

Force Regulation of Ankle Extensor Muscle Activity in Freely Walking Cats

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Donelan JM, McVea DA, Pearson KG. Force regulation of ankle extensor muscle activity in freely walking cats. *J Neurophysiol* 101: 360–371, 2009. First published November 19, 2008; doi:10.1152/jn.90918.2008. To gain insight into the relative importance of force feedback to ongoing ankle extensor activity during walking in the conscious cat, we isolated the medial gastrocnemius muscle (MG) by denervating the other ankle extensors and measured the magnitude of its activity at different muscle lengths, velocities, and forces accomplished by having the animals walk up and down a sloped pegway. Mathematical models of proprioceptor dynamics predicted afferent activity and revealed that the changes in muscle activity under our experimental conditions were strongly correlated with Ib activity and not consistently associated with changes in Ia or group II activity. This allowed us to determine the gains within the force feedback pathway using a simple model of the neuromuscular system and the measured relationship between MG activity and force. Loop gain increased with muscle length due to the intrinsic force-length property of muscle. The gain of the pathway that converts muscle force to motoneuron depolarization was independent of length. To better test for a causal relationship between modulation of force feedback and changes in muscle activity, a second set of experiments was performed in which the MG muscle was perturbed during ground contact of the hind foot by dropping or lifting the peg underfoot. Collectively, these investigations support a causal role for force feedback and indicate that about 30% of the total muscle activity is due to force feedback during level walking. Force feedback's role increases during upslope walking and decreases during downslope walking, providing a simple mechanism for compensating for changes in terrain.

INTRODUCTION

A long-standing issue in motor control is the extent to which afferent feedback from muscle and cutaneous receptors contributes to the activation of motoneurons during normal movements. There is now considerable evidence from studies in humans that reducing afferent feedback during voluntary, locomotor, and respiratory movements reduces the magnitude of ongoing activity in contracting muscles (Collins et al. 1999; Corda et al. 1965; Macefield et al. 1993; Mazzaro et al. 2005). Similarly, reducing afferent feedback from the hind legs of walking cats by removing the ground support markedly reduces the magnitude of activity in weight-bearing muscles (Gorassini et al. 1994; Hiebert and Pearson 1999; Hiebert et al. 1994). Collectively, these studies in humans and cats have indicated that a substantial fraction, roughly 50% in some cases, of suprathreshold activation of motoneurons depends on afferent feedback. Currently there is considerable uncertainty about the identity of the sensory receptors providing the feed-

back signals contributing to motoneuronal activation. Feedback from cutaneous receptors in the fingers likely plays a role in reinforcing motoneuronal activity during grasping (Collins et al. 1999), whereas feedback from muscle spindles has been implicated in regulating the level of activity in ankle extensor muscles during walking and running in humans (Dietz et al. 1979; Mazzaro et al. 2005; Sinkjaer et al. 2000) as well as voluntary contractions of ankle flexor muscles in humans (Macefield et al. 1993). A significant contribution of feedback from muscle spindles to the activation of intercostal muscles is also likely in the respiratory system of the cat (Corda et al. 1965).

In the walking system of the cat, evidence has accrued over the past two decades that afferent feedback is a major contributor to ongoing ankle extensor muscle activity during the stance phase (see reviews by Donelan and Pearson 2004b; McCrea 2001; Pearson et al. 1998). Furthermore, studies in decerebrate and spinal animals have led to the notion that a major component of the reinforcing afferent signal comes from the force-sensitive Golgi tendon organs (GTOs) in the ankle extensor muscles (Donelan and Pearson 2004b). The strongest evidence for this notion is that electrical stimulation of group Ib afferents arising from GTOs in the ankle extensor muscles has an excitatory action on motoneurons innervating these muscles during locomotor activity (Gossard et al. 1994; Pearson and Collins 1993). Because muscle contractions activate the GTOs, this excitatory action means that GTOs operate within a positive feedback pathway to reinforce contractions in the ankle extensor muscles during locomotor activity. The loop gain of this positive feedback pathway in the gastrocnemius muscles has been estimated to range from 0.2 at short muscle lengths to 0.5 at longer muscle lengths (Donelan and Pearson 2004b), demonstrating that force feedback was of modest importance at short muscle lengths, accounting for 20% of total activity and force, and of substantial importance at long muscle lengths, accounting for 50%. Because the evidence that positive force feedback plays a role in regulating activity in the ankle extensor muscles has come entirely from studies of stepping in reduced preparations, an important question is whether positive force feedback also functions to control ankle extensor activity during walking in conscious animals. We know that unexpectedly reducing the loading to the ankle extensors in normal walking animals significantly reduces the level of activity in these muscles (Gorassini et al. 1994). However, these experiments have not provided data for or against the possibility that the reduction in activity is due to a reduction in feedback from GTOs in the ankle extensors. Relevant to this

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question are the recent findings in walking humans that unloading the ankle extensor muscles reduces activity in the soleus muscle and this effect is not mediated by afferents from primary and secondary muscle spindles or from cutaneous receptors (Grey et al. 2004; Mazzaro et al. 2005). Furthermore, a recent study has demonstrated that the magnitude of the unloading effect is proportional to the reduction in force in the ankle extensor muscles and not positively correlated with reductions in muscle length and lengthening velocity (Grey et al. 2007). In short, the findings from human walking and reduced preparations both suggest that force feedback is functioning to regulate ongoing ankle extensor activity.

Our objective in the present study was to gain insight into the relative importance of force feedback to ongoing ankle extensor activity during walking in the conscious cat. To meet this objective, we isolated the medial gastrocnemius muscle (MG) and measured the magnitude of its activity at different muscle lengths, velocities, and forces accomplished by having the animals walk up and down a sloped pegway. MG length and velocity were estimated by combining joint kinematics with anatomical measurements and MG force was estimated by combining ground reaction force measurements with an inverse dynamics analysis. Previously established mathematical models of proprioceptor dynamics predicted afferent activity from the estimated muscle mechanics (Prochazka 1999). Analysis of the predicted proprioceptor activity revealed that the changes in muscle activity under our experimental conditions were strongly correlated with Ib activity and not consistently associated with changes in Ia or group II activity. This allowed us to determine the loop gain of the force feedback pathway using a simple model of the neuromuscular system and the measured relationship between MG activity and force. From the loop gain estimates, we calculated the fractional contribution of force feedback to MG muscle activity during walking over different terrains. In addition to the sloped pegway protocol, a second set of experiments were performed in which the MG muscle was perturbed during walking using drops or lifts of one of the pegs during ground contact of the hind foot. This provided a better test for a causal relationship between modulation of force feedback and changes in muscle activity.

METHODS

Experiments were performed on two female adult cats (cat 1, mass = 2.96 kg; cat 2, mass = 2.80 kg). All procedures were approved by the Health Sciences Animal Policy and Welfare Committee at the University of Alberta.

Sloped pegway experimental procedures

The animals were trained to walk on a pegway (Fig. 1A) at five different slopes (+25, +10, 0, -10, -25°). One peg in the middle of the pegway was instrumented with a force transducer (Model MC3A-3-100; AMTI, Watertown, MA) to measure the vertical and fore-aft reaction forces generated by the ground on the right-side limbs. Positive forces were in the upward and forward directions, respectively. The animals used self-selected speeds and gaits. Once sufficiently trained, which took about 14 days, the animals settled into a comfortable and consistent walking speed regardless of slope with legs from the right and left sides of the body contacting pegs only on the right and left sides of the pegway, respectively.

EMG recording electrodes were then implanted into the main ankle extensor muscles of the right hind leg: medial and lateral gastrocnemius (MG and LG), soleus (SOL), and plantaris (PL). Detailed procedures for implanting electromyographic (EMG) electrodes for recording in intact, walking animals have been described elsewhere (Whelan and Pearson 1997). Briefly, the EMG electrodes consisted of a multistranded stainless steel wire (AS632, Cooner Wire) insulated with Teflon except for an approximately 3-mm length positioned in the muscle. The ends of the electrode wires were secured to a 21-gauge needle that was then passed through the belly of the muscle while the animal was under anesthesia (isoflurane). The two wires of an electrode pairing were then knotted and secured to the muscle with a silk suture. The electrodes wires were initially fed subcutaneously from the head. The proximal ends of the wires were connected to a multipin socket that was secured to the skull with dental acrylic. A cable connection to the amplifiers was inserted into the socket during recording sessions. This cable was supported above the animal by a retractable tether so that the cat was free to move along the pegway. After a 2-day recovery period, the EMG signals were tested while the animal walked on the pegway. This was repeated for 5 days to ensure that the signals were stable across recording sessions.

It is impossible in intact animals to determine forces in individual muscles from external measures alone because multiple muscles cross each joint. To overcome this, the MG muscle of the right hindlimb was isolated by denervation of other main ankle extensors (LG, SOL, and PL). We chose to isolate MG rather than one of the other ankle extensors to facilitate comparisons with previous findings from re-

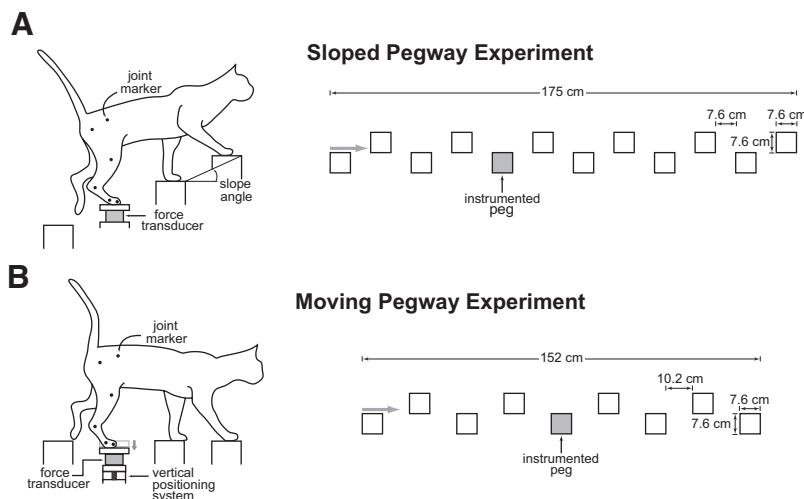


FIG. 1. Illustrations of the experiment procedures used in the sloped pegway experiments (A) and the moving pegway experiments (B).

duced preparations (Donelan and Pearson 2004a). Although muscle force could be estimated using tendon buckle force sensors (Herzog et al. 1993), isolation by denervation served two additional purposes. First, it increased the range of forces, lengths, and velocities experienced by the muscle, allowing for loop gain estimates over a wide range of conditions. Second, it allowed us to study force feedback onto MG in isolation of the heteronymous feedback pathways from the other ankle extensor muscles present in intact animals (Donelan and Pearson 2004a; Nichols 1999). Apart from the gastrocnemius, soleus, and plantaris muscles, there are a few other muscles that can produce extension torques at the ankle, the most prominent being flexor hallucis longus (Bonasera and Nichols 1994). The extent to which this muscle contributes to ankle torque during walking is unknown, but we estimate that it is relatively small because tenotomy of the gastrocnemius, soleus, and plantaris muscles produced a complete collapse at the ankle joint (unpublished observations). The protocol for the denervation procedure was identical to that used by Pearson et al. (1999). Under anesthesia, the common nerve to LG and SOL and the nerve to PL were exposed and transected. The absence of EMG signals in the LG, SOL, and PL muscles was used to establish that the nerves had been transected. Sutures were placed on the proximal ends to allow for later identification (postmortem dissection also confirmed that the correct nerves were transected). About 5 h after recovery from the anesthetic, EMG, ground reaction forces, and sagittal plane video were recorded while the animals walked on the sloped pegway. Prior to the recording sessions, reflective markers were placed on the skin over the iliac crest, the hip, knee, ankle, and metatarsal phalangeal (MTP) joints as well as on the end of the phalanges. Data were analyzed on the first day after denervation during which the animal would complete walking trials at all five pegway slopes. This was on the second day for one animal and on the fifth day for the other.

Moving pegway experimental procedures

Another strategy we used to modify forces in the ankle extensor muscles was to perturb the supporting surface during the stance phase. The animals were trained to walk on a level pegway with one instrumented and motorized peg that could be lowered rapidly (Fig. 1B). This peg was instrumented with a force transducer (Model MC3A-3-100; AMTI, Watertown, MA) to measure ground reaction forces. The force transducer was mounted on a vertical positioning system to allow the peg to be dropped at specified rates and displacements. This system consisted of a rotational stepper motor (Model NEMA 23; Applied Motion Products, Watsonville, CA), controlled by a programmable step motor drive (Model Si3540; Applied Motion Products), and coupled to a ball and screw stage assembly to translate motor rotation into peg vertical displacement (Model 130 series; LinTech, Monrovia, CA). The displacements were triggered by liftoff of the right front paw, signaled by a reduction in its vertical ground reaction force. Because liftoff of the right front paw immediately precedes right hind paw touch down on the same peg, the peg movements were timed to begin close to the initiation of hind-paw ground contact. The drop and lift trials displaced the peg 4 cm over a period of 200 ms. Although this protocol caused measurable decreases in vertical ground reaction force during the peg movement, the animals did not withdraw their paws nor were vertical ground reaction forces reduced to zero. As a consequence, this procedure is distinct from previous trapdoor experiments in which ground reaction forces were eliminated and flexor withdrawal reflexes were induced (Gorassini et al. 1994; Hiebert et al. 1994, 1995). As with the sloped pegway procedures, the animals used self-selected speeds and they settled into a comfortable and consistent walking speed with sufficient training. Control trials in which the peg was held stationary preceded and followed the drop trials.

Data analysis

Amplified EMG and ground reaction force signals were sampled at 1,200 Hz and stored on a computer hard drive. Video was recorded to tape at 60 Hz then captured to hard drive and synchronized with the EMG and force recordings using Peak Motus software (Denver, CO). This same software was used to digitize the position of reflective markers then to transform and scale the results so that pixel coordinates were given in sagittal-plan real-world coordinates. All subsequent analysis was performed in custom programs written in Matlab (The MathWorks, Natick, MA). The raw EMG signals were rectified and filtered with a 20-Hz cutoff, first-order one-way low-pass Butterworth digital filter.

To estimate MG length and velocity, marker coordinates were first filtered with a fourth-order two-way low-pass Butterworth digital filter with a cutoff frequency of 6 Hz and then resampled to match the sampling frequency of force and EMG data using cubic spline interpolation. Due to 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 derived from these joint position coordinates with the convention that positive angles were in the extension direction for both the ankle and knee joints. 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. We visually estimated each joint center as the point with the least movement on manual flexion and extension of the joint. Postmortem dissection determined that for both animals these insertion and origin distances were 15 mm away from the ankle joint along the calcaneum and 5 mm away from the knee joint along the femur. With the knee joint at 100° and the ankle at 110°, these distances equate to ankle and knee moment arm lengths of 14.5 and 5.0 mm, comparing well to the more systematic measurements of others (Burkholder and Nichols 2004). Tendon stiffness was estimated from the product of an assumed 400 MPa elastic modulus (Rack and Westbury 1984) and the tendon cross-sectional area, determined postmortem. We estimated the contribution of tendon to the overall muscle-tendon unit length as the sum of the relaxed tendon length, measured post mortem, and the product of tendon stiffness and MG muscle force (see next paragraph). The estimated muscle fiber length was the overall muscle-tendon unit length less the estimated tendon length. Although we took care to make these measurements carefully, we found that a wide range of tendon stiffnesses had little effect on our overall results.

We used inverse dynamics to estimate the force generated by the MG muscle. The raw ground reaction forces from the instrumented peg were scaled by the manufacturer-determined calibration factors and filtered with a 50 Hz cutoff, fourth-order two-way low-pass Butterworth digital filter. The point at which the force was applied to the body was assumed to be located in the middle of the hind-digits segment. Segment center of mass locations and inertial properties were estimated for the phalanges, tarsals, and shank using regression equations from Hoy et al. (1985) parameterized by body mass measured on the day of the experiment and segment lengths determined postmortem. Segment center of mass accelerations were calculated as the second time derivative of the center of mass position. We used central finite differences as the numerical algorithm for estimating the derivative (Griffiths and Smith 2006) and filtered the data after each derivation with a 6 Hz cutoff, fourth-order two-way low-pass Butterworth digital filter. Having determined the ground reaction forces, segmental accelerations, segmental inertial properties, and segmental geometry, we performed an inverse dynamics analysis on a three-segment rigid body model to solve for the unknown joint forces and moments. Our calculations began with the phalanges and the MTP joint and proceeded proximally, first to the tarsal segment and ankle joint and then to the shank segment and knee joint. Having isolated MG by denervation of the other major ankle extensors, we assumed

that the ankle joint moment was due entirely to force generated by MG. A second assumption was that the line of action of the MG force was along the line that joins its origin to insertion. These assumptions—combined with the measured ankle moment, ankle and knee kinematics, and location of the MG origin and insertion—allowed us to estimate the MG muscle force.

Measured ground reaction forces during the moving peg trials (Fig. 2B) included the inertia of the peg mass. To correct for this nonphysiological force, we measured ground reaction forces during calibration trials in which the peg was displaced under the exact same conditions but without the animal stepping on the peg. This was repeated three times for each condition and averaged to estimate the inertial force of the moving peg (Fig. 2A). This inertial force was then subtracted from the measured ground reaction forces to estimate the forces exerted by the cat paw on the ground (Fig. 2C). The validity of this method is supported by the nearly total elimination of “ringing” in the ground reaction force signal after subtraction of calibration trial data. It works well because the forces exerted by the cat on the moving peg are relatively small compared with the strength of the motor.

Predicted proprioceptor activity

Having determined MG muscle length, velocity, and force, we used mathematical models of proprioceptor dynamics to predict afferent activity. These models are based on those presented in Prochazka (1999) with modifications to better suit our experimental conditions. 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 displacement normalized by rest length. Test length was approximated as the length of the muscle-tendon unit when the ankle and knee are fixed at 90° of flexion. 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. Because the square root of negative velocities will yield an imaginary number, we first calculated the square root of the absolute value of the

velocity and then restored the sign. There are a few notable distinctions between Eq. 1 and the Ia model presented in Prochazka (1999). First, we have removed the bias constant because we are concerned only about modulation of afferent activity and not the absolute activity level. Second, we have removed the term that corrected for alpha-gamma coactivation. This correction involved adding a fraction of the appropriately filtered EMG signal to the Ia activity predicted from position and velocity terms. Ignoring this term in our analysis is equivalent to assuming that animals use the same level of alpha-gamma coactivation at the same period of the step cycle under all measured conditions.

The model for II afferent activity is given by the following equation

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

As with the Ia model, we have removed the bias term and the EMG-dependent term.

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 (w).

We computed the average proprioceptor activity, muscle activity, and muscle mechanics within two regions of the step cycle (Figs. 4–6). The early region was defined as a 50 ms interval immediately preceding ground contact. We evaluated this region to study the effect of changes in Ia and group II afferent on muscle activity in the absence of a significant change in muscle force and Ib activity (Fig. 6). The middle region was defined as a 50 ms interval that began 50 ms after ground contact. This particular interval was chosen because, compared with changes in Ib activity, there was little modulation of Ia and group II activity at different pegway slopes in both animals. This allowed us to study the effects of changes in Ib activity on muscle activity in isolation of contributions from the other proprioceptors. Although defining the middle region as occurring later in the stance phase would have resulted in larger differences in muscle activity (Figs. 4 and 5), it would have prevented us from isolating the effects of force feedback in one of the animals because Ia and II activity depended on slope during late stance.

Estimation of force feedback gain

We used the simple linear model of the neuromuscular system presented in Donelan and Pearson (2004a) to estimate the contribution of homonymous force feedback to total MG muscle activity and force (Fig. 7A). Due to our findings, we assumed that the only afferent pathway responsible for the modulation of muscle activity during the middle region of the MG bursts was the group Ib pathway arising from force-sensitive GTOs. We also assumed that there was linear summation of the central drive e_c to the MG motoneurons and the force feedback signal from group Ib afferents e_f . The constant e_c term may also include the contributions of tonic feedback from other afferent pathways. The sum of the feedforward and feedback contributions yields total motoneuronal activity e_t . Total muscle force f_t is the product of muscle activity and a parameter M , related to the intrinsic properties of muscle (termed “muscle gain”). We used the relationship between EMG (a measure of motoneuronal activity) and force during the middle region of the MG contractions to estimate the model parameters for each animal during each trial at each slope. Since e_t is equal to e_c when the muscle is too short to generate force, we estimated e_c as the y-intercept of the best-fit linear regression line for the relationship between total muscle activity and force (Fig. 7B). We then normalized total activity by e_c and total force by body weight w . This normalization makes our subsequent calculations independent

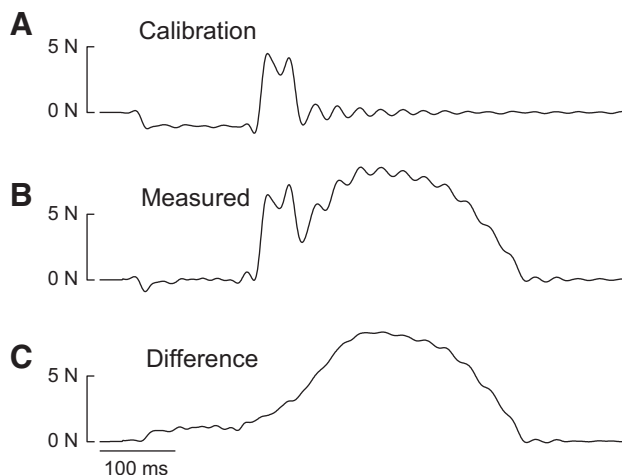


FIG. 2. Representative results for subtracting the component of ground reaction due to peg inertia. A: average measured force during calibration trials when the peg was moved through the same trajectory as the normal trials but without the animal stepping on the peg. B: measured ground reaction force during the moving peg trials with the animal stepping on the peg. C: subtracting the calibration force in A from the measured force in B estimates the force exerted by the cat paw on the ground.

of size and nonphysiological factors, such as electrode placement, allowing for more meaningful comparisons between animals. This estimate of e_c —accompanied by our measurements of e_t and f_t —allows for the algebraic solution of pathway gains. For each stride, we estimated force feedback gain, K , as

$$K = \frac{e_f}{f_t} = \frac{e_t - e_c}{f_t} \quad (5)$$

where K is in units of $e_c \cdot w^{-1}$. The muscle gain M was defined as

$$M = \frac{f_t}{e_t} \quad (6)$$

where M is in units of $w \cdot e_c^{-1}$. The dimensionless product of the muscle and force feedback gains, termed “loop gain” (Prochazka et al. 1997b), is of particular importance. First, it gives the relative contribution of force feedback to total muscle activity and force

$$\frac{e_f}{e_t} = \frac{f_t}{f_t} = K \cdot M \quad (7)$$

where f_t is the contribution of force feedback to f_t . Second, the average loop gain in this positive feedback system must be less than unity for steady-state muscle activity and force (Prochazka et al. 1997a).

Statistical analysis

We tested the significance of measured relationships using best-fit least-squares linear regression. In addition to determining the slope and y-intercept of the line that best fit the data, this procedure yielded a measure of the probability that these coefficients were zero (i.e., P value). If the probability was $<5\%$ ($P = 0.05$), we accepted the relationship as significant.

RESULTS

Comparison of denervated cat data with intact cat data

Isolating the MG muscle resulted in substantial changes in muscle activity and limb dynamics during walking. This is illustrated in Fig. 3 by a comparison of level walking data before and after denervation. Prior to denervation, the measured walking mechanics compare well with previous findings (Goslow Jr et al. 1973; Gregor et al. 2006; Kaya et al. 2005; Smith et al. 1998). Our findings of large increases in MG activity and an increased flexion at the ankle joints after MG isolation are also consistent with previous studies (Pearson et al. 1999). The increase in muscle activity is necessary for MG to generate ankle torque that is normally provided by the denervated ankle extensors. It is unlikely that cutaneous feedback from receptors in the feet is responsible for the increased muscle activity after MG isolation because there was an overall reduction in the vertical ground reaction force as well as a poor correlation between the decreased rate of change in ground reaction force and the increased rate of change in muscle activity.

Sloped pegway experiments

Our objective in the sloped pegway experiments was to gain insight into the relative importance of force feedback to ongoing ankle extensor activity during walking in the conscious cat. To meet this objective, we used a sloped pegway to require the animals to put the isolated MG muscle through a range of

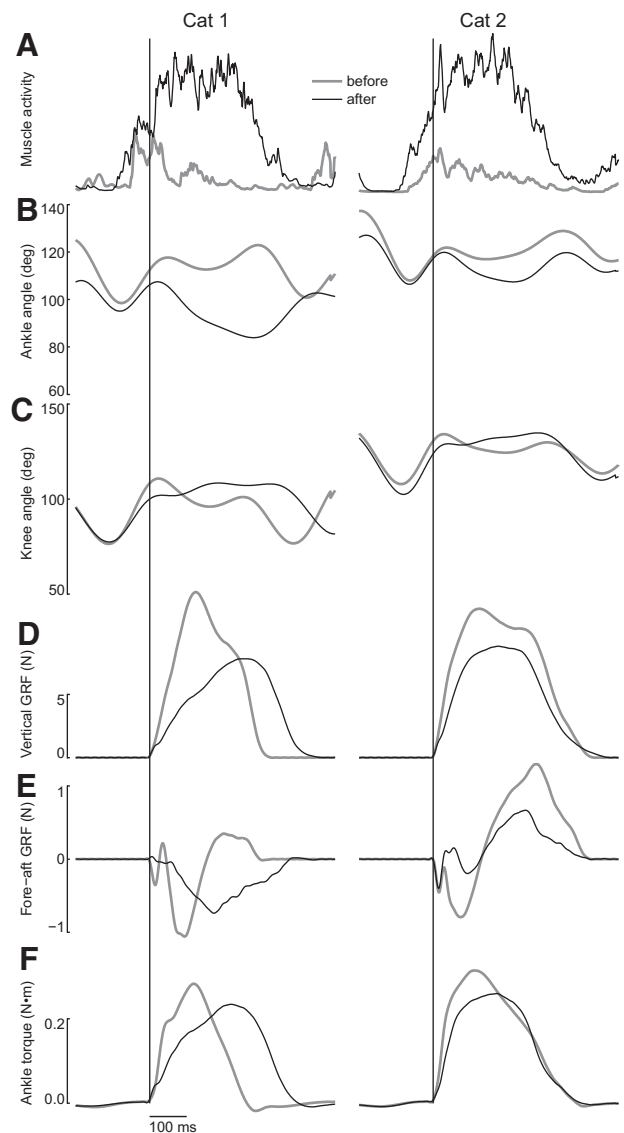


FIG. 3. Isolating the medial gastrocnemius (MG) muscle, accomplished by denervation of the other major ankle extensors, resulted in large changes in muscle activity and limb dynamics during walking compared with animals with intact ankle extensor innervation. The left and right columns are results from cat 1 and cat 2, respectively. The gray and black lines represent results from before and after denervation, respectively. These results are averaged from multiple speed-matched steady-state level walking trials. Comparison of pre- and postdenervation data for cat 1 is compromised by the slower average speed postdenervation. The vertical black line indicates the beginning of stance.

muscle lengths, velocities, forces, and levels of activity. As anticipated, stance phase activity in the isolated MG muscle and leg mechanics changed as a function of pegway slope (Fig. 4). MG activity was substantially greater throughout the stance phase of walking upslope compared with downslope. In contrast, MG activity was relatively unchanged immediately before the foot touched down. This suggests that feedback, rather than feedforward control, is responsible for the observed modulation of stance phase muscle activity (Pearson et al. 1999). To accommodate the higher stairs during upslope walking, the ankle and knee began the stance phase in a flexed position and extended throughout stance, performing a portion of the positive mechanical work required of upslope walking. During downslope walking, the ankle and knee were extended at the

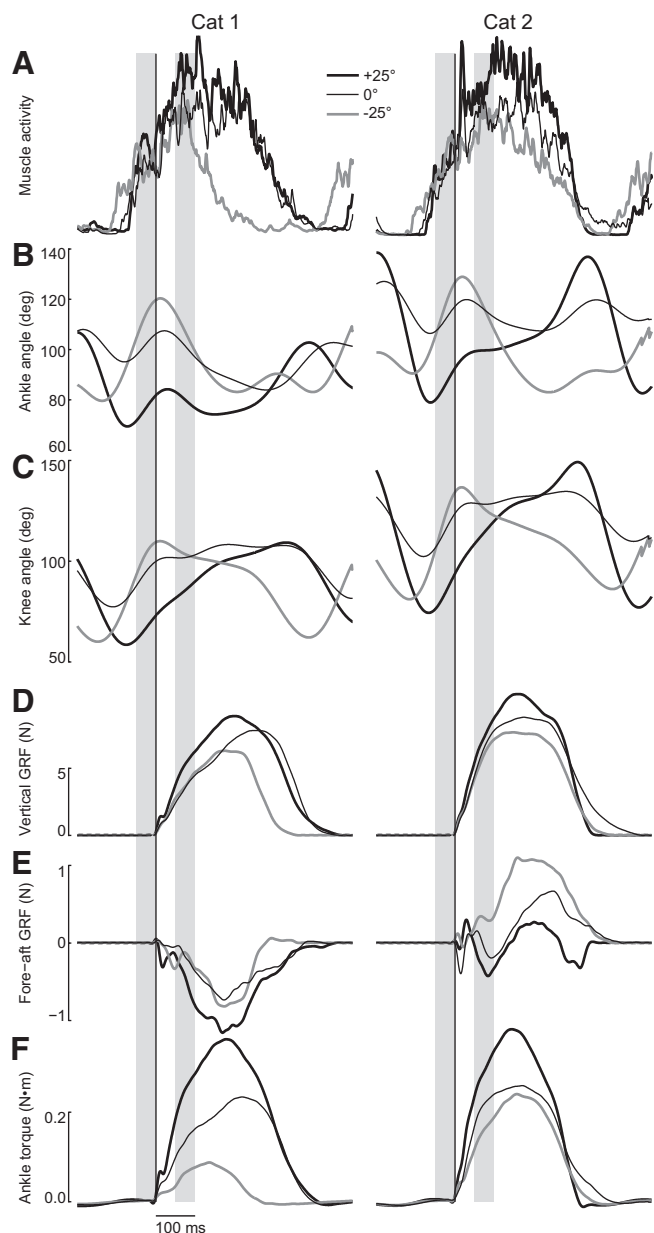


FIG. 4. Pegway slope has a substantial effect on MG muscle activity and limb dynamics. The *left* and *right* columns are results from cats 1 and 2 after MG isolation. The thin black line, thick black line, and gray line are for level, +25°, and -25° trials, respectively (for clarity, we have not presented the +10 and -10° conditions). These results are averages from multiple speed-matched steady-state trials. The vertical black lines indicate the beginning of stance. The shaded vertical bars denote the early and middle regions used in subsequent analyses.

beginning of stance and flexed throughout, performing negative work on the body. The average vertical ground reaction force increased with upslope walking as the responsibility for supporting the majority of body weight shifted from the front legs to the hind legs. The hindlimb fore-aft ground reaction force tended to become more propulsive with a decrease in slope, suggesting that the front legs provided additional braking impulse to keep speed constant. Calculated ankle torque increased substantially during upslope walking relative to level walking as a consequence of the increased ankle flexion and vertical ground reaction force. Similarly, increased ankle exten-

sion and decreased vertical ground reaction force resulted in a decrease in the calculated ankle torque during downslope walking.

Figure 5 illustrates the effect of pegway slope on muscle mechanics and predicted proprioceptor activity. The MG mus-

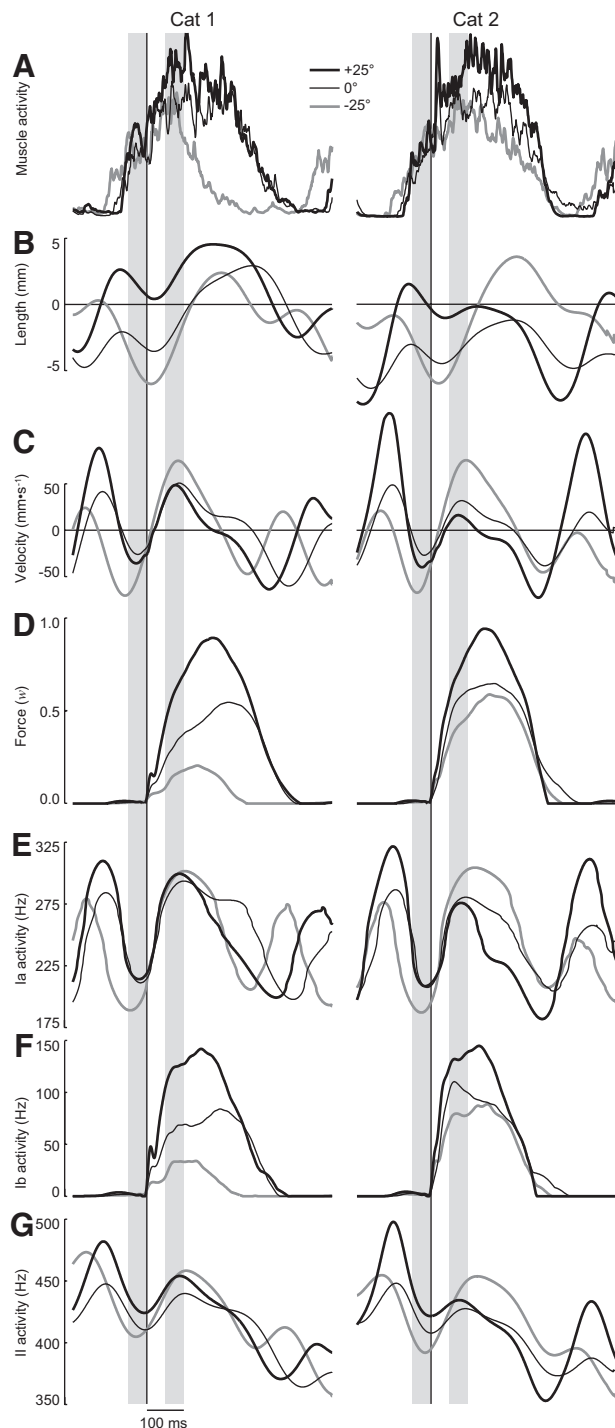


FIG. 5. The effect of pegway slope on MG muscle mechanics and predicted proprioceptor activity. The *left* and *right* columns are results from cats 1 and 2 after MG isolation. The thin black line, thick black line, and gray line are for level, +25°, and -25° trials, respectively (for clarity, we have not presented the +10 and -10° conditions). These results are averages from multiple speed-matched steady-state trials. The vertical black lines indicate the beginning of stance. The shaded vertical bars denote the early and middle regions used in subsequent analyses.

cle is biarticular, crossing both the ankle and knee joints with the extensor moment arm about the ankle approximately three-fold the length of the flexor moment arm about the knee. As a consequence, the length of the MG muscle-tendon unit is most strongly dependent on ankle angle and increases with ankle flexion. Due mainly to the ankle joint kinematics, illustrated in Fig. 4, the isolated MG muscle is substantially longer at stance phase initiation during upslope walking compared with level walking. The muscle velocity in uphill walking is mainly negative as it shortens throughout much of the stance phase. In contrast, MG is shorter at stance phase initiation during downhill walking and the muscle velocity is generally positive as it lengthens throughout stance. This pattern of long and shortening muscle during upslope walking and short and lengthening muscle during downslope walking has an interesting effect on predicted spindle activity. Increases in muscle length or muscle velocity both tend to increase Ia and II activity (*Eqs. 1 and 3*). A decrease in muscle length will tend to counteract the effect of an increase in muscle velocity, or vice versa, resulting in a suppression of the modulation of spindle activity. This effect is illustrated in the middle regions of Fig. 5 where there are negligible differences in predicted Ia and II activity as a function of pegway slope, despite large differences in muscle mechanics. Isolation of MG by denervation of the other main ankle extensor muscles allowed us to use inverse dynamics to accurately predict its force production and thus Ib activity. Due to the strong dependence of muscle force on pegway slope illustrated in Fig. 5, Ib activity increased during the stance phase of upslope walking and decreased during downslope walking, relative to level walking. These large changes in predicted Ib activity are in sharp contrast to the relatively small changes in predicted spindle activity.

Figure 6 presents the changes in muscle activity, velocity, and force, as well as predicted proprioceptor activity, as a function of muscle length during the early and middle regions of the step cycle. Changes in muscle length are caused by the different pegway slopes with longer and shorter muscle lengths occurring during upslope walking and downslope walking, respectively. As is to be expected, middle-region muscle activity and force increased at longer muscle lengths. The slope for the cat 1 linear regression between muscle activity and muscle length was $0.13 \pm 0.10 \text{ mm}^{-1}$ ($P = 0.02$) and for cat 2 the linear regression was $0.12 \pm 0.04 \text{ mm}^{-1}$ ($P = 2.4 \times 10^{-5}$). For the relationship between muscle force and muscle length, the linear regression slopes of cat 1 and cat 2 were $0.07 \pm 0.03 \text{ w} \cdot \text{mm}^{-1}$ ($P = 8.9 \times 10^{-6}$) and $0.07 \pm 0.01 \text{ w} \cdot \text{mm}^{-1}$ ($P = 3.1 \times 10^{-10}$), respectively. As noted previously, muscle velocity tended to decrease at longer lengths (cat 1 slope: $-6.5 \times 10^{-3} \pm 5.9 \times 10^{-3} \text{ m} \cdot \text{s}^{-1} \cdot \text{mm}^{-1}$, $P = 0.03$; cat 2 slope: $-2.4 \times 10^{-3} \pm 2.4 \times 10^{-3} \text{ m} \cdot \text{s}^{-1} \cdot \text{mm}^{-1}$, $P = 0.06$). This resulted in middle-region Ia and II activity that tended to be independent of muscle length. For the predicted Ia activity, the cat 1 slope was $-1.61 \pm 3.33 \text{ Hz} \cdot \text{mm}^{-1}$ ($P = 0.331$) and the cat 2 slope was $1.23 \pm 1.15 \text{ Hz} \cdot \text{mm}^{-1}$ ($P = 0.04$). For the predicted II activity, the cat 1 slope was $1.96 \pm 3.32 \text{ Hz} \cdot \text{mm}^{-1}$ ($P = 0.237$) and the cat 2 slope was $1.78 \pm 2.87 \text{ Hz} \cdot \text{mm}^{-1}$ ($P = 0.211$). This independence from length change suggests that feedback from muscle spindles is not responsible for the regulation of middle-region muscle activity in these sets of experiments. In contrast, predicted Ib activity increased strongly with muscle length (cat 1 slope: $12.7 \pm 4.8 \text{ Hz} \cdot \text{mm}^{-1}$, $P = 1.1 \times 10^{-5}$; cat 2 slope: $14.6 \pm$

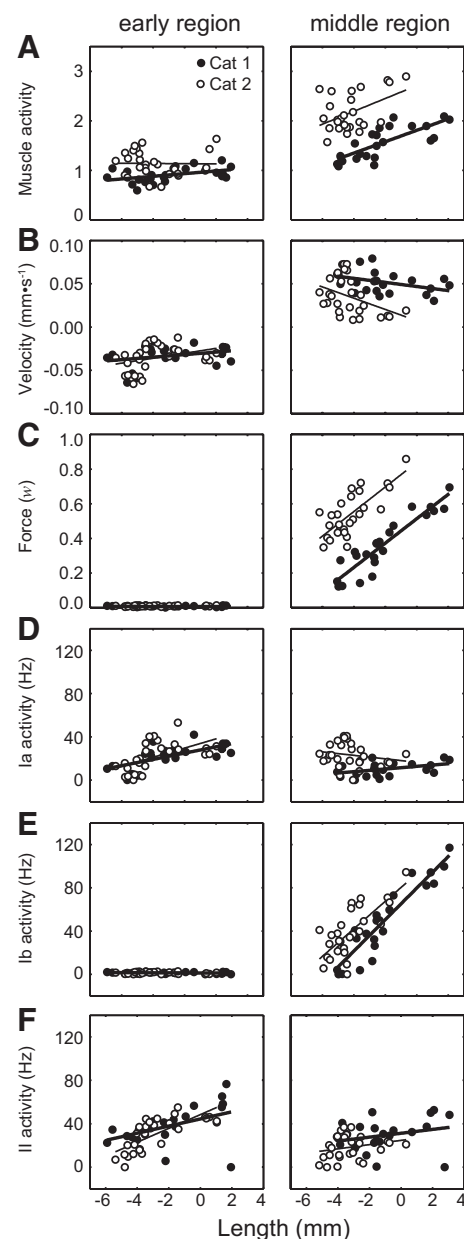


FIG. 6. The dependence of muscle activity, muscle mechanics, and predicted proprioceptor activity on MG muscle-tendon unit length during the early region (*left*) and middle region (*right*) of MG muscle activity (see Fig. 5). Each data point is for a single trial from the +25, +10, 0, -10, and -25° conditions. The closed and open symbols represent data collected from cat 1 and cat 2, respectively. The lines represent best-fit linear regressions.

$2.69 \text{ Hz} \cdot \text{mm}^{-1}$, $P = 2.3 \times 10^{-10}$), suggesting that force feedback from Golgi tendon organs was regulating the ongoing muscle activity.

These findings are supported by analysis of the early-region data (Fig. 6). Prior to foot touchdown, both muscle activity (cat 1 slope: $-2.2 \times 10^{-3} \pm 5.9 \times 10^{-2} \text{ mm}^{-1}$, $P = 0.94$; cat 2 slope: $2.7 \times 10^{-2} \pm 2.5 \times 10^{-2} \text{ mm}^{-1}$, $P = 0.04$) and force (cat 1 slope: $1.6 \times 10^{-4} \pm 6.9 \times 10^{-4} \text{ w} \cdot \text{mm}^{-1}$, $P = 0.63$; cat 2 slope: $-1.6 \times 10^{-4} \pm 6.4 \times 10^{-4} \text{ w} \cdot \text{mm}^{-1}$, $P = 0.62$) were relatively independent of muscle length compared with the middle-region values. Predicted Ib feedback was effectively zero as significant MG muscle force began at foot contact (cat 1 slope: -0.032 ± 0.20

Hz·mm⁻¹, $P = 0.75$; cat 2 slope: -0.072 ± 0.11 Hz·mm⁻¹, $P = 0.19$). Whereas muscle activity was unchanged, predicted Ia and II activity both increased with length. For the early-region predicted Ia activity, the cat 1 slope was 4.25 ± 2.62 Hz·mm⁻¹ ($P = 2.6e-3$) and the cat 2 slope was 2.91 ± 1.43 Hz·mm⁻¹ ($P = 3.7e-4$). For the predicted II activity, the cat 1 slope was 6.37 ± 2.38 Hz·mm⁻¹ ($P = 9.8e-6$) and the cat 2 slope was 3.29 ± 2.87 Hz·mm⁻¹ ($P = 2.7e-2$). The relatively large changes in predicted spindle activity and the relatively small changes in early-region muscle activity suggest small feedback gains for these proprioceptive signals.

Our above-cited findings suggest that the measured modulation of middle-region MG activity with pegway slope was entirely due to feedback from force-sensitive afferents originating from MG muscle. This allowed us to use a linear model for positive force feedback (Fig. 7A) and empirical data for the relationship between middle-region muscle activity and force (Fig. 7B) to estimate the contribution of force feedback to muscle activity as a function of muscle length. Figure 7C presents the estimated force feedback gain K at different muscle lengths (Eq. 5). Although the magnitude of K varied between the two animals, a consistent finding was that it was independent of MG length ($P = 0.57$ and $P = 0.37$ for cat 1 and cat 2, respectively). Linear regression between force feedback gain and muscle length yielded nonsignificant slopes of 0.05 ± 0.16 e_c·w⁻¹·mm⁻¹ for cat 1 and -0.07 ± 0.15 e_c·w⁻¹·mm⁻¹ for cat 2; y-intercepts were 1.60 ± 0.39 and 1.95 ± 0.54 e_c·w⁻¹, respectively. The average magnitude of K , a meaningful measure because force feedback gain was inde-

pendent of muscle length, was 1.55 ± 0.78 e_c·w⁻¹ for cat 1 and 2.17 ± 0.51 e_c·w⁻¹ for cat 2.

In contrast to force feedback gain, the estimated muscle gain M generally increased with muscle length (Fig. 7D; Eq. 6). Linear regression between muscle gain and length yielded significant slopes of 0.03 ± 0.01 w·e_c⁻¹·mm⁻¹ for cat 1 and 0.02 ± 0.01 w·e_c⁻¹·mm⁻¹ for cat 2 ($P = 3.2e-6$ and $P = 3.9e-3$, respectively); y-intercepts were 0.26 ± 0.02 and 0.30 ± 0.04 w·e_c⁻¹, respectively. The dependence of muscle gain on muscle length as expected due to the well-known force-length properties of muscle (Gordon et al. 1966; Rack and Westbury 1969).

The estimated loop gain $K \cdot M$ increased at longer muscle lengths (Fig. 7E; Eq. 7). Linear regression between loop gain and length yielded significant slopes of 0.05 ± 0.02 for cat 1 and 0.02 ± 0.02 for cat 2 ($P = 4.1e-5$ and $P = 3.1e-2$, respectively); y-intercepts were 0.39 ± 0.05 and 0.60 ± 0.08 , respectively. The increase in loop gain with muscle length is a result of it being the product of force feedback gain that was independent of muscle length and muscle gain that monotonically increased with muscle length. Cat 1 loop gain increased from 0.20 ± 0.14 at -25° slope to 0.46 ± 0.06 at $+25^\circ$ slope. Loop gain during level walking was 0.26 ± 0.13 . Cat 2 loop gain was consistently greater in magnitude than cat 1 loop gain but had a smaller dependence on muscle length. Loop gain increased from 0.49 ± 0.05 at -25° slope to 0.61 ± 0.08 at $+25^\circ$ slope, with loop gain during level walking equal to 0.51 ± 0.10 . The difference in loop gain between animals can be attributed to the differences in their estimated force feedback and muscle gains. Since loop gain is the relative contri-

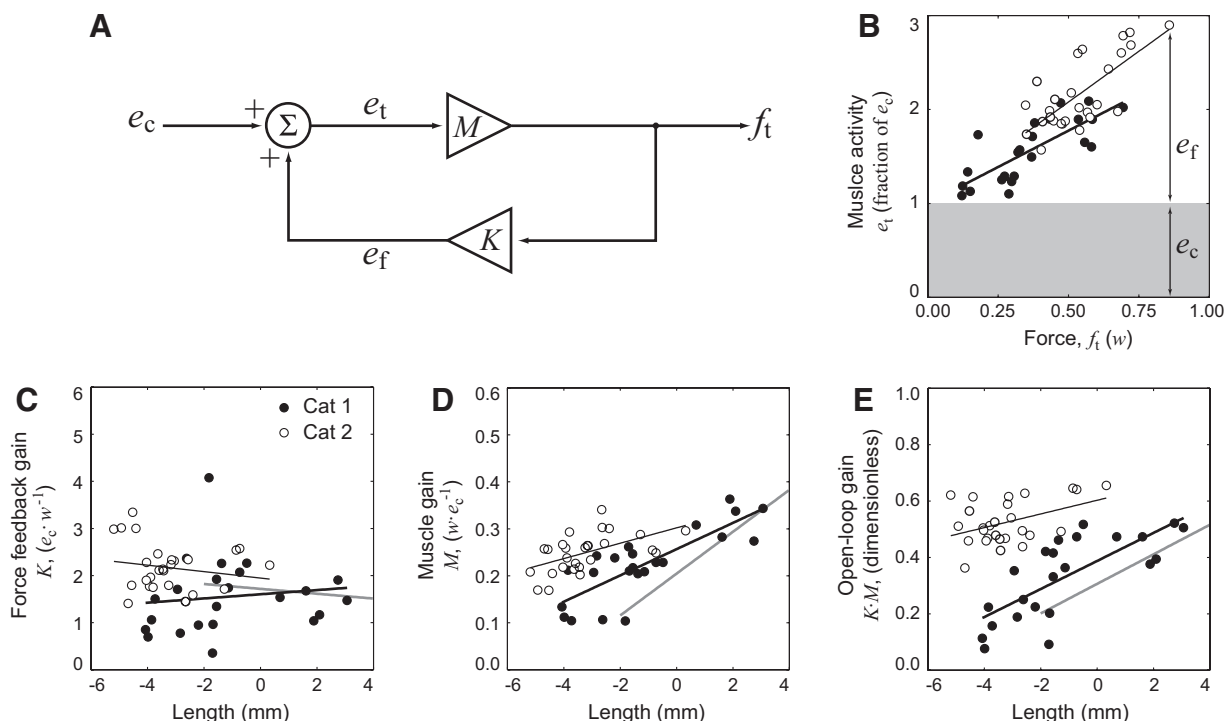


FIG. 7. Estimates of force feedback gain, muscle gain, and loop gain (C, D, and E, respectively) derived using a simple linear model of the neuromuscular system (A) and the relationship between MG activity and MG force (B). Each data point is for a single trial from the $+25^\circ$, $+10^\circ$, 0° , -10° , and -25° conditions (upslope and downslope walking resulted in longer and shorter muscle lengths, respectively). Cat 1 data are represented by closed symbols and cat 2 data by open symbols. The thick black and thin black lines represent best-fit linear regressions for cat 1 and cat 2, respectively. For comparison, the gray lines represent average relationships determined in our previous decerebrate cat experiments. In B, the y-axis intercept estimates the feedforward contribution to muscle activity, e_c (denoted by the horizontal shaded area).

bution of force feedback to total muscle activity and force (Eq. 7), these results indicate that force feedback was of substantial importance during level walking, accounting for about 39% total muscle activity and force. Force feedback played a lesser role during downslope walking, accounting for 35% of muscle activity and force, and a substantially greater role during walking upslope, accounting for about 54% of muscle activity and force. Loop gain was always less than unity, indicating that this positive feedback system was stable (Prochazka et al. 1997a).

Moving pegway experiments

Although the sloped pegway experiments found strong correlations between modulation of force feedback and changes in muscle activity, the same changes in muscle activity could be explained by other mechanisms such as phasic feedforward control or gain scheduling of other feedback pathways. The purpose of the moving pegway experiments was to better test for a causal relationship between modulation of force feedback and changes in muscle activity by perturbing the MG muscle during walking, using drops or lifts of one of the pegs during ground contact of the hind foot. Three general patterns that were supportive of the effects of force feedback on muscle activity emerged from our moving pegway experiments. First, changes in muscle activity appeared to correlate much better with force feedback modulation than with predicted Ia and II feedback. Second, we found no examples of major increases in muscle activity without a corresponding increase in predicted Ib activity. Finally, increases in Ib activity tended to lead increases in muscle activity.

These patterns supporting a causal influence of force feedback are exemplified by the -4 cm drop trials in one of the animals (Fig. 8). The peg is dropping away from the foot in early stance, resulting in a relatively constant level of muscle activity. Once the peg begins to decelerate in late stance, there is a rapid increase in muscle activity to double the early stance activity. This late stance increase is preceded by increases in predicted Ia and Ib activity, suggesting that increased activity in one of both these afferents caused the increase in muscle activity. However, there is a similar sized early stance increase in Ia activity without a consequent increase in muscle activity. This suggests that the changes in muscle activity produced by the drop are caused by modulation of positive force feedback, whereas Ia feedback gain is small or zero (Donelan and Pearson 2004b). Modulation in Group II activity is not strong and thus is unlikely to play a large role. These general patterns were also evident at different speeds, during lifts as well as drops, and in different animals.

DISCUSSION

Our analysis has indicated that positive feedback from force-sensitive afferents in the medial gastrocnemius (MG) muscle contributes substantially to the activation of motoneurons innervating the MG muscle during the stance phase in conscious walking cats. These findings complement previous conclusions from numerous studies in decerebrate and spinal cats that afferents arising from the force-sensitive Golgi tendon organs in the gastrocnemius muscles have an excitatory action on gastrocnemius motoneurons during stepping and during fivive

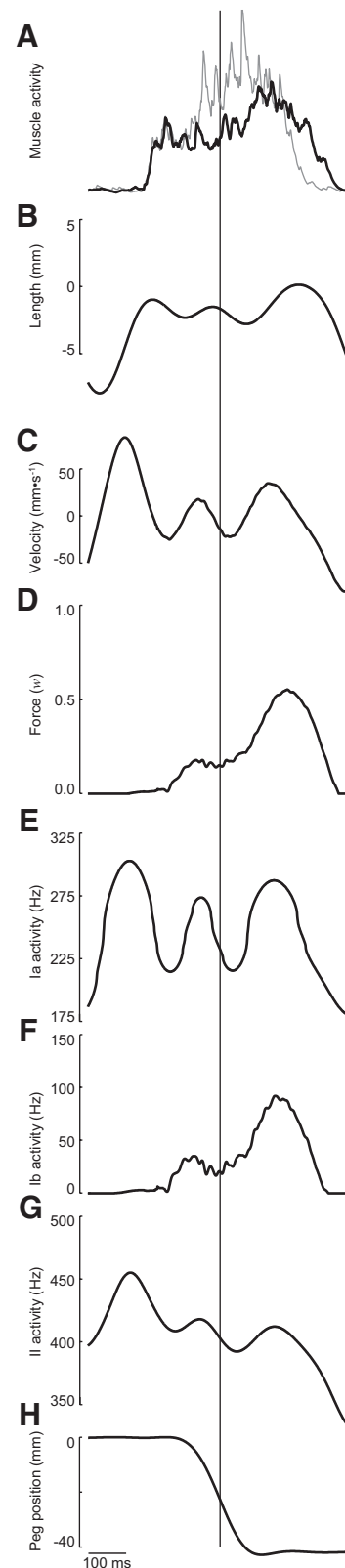


FIG. 8. The effect of a -4 cm peg displacement (*H*) on cat 1 muscle mechanics and predicted proprioceptor activity. The black line represents average results from 3 speed-matched steady-state level-walking moving-peg trials. For comparison, the gray line in *A* is the muscle activity in a speed-matched control trial that occurred immediately before the moving peg trials. The vertical black lines indicate the middle of the peg displacement.

locomotion (Conway et al. 1987; Donelan and Pearson 2004a; Duysens and Pearson 1980; Gossard et al. 1994; Hiebert and Pearson 1999; McCrea et al. 1995; Pearson and Collins 1993). The evidence also parallels a recent finding in walking humans that positive force feedback contributes to the activation of the soleus muscle during stance (Grey et al. 2007). Positive force feedback onto motoneurons during the stance phase is also a characteristic of walking systems of insects, suggesting that this is a general mechanism for regulating ongoing muscle activity (Buschges 2005).

A number of observations in this study support our claim that positive force feedback contributes to the activation of MG in conscious walking cats. First, the magnitude of muscle activity increased or decreased in parallel with increases or decreases in muscle force when the animals walked up and down a sloped pegway, respectively. Second, estimates of proprioceptor activity revealed that modulation of afferents arising from muscle spindles did not match the measured modulation of muscle activity. The changes in muscle activity were matched by modulation of afferents arising from Golgi tendon organs. Indeed, the middle-region increases in muscle activity and force were paralleled by large changes in predicted Ib activity, whereas Ia and group II activity were essentially unchanged. Third, the increase in early stance MG activity after isolating the muscle was accompanied by a reduction in the ground reaction force, thus making it unlikely that cutaneous afferents responding to forces on the paws have a significant role in activating MG motoneurons. Fourth, perturbing the MG muscle during walking using a moving peg during hind foot ground contact resulted in changes to muscle activity that correlated well with the predicted modulation of Ib activity but not Ia and group II activity. Increases to Ib activity tended to occur prior to increases in muscle activity and we found no examples of major increases in muscle activity without a corresponding increase in predicted Ib activity. Considered independently, none of these observations provides unequivocal evidence for positive force feedback. However, when these results from conscious animals are collectively considered and combined with the more direct data from reduced preparations, it becomes reasonable to conclude that a substantial fraction of the activation of MG motoneurons in conscious walking cats is due to positive feedback from force-sensitive afferents.

Our quantitative analysis and the conclusions we have drawn from these analyses depend on a number of major assumptions. The first is that the models for describing afferent activity are appropriate when animals walk up and down slopes. These models are based on those described by Prochazka (1999) that were derived from cats walking on a horizontal surface. The extent to which fusimotor drive to spindles is modified during slope walking is currently unknown. It is conceivable that it could be altered in a manner that enhances spindle feedback during upslope walking and attenuates it during downslope walking, thereby quantitatively reducing our estimate of the contribution of positive force feedback to ongoing muscle activity. A second major assumption in our analysis is that removal of heteronymous sensory input to medial gastrocnemius motoneurons does not alter the gains of homonymous feedback pathways. If gains were indeed altered then the most likely effect would be a reduction of the gain in medial gastrocnemius length and velocity feedback pathways because of the withdrawal of the synergistic action of spindle activity

from the denervated muscles onto spinal networks. If this gain change were to occur the effect on motoneuron depolarization would likely be minor because there is little modulation in Ia and II activity (Figs. 5 and 6). Nevertheless, if the contribution of these pathways to motoneuron depolarization were to be reduced, our analysis would underestimate the contribution of force feedback to the activation of medial gastrocnemius. Less of an effect of denervation would be expected on the force feedback pathway itself because of the transfer of force to the isolated medial gastrocnemius muscle. A third major assumption is that denervation does not result in modification of the homonymous force feedback gain. Our current predictions are based on measurements made as long as 5 days after denervation and there are large changes to the motor program that occur within this time window (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 feedback gains. Accepting these major assumptions—and the more minor ones used throughout this analysis—means that the quantitative values derived from our analysis must be treated with caution.

Our current results are quantitatively and qualitatively similar to those of a previous experiment on stepping in decerebrate cats (Donelan and Pearson 2004a). The previous work allowed for more direct and controlled estimates of feedback gains because we could directly adjust muscle length by fixing one hind leg, isolating the MG muscle, and attaching it to a motor. We were also able to directly measure proprioceptor activity rather than relying on predictions. The gray lines in Fig. 7, C–E represent the average relationships between measured gains and muscle length determined in our previous experiment. As with our current finding in conscious cats, force feedback gain was independent of muscle length (Fig. 7C). Muscle gain increased with muscle length in both sets of experiments (Fig. 7D) due mainly to the force–length property of muscle (Gordon et al. 1966; Rack and Westbury 1969). The

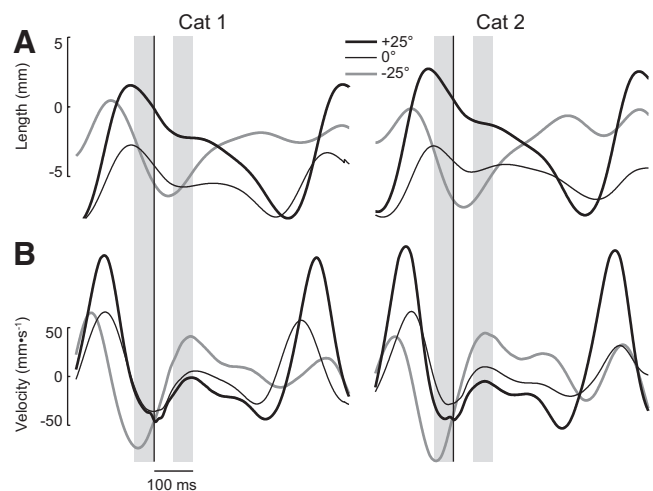


FIG. 9. The effect of pegway slope on muscle mechanics in animals with intact innervation. The *left* and *right* columns are results from cats 1 and 2. The thin black line, thick black line, and gray line are for level, +25°, and -25° trials, respectively (for clarity, we have not presented the +10 and -10° conditions). These results are averages from multiple speed-matched steady-state trials. The vertical black lines indicate the beginning of stance. The shaded vertical bars denote the early and middle regions.

larger y-intercepts and shallower slopes in the current experiment were expected due to the force–velocity property of muscle (Hill 1938). Muscles were held isometric at all lengths in the previous experiment and in the current experiment, the muscles were lengthening during the middle region, increasing muscle gain, and the lengthening velocity was larger at shorter muscle lengths (Figs. 5 and 6). The dependence of loop gain on muscle length was similar in both preparations (Fig. 7E). The larger loop gains in the conscious cats are a result of the muscle lengthening velocity and its consequent effect on muscle gains. Although the advantages of reduced preparations are considerable, the applicability of the results to conscious cats is always only tentative. The remarkable correspondence between our reduced and intact work not only confirms our previous force feedback findings, but also generally supports the use of the decerebrate preparation for quantitative estimation of the physiological parameters used during walking in conscious animals in addition to its more traditional role of providing qualitative insight into underlying physiological mechanisms.

To understand the functional relevance of our findings, one must consider the muscle mechanics used by intact animals during level and slope walking. Figure 9 illustrates estimated muscle lengths and velocities used by our animals prior to MG isolation. Muscle length during the middle region of level walking was -5 mm on average for the two animals studied. At this length, force feedback to MG contributes about 30% of the ongoing muscle activity and force (Fig. 7E). During downslope walking, the middle-region muscle length is shorter, thus reducing the contribution of force feedback. During upslope walking, muscle lengths were substantially longer, approximately -1.5 mm, and the contribution of force feedback increases to about 40%. Although the predicted contribution of force feedback in intact walking is substantial, it does not account for the entire muscle activity. The remainder is due to other contributors that may include central drive, heteronymous force feedback, and feedback from spindles or other receptors. Specifically, our study does not exclude the contribution of spindle feedback signals in regulating muscle activity during the stance phase. In humans, for example, there are indications that length and velocity-related signals make a contribution to the activation of the soleus muscle during early stance (Sinkjaer et al. 2000; Yang et al. 1991). It should also be noted that the role of force feedback will depend on the biomechanical context—its contribution will likely differ in different muscles and for the same muscles in animals that use different walking postures.

Our findings regarding feedback pathway gains suggest that this modulation of muscle activity and force with the slope of walking does not necessarily require a modification of nervous system gains or central drive (Fig. 7). The requirement of a more flexed leg in early stance during upslope walking results in an initially longer muscle length with a greater muscle gain. This increase in muscle gain results in a feedback pathway with a greater loop gain. Similarly, the more extended leg required in early stance during downslope walking results in an initially shorter muscle length and a reduced contribution of force feedback. Force feedback combined with intrinsic muscle properties appears to provide a simple mechanism for automatically compensating for changes in terrain with-

out requiring different commands from the brain or even modification of CNS gains.

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