Afferent and spinal reflex aspects of muscle fatigue: Issues and Speculations

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"...during fatigue, motoneurone firing rates may be regulated by a peripheral reflex originating in response to fatigue-induced changes in the muscle..." (Bigland Ritchie et al. 1986)

Abstract In this article, the above quote from the work of Bigland-Ritchie and her colleagues is discussed in relation to afferent and spinal reflex mechanisms that could conceivably contribute to the reflex. The argument is first advanced that evaluation of this hypothesis should not be limited to studies on humans and other mammalian species. Rather, it should be extended to include invertebrates and other vertebrate groups, because it is likely that the neuromuscular mechanisms that reduce and delay muscle fatigue in glycolytic muscle cells have been subject to evolutionary conservation. Next, we address a concern of Bigland-Ritchie et al. (1986) that a controlled reduction in motoneurone firing rates during fatigue is attributable in part to the cells' intrinsic (biophysical) properties. We consider this possibility less likely than the operation of a more complex control strategy in which CNS-induced changes in the biophysical properties of motoneurones serve, themselves, to delay and reduce fatigue. In regard to the afferent and spinal reflex aspects of the Bigland-Ritchie hypothesis, we have argued that no single afferent species is dominant in the effects of afferent feedback on motoneurone discharge during fatiguing muscle contractions, at least before the onset of pain. Rather, as with reflex control of sustained and intermittent movements in the fresh (unfatigued) state, it is likely that *all* the limb afferents contribute, in a context-dependent fashion. Finally, it is proposed that the role of limb afferent input during fatigue should not be limited to consideration of restricted (private, specialized) spinal pathways. Instead, since at least the proprioceptive component of this sensory input has multifaceted responsibilities in motor control, all such responsibilities should be examined in the face of muscle fatigue.

The study of muscle fatigue (hereafter termed fatigue) can provide a framework for new perspectives on the operation of the motor control system, at both segmental and suprasegmental levels. For work at the segmental level, the topic of this article, it is sufficient to define fatigue as a "... failure to maintain the required or expected force" (Edwards 1981; for suprasegmental considerations, see Enoka & Stuart 1992). The segmental motor system is a term used to describe the integrated (systems) operation of brainstem/spinal motor circuitry, motor units, muscle receptors, and the segmental actions of muscle, joint and cutaneous afferents (reviewed in Binder & Mendell 1990). As reviewed elsewhere (Stuart & Enoka 1990), the systems approach to the segmental motor system has been dominated for thirty years by three areas of study: 1) the role of spinal interneurons in integrating descending command and sensory-feedback signals for the elaboration of spinal reflexes; 2) the mechanisms underlying the interneuronal pattern generation required for the execution of relatively stereotyped movements like breathing, chewing, swimming and walking; and 3) the phenomenon of orderly motor unit recruitment and its potential underlying mechanisms, such as Henneman's size principle. Now, a fourth area of study seems fruitful: testing ideas pertaining to muscle fatigue, such as the idea of Bigland-Ritchie et al. (1986) that is quoted above. It is argued below that the testing of their *sensory-feedback hypothesis* in a wide variety of animal species has important implications for furthering the understanding of the segmental motor system.

Evolutionary and phylogenetic considerations

To this point, the study of segmental aspects of fatigue has been limited almost exclusively to studies undertaken on mammalian species; notably cat, rat and human. However, the appearance of fatigue and the neural strategies employed to reduce and delay it are as ubiquitous in the animal kingdom as movement itself. Furthermore, the ability to cope with fatigue, even in a transitory fashion, is fundamental to the survival of all species. Hence, neural, neuromuscular, and muscular mechanisms of fatigue must surely be as subject to *evolutionary conservation* as other molecular, cellular and intercellular (systems) mechanisms that are fundamental to survival.

This need for *interphyletic awareness* (cf. Stuart 1985) in the study of fatigue is also supported by the proposition that the neurobiological aspects of muscle fatigue largely involve consideration of interactions between the CNS and glycolytic, rapidly-fatiguing muscle cells. The fatigue literature suggests that it is these cells on which the CNS and peripheral neuromuscular mechanisms can exert the most fatigue-reducing/delaying effect, whereas the eventual fatigability of oxidative, fatigue-resistant muscle cells is determined primarily by metabolic processes within the active muscle cells. Similarly, the presence or absence of temperature regulatory mechanisms (which primarily affect the rates of chemical and physical processes, rather than underlying mechanisms) and blood flow are not crucial for anaerobic metabolism during fatiguing contractions, but become critical factors when considering aerobic mechanisms during fatigue. This *neural vs. metabolic* division of fatigue mechanisms has presumably also been subject to the same evolutionary conservation that has resulted in a division of labor between the anaerobic *vs.* aerobic types of muscle fiber so prominent in both invertebrates (e.g., arthropods; Rathmayer & Maier 1987), which evolved in the Cambrian Period (approx. 570 million years ago) and non-mammalian vertebrates (e.g., lampreys, elasmobranchs and teleost fishes; Ogata 1988, Rome et al. 1988), which likewise appear very early in the fossil record. These points are emphasized first in this article, because investigations of motor control (including fatigue) in mammals can continue to derive much inspiration from considering the neural mechanisms and strategies that nature found so useful many millions of years ago, well before the appearance of mammalian species (e.g., Callister et al. 1992). Interestingly, while this viewpoint is now well accepted for molecular (e.g., genes, ion channels, myosin isoforms, Ca^{2+} binding proteins) and cellular (e.g., mitosis, metabolic pathways, synaptic transmission) mechanisms, it is less well appreciated at the systems and organismic levels of inquiry except perhaps in the study of the neural control of locomotion. In this area, the work of Grillner and colleagues on the lamprey (reviewed in Grillner et al. 1988, 1991) has provided new openings in the study of mammalian locomotion. Similarly, new insights into the control of multi-jointed movement have been provided by the study of the wiping reflex in frogs (Giszter et al. 1989; Ostry et al. 1991).

Muscle wisdom and the sensory-feedback hypothesis

As fatigue proceeds in conscious humans during both maximum voluntary contractions (MVCs) and imposed contractions of a selected pattern, there is a decrease in the rate of whole-muscle relaxation which lowers fusion frequency. This occurs concomitantly with a reduction in the rate of motoneurone discharge (e.g.: Dietz 1978; Marsden et al. 1976, 1983; Bigland-Ritchie et al. 1986). This association between force, relaxation and discharge rates is referred to as muscle wisdom. It should ensure that the CNS drive to fatiguing muscle does not exceed that necessary to produce the required force, and as such should serve to reduce and delay "central" fatigue within the CNS (cf. Enoka & Stuart 1992).

While the findings to date are particularly interesting, several features of muscle wisdom now require systematic investigation. For example: 1) several observations in the Marsden et al. (1983) report are puzzling (e.g., the EMG data in their Fig. 6) and require confirmation and extension; 2) similarly, an observation of Bigland-Ritchie et al. (1983; their Fig. 4B) is possibly at odds with a subsequent one of Binder-Macleod and McDermond (1992; their Figs. 1-4; cf. also Botterman & Cope 1988, and Cooper et al. 1988); 3) the boundary conditions of muscle wisdom remain relatively unexplored, such as comparison of repetitive *vs.* sustained contractions (e.g.: Duchateau & Hainaut 1985; Bergstrom & Hultman 1988), fatigue brought on by low- *vs.* high-frequency contractions (cf. Garland et al. 1988), short- *vs.* long-duration

contractions (Bergstrom & Hultman 1988), and by different patterns of activation, including those of variable duty cycle (cf. Gandevia 1990; McKenzie & Gandevia 1991) and interpulse interval (Binder-Macleod & Barker 1991; Bevan et al. 1992; Laouris & Stuart, this volume); and 5) the relation of muscle wisdom to motor-unit type is relatively unexplored. However, indirect evidence suggesting that slow-twitch units may be less effected than fast-twitch ones (Dubose et al. 1987; Gordon et al. 1990) is in keeping with the evolutionary and phylogenetic considerations emphasized above. This latter evidence reinforces the need to test for the manifestation of muscle wisdom during fatiguing muscle contractions in a variety of animal species, in order to test the appealing notion that this strategy, too, has been subject to evolutionary conservation.

To account for muscle wisdom, Bigland-Ritchie and her colleagues have proposed the sensory-feedback hypothesis under consideration in this article. This hypothesis must coexist with orderly motor-unit recruitment and Henneman's size principle (for review: Binder & Mendell 1990) and, like the latter (Stuart & Enoka 1983), Bigland-Ritchie's hypothesis is simple to comprehend, it provides a unified means of viewing previous, present and future studies, and it is testable with present-day techniques in a variety of animal species.

Sensory feedback vs. motoneurone adaptation

In the same report in which Bigland Ritchie et al. (1986) advanced the sensory-feedback hypothesis, they cautioned that *"...the decline in motoneurone firing rates seen during fatigue of a sustained maximum voluntary contraction may result primarily from changes in central motoneurone excitability; the time course of frequency changes are quite similar to that reported by Kernell and colleagues for changes in the discharge rates of cat single motoneurones in response to constant current injection (...Kernell & Monster 1982 a,b)"*. This caveat was prompted by the authors' recognition of the similarity in the on-average magnitude of the drop in firing rate (approx. 33 to 18 Hz) of motor units in their human subjects during a 40 second MVC and that (approx. 29 to 16 Hz) over the same time period during sustained intracellular stimulation of motoneurones in deeply anesthetized cats (e.g., compare Fig. 4A-B in Bigland-Ritchie et al. 1983 to Fig. 5 in Kernell & Monster 1982b). In this comparison, the adaptation reported by Kernell and Monster (1982a,b) is termed *late*: it occurs after the first 1-2 s of sustained stimulation in contrast to the more rapid drop in firing rate, termed *initial,* that occurs at the onset of stimulation. Our group (Spielmann et al. 1991) has considered these firing-rate declines in relation to evidence on: initial *vs.* late adaptation following sustained stimulation and *within-train vs. between-train* adaptation following intermittent stimulation (Llinás & Lopez-Barneo 1988; Spielmann et al. 1990; Spielmann 1991; Nordstrom et al. 1991); the neuropharmacology of after-hyperpolarization (e.g., Zhang & Krnjevic 1987; Hounsgaard et al. 1988) and; after-hyperpolarization under near passive and active (fictive locomotion) conditions (Brownstone et al. 1992). Collectively these results suggest: 1) similarities between initial and within-train, and late and between-train adaptation; 2) the obligatory nature of initial and late adaptation (but probably involving different mechanisms) in the presence of motoneurone after-hyperpolarization; 3) the mutability of motoneurone after-hyperpolarization (and hence initial and late adaptation), as effected by descending command signals, CNS state (e.g., passive *vs.* active) and associated transmitters and neuromodulators. On this basis, we believe it is premature to assume that after-hyperpolarization and its obligatory initial and late adaptation are features of motoneurone discharge during natural movements, such as during an MVC. Rather, it seems more attractive to test the possibility that the intrinsic (biophysical) properties are subject to an extrinsic (synaptically mediated) control by the CNS. Such a control mechanism could be context (task) dependent and serve to reduce and delay fatigue, at least on a temporary basis. It would seem that the intrinsic *vs.* extrinsic control of after-hyperpolarization (and hence intitial and late adaptation) is an important issue that must be resolved in parallel with consideration of the evidence (vide infra) that implicates sensory feedback in reducing motoneurone firing during fatiguing contractions.

Sensory-feedback vs. "interneuronal wisdom"

In a sense, the concept of muscle wisdom is an extension to dynamic (muscle activation) conditions of the now well-accepted principle that the morphological, biochemical, biophysical and physiological properties of spinal motoneurones are related in an interdependent manner to those of the muscle cells they innervate. Evidence for these interdependencies and the testing of additional ones are described in the literature on the size principle (e.g., Binder & Mendell

1990; Gardiner & Kernell 1990), nerve-to-muscle trophism in reduced animal preparations (Vrbová 1989) and muscle-to-nerve trophism (e.g., Czeh et al. 1978). In simple, but intuitively attractive language, the notion is now well accepted that motoneurones have an **a priori** knowledge about the force developing potential of the muscle cells they innervate. Of at least equal importance is a newly emerging literature which suggests that spinal interneurones have a similar **a prioi** knowledge about the mechanical properties of an entire limb when performing a task that involves more than one joint (e.g., Gielen et al. 1988; Gurfinkel et al. 1988; Koshland et al. 1991; Lacquaniti et al. 1991). This point is introduced here to emphasize that a thorough testing of the sensory-feedback hypothesis will not only require consideration of interactions between sensory-feedback during fatiguing contractions and the intrinsic (biophysical) *vs.* extrinsic (synaptically mediated) properties of motoneurones, but also between this feedback and populations of spinal interneurones that may respond to fatigue-induced sensory input in a fashion appropriate for the biomechanics of the entire limb.

Issues concerning sensory afferents and their central actions

Indirect evidence, derived from experiments on conscious humans using a variety of imaginative protocols, has implicated small diameter group III-IV afferents, presumably signaling changes in the metabolic status of muscle cells, in a reflex inhibition of motoneurones during fatigue (Bigland-Ritchie et al. 1986; Woods et al. 1987; Garland et al. 1988; Gandevia et al. 1990; Garland & McComas 1990; Garland 1991; Macefield et al. 1992; cf. Kulkulka et al. 1986). Direct evidence from reduced animal experiments supporting this logically appealing notion is limited and somewhat contradictory. While it is firmly established that muscle contraction reflexly increases cardiovascular and ventilatory function via group III-IV muscle afferent input (reviewed in Kniffki et al. 1981), the identity of the contraction-induced stimuli responsible for the increased activity in these small diameter afferents was unknown until recently. Now, however, their is evidence to suggest that known products of muscle metabolism (e.g., K^+, H^+ and arachadonic acid) can increase the discharge rates of some group III-IV afferents (Kaufmann et al. 1988; Rotto & Kaufmann 1988). It remains to be proven that such excitation can occur beneath the threshold for activation of nociceptive afferents. Furthermore, the discharge of many slowly conducting, *non-nociceptive* group III-IV mechanoreceptor afferents has been shown to exhibit a *decline* in their discharge during the initial phase of fatigue (Hayward et al. 1991).

At this stage, there is clearly need for a multi-laboratory attack on this issue using both experimental paradigms. For work on conscious humans that test for involvement of group III-IV afferents in the wisdom phenomenon, it will be a formidable problem to discriminate (with microneurography) unitary activity in group III-IV afferents supplying a fatiguing muscle and prove whether the axons subserve nociceptive *vs.* ergoreceptive (exercise related) function (Hasan & Stuart 1984). In the case of reduced-animal experimentation, there are also formidable technical difficulties when recording the activity of single group III-IV afferents (particularly those signaling non-noxious events); but nevertheless, a substantial data base was recently assembled on a somewhat analogous problem (afferent discharge from control vs. inflamed joints; Grigg et al. 1986). Hence, the prospects are promising that a more complete understanding is attainable of the responses of group III-IV chemoreceptor and mechanoreceptor afferents in fatiguing muscle before and after the onset of pain.

Such group III-IV involvement must also be considered in relation to the potential contribution from large diameter group I-II mechanoreceptor afferents. For example, because motor units in humans do not exhibit a decline in discharge rate during sustained activity (brought on by several means) until recovery from anesthetic block is complete, Bongiovanni and Hagbarth (1990) proposed that the decline in discharge rate from a high value is a result of disfacilitation (i.e., reduced post-synaptic excitation of motoneurones via a reduction in fusimotor-driven feedback from muscle spindles; cf. also Gandevia et al. 1990; Macefield et al 1992). This possibility has been supported by evidence showing a fatigue-induced decline in the firing rate of human muscle spindle afferents (Macefield et al. 1991), but the relative roles of reflex inhibition mediated by small diameter afferents and disfacilitation of motoneurones is unresolved. As work continues on this problem, the temporal aspects of muscle wisdom will require special consideration. For example, there is need to evaluate the recent suggestion that *"...One plausible way to amalgamate the current findings is to suggest that any decline in motoneurone discharge rate during the first 5-10s of a maximal voluntary contraction may reflect the reduction in muscle spindle input and increase in presynaptic inhibition, while*

metabolic effects exerted reflexly through small-diameter afferents contribute more later in the contraction" (Gandevia 1990).

At present, there is a limited and conflicting set of observations on the effects of fatigue on the sensitivity of large diameter, mechanoreceptor afferents and their spinal-reflex efficacy. For muscle spindle afferent (Ia and spII) sensitivity, the initial results on reduced animals are generally in agreement, with fatigue shown to enhance their responsiveness to single motor unit contractions (Christakos & Windhorst 1986; Enoka et al. 1990; cf. also the 1985 work of Nelson & Hutton on spindle responses to whole muscle stretch). However, of similar merit is evidence from experiments on humans that fatigue results in a decline of fusimotor drive to muscle spindles and consequently reduces spindle discharge (vide supra). For tendon organ (Ib) afferents, the effects of fatigue are also uncertain. In studies on reduced animals, there is evidence of little (Stephens et al. 1975) or no (Gregory 1990) change in their responsiveness to single motor unit contractions; whereas, in similar preparations, there is equally convincing evidence of a reduction in Ib responsiveness to whole muscle stretch (Hutton & Nelson 1986). Similar uncertainty abounds concerning the spinal-reflex efficacy of this sensory input. On the one hand, there is evidence that fatigue enhances the efficacy of short and long latency reflex EMG and motoneurone responses to brief muscle perturbations in humans (Darling & Hayes 1983; Kirsch & Rymer 1987) and reduced animals (Windhorst et al. 1986). However, these results are in possible conflict with those reported for humans by Hunter and Kearney (1983), Crago and Zacharkiw (1985) and Balestra et al. (1992). As this field of investigation continues, studies will be required on the effects of contraction of type-identified motor units on afferent fibers during fatigue in both reduced animals (i.e., as introduced by Stephens et al. 1975) and conscious humans. In the latter instance, a valuable stimulation technique (Westling et al. 1990) has already been applied to the study of motor unit fatigue (Thomas et al. 1991). Also, our understanding of the effects of fatigue on spinal reflex transmission requires analysis of interneuronal pathways (cf. interneuronal wisdom; vide supra) in the conscious human, making use of refined conditioning volley/test shock techniques (e.g., Fournier & Pierrot-Deseilligny 1989) that derive their inspiration from the virtuosic work of the Lundberg group (Baldissera et al. 1981; Jankowska 1992).

On the basis of our current understanding of the spinal actions of muscle afferents, we would propose that any *precise* matching of motoneurone discharge to the stimulus frequency-force relation of its fatiguing muscle unit, on a moment-to-moment basis, is more likely to be attributable to the action of large diameter spindle afferents rather than small diameter ones, with the latter's input providing a more general, sustained inhibition (firing rate reduction) of motoneurone discharge. This speculation is summarized in Fig. 1. It is based on our interpretation of evidence generated largely by Lundberg and Jankowska and their colleagues on the spinal connectivity patterns of limb afferents in reduced cat preparations (reviewed in: Baldissera et al. 1981; McCrea 1996; Stuart 1986; Schomburg 1990; Jankowska 1992).

In considering the implications for the sensory-feedback hypothesis of the organizational scheme proposed in Fig. 1, it must be recognized, of course, that far more is known about the spinal connectivity patterns of group III-IV afferents in cutaneous than in muscle nerves. However, there is evidence that under selected circumstances, such cutaneous input can combine with large diameter, muscle afferent input to achieve a relatively private (concentrated) effect on a particular population of motoneurones (for review: McCrea 1992; Jankowska 1992; cf. also He et al. 1988; Ferrell et al. 1988). Hence, the possibility can not be dismissed at this time, that under the conditions that bring on muscle fatigue, some specialized effects from homonymous, non-nociceptive group III-IV afferent input can be exerted on motoneurones which drive the fatiguing muscle. However, it is parsimonious to consider that this possibility is far less likely than our proposition that a precise reflex control of motoneurone firing rate is far more likely to be attributable to changes in Ia afferent input, with a tonic inhibition progressively building as brought on by the non-nociceptive group III-IV input. Once pain sets in, it is also unlikely that the nociceptor input exerts a private-line effect on homonymous motoneurones or that it could regulate their firing rate in attune with the changing mechanical status of the fatiguing muscle.

As a final reflection on the sensory-feedback hypothesis, it is important to remember that fatigue occurs during sustained and intermittent activation of muscle; it is part and parcel of the numerous problems that must be solved by the CNS in its overall control of movement. The viewpoint has been advanced by Lundberg and Jankowska and their colleagues that *no* one

single afferent species dominates in the effect of afferent feedback on movement. Rather, the evidence to date points to the scheme we have outlined in Fig. 1: the role of peripheral afferent input from active muscles during fatigue is to support descending command signals that are mediated largely by interneurons on which the majority of afferent input converges. Their argument that *"...it seems much more sensible that different receptors which can give useful information combine in the feedback control and this is best achieved by convergence on interneurons in a common reflex pathway"* (Jankowska & Lundberg 1981) should well apply to fatigue with the added proviso that as fatigue ensues, the reflex control will be influenced to a progressively greater extent by group III-IV sensory input that, itself, becomes progressively more dominated by the nociceptive input.

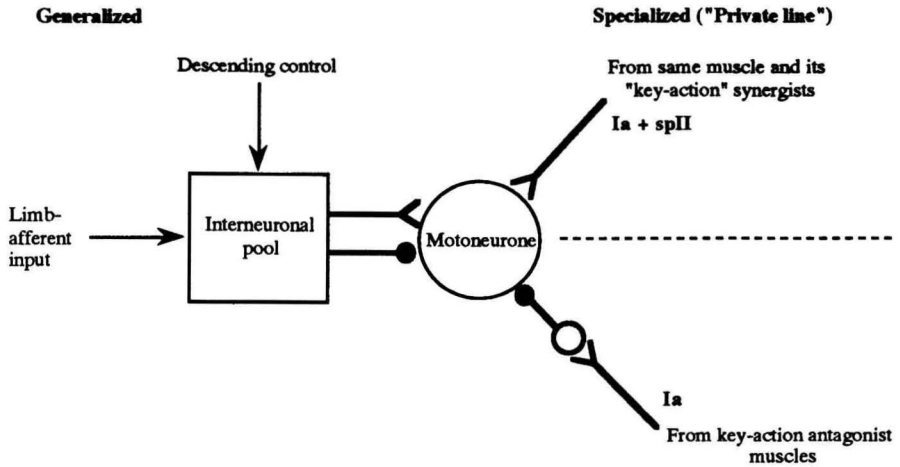

Figure 1. ***Overall organization of the central connections and actions of limb afferents.*** Shown is a generalized hindlimb extensor motoneurone receiving excitation (—<) and inhibition (—●) from a generalized interneuronal pool responsive to descending control and afferent input from the *entire* limb. In addition, the motoneurones of each single muscle receive relatively discrete (specialized, private line) monosynaptic Ia and spII excitation from their own muscle and its close synergists, and somewhat less discrete disynaptic inhibition (the open circle is generalized in this pathway). These pathways, too, are subject to controls emanating from the generalized interneuronal pool. In this schema, note that the Ia input projects both directly (as shown) to the motoneurone and indirectly (not shown) via the limb afferent input. Also, the interneurons providing disynaptic inhibition to the motoneurone are, in reality, a part of the generalized interneuronal pool.

The Fig. 1 model is based on four lines of evidence:

1. By far the majority of limb afferent input to the spinal cord (including that from Ia and spII afferents) is directed to spinal interneurons on which the descending command signals also converge. The output of this massive interneuronal pool effects motor pools (nuclei) supplying the whole limb. This convergent-divergent arrangement of interneuronal connectivity suggests that sensory input from single muscles contribute more to the integrated control of the limb rather than the singular control of their same (homonymous) muscle.

2. While the mechanical status of single muscles is signaled accurately by the combined ensemble input from their spindles (Ia, spII) and tendon organs (Ib), the central actions of the Ib and shared Ia-Ib feedback (the latter onto interneurons receiving monosynaptic excitation from both Ia and Ib afferents) suggest that their role is to ensure the integrated

actions of many muscles across several joints, rather than to the exclusive regulation of a single muscle.

3. The possibility of an exclusive ("private line"; cf. McCrea 1992) mechanoreceptor reflex control of the homonymous muscle (or, at least, of it and its close synergists) is limited to that derived from the monosynaptic input of Ia and spII afferents. This arrangement is present in most but not all muscle systems, and it, too, is subject, under certain conditions, to a presynaptic inhibitory control from the interneuronal pool (see Rudomin's chapter in Binder & Mendell 1990).

4. A degree of exclusivity may also be provided in disynaptic reciprocal inhibitory pathways activated by Ia afferent input. While interneuronal modulation is ever-present in this pathway, the spinal connectivity pattern of this pathway is at least suggestive of some focus of attention (specialization) on a selected group of muscles, rather than that of the entire limb.

Proprioceptive usage in motor control in the presence of muscle fatigue

As a final comment, we would propose that while the systematic testing of the sensory-feedback hypothesis will contribute to our understanding of segmental motor mechanisms, the study of muscle fatigue has even broader implications for the control of movement. For example, experimental evidence derived from several invertebrate and vertebrate species, performing a wide variety of tasks, now suggests several roles for proprioceptive information (Hasan & Stuart 1988). Table 1 summarizes these roles which are exhibited during sensorimotor integration at *all* levels of the CNS, including the operation of segmental reflexes (***Note:*** Proprioceptors are the receptors that respond to the mechanical variable associated with muscles and joints. In the strictest sense, the proprioceptors have an adequate stimulus that arises from the actions of the organism itself and they include muscle spindles, Golgi tendon organs, and joint receptors in vertebrates, and a variety of stretch receptors and chordotonal organs in invertebrates. In contrast, exteroceptors such as tactile receptors respond primarily to external stimuli. However, the force-sensitive receptors in the exoskeleton of many invertebrates can function as proprioceptors).

An intriguing feature of Table 1 is that neurophysiologists have focused almost exclusively on **only two** of the proposed roles (1.1 & 2.1 in Table 1), with the sensory-feedback hypothesis fitting most closely with studies of conventional reflex testing (i.e., 2.1 in Table 1; appropriate responses to unexpected perturbations). It will be of great utility and interest to arrive at a more complete understanding of the effects of muscle fatigue on the functions summarized in Table 1, and on many other motor functions, as well, when the non-proprioceptive group III-IV input and suprasegmental aspects of muscle fatigue are also taken into account.

Table 1. The role of proprioceptors in motor control

1. Three roles arise from mechanics of the musculoskeletal system. They involve *smoothing* and *stabilizing* of *internally generated* programs.
   - 1.1 linearization of (correction for) muscle properties
   - 1.2 compensation for lever-arm variations
   - 1.3 correction of interjoint interaction effects
2. Three additional roles arise from *interactions* between the *mechanics* of the musculoskeletal system and the *physical environment.*
   - 2.1 appropriate responses to unexpected perturbations
   - 2.2 selections of appropriate synergies of response
   - 2.3 assist external forces, particularly in interlimb coordination

Summary

Muscle wisdom and its proposed sensory-feedback mechanism provide a new opening in the study of muscle fatigue and the function of the segmental motor system, particularly in regard to the neuromuscular control of glycolytic, rapidly fatiguing muscle cells. Numerous experiments on both reduced animal preparations in a wide variety of species and conscious humans are necessary on: *motoneurones,* the relationship between their adaptive properties, size principle issues and mechanisms of motor unit fatigue; *motor units,* associations between the magnitude of fatigue-induced slowing in force-relaxation rate and motoneurone firing rate, recruitment order, force and fatigability; *muscle receptors,* effects of fatigue on their adaptive and transducing properties and; *spinal reflexes*, fatigue-induced modulation of reflex efficacy. In addition, the broad and multifaceted role of proprioceptive usage in the control of movement (also, in a wide variety of species) should now be examined in the presence of muscle fatigue. Clearly, an increased emphasis on the study of muscle fatigue, as guided by clearly defined and perceived issues, will contribute greatly to further advances in our understanding of the segmental motor system, particularly if the work is also stimulated by the spirit of adventurous speculation advanced in this article!

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