Use-dependent gain change in the reflex contribution to extensor activity in walking cats

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Abstract

Denervation of the synergists of the medial gastrocnemius (MG) muscle in the cat hind leg results in a progressive increase in the magnitude of burst activity in the MG muscle during walking. The increase in burst magnitude is associated with an increase in the slope of the relationship between the magnitude of individual MG bursts and the amplitude of ankle flexion during stance. This finding is consistent with the hypothesis that the increase in MG burst magnitude is due to an increase in gain of reflex pathways reinforcing the activation of MG. The increase in slope is use-dependent since it was not observed when the leg was released from a cast that immobilized the leg for 6 days. © 2000 Elsevier Science B.V. All rights reserved.

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A number of recent studies in humans and cats have demonstrated that afferent feedback from proprioceptors in the leg muscles contributes a substantial fraction of the excitatory input to extensor motoneurons during the stance phase of walking [2,8,9,11]. The large contribution of afferent feedback to the activation of extensor motoneurons raises the issue of how the gains of reinforcing pathways are set to be appropriate for the mechanical properties of the limbs and the physiological properties of the muscles. Because these properties change considerably during development and aging, it seems reasonable to expect that the gains of reinforcing pathways might be set to be appropriate for the mechanical and physiological properties of the system. Data consistent with this expectation has come from a recent study on the effect of partially denervating the ankle extensor muscles in the walking cat [5]. This study reported an increase in the magnitude of activity in the medial gastrocnemius (MG) muscle following transection of the nerves supplying close synergists (lateral gastrocnemius, soleus and plantaris). One component of the MG bursts (beginning prior to ground contact) increased relatively slowly over a period of about 7 days. Another component (beginning after ground contact) increased more rapidly and was maximal 2–3 days after the nerve transections. It was hypothesized that the increase in the late component was due to an increase in the gain of afferent pathways reinforcing the generation of the MG bursts.

We have now tested this hypothesis by examining the relationship between the magnitude of the late component of individual MG bursts and the magnitude of the corresponding flexion at the ankle joint during early stance (Fig. 1A). The rationale for this analysis is that ankle flexion during early stance results in a lengthening of the active ankle extensor muscles, which then naturally evokes a stretch reflex in MG. A contribution of a stretch reflex to the activation of MG motoneurons is consistent with a previous finding of a linear relationship between the magnitude of MG bursts and the magnitude of ankle flexion [5]. The slope of the relationship between MG burst amplitude and ankle flexion thus provides a measure of the gain of afferent pathways contributing to MG burst

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Fig. 1. (A) Plots of ankle angle (top) and the rectified and filtered EMG in MG (bottom) for one step cycle showing the parameters measured in this study. The change in ankle angle (Δθ) was measured as the difference between the ankle angle at the onset of stance and the angle when the ankle was maximally flexed during stance. The magnitude of the MG EMG was averaged over a period of 100 ms centered around maximal ankle flexion (shaded). The stick figures show the leg configurations at the times of ankle angle measurements. (B) Example of the linear relationship between the magnitude of EMG activity in MG and the change in ankle angle during early stance measured during a continuous walking sequence. Each data point represents a single step and the open squares are data points obtained when the hindquarters were lifted slightly to reduce ankle flexion. Data from cat one day after removing immobilizing cast. (C, D) Increase in the slope of the relationship between MG EMG amplitude and the change in ankle angle on the day following transection of the nerves supplying the LG, SOL and PL muscles in two different cats. Filled circles, day of nerve transections; open circles, 1 day after nerve transections. EMG values in C and D are normalized to the average value on day 0.

generation. We predicted that the increase in the magnitude of the late component of the MG bursts that occurs during the first few days following denervation of synergists would be associated with an increase in the slope of the relationship between MG burst amplitude and ankle flexion.

Data were collected from six adult cats walking on a horizontal treadmill. These were the same animals used in an earlier study [5]. The procedures for implanting electromyographic (EMG) recording electrodes and transecting the nerves to the lateral gastrocnemius, soleus and plantaris muscles are described in that study. In the present study, EMG and video data were analyzed when the animals were walking at 0.6 m/s. This was the speed at which all animals walked continuously for some time and remained positioned near the centre of treadmill. Insufficient data were available for examining the effect of walking speed on the relationship between MG burst amplitude and ankle flexion. Over the range of preferred walking speeds (0.5–0.7 m/s) we would expect this to be minimal since the rate and extent of ankle flexion during early stance is similar (as is the case in normal animals [7]), but there may be effects at higher speeds when the ankle flexion during early stance is larger [7]. Each EMG burst triggered a computer generated pulse code that was simultaneously placed in the EMG and video recordings. This allowed the matching of an individual step with the corresponding EMG burst in MG. The raw EMG records were rectified, filtered (50 Hz) and digitized using an Axotape (Axon Instruments) data acquisition system. The amplitude of the individual MG bursts was determined by averaging the amplitude each burst of over a period of 100 ms centered around the time of maximum flexion of the ankle (shaded region in Fig. 1A). Measurements were made using custom software that allowed retrieving Axotape files. The magnitude of ankle flexion for the step corresponding to each EMG burst was measured directly from a video monitor using a flexible protractor. One measurement was made at the instant of ground contact and the other was made 200 ms (12 frames) later. At this time the ankle was fully
flexed and remained relatively constant for a period of 100–200 ms (Fig. 1A). An analysis of covariance (ANCOVA) was used to assess differences in the slopes of the linear regression of MG burst amplitude versus ankle flexion on different days.

In all six animals, a linear relationship was found between the magnitude of the MG bursts and the magnitude of ankle flexion during early stance on the day of the nerve transections (day 0). Data from four animals (filled circles) are shown in Fig. 1C,D and in Fig. 2A,B. The correlation coefficient of this relationship varied from animal to animal, with the range being from 0.35 to 0.69, mean=0.59. One of the main results of this investigation was that the slope of this relationship was increased on the day following the nerve transections in four of the animals (the remaining two animals had their leg placed in cast on day 0). Examples from two animals are shown in Fig.

1C,D. Statistical analysis revealed the slope increase was significant in all four animals (P<0.05). By contrast, there was no consistent change in the y-intercept of the regression lines fitted to the data for day 0 and day 1. The mean values for the y-intercepts on days 0 and 1 were 0.58 (range 0.34–0.84) and 0.60 (range 0.53–0.74), respectively.

Because the measurements on day 0 were made a fairly short time after the nerve transections (5 h), one possible explanation for the increase in slope of the relationship between MG burst magnitude and ankle flexion is that the reflex contribution to MG burst generation was depressed on day 0 due to the surgical procedure. If this were the case then we would expect that the slope of relationship would also be increased on the day of cast removal in the two animals in which the hind leg was immobilized for 6 days. Contrary to this expectation there was not a significant difference in the slopes on day 0 and day 6, P>0.05 (Fig. 2). There was, however, a shift in the position of the regression lines, slightly down in one animal (Fig. 2A) and up in the other (Fig. 2B). These shifts are most likely due to alterations in the electrode properties or position in the muscles, since the changes in the average values of the initial and late components of the MG EMGs were proportionally similar (not shown). On the day following cast removal (day 7) the slope of the relationship between MG burst amplitude and ankle flexion increased significantly (P<0.05) in both animals. This was qualitatively similar to the slope increases seen in the other four animals on the day after the nerve transections. Another similarity was that the y-intercept of the relationship was similar on days 6 and 7 (the means were 0.62 and 0.60, respectively).

An important assumption in this investigation was that the natural lengthening of the MG muscle during early stance evoked a stretch reflex response in the MG muscle, and that this response contributes to the generation of the MG bursts during the stance phase of walking. The evidence that it occurs in conscious walking cats is meager [5] although previous studies in decerebrate animals have indicated a large reflex contribution [1–4,6,9]. We obtained additional evidence in conscious animals by examining this relationship when ankle flexion was decreased by lifting the hindquarters (Fig. 1B). In three animals we were able to gently lift the hindquarters for short periods of times (three- to six-step cycles) without causing a disruption of regular walking. In all three animals lifting the hindquarters reduced MG burst magnitude, with the largest reductions associated with the smallest flexions of the ankle. Furthermore the relationship between ankle flexion and MG burst magnitude when the hindquarters were lifted was an extrapolation of this relationship during normal walking. The data illustrated in Fig. 1B were collected on the day following cast removal in one of the animals in which the leg was immobilized. The simplest explanation of these data is that lifting the hindquarters reduces lengthening and loading of the MG muscle during early
stance thus reducing the contribution of proprioceptive signals to the generation of the MG bursts.

A number of factors that might explain the use-dependent increase in slope can be excluded. First it is unlikely to be due to recovery from the experimental procedure since the slopes were similar on day 0 and on the day of cast removal in the two animals in which the hind leg was immobilized for 6 days. Cast removal was done without application of anaesthetic or any additional surgery, and by 6 days we assume that acute trauma to tissue was reduced. Second, the increase in slope cannot be easily explained by a generalized increase in central drive to the MG motoneurons during the stance phase. If this was true then it is difficult to understand how the increased drive could be linearly scaled to the magnitude of ankle flexion without changing the y-intercept of the EMG–flexion relationship. For this to occur there would have to be some sort of predictive component to the increased central activation of the MG motoneurons related to the anticipated degree of ankle flexion. Since the variation in ankle flexion is most likely due to unpredictable changes in loading of the leg from step to step we believe this explanation is improbable.

The explanation we favor is that the increase in slope results from a use-dependent increase in the gain in afferent pathways contributing to the activation of MG motoneurons during the stance phase (see Ref. [4] for a review of these pathways). A gain increase in afferent pathways contributing to MG activation could occur either by modification of synaptic transmission in the spinal cord or, in the case of afferent pathways from muscle spindles, by an increase in the fusimotor input to the spindles during the stance phase. The plausibility of the latter is based on findings that spindles in the ankle extensor muscles receive phasic fusimotor drive during the stance phase [10]. Reduction in presynaptic inhibition of group I afferents and/or use-dependent potentiation of synaptic junctions within the reflex pathways could be mechanisms for modifying central transmission of afferent signals. Future investigations using intracellular recording techniques will be required to resolve which, if any, of these mechanisms is utilized.

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References