

Control of ankle extensor muscle activity in walking cats

Kathrin Hatz,¹ Katja Mombaur,¹ and J. Maxwell Donelan²

¹Interdisciplinary Center for Scientific Computing (IWR), Heidelberg University, Heidelberg, Germany; and ²Department of Biomedical Physiology and Kinesiology, Simon Fraser University, Burnaby, British Columbia, Canada

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Hatz K, Mombaur K, Donelan JM. Control of ankle extensor muscle activity in walking cats. *J Neurophysiol* 108: 2785–2793, 2012. First published August 29, 2012; doi:10.1152/jn.00944.2011.—Our objective was to gain insight into the relative importance of feedforward control and different proprioceptive feedback pathways to ongoing ankle extensor activity during walking in the conscious cat. We asked whether the modulation of stance phase muscle activity is due primarily to proprioceptive feedback and whether the same proprioceptive gains and feedforward commands can automatically generate the muscle activity required for changes in walking slope. To test these hypotheses, we analyzed previously collected muscle activity and mechanics data from cats with an isolated medial gastrocnemius muscle walking along a sloped pegway. Models of proprioceptor dynamics predicted afferent activity from the measured muscle mechanics. We modeled muscle activity as the weighted sum of the activity predicted from the different proprioceptive pathways and a simple model of central drive. We determined the unknown model parameters using optimization procedures that minimized the error between the predicted and measured muscle activity. We found that the modulation of muscle activity within the stance phase and across walking slopes is indeed well described by neural control that employs constant central drive and constant proprioceptive feedback gains. Furthermore, it is force feedback from Ib afferents that is primarily responsible for modulating muscle activity; group II afferent feedback makes a small contribution to tonic activity, and Ia afferent feedback makes no contribution. Force feedback combined with tonic central drive appears to provide a simple control mechanism for automatically compensating for changes in terrain without requiring different commands from the brain or even modification of central nervous system gains.

locomotion; motor control; proprioceptive feedback; feedforward control

MUSCLE ACTIVITY DURING WALKING has important contributions from both centrally generated commands and feedback control. Perhaps the strongest experimental evidence for a central contribution comes from studies where sensory feedback is effectively eliminated by transection of the major afferent pathways. In the near absence of sensory feedback, animals still produce the alternating flexor and extensor muscle activity that is characteristic of walking (Brown 1911; Grillner and Zangger 1979, 1984; Pearson et al. 1999). However, this feedforward control does not normally act in isolation; when available, sensory feedback appears to contribute substantially to the centrally generated pattern. This is clearly demonstrated by experiments that remove ground support from under the hind legs of walking cats or forcibly unload the ankle of walking humans. This unexpected reduction in afferent feedback markedly reduces the magnitude of muscle activity in the

weight-bearing muscles of the leg (Gorassini et al. 1994; Hiebert et al. 1994; Hiebert and Pearson 1999; Sinkjaer et al. 2000).

Although the above-mentioned experiments indicate a role for both central drive and feedback control, it has proven more difficult to quantify their relative contributions, including those of the various feedback pathways. One approach used to address this question has been to find phases of the step cycle where the modulation of muscle activity can only be attributed to one feedback pathway because the activity in other feedback pathways is constant (Donelan and Pearson 2004a, 2004b). This approach is limited in that it can only be applied to short periods within the step cycle which fulfill the condition that only one feedback pathway is modulated; throughout the remainder of the step cycle, the modulation of afferent signals is considerably more complex (Donelan and Pearson 2004a; Donelan et al. 2009; Prochazka and Gorassini 1998; Prochazka et al. 1976). A second general approach toward quantifying the contribution of an individual afferent pathway has been to selectively remove or decrease activity within that pathway by using methods such as nerve transections or nerve blocks (Bouyer and Rossignol 2003; Grey et al. 2001). This instructive approach is nevertheless limited because it does not instantly and transiently decrease feedback. Consequently, there is the real possibility that the control system has adapted, upregulating the role of other pathways in the absence of the missing feedback. Rather than reduce afferent activity, a third approach is to selectively increase it through electrical stimulation or mechanical perturbation (Guertin et al. 1995; Hiebert et al. 1995; Whelan and Pearson 1997). The limitation here is that it is not clear whether the same feedback pathways responsible for the response to the perturbation also underlie the activity during normal walking (Donelan and Pearson 2004b).

In this article, we attempt to overcome some of the limitations of these prior approaches by modeling combinations of central drive and feedback control and then determining whether their summed contribution can explain the measured modulation in muscle activity. This avoids the limitation of the first approach described above in that it can be applied during walking periods where more than one contributor to muscle activity is undergoing change. Also, unlike the second and third approaches, it does not require a perturbation to the walking animal that may change the nature of the control system that the animal is employing. There are, of course, an infinite number of candidate control systems that may explain the measured muscle activity. To overcome this problem, we constrained the control system topology on the basis of physiologically realistic assumptions about the nature of central drive and the important feedback pathways (see Fig. 1). More

Address for reprint requests and other correspondence: J. M. Donelan, Dept. of Biomedical Physiology & Kinesiology, Simon Fraser Univ., Burnaby, BC, Canada V5A 1S6 (e-mail: mdonelan@sfu.ca).

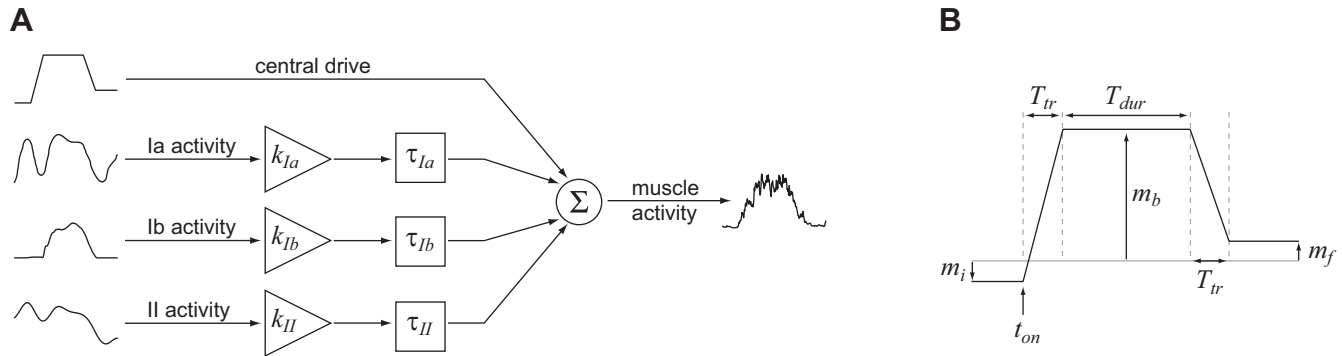


Fig. 1. **A**: muscle activity was modeled as the sum of contributions from central drive and Ia, Ib, and II afferent feedback signals. The contributions of the different afferent pathways were determined by the gains k_{Ia} , k_{Ib} , and k_{II} , respectively. Time delays τ_{Ia} , τ_{Ib} , and τ_{II} allowed for different feedback delays in the different afferent pathways. **B**: central drive was modeled as a trapezoidal step-up/step-down function described with 6 parameters: initial value m_i , burst onset time t_{on} , duration of the transition periods T_{tr} , burst magnitude m_b , burst duration T_{dur} , and final value m_f .

specifically, we modeled muscle activity as the weighted sum of the activity predicted from the different proprioceptive pathways and a simple model of central drive. We determined the unknown parameters, including the feedback gains, using optimization procedures that minimized the sum of the squared error between the model predictions and the measured muscle activity across all walking slopes.

We used this analysis to gain insight into the relative importance of different proprioceptive feedback pathways, as well as feedforward control, to ongoing ankle extensor activity during walking in the conscious cat. We tested two main hypotheses: 1) the modulation of stance phase muscle activity is due primarily to proprioceptive feedback, and 2) the same proprioceptive gains and feedforward commands can automatically generate the muscle activity required for changes in walking slope. To test these hypotheses, we analyzed previously collected muscle activity and mechanics data from cats with an isolated medial gastrocnemius muscle (MG) walking along a sloped pegway (Donelan et al. 2009). Established mathematical models of proprioceptor dynamics were used to predict afferent activity from the measured muscle mechanics (Prochazka 1999). We then determined whether the modulation of measured muscle activity within the stance phase and across walking slopes was well described by a model with constant central drive and constant feedback gains (Fig. 1).

MATERIALS AND METHODS

Experimental procedures. These procedures have been previously described in detail by Donelan et al. (2009). Here, we review them in brief with an emphasis on the details most relevant to the current analysis. All procedures were approved by the Health Sciences Animal Policy and Welfare Committee at the University of Alberta.

Experiments were performed on two female adult cats (*cat 1*, mass = 2.96 kg; *cat 2*, mass = 2.80 kg) with the MG of the right hindlimb isolated by denervation of the other main ankle extensors. After recovering from surgery, the animals walked at self-selected speeds on a pegway at five different slopes (+25°, +10°, 0°, -10°, -25°). One peg in the middle of the pegway was instrumented with a force transducer to measure the ground reaction forces from the right hindlimb (Fig. 2). Implanted electromyography (EMG) electrodes measured MG muscle activity. Amplified EMG and ground reaction force signals were sampled at 1,200 Hz and stored for subsequent analysis. Sagittal-plane leg kinematics were measured using reflective markers placed on the skin over the hip, knee, ankle, and metatarsal-phalangeal joints as well as on the end of the phalanges. The positions

of these markers were recorded at 60 Hz using video synchronized to the EMG and force measurements.

To estimate MG length and velocity, marker coordinates were first resampled to match the sampling frequency of force and EMG data. Because of the substantial skin movement under the knee marker, knee position was estimated from triangulation of the hip and ankle markers based on measured thigh and shank lengths (Pearson et al. 1999). Joint angles were then derived from these joint position coordinates. The origin-to-insertion length of the MG muscle-tendon unit was calculated using the ankle and knee joint angles as well as the distance along the segments from the joint centers at which the muscle originates and inserts, measured postmortem. The contribution of tendon to the overall muscle-tendon unit length was estimated as the sum of the relaxed tendon length, measured postmortem, and the quotient of MG muscle force and tendon stiffness. Tendon stiffness was determined from the relaxed tendon cross-sectional area, determined postmortem, and an assumed elastic modulus of 400 MPa (Rack and Westbury 1984). The estimated muscle fiber length was the overall muscle-tendon unit length less the estimated tendon length. The muscle fiber velocity was the time derivative of this length.

To estimate MG muscle force, it was first assumed that the ankle joint moment was due entirely to force generated by MG, since all other major ankle extensors were denervated. The ankle joint moment was calculated using an inverse dynamics analysis of a three-segment, two-joint, rigid body model consisting of the phalanges, tarsals, and shank joined by the metatarsal-phalangeal and ankle joints. As inputs, this analysis required the measured ground reaction forces as well as calculated segmental accelerations, segmental inertial properties, and segmental geometry. Repeated trials for each condition were averaged

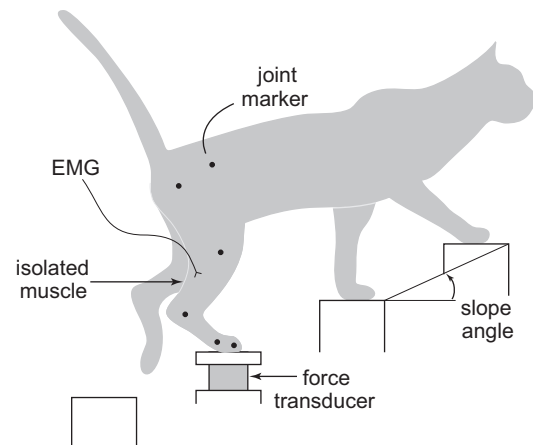


Fig. 2. Illustration of the experiment procedures. EMG, electromyogram.

to produce average time series for muscle force, length, velocity, and EMG.

Having determined MG muscle length, velocity, and force, we used mathematical models of proprioceptor dynamics to predict afferent activity. These models of Ia, Ib, and group II dynamics were based on those presented in Prochazka (1999) and Houk and Simon (1967). The equations are presented briefly here; a more complete description of the models and their modifications can be found in Donelan et al. (2009). The model for Ia afferent activity is given by the following equation:

$$Ia(t) = 65 \cdot \sqrt{v(t)} + 200 \cdot d(t), \quad (1)$$

where t indicates that this function is in the time domain, and d is muscle-tendon length normalized by rest length (Donelan et al. 2009). The velocity-dependent term, v , is calculated using the following transfer function:

$$v(s) = \frac{200 \cdot s}{s + 200} d(s), \quad (2)$$

where s indicates that this function is in the frequency domain. The model for group II afferent activity is given by the following equation:

$$II(s) = 40 \cdot \frac{200 \cdot (s + 0.4) \cdot (s + 11)}{(s + 0.8) \cdot (s + 200)} d(s), \quad (3)$$

where the variables are as defined in the previous equations. After Prochazka (1999), we used the tendon organ Ib afferent model of Houk and Simon (1967):

$$Ib(s) = 333 \cdot \frac{(s + 0.15) \cdot (s + 1.5) \cdot (s + 16)}{(s + 0.2) \cdot (s + 2) \cdot (s + 37)} f(s), \quad (4)$$

where f is MG muscle force normalized for body weight.

Modeling muscle activity. We modeled the measured muscle activity M as the sum of contributions from central drive c and the predicted afferent feedback signals Ia, Ib, and II:

$$M(t) = k_{Ia}Ia(t - \tau_{Ia}) + k_{Ib}Ib(t - \tau_{Ib}) + k_{II}II(t - \tau_{II}) + c(t), \quad (5)$$

where t denotes the time (Fig. 1A). The relative contributions of the different afferent pathways are determined by the gains k_{Ia} , k_{Ib} , and k_{II} . Time delays τ_{Ia} , τ_{Ib} , and τ_{II} allow for different feedback delays between the different afferent pathways.

Our model for the centrally generated motor signal $c(t)$ was a simple on-off command, augmented with some physiologically realistic features. First, rather than jump instantaneously between on and off states, the model allowed for sloped transitions. The physiological rationale is that measured muscle activity is the compound activity from a collection of motor units; the sloped transitions approximate the effect of different motor units that are activated instantly and simultaneously by a central command but then conduct the signals to the muscle with differing velocities and activate the muscle fibers with differing rates. Second, rather than have the centrally generated signal have zero contribution to muscle activity when it is in the off state, it was allowed to have positive or negative offsets. This was intended to capture the possibility that there may be central drive to the extensor motoneurons during the swing phase, as well as feedback from other muscles (such as reciprocal inhibition from flexors). The result is that central drive is modeled as a trapezoidal step-up/step-down function that can be described with six parameters (Fig. 1B). Two parameters are required for the initial and final values of the central drive, and one parameter is required for the duration of the transition periods. The remaining three parameters are the minimal set required to describe a simple on-off command: the burst onset time, duration, and magnitude.

Numerical methods. The model described above has 12 unknown parameters: 3 gains, 3 time delays, and 6 parameters to describe the central drive. Importantly, these parameters were not allowed to vary

within the stride cycle or between up and down slope conditions. Instead, we determined whether a model with the same central drive and constant feedback gains could describe the modulation of muscle activity within the stance phase across different walking slopes.

We determined the optimal model parameters by systematically varying them until the sum of the squared error between the model prediction and the measured muscle activity was minimized. We constrained this optimization problem in two ways. First, the time delays were required to be greater than zero; future afferent feedback cannot affect present muscle activity. Second, all feedback gains were required to be greater than zero. This assumption was based on the empirical findings that Ia, Ib, and group II feedback from ankle extensors are all excitatory during the stance phase of walking in cats (Pearson 2004). We solved this optimization problem using the software package MUSCOD-II (Bock and Plitt 1984; Leineweber et al. 2003a, 2003b).

For this procedure, the optimal parameters for each animal were estimated using the measured data from only the level walking trials (0° slope). We then validated these parameters by comparing the model prediction with the measured data from the four slope walking conditions ($+25^\circ$, $+10^\circ$, -10° , -25°). Our analysis focused on the region of the stride cycle beginning 200 ms before foot contact and ending 500 ms after foot contact. We choose this region because it included the full burst of MG stance phase muscle activity at all slopes for both animals. Foot contact was determined from the onset of the vertical ground reaction force. Before analysis, the raw EMG signals were first rectified and filtered with a 20-Hz-cutoff first-order one-way low-pass Butterworth digital filter. To get a continuous representation of the discrete-time measured data, we interpolated the muscle and afferent activity data with cubic splines.

We quantified the degree to which the model captured the measured muscle activity in two ways. First, we calculated the coefficient of determination, or R^2 value, which quantified the amount of variability in the data set captured by the model. We report R^2 values for the fit between the model and the average muscle activity at each slope for each animal. Second, we visually examined the residuals, defined as the difference at each time point between the model prediction and the measured data. A good fit will demonstrate residuals that are small in magnitude, randomly distributed around zero, and show no particular pattern with time.

RESULTS

A simple control system with constant feedback gains and the same central drive well describes the modulation of ankle extensor muscle activity across walking slopes (Fig. 3). The R^2 values at different walking slopes ranged from 0.89 to 0.96 for *cat 1* and from 0.77 to 0.94 for *cat 2*. These values indicate that the model explained no less than 89% and 77% of the modulation in muscle activity in *cat 1* and *cat 2*, respectively. The relatively small residual errors also support the conclusion that this simple control system was overall a good fit to the measured data (Fig. 3, right). It should be emphasized that the optimal parameters for each animal were estimated using only the measured data from the level walking trials (0° slope). Having thus gained some confidence in the explanatory power of the model, we can next examine the contribution to muscle activity of central drive and the different feedback pathways, an important analysis not possible in the intact physiological system.

Central drive has a major contribution to muscle activity throughout ankle extensor burst duration and across walking slopes (Fig. 4). During the prestance phase, defined as beginning when the burst in muscle activity begins and ending when the foot contacts the ground, central drive is the dominant

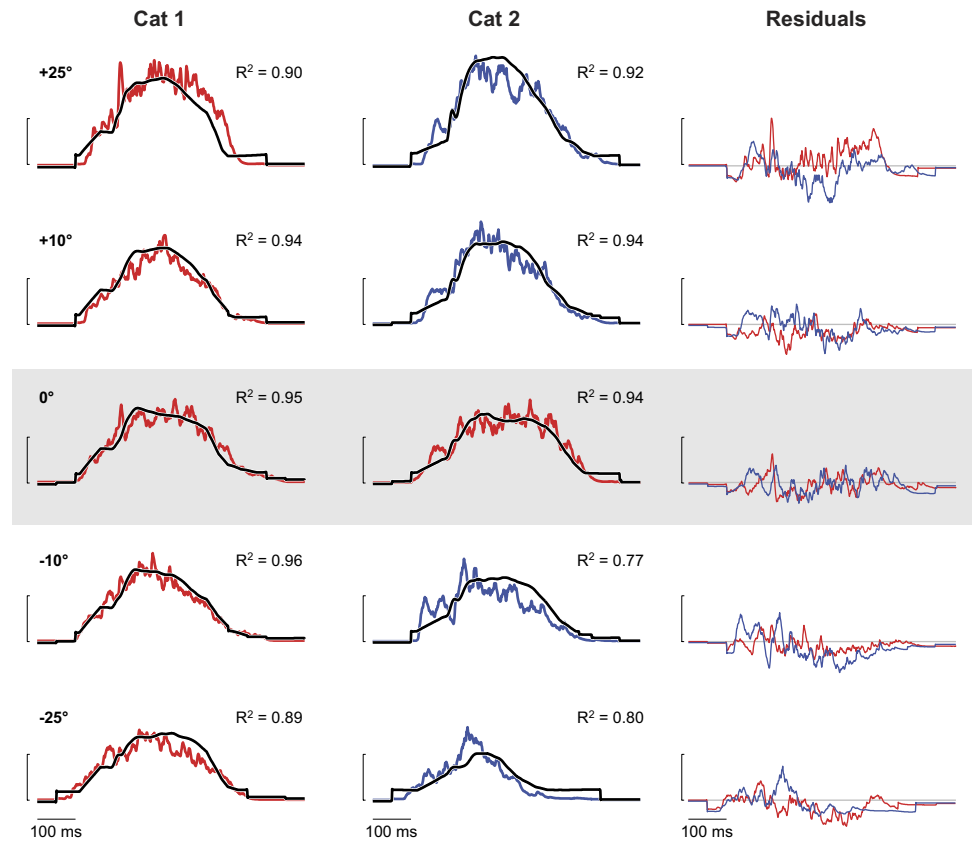


Fig. 3. Comparison between measured and predicted muscle activity. The black lines in *left* and *middle* panels are the model predictions, and the colored lines are the measured muscle activity. *Right* panel illustrates the residuals, the difference between the measured data and the model predictions at each walking slope, for *cat 1* (red) and *cat 2* (blue). The shaded box illustrates that the 0° slope condition was used to estimate all model parameters, whereas the other 4 slopes were used to validate the model predictions. All scale bars are the same magnitude.

contributor, responsible for ~60% of the total activity for *cat 1* and 40% of the total activity for *cat 2* (Fig. 5). During the stance phase, defined as beginning when the foot contacts the ground and ending when the foot lifts off the ground, central drive also has a major contribution (Figs. 4 and 5). This contribution is greatest during downslope walking and is equal to ~40% of the total activity for *cat 1* and 28% of the total activity for *cat 2*. The role of central drive decreases as slope increases, falling to 32% in *cat 1* and 8% in *cat 2* at +25°. It is important to note that although the relative role of central drive may change, we have used a model of central drive that has a constant absolute contribution within the stance phase and across walking slopes. Thus modulation of muscle activity to compensate for changing muscle force requirements must be accomplished with feedback.

Force feedback from Ib afferents is primarily responsible for the modulation of muscle activity within the stance phase and across walking slopes (Fig. 4). This modulation is due entirely to changes in afferent activity; feedback gains within this model are kept constant within the walking cycle and across slope conditions. During level walking, force feedback is the dominant contributor to muscle activity, responsible for 46% of the stance phase muscle activity in *cat 1* and 69% in *cat 2* (Fig. 5). This large contribution is due to the combined effects of a large feedback gain (Table 1) and significant Ib activity during the stance phase (Table 2). Upslope walking requires greater muscle activity, and force feedback automatically compensates, increasing its contribution to 54% and 77% in *cat 1* and *cat 2*, respectively. It similarly compensates during downslope walking, where less muscle activity is required, decreasing its contribution to 42% in *cat 1* and 41% in *cat 2*. During

prestance, force feedback has a negligible contribution to muscle activity despite its large feedback gain (Fig. 5). This is due to low Ib activity; the force in the muscle is small until stance begins.

Feedback from group II afferents plays a similar, albeit smaller, role as central drive in regulating ongoing muscle activity. Its contribution is a nearly tonic addition to both prestance and stance phase activity. This is because the contribution of muscle length to group II activity tends to counteract the contribution from muscle velocity under our experimental conditions; the muscle is long but shortening during upslope walking and short but lengthening during downslope walking (Donelan et al. 2009). Consequently, the modulation of group II activity is low relative to its average activity; across slopes in both cats, the average activity was greater than 400 Hz, but the average modulation was only 4% root mean square (Table 2). This low modulation, combined with a feedback gain that is ~20 times smaller than the magnitude of the Ib gain (Table 1), results in a small contribution that is essentially static (Fig. 4). Group II feedback is nevertheless important, especially to prestance, where it contributes 35% and 54% of the ankle extensor activity in *cat 1* and *cat 2*, respectively. The contribution to stance phase activity is smaller, averaging ~20% across walking slopes in both cats.

Ia afferent feedback makes no contribution to ankle extensor muscle activity (Figs. 4 and 5). Whereas average Ia afferent activity was always high (~250 Hz), the feedback gain that optimizes the fit between the measured and modeled muscle activity was three orders of magnitude smaller than the Ib feedback gain (Table 1). This feedback gain is the smallest value possible in our optimization procedure.

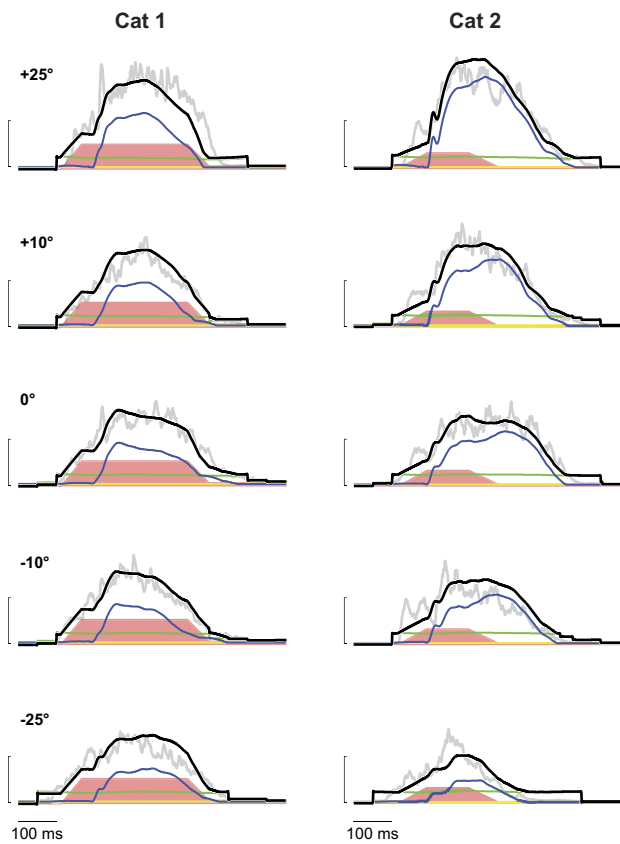


Fig. 4. Individual contributions of central drive and the different feedback pathways to ankle extensor muscle activity. The black and gray lines are predicted and measured muscle activity, respectively. Central drive, modeled as a step-up/step-down trapezoidal function (red shape) is constant across walking slopes for each animal. Contributions from Ia, Ib, and group II feedback are shown as yellow, blue, and green lines, respectively. All scale bars are the same magnitude.

DISCUSSION

Positive force feedback from Ib afferents appears to be necessary for a simple feedback model to explain the measured results. One way to derive additional insight into the importance of positive force feedback is to eliminate it from the model and then reoptimize to determine the best fit between model prediction and measured results for the 0° slope condition. This yields decidedly poor fits between model predictions and measured data at all slopes. For the +25° slope condition, for example, the R^2 values decreased for *cat 1* and *cat 2* from 0.90 and 0.92 when the model prediction included Ib feedback to 0.83 and 0.80 when Ib feedback was removed (Fig. 6, A and B). It is also possible for force feedback to play an important role in modulating ongoing activity using negative feedback, rather than positive feedback (Lundberg et al. 1977; Ross and Nichols 2009). Constraining the Ib gain in the model to be less than or equal to zero and reoptimizing also demonstrates poor fits with R^2 values of 0.86 and 0.72 at +25° (Fig. 6C). Indeed, the optimal gains for force feedback when constrained to be less than or equal to zero were zero. Eliminating Ia and group II feedback and reoptimizing a model that includes only force feedback in addition to central drive yields fits that are as good as those with complete feedback (Fig. 6D). However, force feedback alone cannot generate the observed patterns; eliminating central drive in addition to the other feedback pathways

yields worse fits (Fig. 6E). This is to be expected because contributions from sources other than force feedback are required to describe activity during the prestance region, where muscle force is effectively zero, and provide some degree of background muscle force during stance on which force feedback can act. We also considered a more complex model topology to simulate the modulation of central drive by afferent feedback, as has been observed in fictive locomotion experiments (Guertin et al. 1995; Rybak et al. 2006). Rather than model the effect of a particular afferent pathway, we assumed that any feedback could affect central drive and allowed all central drive parameters to change with slope. This resulted in modest increases in model fits (from 0.90 and 0.92 to 0.93 and 0.95, at +25°), with some of the improvement in fit attributed to the fact that all the model parameters were optimized for each slope, rather than just the 0° condition as before. We found that the contribution of central drive changed only modestly with slope, resulting in the same general patterns exhibited in our original model. Taken together, the successes and failures of these alternative models in explaining the measured data suggest that the ankle extensor muscle activity required within the step cycle and across walking slopes can be supplied with a simple combination of central drive for tonic background activity and positive force feedback for modulation.

Despite the good fit between model and measurements, we cannot definitively conclude that this model control system underlies the neural control employed by walking animals. We expect, for example, that more sophisticated models that better capture the complex underlying physiology would also better

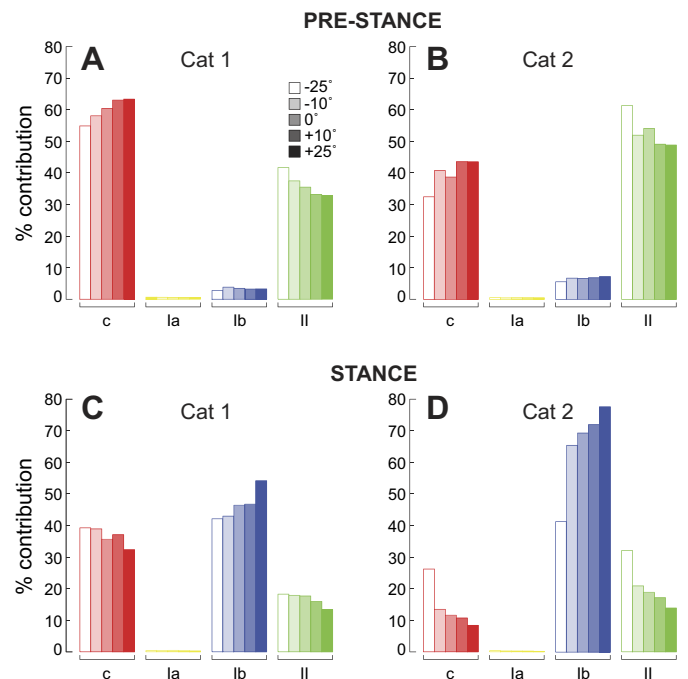


Fig. 5. Averaged contributions of central drive and the different feedback pathways to ankle extensor muscle activity. A and B: contributions during the prestance phase, defined as beginning when the burst in muscle activity begins and ending when the foot contacts the ground. C and D: contributions during the stance phase, defined as beginning when the foot contacts the ground and ending when the foot lifts off the ground. Shading of bars increases from the -25° slope condition (light) to the +25° slope condition (dark). c, Central drive.

Table 1. *Optimal model parameters*

	Ia		Ib		II		Central Drive					
	k_{Ia}	τ_{Ia}	k_{Ib}	τ_{Ib}	k_{II}	τ_{II}	m_i	t_{on}	T_{tr}	m_b	T_{dur}	m_f
<i>Cat 1</i>	0.01	2.3	4.6	0.0	0.26	0.2	-0.03	-87	53	0.35	383	0.02
<i>Cat 2</i>	0.01	1.6	7.7	2.0	0.3	0.1	-0.03	-84	72	0.34	265	0.01

All variables of time (τ , t , and T) are in units of milliseconds. The gain variables k_{Ia} , k_{Ib} , and k_{II} , which convert afferent activity measured in Hz to dimensionless muscle activity, have units of Hz^{-1} and are presented as $1,000\times$ their actual value. Time delays τ_{Ia} , τ_{Ib} , and τ_{II} allow for different feedback delays between the different afferent pathways. The initial (m_i) and final (m_f) values of the central drive signal, as well as its burst magnitude (m_b), are expressed as a fraction of each cat's peak measured muscle activity during level walking. t_{on} , burst onset time; T_{tr} , duration of the transition periods.

describe the measured data. Also, if we were to have allowed central drive to continuously vary its magnitude within the stride cycle and across slopes, it could exactly describe the measured muscle activity without the need for feedback. We consider this to be trivially true; arbitrarily complex feedforward control is always one candidate controller underlying the neural control of any movement. We can conclude, however, that this complexity is not needed to describe the vast majority of the behavior; a controller can be impressively simple and still automatically compensate for the changes in ankle extensor muscle activity that are required within the step cycle and across walking slopes.

Our methods and analyses have a number of important limitations. First, all measurements were taken from animals with an isolated MG muscle through denervation of other ankle extensors. Although isolation of MG was required to estimate proprioceptor activity, the intervention increased the loads placed on the muscle and may have changed the underlying neural control. Our measurements were made as long as 5 days after denervation, a time period sufficient to allow large changes to occur to the motor program (Maas et al. 2010; Pearson et al. 1999). Although most of the gradual adaptations to denervation have been interpreted as changes to feedforward commands (Pearson et al. 1999), it is nevertheless possible that denervation results in large changes to autogenic feedback gains. Denervation certainly changed the role of heterogenic control by removing the influence of length and force dependent reflexes from close MG synergists on MG activity (Eccles et al. 1957a, 1957b; Nichols 1999).

A second limitation is that our analysis only included data from two animals. This occurred because we leveraged data collected during a previous experiment (Donelan et al. 2009). Although this low sample size certainly constrains our ability to generalize, it should be noted that the observed patterns were consistent between animals and this was in no way prescribed by the analysis.

A third limitation concerns the identified feedback time delays. Although these were included as free parameters in the

model, the best-fit values were generally faster than is physiologically realistic (Table 1). We attribute this imprecision to methodological limitations. The kinematic data required for the proprioceptor models was captured with a slow sampling frequency (60 Hz), suggesting that we can only estimate time delays to within about 17 ms. Within this very limited precision, the identified delays (which ranged from 0.0 to 2.3 ms; Table 1) were almost in the range of values found in empirical experiments ($\sim 5\text{--}10$ ms; Donelan et al. 2009).

A final important limitation is the many assumptions required in estimating proprioceptor activity from measured kinematics and ground reaction forces. These include assumptions typical of inverse dynamics analyses (e.g., rigid bodies and no soft tissue movement) as well as assuming that only MG was responsible for generating the measured ankle extensor torque (Donelan et al. 2009). One consequence of this latter assumption is to neglect a possibly important role for passive tissue; Prilutsky et al. (2011) have demonstrated that it makes a major contribution to ankle extensor torque, especially after partial denervation of the ankle extensors. To correctly account for this contribution, as well as that from other intact muscles such as plantaris and flexor hallucis longus, requires different methods than originally used (e.g., tendon-buckle force transducers). A reasonable first approximation is to assume that actual MG forces were a fraction of our estimates. If this is indeed the case, our conclusions would be unchanged; a proportional reduction in Ib activity would result in a proportional increase in the optimal Ib feedback gain. Perhaps the most important of this class of assumptions was that proprioceptor models developed for level walking can also be applied to slope walking conditions. This is particularly important for feedback from spindles where modification in fusimotor drive will change the dynamic response of Ia and group II afferents. In light of these major limitations, as well as the many more minor ones present throughout this analysis, our quantitative findings are best viewed as predictions that must be further validated by existing data and tested using new experiments.

Conclusions drawn from this analysis are very similar to those drawn from other approaches. During the stance phase of level walking, our estimate of the contribution of central drive to ongoing activity is $\sim 25\%$ (Fig. 5). This value is similar to that estimated from unexpectedly removing the supporting surface immediately before ground contact in intact, decerebrate, and spinal cats (Angel et al. 1996; Bennett et al. 1996; De Serres et al. 2002; Donelan and Pearson 2004a, 2004b; Donelan et al. 2009; Gorassini et al. 1994; Hiebert and Pearson 1999; Hiebert et al. 1994; McCrea et al. 1995; Stein et al. 2000). In addition, comparable estimates of the contribution of central drive have been made for ankle extensors in walking

Table 2. *Characteristics of afferent activity*

	Ia		Ib		II	
	Avg, Hz	RMS, %	Avg, Hz	RMS, %	Avg, Hz	RMS, %
<i>Cat 1</i>	251	13	76	57	416	4
<i>Cat 2</i>	263	12	53	56	429	4

For each afferent type, values are the average activity (Avg) during the stance phase, averaged across walking slopes, and the root mean square (RMS) variability of the afferent activity during the stance phase, normalized for average activity and then averaged across walking slopes.

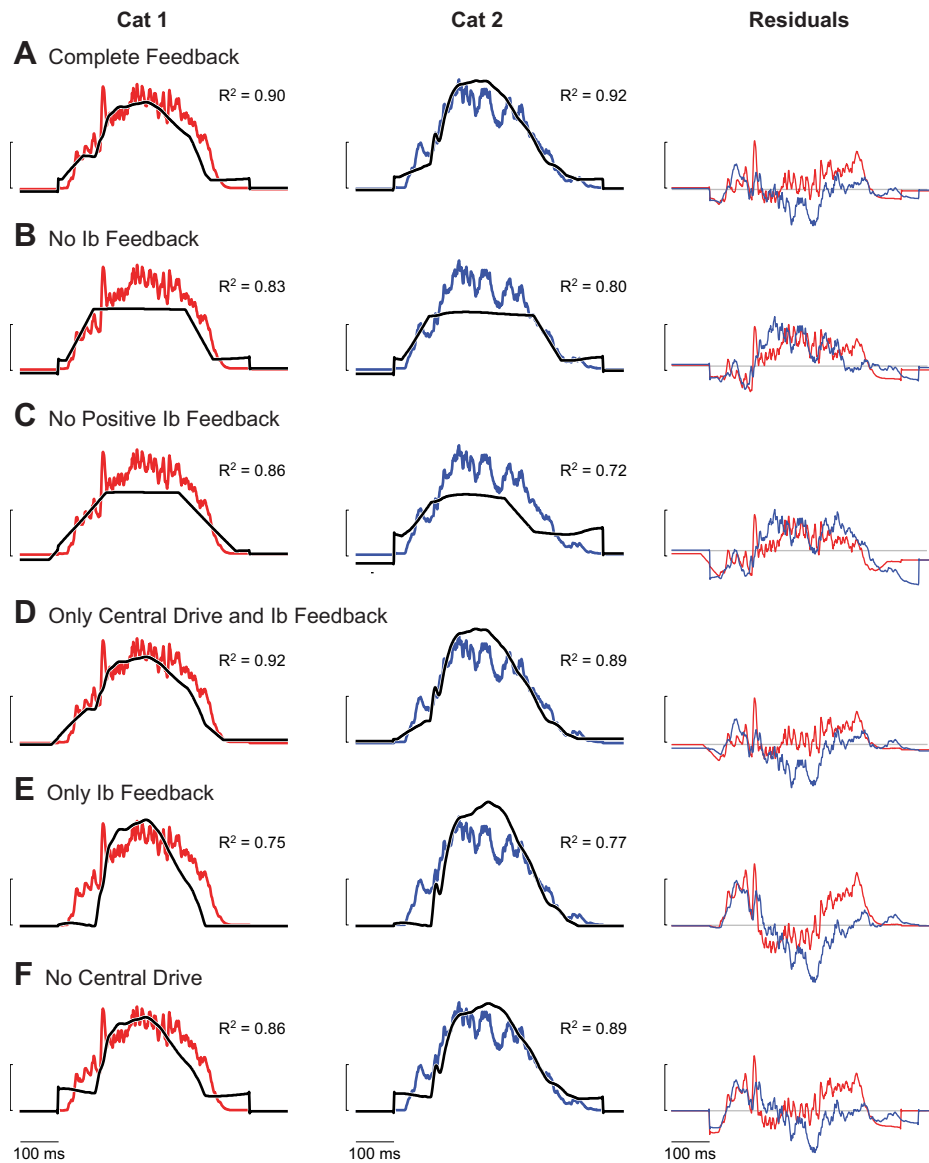


Fig. 6. Comparison between measured and predicted muscle activity for 6 alternative models (A–F). The optimal parameters for each model were estimated using the measured data from only the level walking trials (0° slope). All illustrated comparisons are at the $+25^\circ$ slope condition. The black lines in *left* and *middle* panels are the model predictions, and the colored lines are the measured muscle activity. *Right* panel illustrates the residuals, the difference between the measured data and the model predictions at each walking slope, for *cat 1* (red) and *cat 2* (blue). All scale bars are the same magnitude.

humans by forcibly flexing or extending the ankle joint (Sinkjaer et al. 2000; Yang et al. 1991). One discrepancy between our data and that from the literature concerns the prestance muscle activity. Our data demonstrated little effect of slope on prestance activity. However, Maas et al. (2010) also used denervation to isolate MG and found that there was a significant increase in prestance activity when comparing upslope to downslope walking. Although the discrepancy may be readily explained by differences between the two protocols, it nevertheless suggests that a model with constant central drive will not describe their measurements as well as it described ours.

Previous research also supports our finding that force feedback plays an important role in modulating ongoing stance phase muscle activity and that this role increases during upslope walking. A previous experiment on stepping in decerebrate cats, in which the MG muscle was held at different lengths and forcibly stretched using a motor while afferent activity was measured directly, found that force feedback accounted for 20% of muscle activity at short muscle lengths and 50% of activity at long muscle lengths (Donelan and

Pearson 2004a). Similarly, we found that the role of force feedback increased at the longer muscle lengths used during upslope walking, contributing about 63% of the activity, compared with downslope walking, when it contributed about 41%. Using the same data set that we used here but employing a different approach to estimate the contribution of force feedback yielded very similar quantitative and qualitative results (Donelan et al. 2009). Although this current research, as well as the above-referenced work, provides quantitative estimates for the role of positive force feedback, many studies have previously demonstrated an important role for this pathway (Donelan and Pearson 2004b; Duysens and Pearson 1980; Duysens et al. 2000; Hiebert et al. 1995; Pearson 2008; Pearson et al. 1992; Prochazka et al. 1997a, 1997b, 2002). Quantitative estimates of the role of force feedback in human walking do not yet exist, but experiments by Grey et al. (2004) clearly suggest an important role. Grey and colleagues found a large reduction in muscle activity during stance when the ankle is forcibly extended, and this reduction persisted when Ia, group II, and cutaneous feedback were eliminated using ischemic and

pharmaceutical nerve blocks. Our conclusions are restricted to autogenic feedback. Our analysis was not designed to estimate the contribution of MG feedback to the activity of other muscles, nor was it designed to estimate the contribution of feedback from other muscles to the activity of MG. The role of these heterogenic pathways could differ substantially. For example, Ross and Nichols (2009) report negative force feedback from the gastrocnemius muscles onto plantaris and flexor hallucis longus and from the quadriceps onto the gastrocnemius muscles.

The biggest discrepancy between our findings and those from the literature concerns the role of group II afferent feedback. Our modeling results suggest a minor but important tonic contribution to both prestance and stance phase activity (Figs. 4 and 5). Experimentally, the role of group II afferents in cats has been explored by electrically stimulating ankle extensor nerves first below the threshold for recruiting group II fibers and then above. During fictive locomotion in both spinal and decerebrate cats, as well as stepping in decerebrate cats, the incremental increase in stimulation intensity does not result in an incremental increase in motoneuron or muscle activity, suggesting that group II feedback has no contribution to ongoing activity (Donelan and Pearson 2004a; Gossard et al. 1994; Perreault et al. 1995). This evidence is by no means conclusive, because the absence of any effects of stimulating group II afferents also might be explained by a saturation of motoneuron activity by high-frequency stimulation of group I afferents. The evidence is similarly mixed in walking humans, where group II feedback appears to contribute to the increase in muscle activity when ankle extensors are forcibly stretched but not to the decrease in activity when they are forcibly shortened (Grey et al. 2001, 2002). Although these collective experimental results suggest a small role for group II feedback, they are certainly not definitive (Donelan and Pearson 2004a). Thus it is difficult to determine whether this particular model prediction is best viewed as spurious or as insight into a feedback mechanism that has been difficult to explore experimentally. If it is indeed spurious, we suspect that the role we currently ascribe to group II feedback is actually performed by central drive given their similar patterns of tonic activity (Fig. 4) as well as the respectable fits obtained by a model that does not include group II feedback (Fig. 6D) and a model that does not include central drive (Fig. 6F).

Our findings contribute to the growing body of evidence that Ia feedback plays a limited role in contributing to ongoing ankle extensor activity during walking. In the current analysis, we found that the Ia feedback gain that optimizes the fit between the measured and modeled muscle activity is nearly zero (Table 1). This is consistent with studies demonstrating presynaptic inhibition on monosynaptic group I connections to motoneurons in the decerebrate cat (Gosgnach et al. 2000), no effect of muscle vibration on ankle extensor activity during human walking (Verschuere et al. 2003), and reduced H-reflex magnitudes during walking compared with standing in humans (Capaday and Stein 1986). It is also consistent with the work of Sinkjaer et al. (2000) who demonstrated that the reduction in muscle activity which occurs when the ankle extensors are forcibly shortened during human walking persists after feedback from Ia afferents is eliminated with the use of an ischemic block. This does not necessarily mean that Ia feedback has no functional role during walking; it may be essential

for rapid responses to perturbations (Grey et al. 2001) even if it has no role in modulating muscle activity during normal walking (Donelan and Pearson 2004b).

In summary, our results indicate that the modulation of ankle extensor muscle activity within the step cycle and across walking slopes is indeed well described by neural control that employs constant central drive and constant proprioceptive feedback gains. Because central drive is constant, this modulation of muscle activity must be due to sensory feedback. The analysis suggests that force feedback from Ib afferents is primarily responsible for regulating muscle activity within the stance phase and across slopes; group II afferent feedback makes a small contribution to tonic activity, and Ia afferent feedback makes no contribution whatsoever. Our analysis suggests that neural control can be impressively simple and still automatically compensate for the changes in ankle extensor muscle activity that are required within the step cycle and across walking slopes.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

K.H., K.M., and J.M.D. conception and design of research; J.M.D. performed experiments; K.H., K.M., and J.M.D. analyzed data; K.H., K.M., and J.M.D. interpreted results of experiments; K.H. and J.M.D. prepared figures; K.H. and J.M.D. drafted manuscript; K.H., K.M., and J.M.D. edited and revised manuscript; K.H., K.M., and J.M.D. approved final version of manuscript.

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