed for the development of tools for genetically targeting the individual components of spinal circuits in the mouse (Catela et al., 2015). The recent development of genetic approaches in mice has allowed the beginning of a much deeper understanding of the organization of spinal interneuron circuits (Bikoff et al., 2016; Gabitto et al., 2016). We would like to suggest that the common marmoset offers the opportunity to isolate the cortical contributions to spinal interneuron-mediated motor control in that it has a corticospinal system where corticomotoneuronal projections are sparse or absent.

WORKING WITH MARMOSETS TO STUDY THE MOTOR SYSTEM

While marmosets are an interesting model species that shows potential for the study of motor systems, they are in the early stages of their development as a model species for neurophysiology. Marmosets are thought to be more fragile than other non-human primates used in neurophysiology. Additionally, their small size means that they will likely perform fewer trials in standard experimental sessions where trials are exchanged for food or fluid rewards. When viewed from a lens of macaque work, these aspects of the marmoset might be seen as disadvantages, but we would like to suggest that these aspects of marmoset behavior and physiology offer opportunities to reevaluate standard approaches to working with non-human primates in neurophysiology.

Neuroscientific work with macaque monkeys benefits from their willingness to perform hundreds to thousands of trials of a given experimental task. In contrast, reports vary about how well marmosets are able to perform comparable numbers of trials. There seems to be a task dependent range. In a study of the capacity for flexible control in a reinforcement learning-based brain machine interface task, many of the analyses of experimental sessions were limited to 30 trials due to fidgeting marmosets (Pohlmeyer et al., 2014). In a couple of recent studies demonstrating the suitability of the common marmoset for studying the visual system, marmosets were found to perform 300–800 fixation trials but on average only 50 trials of a smooth pursuit paradigm (Mitchell et al., 2014, 2015). Studies reporting marmoset performance on different touch screen tasks varied from 60 to 150 trials in a session (Roberts et al., 1988; Clarke et al., 2015; Yamazaki et al., 2016).

It seems clear from the experiences of multiple groups that the quality and quantity of marmosets' performance of experimentally useful behavior is dependent on their comfort and motivation. There are multiple reports of acclimating marmosets to experimental constraints in the literature (Schultz-Darken et al., 2004; Remington et al., 2012; Belcher et al., 2013). Yet there are also reports of experimental constraints, of the style imposed on macaques, inhibiting marmoset behavior (Eliades and Wang, 2008; Roy and Wang, 2012). In our own experience, following acclimation protocols similar to those used in the studies mentioned above, almost all experimentally usefully behavior was extinguished, where it had been reliably expressed in the unconstrained marmoset. The Wang group pioneered a solution to this problem by developing a wireless neural recording solution that allowed them to record multichannel single unit neural recordings from freely moving marmosets (Roy and Wang, 2012). The marmoset's relative intolerance to restraint may compel a refinement in the default use of neural recording techniques requiring head fixation. More routine use of wireless neural recording would allow for the development of more flexible training and recording setups that could be integrated into the marmoset vivarium. By automating behavioral training and making it available throughout the day we could address the experimental bottleneck of training non-human primates and allow for voluntary participation in experiments.

Most groups do not seem to use fluid control as a motivation to engage marmosets in experimental tasks, but instead find success with rewards that marmosets like (e.g., banana milkshake, peach yogurt or marshmallow slurry). One recent study did find that motivation manipulation through food restriction could improve experimental performance in one individual; importantly they found the performance of the other marmoset in the study to be adequate without any restriction (Mitchell et al., 2014). In our lab we have found that marmosets will engage in behavior within an experimental apparatus repeatedly throughout the day without imposing any sort of food or fluid control. The fact that some marmosets will engage in experimentally useful behavior without any restriction should compel case by case consideration of the use of restriction with marmosets. This would represent a refinement in the default use of fluid control in most non-human neuroscientific studies.

The experimental challenges that marmosets present seem to compel refinement in techniques for using non-human primates in behavioral and systems neuroscience research. As the marmoset becomes more established as a model species for the study of auditory processing, vocal production, active vision, and social behavior (Miller et al., 2009, 2016, Mitchell et al., 2014, 2015), it seems like a good opportunity to design approaches utilizing newly available technology so that the precedents set for working with marmosets represent refinements on older standard operating procedures received from working with macaques.

Studies of motor control in behaving animals often require recording the kinematics of motor behaviors. Takemi et al., (2014) used small reflective markers placed on the hand to record marmoset reach to grasp movements in the context of a single pellet reaching task. However, these experimenters noted that sessions were limited to 30 minutes because marmosets would begin to remove the markers. A similar marker based solution has also been used to record the kinematics of marmoset gait (Chadwell and Young, 2015; Young et al., 2016). In these studies, marmosets were anesthetized for marker application. We have also found it difficult to acclimatize marmosets to reflective markers for motion capture. However, we have had success recording upper limb kinematics using subcutaneous markers in the context of an X-Ray Reconstruction of Moving Morphology system (Brainerd et al., 2010). These markers go unnoticed by the marmoset and allow for recording across multiple days without the need to reapply markers.

One of the most promising aspects of the marmoset as a model system for neuroscience derives from its potential for genetic manipulation, since the initial demonstration of transgenic marmosets expressing enhanced green fluorescent protein (Sasaki et al., 2009; Cyranoski, 2014; Sasaki, 2015). More recently there have been demonstrations of using viral strategies to introduce genes for expressing calcium indicators which have allowed for in vivo calcium imaging in anesthetized marmosets (Sadakane et al., 2015; Santisakultarm et al., 2016). Successful optogenetic stimulation has also recently been reported (MacDougall et al., 2016). While some systematic evaluation of viral strategies has been carried out, the approaches to gene transfer are still in early stages of development (Watakabe et al., 2015). For a review of efforts and prospects for applying genetic tools to aid investigations of the primate brain see Belmonte et al. (2015).

CONCLUSION

This brief review of marmoset motor system anatomy provides a picture of a primate expressing the basic musculoskeletal, cortical and spinal organization we recognize in the motor systems of Old World monkeys and humans. Differences lie in the extent of cortical field differentiation and corticospinal termination. In these differences we can find insights about the principles of motor system organization. Additionally the small size and smoothness of the marmoset brain will allow integration of our understanding of motor cortical functioning at multiple scales using both multielectrode array and imaging techniques in a way that has not been possible so far in a non-human primate. While the marmoset is still in the early stages of its development as a model species for the study of motor systems, the prospects for cell type specific access to interrogate and monitor the nervous system promise to deepen our understanding of motor cortical activity and its integration into the spinal circuitry for movement by spinal interneurons.

REFERENCES

Abreu F, De la Fuente MFC, Schiel N, Souto A. 2016. Feeding ecology and behavioral adjustments: Flexibility of a small neotropical primate (Callithrix jacchus) to survive in a semiarid environment. Mamm Res 61:221–229.

Aflalo TN, Graziano MSA. 2007. Relationship between unconstrained arm movements and single-neuron firing in the macaque motor cortex. J Neurosci 27:2760–2780.

Akkal D, Dum RP, Strick PL. 2007. Supplementary motor area and presupplementary motor area: Targets of basal ganglia and cerebellar output. J Neurosci 27:10659–10673.

Alstermark B, Isa T. 2012. Circuits for skilled reaching and grasping. Annu Rev Neurosci 35:559–578.

Alstermark B, Isa T, Pettersson L-G, Sasaki S. 2007. The C3?C4 propriospinal system in the cat and monkey: A spinal pre-motoneuronal centre for voluntary motor control. Acta Physiol 189:123–140.

Bakola S, Burman KJ, Rosa MGP. 2014. The cortical motor system of the marmoset monkey (Callithrix jacchus). Neurosci Res 93:72–81.

Barbas H, Pandya DN. 1987. Architecture and frontal cortical connections of the premotor cortex (area 6) in the rhesus monkey. J Comp Neurol 256:211–228.

Belcher AM, Yen CC, Stepp H, Gu H, Lu H, Yang Y, Silva AC, et al. 2013. Large-scale brain networks in the awake, truly resting marmoset monkey. J Neurosci 33:16796–16804.

Belmonte JCI, Callaway EM, Caddick SJ, Churchland P, Feng G, Homanics GE, Lee K-F, et al. 2015. Brains, genes, and primates. Neuron 86:617–631.

Bikoff JB, Gabitto MI, Rivard AF, Drobac E, Machado TA, Miri A, Brenner-Morton S, et al. 2016. Spinal inhibitory interneuron diversity delineates variant motor microcircuits. Cell 165:207–219.

Bortoff G, Strick P. 1993. Corticospinal terminations in two new-world primates: further evidence that corticomotoneuronal connectionsp provide part of the neural substrate for manual dexterity. J Neurosci 13:5105–5118.

Bostan AC, Dum RP, Strick PL. 2013. Cerebellar networks with the cerebral cortex and basal ganglia. Trends Cogn Sci 17:241–254.

Brainerd EL, Baier DB, Gatesy SM, Hedrick TL, Metzger KA, Gilbert SL, Crisco JJ. 2010. X-ray reconstruction of moving morphology (XROMM): Precision, accuracy and applications in comparative biomechanics research. J Exp Zool Part Ecol Genet Physiol 313:262–279.

Bremner LR, Andersen RA. 2014. Temporal analysis of reference frames in parietal cortex area 5d during reach planning. J Neurosci 34:5273–5284.

Burish MJ, Stepniewska I, Kaas JH. 2008. Microstimulation and architectonics of frontoparietal cortex in common marmosets (Callithrix jacchus). J Comp Neurol 507: 1151–1168.

Burman KJ, Palmer SM, Gamberini M, Rosa MGP. 2006. Cytoarchitectonic subdivisions of the dorsolateral frontal cortex of the marmoset monkey (Callithrix jacchus), and their projections to dorsal visual areas. J Comp Neurol 495:149–172.

Burman KJ, Palmer SM, Gamberini M, Spitzer MW, Rosa MGP. 2008. Anatomical and physiological definition of the motor cortex of the marmoset monkey. J Comp Neurol 506:860–876.

Burman KJ, Bakola S, Richardson KE, Reser DH, Rosa MGP. 2014a. Patterns of cortical input to the primary motor area in the marmoset monkey: Afferent connections of the motor cortex. J Comp Neurol 522:811–843.

Burman KJ, Bakola S, Richardson KE, Reser DH, Rosa MGP. 2014b. Patterns of afferent input to the caudal and rostral areas of the dorsal premotor cortex (6DC and 6DR) in the marmoset monkey: Afferent Connections of Dorsal Premotor Cortex. J Comp Neurol 522:3683–3716.

Burman KJ, Bakola S, Richardson KE, Yu H-H, Reser DH, Rosa MGP. 2015. Cortical and thalamic projections to cytoarchitectural areas 6Va and 8C of the marmoset monkey: Connectionally distinct subdivisions of the lateral premotor cortex: Connections of marmoset lateral premotor cortex. J Comp Neurol 522:1222–1247.

Catela C, Shin MM, Dasen JS. 2015. Assembly and function of spinal circuits for motor control. Annu Rev Cell Dev Biol 31:669–698.

Chadwell BA, Young JW. 2015. Angular momentum and arboreal stability in common marmosets (*Callithrix jacchus*): Mechanics of Arboreal Stability in Marmosets. Am J Phys Anthropol 156:565–576.

Clarke HF, Horst NK, Roberts AC. 2015. Regional inactivations of primate ventral prefrontal cortex reveal two distinct mechanisms underlying negative bias in decision making. Proc Natl Acad Sci 112:4176–4181.

Cyranoski D. 2014. Marmosets are stars of Japan's ambitious brain project. Nature 514:151.

Dasen JS, Liu J-P, Jessell TM. 2003. Motor neuron columnar fate imposed by sequential phases of Hox-c activity. Nature 425:926–933.

Dum RP, Strick P. 2002. An unfolded map of the cerebellar dentate nucleus and its projections to the cerebral cortex. J Neurophysiol 89:634–639.

Eliades SJ, Wang X. 2008. Chronic multi-electrode neural recording in free-roaming monkeys. J Neurosci Methods 172:201–214.

Esposito MS, Capelli P, Arber S. 2014. Brainstem nucleus MdV mediates skilled forelimb motor tasks. Nature 508: 351–356.

Evarts EV. 1968. Relation of pyramidal tract activity to force exerted during voluntary movement. J Neurophysiol 31:14–27.

Fetz EE, Perlmutter SI, Prut Y, Seki K. 2002. Functional properties of primate spinal interneurones during voluntary hand movements. In: Gandevia SC, Proske U, Stuart DG, editors. Sensorimotor Control of Movement and Posture. New York: Springer, pp 265–271.

Francisco TM, Couto DR, Zanuncio JC, Serrão JE, Silva I, de O, Boere V. 2014. Vegetable exudates as food for callithrix spp. (callitrichidae): Exploratory patterns. PLoS ONE 9:e112321.

Fujiyoshi K, Yamada M, Nakamura M, Yamane J, Katoh H, Kitamura K, Kawai K, et al. 2007. In vivo tracing of neural tracts in the intact and injured spinal cord of marmosets by diffusion tensor tractography. J Neurosci 27: 11991–11998.

Gabitto MI, Pakman A, Bikoff JB, Abbott LF, Jessell TM, Paninski L. 2016. Bayesian sparse regression analysis documents the diversity of spinal inhibitory interneurons. Cell 165:220–233.

Georgopoulos A, Schwartz A, Kettner R. 1986. Neuronal population coding of movement direction. Science 233: 1416–1419.

Georgopoulos AP, Kettner RE, Schwartz AB. 1988. Primate motor cortex and free arm movements to visual targets in three-dimensional space. II. Coding of the direction of movement by a neuronal population. J Neurosci 8:2928–2937.

Georgopoulos AP, Merchant H, Naselaris T, Amirikian B. 2007. Mapping of the preferred direction in the motor cortex. Proc Natl Acad Sci 104:11068–11072.

Griffin D, Hoffman DS, Strick P. 2015. Corticomotoneuronal cells are "functionally tuned.". Science 350:667–670.

Harel R, Asher I, Cohen O, Israel Z, Shalit U, Yanai Y, Zinger N, et al. 2008. Computation in spinal circuitry: Lessons from behaving primates. Behav Brain Res 194: 119–128.

Hochberg LR, Serruya MD, Friehs GM, Mukand JA, Saleh M, Caplan AH, Branner A, et al. 2006. Neuronal ensemble control of prosthetic devices by a human with tetraplegia. Nature 442:164–171.

Hochberg LR, Bacher D, Jarosiewicz B, Masse NY, Simeral JD, Vogel J, Haddadin S, et al. 2012. Reach and grasp by people with tetraplegia using a neurally controlled robotic arm. Nature 485:372–375.

Holsapple JW, Preston JB, Strick PL. 1991. The origin of thalamic inputs to the "hand" representation in the primary motor cortex. J Neurosci 11:2644–2654.

Hoover JE, Strick PL. 1999. The organization of cerebellar and basal ganglia outputs to primary motor cortex as revealed by retrograde transneuronal transport of herpes simplex virus type 1. J Neurosci 19:1446–1463.

Huerta MF, Pons TP. 1990. Primary motor cortex receives input from area 3a in macaques. Brain Res 537:367–371.

Huffman KJ, Krubitzer L. 2001a. Area 3a: Topographic organization and cortical connections in marmoset monkeys. Cereb Cortex 11:849–867.

Huffman KJ, Krubitzer L. 2001b. Thalamo-cortical connections of areas 3a and M1 in marmoset monkeys. J Comp Neurol 435:291–310.

Iwanami A, Yamane J, Katoh H, Nakamura M, Momoshima S, Ishii H, Tanioka Y, et al. 2005. Establishment of graded spinal cord injury model in a nonhuman primate: The common marmoset. J Neurosci Res 80:172–181.

Jenny AB, Inukai J. 1983. Principles of motor organization of the monkey cervical spinal cord. J Neurosci 3:567–575.

Jones EG, Porter R. 1980. What is area 3a?. Brain Res Rev 2:1–43.

Kalaska JF, Scott SH, Cisek P, Sergio LE. 1997. Cortical control of reaching movements. Curr Opin Neurobiol 7: 849–859.

Kelly RM, Strick PL. 2003. Cerebellar loops with motor cortex and prefrontal cortex of a nonhuman primate. J Neurosci 23:8432–8444.

Kinoshita M, Matsui R, Kato S, Hasegawa T, Kasahara H, Isa K, Watakabe A, et al. 2012. Genetic dissection of the circuit for hand dexterity in primates. Nature 487:235–238.

Kipping JA, Grodd W, Kumar V, Taubert M, Villringer A, Margulies DS. 2013. Overlapping and parallel cerebello-cerebral networks contributing to sensorimotor control: An intrinsic functional connectivity study. NeuroImage 83:837–848.

Kondo T, Yoshihara Y, Yoshino-Saito K, Sekiguchi T, Kosugi A, Miyazaki Y, Nishimura Y, et al. 2015. Histological and electrophysiological analysis of the cortico-spinal pathway to forelimb motoneurons in common marmosets. Neurosci Res 98:35–44.

Krubitzer LA, Kaas JH. 1990. The organization and connections of somatosensory cortex in marmosets. J Neurosci 10:952–974.

Krubitzer LA, Seelke AMH. 2012. Cortical evolution in mammals: The bane and beauty of phenotypic variability. Proc Natl Acad Sci 109:10647–10654.

Krubitzer L, Huffman KJ, Disbrow E, Recanzone G. 2004. Organization of area 3a in macaque monkeys: Contributions to the cortical phenotype. J Comp Neurol 471:97–111.

Kuypers HGJM. 1981. Anatomy of the descending pathways. In: Kuypers HGJM, Martin GF, editors. Handbook of Physiology ~ The Nervous System, pp 597–666.

Kuypers HG, Lawrence DG. 1967. Cortical projections to the red nucleus and the brain stem in the rhesus monkey. Brain Res 4:151–188.

Kwan HC, MacKay WA, Murphy JT, Wong YC. 1978. Spatial organization of precentral cortex in awake primates. II. Motor outputs. J Neurophysiol 41:1120–1131.

Lemon RN, Griffiths J. 2005. Comparing the function of the corticospinal system in different species: Organizational differences for motor specialization?. Muscle Nerve 32:261–279.

Lu X, Miyachi S, Ito Y, Nambu A, Takada M. 2007. Topographic distribution of output neurons in cerebellar nuclei and cortex to somatotopic map of primary motor cortex: Somatotopic cerebrocerebellar linkage. Eur J Neurosci 25:2374–2382.

MacDougall M, Nummela SU, Coop S, Disney A, Mitchell JF, Miller CT. 2016. Optogenetic manipulation of neural circuits in awake marmosets. J Neurophysiol 116:1286–1294.

Matelli M, Luppino G, Fogassi L, Rizzolatti G. 1989. Thalamic input to inferior area 6 and area 4 in the macaque monkey. J Comp Neurol 280:468–488.

McHanwell S, Watson C. 2009. Localization of motoneurons in the spinal cord. In: Watson C, Paxinos G, Kayalioglu G, editors. The Spinal Cord: A Christopher and Dana Reeve Foundation Text and Atlas. Academic Publishers.

Meier JD, Aflalo TN, Kastner S, Graziano MSA. 2008. Complex organization of human primary motor cortex: A high-resolution fmri study. J Neurophysiol 100:1800–1812.

Merchant H, Naselaris T, Georgopoulos AP. 2008. Dynamic sculpting of directional tuning in the primate motor cortex during three-dimensional reaching. J Neurosci 28: 9164–9172.

Miller CT, Eliades SJ, Wang X. 2009. Motor planning for vocal production in common marmosets. Anim Behav 78:1195–1203.

Miller CT, Freiwald WA, Leopold DA, Mitchell JF, Silva AC, Wang X. 2016. Marmosets: A neuroscientific model of human social behavior. Neuron 90:219–233.

Miri A, Azim E, Jessell TM. 2013. Edging toward Entelechy in motor control. Neuron 80:827–834.

Mitchell JF, Leopold DA. 2015. The marmoset monkey as a model for visual neuroscience. Neurosci Res 93:20–46.

Mitchell JF, Reynolds JH, Miller CT. 2014. Active vision in marmosets: A model system for visual neuroscience. J Neurosci 34:1183–1194.

Mitchell JF, Priebe NJ, Miller CT. 2015. Motion dependence of smooth pursuit eye movements in the marmoset. J Neurophysiol 113:3954–3960.

Miyachi S, Lu X, Imanishi M, Sawada K, Nambu A, Takada M. 2006. Somatotopically arranged inputs from putamen and subthalamic nucleus to primary motor cortex. Neurosci Res 56:300–308.

Napier JR, Napier PH. 1967. A Handbook of Living Primates: Morphology, ecology and nehavior of nonhuman primates. New York: Academic Press, 456 p.

Nei M, Glazko GV. 2002. The Wilhelmine E. Key 2001 Invitational Lecture. Estimation of divergence times for a few mammalian and several primate species. J Hered 93: 157–164.

Nudo RJ, Masterton RB. 1988. Descending pathways to the spinal cord: A comparative study of 22 mammals. J Comp Neurol 277:53–79.

Nudo RJ, Masterton RB. 1990. Descending pathways to the spinal cord, III: Sites of origin of the corticospinal tract. J Comp Neurol 296:559–583.

Nudo RJ, Frost SB. 2007. The Evolution of motor cortex and motor systems. In: Kaas JH, Krubitzer LA, editors. Evolution of Nervious Systems. New York: Elsevier Academic Press. 554 p.

Padberg J, Franca JG, Cooke DF, Soares JGM, Rosa MGP, Fiorani M, Gattass R, Krubitzer L. 2007. Parallel evolution of cortical areas involved in skilled hand use. J Neurosci 27:10106–10115.

Park MC, Belhaj-Saï f. A, Gordon M, Cheney PD. 2001. Consistent features in the forelimb representation of primary motor cortex in rhesus macaques. J Neurosci 21: 2784–2792.

Paxinos G, Watson C, Petrides M, Rosa M, Tokuno H. 2012. The Marmoset Brain in Stereotaxic Coordinates. New York: Academic Press.

Picard N, Smith AM. 1992. Primary motor cortical activity related to the weight and texture of grasped objects in the monkey. J Neurophysiol 68:1867–1881.

Pohlmeyer EA, Mahmoudi B, Geng S, Prins NW, Sanchez JC. 2014. Using reinforcement learning to provide stable brain-machine interface control despite neural input reorganization. PLoS ONE 9:e87253.

Porter R, Lemon R. 1993. Corticospinal Control and Voluntary Movement. New York: Oxford University Press. 428 p.

Proville RD, Spolidoro M, Guyon N, Dugué GP, Selimi F, Isope P, Popa D, et al. 2014. Cerebellum involvement in cortical sensorimotor circuits for the control of voluntary movements. Nat Neurosci 17:1233–1239.

Prut Y, Perlmutter SI. 2003a. Firing properties of spinal interneurons during voluntary movement. II. Interactions between spinal neurons. J Neurosci 23:9611–9619.

Prut Y, Perlmutter SI. 2003b. Firing properties of spinal interneurons during voluntary movement. I. State-dependent regularity of firing. J Neurosci 23:9600–9610.

Rathelot J-A, Strick PL. 2009. Subdivisions of primary motor cortex based on cortico-motoneuronal cells. Proc Natl Acad Sci 106:918–923.

Remington ED, Osmanski MS, Wang X. 2012. An operant conditioning method for studying auditory behaviors in marmoset monkeys. PLoS ONE 7:e47895.

Roberts AC, Robbins TW, Everitt BJ. 1988. The effects of intradimensional and extradimensional shifts on visual discrimination learning in humans and nonhuman primates. Q J Exp Psychol Sect B 40:321–341.

Roy S, Wang X. 2012. Wireless multi-channel single unit recording in freely moving and vocalizing primates. J Neurosci Methods 203:28–40.

Sadakane O, Masamizu Y, Watakabe A, Terada S-I, Ohtsuka M, Takaji M, Mizukami H, et al. 2015. Long-term two-photon calcium imaging of neuronal populations with subcellular resolution in adult non-human primates. Cell Rep 13:1989–1999.

Santisakultarm TP, Kersbergen CJ, Bandy DK, Ide DC, Choi S-H, Silva AC. 2016. Two-photon imaging of cerebral hemodynamics and neural activity in awake and anesthetized marmosets. J Neurosci Methods 271: 55–64.

Sasaki E. 2015. Prospects for genetically modified non-human primate models, including the common marmoset. Neurosci Res 93:110–115.

Sasaki E, Suemizu H, Shimada A, Hanazawa K, Oiwa R, Kamioka M, Tomioka I, et al. 2009. Generation of transgenic non-human primates with germline transmission. Nature 459:523–527.

Schiel N, Souto A, Huber L, Bezerra BM. 2010. Hunting strategies in wild common marmosets are prey and age dependent. Am J Primatol 72:1039–1046.

Schultz-Darken NJ, Pape RM, Tannenbaum PL, Saltzman W, Abbott DH. 2004. Novel restraint system for neuroendocrine studies of socially living common marmoset monkeys. Lab Anim 38:393–405.

Schultz-Darken N, Braun KM, Emborg ME. 2016. Neurobehavioral development of common marmoset monkeys: Marmoset neurobehavioral development. Dev Psychobiol 58:141–158.

Sherman SM, Guillery RW. 2011. Distinct functions for direct and transthalamic corticocortical connections. J Neurophysiol 106:1068–1077.

Sherman SM, Guillery RW. 2013. Functional Connections of Cortical Areas: A New View from the Thalamus. Cambridge: The MIT Press, 296 p.

Strick PL, Preston JB. 1982. Two representations of the hand in area 4 of a primate. II. Somatosensory input organization. J Neurophysiol 48:150–159.

Sussman RW, Kinzey WG. 1984. The ecological role of the Callitrichidae: A review. Am J Phys Anthropol 64: 419–449.

Takemi M, Kondo T, Yoshino-Saito K, Sekiguchi T, Kosugi A, Kasuga S, Okano HJ, et al. 2014. Three-dimensional motion analysis of arm-reaching movements in healthy and hemispinalized common marmosets. Behav Brain Res 275:259–268.

Wang X, Lu T, Snider RK, Liang L. 2005. Sustained firing in auditory cortex evoked by preferred stimuli. Nature 435:341–346.

Wang Y, Fang Q, Gong N. 2014. Motor assessment of developing common marmosets. Neurosci Bull 30:387–393.

Watakabe A, Ohtsuka M, Kinoshita M, Takaji M, Isa K, Mizukami H, Ozawa K, et al. 2015. Comparative analyses of adeno-associated viral vector serotypes 1, 2, 5, 8 and 9 in marmoset, mouse and macaque cerebral cortex. Neurosci Res 93:144–157.

Watson C, Sengul G, Tanaka I, Rusznak Z, Tokuno H. 2015. The spinal cord of the common marmoset (Callithrix jacchus). Neurosci Res 93:164–175.

Yamazaki Y, Echigo C, Saiki M, Inada M, Watanabe S, Iriki A. 2011. Tool-use learning by common marmosets (Callithrix jacchus). Exp Brain Res 213:63–71.

Yamazaki Y, Saiki M, Inada M, Watanabe S, Iriki A. 2016. Sustained performance by common marmosets in a delayed matching to position task with variable stimulus presentations. Behav Brain Res 297:277–284.

Yoshino-Saito K, Nishimura Y, Oishi T, Isa T. 2010. Quantitative inter-segmental and inter-laminar comparison of corticospinal projections from the forelimb area of the primary motor cortex of macaque monkeys. Neuroscience 171:1164–1179.

Young JW, Stricklen BM, Chadwell BA. 2016. Effects of support diameter and compliance on common marmoset (*Callithrix jacchus*) gait kinematics. J Exp Biol 219: 2659–2672.

Ziv Y, Burns LD, Cocker ED, Hamel EO, Ghosh KK, Kitch LJ, Gamal AE, et al. 2013. Long-term dynamics of CA1 hippocampal place codes. Nat Neurosci 16:264–266.