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SENSORI-SENSORY AFFERENT CONDITIONING WITH LEG MOVEMENT: GAIN CONTROL IN SPINAL REFLEX AND ASCENDING PATHS

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Abstract—Studies are reviewed, predominantly involving healthy humans, on gain changes in spinal reflexes and supraspinal ascending paths during passive and active leg movement. The passive movement research shows that the pathways of H reflexes of the leg and foot are down-regulated as a consequence of movement-elicited discharge from somatosensory receptors, likely muscle spindle primary endings, both ipsi- and contralaterally. Discharge from the conditioning receptors in extensor muscles of the knee and hip appears to lead to presynaptic inhibition evoked over a spinal path, and to long-lasting attenuation when movement stops. The ipsilateral modulation is similar in phase to that seen with active movement. The contralateral conditioning does not phase modulate with passive movement and modulates to the phase of active ipsilateral movement. There are also centrifugal effects onto these pathways during movement. The pathways of the cutaneous reflexes of the human leg also are gain-modulated during active movement. The review summarizes the effects across muscles, across nociceptive and non-nociceptive stimuli and over time elapsed after the stimulus. Some of the gain changes in such reflexes have been associated with central pattern generators. However, the centripetal effect of movement-induced proprioceptive drive awaits exploration in these pathways. Scalp-recorded evoked potentials from rapidly conducting pathways that ascend to the human somatosensory cortex from stimulation sites in the leg also are gain-attenuated in relation to passive movement-elicited discharge of the extensor muscle spindle primary endings. Centrifugal influences due to a requirement for accurate active movement can partially lift the attenuation on the ascending path, both during and before movement. We suggest that a significant role for muscle spindle discharge is to control the gain in Ia pathways from the legs, consequent or prior to their movement. This control can reduce the strength of synaptic input onto target neurons from these kinesthetic receptors, which are powerfully activated by the movement, perhaps to retain the opportunity for target neuron modulation from other control sources.

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1. INTRODUCTION

"*Machine-like regularity and fatality of reaction, although characteristic of spinal reflexes, is yet not exemplified by them to such an extent that similar stimuli will always elicit from the spinal animal similar responses.*" (Sherrington, 1900). The characteristics of spinal reflexes, as noted by Sherrington, are not immutably associated with the characteristics of the delivered stimulus. Sherrington highlighted such modifiability of the reflex pathway by noting the influence of the passive changes in limb posture on the magnitude and often direction of responses evoked by a common stimulus. Yet, it appears that ideology displaced these experimental observations, for by the 1920s we read in a neurology text: "*A reflex act... is an invariable mechanically determined adaptive response to the stimulation of a sense organ*" (Herrick, 1920). Fortunately, there has been much recent support of the ideas of Sherrington, revealing that the output from reflex pathways alters due to altered convergence even when the stimulus input is held constant. These pathway gain changes and the extent and complexity of this convergence onto the target neurons of reflex pathways in acute animal preparations have been well characterized (Baldissera *et al.*, 1981; Jankowska, 1992). What has proved interesting recently is the modulation of certain human pathways involving somatosensory afferents, observed as a direct consequence of movement. This modulation, evoked by quite natural movement conditions, is so powerful that the gain of specific neural pathways can fall close to zero.

Particularly intriguing has been the modulation of pathways serving mammalian muscle stretch receptors. Presently we review these matters in studies of leg movements, with the predominant focus being healthy humans; reflexes in the upper limb are not included. The generalizability between upper and lower limbs remains to be explored.

It is important to understand the control of somatosensory transmission, in that motor plans interact with sensory flow to determine limb movement. For vertebrate locomotion, the sites of pattern generation in the brain and spinal cord both receive sensory input consequent to movement. In the studies presently reviewed, test pulses were put through sensory, and sensorimotor pathways, to establish change in input–output relationships with movement. Two test pulse inputs are considered here, being stimulation of: (1) group I afferents, often those originating from triceps surae; and (2) cutaneous afferents arising from the foot. The output magnitude from these test pulses is measured from muscle electrode activity and/or somatosensory evoked potentials (SEPs) recorded from the brain via scalp electrodes. Careful control of the magnitude of the test pulse input allows one to infer about changes observed in the magnitude of the test pulse output. This can lead to inferences about spinal control and locomotion, centrifugal and centripetal sources of modulation, synaptic plasticity, presynaptic inhibition and co-ordinative organization of the motor plan with sensory feedback. There are related reviews on reflex modulation and presynaptic inhibition (Stein and Capaday, 1988; Stein, 1995), spinal interneuronal relays (Jankowska, 1992), gain control in motor tasks (Prochazka, 1989) and the H reflex (Schieppati, 1987).

As noted, one of the target test pulses features stimulation of the large diameter afferents from skeletal muscle. The initial electrical reflex measured at the muscle, in response to such afferent stimulation, is referred to as the Hoffmann (H) reflex. The afferents involved also serve as the foundation for the autogenic stretch reflex which occurs when muscle stretch receptors, particularly the primary sensory endings of spindles, are activated leading to autogenic excitation. The H reflex can be used as a partial analogue of the autogenic stretch reflex, with

the stimulus being a low threshold electrical pulse to the mixed nerve trunk serving the muscle, i.e. proximal to the receptors, muscle and tendon (Hoffmann, 1918). Both reflexes can be evoked in a variety of mammals, including humans, non-human primates (Wolpaw and Carp, 1993), rats (Chen and Wolpaw, 1994), cats (Akazawa *et al.*, 1982) and dogs (Knecht and Redding, 1981). The magnitude usually is measured as electromyographic activity (EMG), although the muscle force produced also has been observed. It has been known since the early 1980s that the magnitudes of stretch reflexes and of H reflexes alter when people walk, even when the stimulus is kept constant (Morin *et al.*, 1982). (Also see reviews by Schieppati, 1987; Stein and Capaday, 1988.)

Since the initial identification of the phasic modulation of sensorimotor pathways associated with locomotion, a body of work has been completed providing detailed information on: (1) initiating source(s); (2) pathways; (3) modes of depression of the group I and cutaneous mediated reflexes; and (4) possible functional relevance. The majority of the work has been focused on group I reflexes, specifically the H reflex. It is clear that the pathways of these reflexes receive modulatory convergence from transmission through other primary afferents, i.e. centripetally induced modulation. This sensori-sensory conditioning for the lower limb is the focus of this review. Also clear is that convergence initiated from more complex CNS centres of the brain and spinal cord modulates these reflex paths, i.e. centrifugal modulation. Progress has been made recently in showing the separate contributions of these two sources. It should be noted that this review does not cover the primate and human work on long-term changes of the magnitude of H and stretch reflexes, as this is a domain in itself (Wolpaw and Carp, 1993; Wolf *et al.*, 1995).

Locomotor movements also modulate cutaneous reflex responses, which are multiphasic and of latency longer than the H reflex, evoked in muscles of the leg by stimulation of the cutaneous nerves. Active movement of the leg induces modulation of the amplitudes of these reflexes, reflecting similarity to the receptiveness of the H reflex to movement-induced conditioning.

In addition to the focus directed to these spinal sensori-motor pathways, recent work has focused on movement-induced modulation of somatosensory evoked potentials (SEPs) measured from the scalp. This provides meaningful information about how gating of sensory input to the cortex is processed in comparison to spinal sensori-motor pathways. Progress has been made on the understanding of differential and parallel modulation of the spinal and supraspinal pathways. The technique for SEPs arising from the lower limb usually involves stimulation of tibial nerve or sural nerve and recording from surface electrodes over the lumbar cord or from scalp electrodes over the cerebral cortex.

The current review will address research emphasizing the evidence and characteristics of peripherally and centrally mediated regulation of pathway gain underlying human lower limb movements. The principal focus is on the evidence supporting a significant role played by sensory discharge arising from ongoing movement as an important mediator of afferent conditioning. This body of work provides a foundation for understanding of the complex interplay between sensory inputs and the control of ongoing movement. Eventually, understanding about how the task parameters and the transient status of the CNS influence this sensori-sensory conditioning will help define the broader range of characteristics of such modulation present in everyday behaviour.

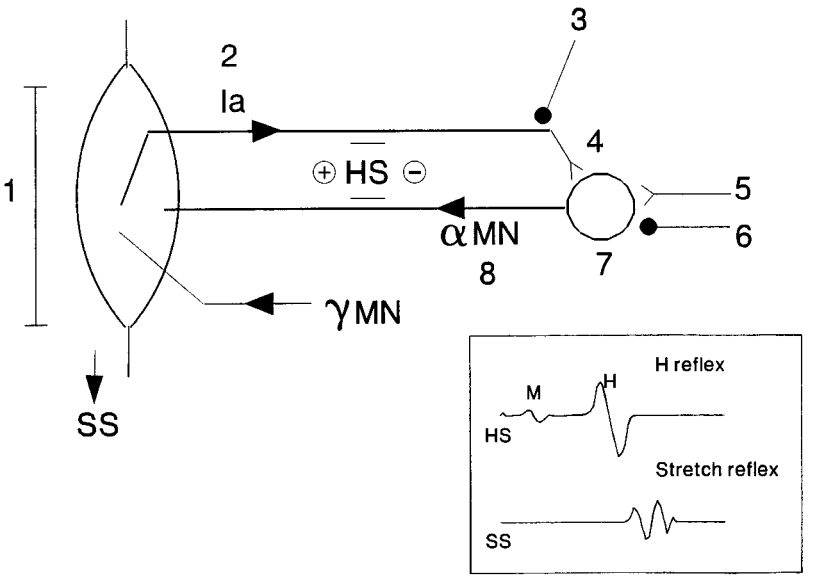

Fig. 1. Schematics of some main components of the stretch reflex and the H reflex. For numbered components, see details in text. Abbreviations: HS, H reflex stimulation; SS, stretch reflex stimulation.

2. MODULATION OF THE GAIN OF H REFLEX PATHS OF THE LEG

2.1. Methodology

Figure 1 is a schematic of the EMG of the stretch and H reflexes, their neural path and major factors determining the magnitude of the responses. Change in any of the factors will be reflected in the gain of the pathway. Failure to acknowledge the range of possible factors influencing the reflex gain makes some studies difficult to interpret. For example, it is wrong to view the magnitude of the H reflex as an expression of the excitability of the motoneuron. It is clear that changes in this magnitude, representing changes in gain of the overall path of the reflex, quite often represent events which are presynaptic to the motoneuron, the excitability of the motoneuron not necessarily changing to any appreciable degree (Hultborn and Nielsen, 1995).

As denoted in Fig. 1, to maintain the same reflex magnitude, for both stretch and H reflexes, the experiment must maintain constant: (1) the muscle length, hence tonic discharge of spindle receptors (Hultborn *et al.*, 1996); (2) the level of ongoing traffic in the transmitting afferents; (3) the presynaptic inhibition, autogenically and heteronymously induced, from axo-axonal synapses close to the afferent terminal branches; and (4) availability of transmitter vesicles, which is often dependent on immediately prior history of discharge at that terminal branch. Postsynaptic modulators of reflex amplitude include (5) EPSPs; and (6) IPSPs; together with (7) longer-lasting changes in the postsynaptic cell, such as metabotropic and plateau potential effects. Ongoing contractions (8) also will play a part, as the action potentials may render refractory some motoneurons, temporarily prohibiting their participation in the reflex response. Accordingly, at such times, H waves can alter in magnitude as a reflection of the recent recruitment of alpha motoneurons for voluntary contraction (Brooke and McIlroy, 1985). When this occurs, the M wave magnitude appears to be inversely proportional to the H wave and large H waves can appear at M_{max} levels of stimulation. These factors are all potentially available to the motor control system and can account for changes in reflex gain. Thus, care in experimental control and interpretation of results is necessary.

The stretch reflex is elicited by a force (SS), commonly a tendon tap or brief vibration in human studies, to stretch the muscle. This force likely also discharges receptors additional to those in muscle spindles. Constancy in the resulting action potential volley in Ia fibres requires constancy of muscle fibre tension, extrafusal and intrafusal via gamma drive. As the trace in Fig. 1 shows, the stimulus for the stretch reflex is a complex of forces and the reflex response in the EMG is quite distributed in time and magnitude, compared with the more discreet stimulus and response for the H reflex. In the remainder of this review, there is only limited data from experiments on stretch reflexes. This likely is because stimulus input when using the H reflex technically is easier to evoke during movement and therefore most studies have used this as a probe.

As the trace in Fig. 1 shows, compared with the stretch reflex, the electrical stimulus of the H reflex results in a more synchronized stimulus artefact of brief duration and a more synchronized and brief reflex response in the EMG. However, the ecological validity of the H reflex procedure is weak. In addition to the artificial synchrony of the afferent volley, the largest stretch-evoked reflex responses of the EMG are comparable in area to responses that occur very early in the stimulus range for the H reflex (McIlroy and Brooke, 1986). A conclusion on the comparison of the two reflexes is that they are both useful experimental probes, different from each other and both having a number of constraining factors which need to be attended to in experimental design and interpretation. (Note that Schieppati, 1987, is still the most current review for further factors pertaining to the H reflex.)

The H reflex is elicited by electrical activation of large diameter afferents (HS). This also can set up, in alpha motoneuronal axons, orthodromically proceeding action potentials which result in an M wave in the EMG. Additionally, from the alpha motoneuronal axons, antidromic action potentials can proceed which, through collision with reflex-elicited action potentials, lead to diminished reflex amplitudes. Inconstancy of this antidromic consequence of the stimulation will compromise interpretation of reflex gain.

High levels of stimulation, intended to evoke M and H waves, also can elicit F waves at times. These are held to arise from antidromic stimulation of alpha motoneuronal axons leading to action potentials set up at motoneuronal soma, resulting eventually in excitation of the muscle (Ma and Liveson, 1983). One can screen against the confusion of mistaking F waves for H waves, as the former only appear intermittently over consecutive samples and disappear at lower stimulus intensities which are yet adequate to evoke H waves. The matter is discussed further (Ma and Liveson, 1983; Hultborn and Nielsen, 1995). The latter authors show that F waves are much less sensitive to conditioning from heteronymous nerve, compared with H reflexes.

When change in gain is to be denoted by a change in reflex magnitude, maintaining constancy of stimulation is paramount. For the stretch reflex, this involves not simply consistent force applied to stretch the muscle, but also the transmission of that force to the muscle receptors, i.e. the intrinsic stiffness and the stiffness imposed by voluntary contraction. For the H reflex, it involves consistent activation of the Ia afferents (Crone *et al.*, 1990). When movement conditions are studied, this presents problems for the stimulus control in both types of reflex. In the H reflex, a common procedure is to use stability of a concomitantly evoked and small M wave as a biocalibration (Swett and Bourassa, 1981) of the effect of the stimulus. The argument is that the M wave represents activation of large diameter efferents and reflects the accompanying activation of the large diameter afferents in the shared mixed nerve trunk (Mayer and Mawdsley, 1965). It is hoped that the afferents are substantially Ia fibres. There is experimental support for this argument. Neurographic studies have shown that the magnitude of the

M wave is correlated with the magnitude of the afferent volley, which is conducted at a group I velocity (Abbruzzese *et al.*, 1985; Fukoshima *et al.*, 1982). Further, it is likely that Ia fibres comprise the bulk of the H reflex. The movement-induced attenuation of that reflex was studied across the range of stimulation from the threshold for H responses (H_t) to the stimulation evoking the maximum M wave (M_{max}) (Misiaszek *et al.*, 1995c). The curve of the H reflex magnitudes did not show evidence of recruitment of a different afferent group as stimulus intensity rose. That study also provides some reassurance against the worry that small changes in M wave amplitude may confound the results of movement-induced conditioning of H reflexes. The depression of reflex magnitude was so complete, across the stimulus range, as to make any small shifts in M wave magnitude comparatively minor in effect. Such small shifts, with control of stimulus to $\pm$ 5% M_{max}, were not correlated with variations in H reflex magnitude (Collins *et al.*, 1993b). Further reassurance that movement conditioning of H reflexes is real, not an artefact of poor stimulus control, is shown by the effect continuing when the knee (the site of stimulation) is immobilized and the hip is moved (Brooke *et al.*, 1993).

There must also be concern about the rate of stimulation selected. Close-spaced stimulation runs the risk that there will be a decrease in H reflex amplitude due to a reduced release of neurotransmitter (Hultborn *et al.*, 1996). Also, a long succession of H reflex magnitudes evoked at a rate of 1 sec^{-1} appears like a fractal time series, with strong time autocorrelations over durations of 23 ± 17 sec (Nozaki *et al.*, 1995). The effect may be arising at the synaptic connections to alpha motoneurons. There is an opportunity for research to establish the basis for this slow DC effect. Unless accounted for, it will increase the error variance in trials made up of many samples which are continuous in time.

The introduction of movement as a conditioning source presents several other important methodologic matters. In recent studies, use has been made of "passive" movement to dissociate the effect of afferent inputs associated with the movement from that of the descending motor drive that controls active movements. The subject's body and head are supported. An external manipulator (motor and gear/crank system or robot or experimenter's hands) directs the path of the limb segment(s) about the joint(s). The subject is asked to keep the muscles relaxed and the lack of activity in the EMGs of those muscles is confirmed by online monitoring. The fear of confounding from undetected muscle activity, subliminal for the EMG electrodes on the surface of the skin, is diminished with demonstration of similar modulations with passive movement where tonic isometric contraction of the muscles is introduced (Brooke *et al.*, 1995a; Cheng *et al.*, 1996; Misiaszek *et al.*, 1995b).

A general question to raise about studies relying on movement is: "Does the reduced H reflex amplitude simply reflect occlusion of the stimulated afferents, due to the receptor traffic set up as a consequence of the movement itself?". The answer is likely to be "No". As early as 1982, it was shown that ischaemic block just below the stimulation site of the H reflex did not alter the movement-induced modulation (Morin *et al.*, 1982). Subsequent studies also have rejected this possibility, e.g. Capaday and Stein, 1987a). Further, in recent studies showing modulation of the reflex amplitude in the ankle extensor muscle soleus with passive movement, the ankle was immobilized, much reducing the possibility of test afferent occlusion from the movement.

2.2. Active Movement of the Leg(s)

The gain of H reflexes is modulated when people actively move their legs. Early work on this topic was reviewed in the 1980s (Schieppati, 1987; Stein and Capaday, 1988). The modulation has now been seen in walking, running, stepping, hopping and pedalling, as well as elevated beam-walking and rock-climbing (Garrett *et al.*, 1981; Capaday and Stein, 1986, 1987a; Crenna and Frigo, 1987; Brooke *et al.*, 1995a; Moritani *et al.*, 1990; Brooke *et al.*, 1991a; Boorman *et al.*, 1993; Llewellyn *et al.*, 1990; Bennett *et al.*, 1993). [Compared with lying horizontal, attenuation of magnitude occurs in standing (Chan and Kearney, 1982; Koceja *et al.*, 1993; Brooke *et al.*, 1995a).] The gain modulation is retained if the activity is restricted to one leg walking on a treadmill or stationary stepping (Crenna and Frigo, 1987; Brooke *et al.*, 1995a). It has been observed in the pathways for human soleus (many of the references in this review), tibialis anterior (Brooke *et al.*, 1991a), gastrocnemius (Moritani *et al.*, 1990) and quadriceps muscles (Dietz *et al.*, 1990; for vastus medialis, see Brooke *et al.*, 1991a). Reflex responses in soleus, an extensor of the ankle, during active stepping are shown in Fig. 2 as the mean amplitudes for a group of subjects and also data from one subject stepping uni- and bipedally (Brooke *et al.*, 1995a). The main components of the pattern are common across the activities of stepping, walking, running and pedalling. There is high gain during much of the phase when soleus is active and low gain as the leg returns to that phase. On average over the cycle of movement, the reflex gain is lower than that observed when the subjects sit or stand still. Neither M waves nor latencies of the reflex responses are systematically changed.

2.2.1. *Relationship of Modulation to Ongoing EMG*

An obvious question about this modulation of reflex gain with active movement is: "Is the gain change a function of the changes in ongoing EMGs?". Many papers show that isometric contractions of the autogenic muscle result in increased H reflex magnitude (Paillard, 1955), particularly for low levels of contraction (Cheng *et al.*, 1994; Verrier, 1985). However, data show that this simple relationship is not a satisfactory explanation of the gain changes during active movement (Crenna and Frigo, 1987). Over the stance phase of gait, soleus, vastus lateralis and rectus femoris H reflex gains fall, yet the ongoing EMG activity is little changed (Morin *et al.*, 1982; Dietz *et al.*, 1990). In the swing phase, the gain remains low even when a tonic contraction of soleus is introduced during a stepping-like active movement (Brooke *et al.*, 1995a), or during walking

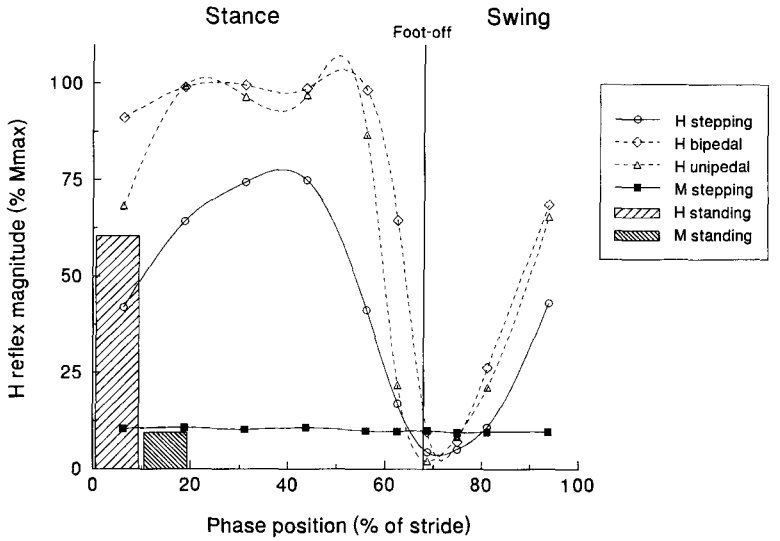

Fig. 2. Soleus H reflex modulation over the active stepping cycle. The solid line shows average data for bipedal stepping from six subjects. The dotted line shows data for one subject, for bipedal stepping and for stepping with one leg. (Data from Brooke *et al.*, 1995a.)

(Yang and Whelan, 1993). Further, the reflex increase in soleus over the cycle of human gait tends to precede the change in EMG activity (Capaday and Stein, 1986; Yang *et al.*, 1991a; Fig. 1 in Brooke *et al.*, 1992). This occurs also in the locomoting decerebrate cat, during mesencephalic locomotor region stimulation (Akazawa *et al.*, 1982). The additional effect of activity in the antagonist muscle has been studied. Removing the burst of activity in tibialis anterior little altered the depressed reflex in soleus during the swing phase of walking (Yang and Whelan, 1993). Increasing tibialis anterior activity further depressed the reflex in soleus during cycle pedalling with both legs (Brooke *et al.*, 1992). Presently, the conclusion appears to be that the background excitability of the autogenic motoneuronal pool plays a role in reflex modulation, but that the story is more complex than that. The studies on passive movement (Section 2.3) add further insight. Descending control of gain also may be involved.

2.2.2. *Role of Presynaptic Inhibition in Modulation*

During active movement, presynaptic inhibition seems to be the main source of the observed attenuation of H reflexes. Briefly, the grounds for this statement are as follows.

1. The reflex modulation fails to follow the motoneuronal excitation, as reflected by the EMG ongoing for the movement of walking (Capaday and Stein, 1986). Further confirmation comes from comparing running to walking, where, for running, the reflex gain attenuates further, yet the ongoing EMG increases considerably (Capaday and Stein, 1987a). The implication is that pre-motoneuronal matters are involved, at least in part.

2. Equivalent ongoing EMG activity has been obtained by matching the movement condition with a stationary one. Despite this matching, reflex gains are lower in the movement condition (Morin *et al.*, 1982). Further, compared with standing with different levels of autogenic muscle contraction, reflexes attenuate for the different contraction levels when they are sampled across the movement cycle of walking (Capaday and Stein, 1986). This separation between gain and ongoing EMG was confirmed in later studies (Brooke *et al.*, 1991a), which removed the potential confounding of different levels of movement EMG obtained from different points in the movement cycle.

3. Heteronymous group I reflexes from the common peroneal nerve to the vastii muscle (Brooke and McIlroy, 1990a, 1990b) were not attenuated with movement even though homonymous H reflexes in vastus medialis were attenuated (Brooke *et al.*, 1991a). One would have anticipated that both the homonymous and heteronymous excitatory inputs onto the vastii motoneurons would have been attenuated if the mechanism of attenuation was postsynaptic. As a result, pre-motoneuronal inhibition of the H reflex is the most likely explanation.

4. Antidromic gastrocnemius nerve stimulation, that elicits recurrent inhibition of the motoneuronal membrane through Renshaw cell activation, does not produce sufficient monosynaptic reflex gain attenuation to match that seen with movement, in the crossed extensor excited, motoneuronal membrane of the decerebrate cat (Capaday and Stein, 1989). The Renshaw cells induce substantial gain attenuation with the motoneuronal membrane in a resting state. However, there is little effect when the excitation is added, mimicking the excitation for active movement. The suggestion again is that premotoneuronal events drive the gain attenuation.

5. In a computer model of the motoneuron, it was not possible to manipulate within a physiological range the variables converging onto the postsynaptic membrane, so as to replicate the levels of gain attenuation seen during active movement (Capaday and Stein, 1987b). Presynaptic inhibition is implied.

These demonstrations could be considered conclusive. It might, however, be wise to show some caution, since all are indirect. Further, our knowledge of intracellular matters in the presynaptic interneuron is limited. Also, to proceed logically from premotoneuronal to presynaptic inhibition assumes that H reflexes are monosynaptic and this has been questioned. One of the grounds is that of a possible contribution from cutaneous afferents with diameters as large as Ia afferents in the human leg (Burke *et al.*, 1984; Macefield *et al.*, 1989). Partly counterbalancing this, no evidence was found for more than one type of afferent conditioning when the stimulus range for H reflexes was submitted to movement-induced gain attenuation (Misiaszek *et al.*, 1995c). Further, estimated rise times of EPSPs from single motor units activated at low threshold autogenically, suggest a monosynaptic path (Mao *et al.*, 1984; Miles *et al.*, 1989). A recent review summarized the evidence for and against presynaptic inhibitory interpretations for such gain changes in humans (Stein, 1995). It also spotlighted an additional technique which should prove useful. Following distal stimulation of the sural nerve, sensory nerve action potentials were recorded from successively more proximal sites on the human leg, to demonstrate an antidromic volley suggestive of a dorsal root reflex (Shefner *et al.*, 1992). This was attributed to primary afferent depolarization (PAD) at the terminals. The PAD is taken as an indicator that presynaptic inhibition is occurring.

The putative presynaptic inhibition brought to bear on H reflexes during movement may arise from a variety of sources. Such conditioning from an antagonist nerve is strong when standing, yet appears weak or non-existent when studied in the stance phase of walking (Capaday *et al.*, 1995). This altered conditioning may arise from saturation of presynaptic inhibitory interneurons onto autogenic Ia afferents during the movement or may arise from selective modulation of the presynaptic inhibitory interneurons from the antagonist nerve. There may be a number of examples of such change in conditioning with movement, given the complexity of convergence onto primary afferents and spinal neurons. There is an opportunity for more research.

2.2.3. *Initiating Source and Neural Path for Modulation*

In the studies of gain attenuation with active movement, there is little evidence as to what are the initiating sources for the modulation. Neither is there much evidence as to the path taken from the initiating sources to the presumed presynaptic inhibitory interneurons. One initiating source is suggested to be centrifugal, being convergence from the brain (see Section 2.4.1). Another appears to be centripetal, i.e. initiated from peripheral somatosensory receptor discharge. For example, in walking, cutaneomuscular stimulation from the medial plantar nerve attenuates H reflex gain in soleus over all phases, whereas there is little effect during quiet stance (Fung and Barbeau, 1994). The attenuation with movement is less pronounced in spastic paretic patients (Fung and Barbeau, 1994). The extensiveness of such sensori-sensory afferent conditioning, centripetally through oligosegmental circuits or utilizing centrifugal influences through longer loops, is not clear for active movement. There is opportunity for research on both specific sources and neural routes.

2.3. Passive Movement of the Leg(s)

The modulation of H reflex gain seen with active movement likely arises from many sources. To reduce the complexity of the preparation, delimitation has been made to passive movement, with results existing on pathways for the human muscles of soleus (many references below), tibialis anterior (Brooke *et al.*, 1996c) and abductor hallucis (Misiaszek *et al.*, 1995a), and for the second interosseus muscle of the anaesthetized dog (Misiaszek *et al.*, 1995, 1996). Passive movement removes the descending commands which result in voluntary EMGs and quite likely other descending effects onto segmental interneurons. It also removes the kinesthetic receptor discharges that result from muscle contraction. This substantially removes potential influence from Golgi tendon organs, which are sensitive to the force of contraction but much less sensitive to passively imposed forces (Baldissera *et al.*, 1981). Passive movements also delimit the muscle spindle involvement, substantially reducing changes in gamma motoneuronal drive, as described in the cat (Prochazka *et al.*, 1977a; Loeb and Hoffer, 1985) and contraction-induced alterations in spindle length and hence discharge. The passive movement applied in the human studies usually has been with the ankle braced, to limit possible changes in H reflex gain which might be attributable to length changes of the soleus muscle. In part, such an effect from the length of the autogenic muscle may arise from reduced availability of neurotransmitter for release by the reflex action potentials at the afferent terminals (Nielsen *et al.*, 1992; Hultborn *et al.*, 1996).

2.3.1. *Ipsilateral Movement*

Pedalling action, forward (many references below) and reverse (Brooke *et al.*, 1996a) has been used mainly for passive movement, through a motor or through an additional ergometer moving the subject's feet when they are attached to a pedal of a bicycle crank/chainwheel system. There is also complementary information on stepping and on rotation about the single joints of hip and knee. At a normal pedalling rate of 60 rpm, similar in cadence to a typical walking rate of 120 steps/min, passive movement strongly depresses the reflex gain in soleus (McIlroy *et al.*, 1992), with the effect occurring across the whole cycle of movement. At movement rates of 60–90 rpm, the reflex gain can be reduced virtually to zero in the majority of the subjects. Thus, a control reflex recruiting as much as 90% of the maximum EMG (as M_{max}) can be completely shut down. As the movement rate is reduced, the gain attenuation reduces (McIlroy *et al.*, 1992; Collins *et al.*, 1993a). At slower rates, such as 20 or 10 rpm, the attenuation is still evident. At these slow rates it also shows clear phase modulation (McIlroy *et al.*, 1992), the strongest attenuation occurring at the point where the

leg under study is most fully flexed (Cheng *et al.*, 1995a).

These effects persist if only one leg is moved. At a rate of 60 rpm, the effect from one leg (the ipsilateral test leg) or both legs moving is indistinguishable (McIlroy *et al.*, 1992). Thus, the gain attenuation is not dependent upon bipedality of movement. Also, deprivation of vision or hearing during the movement leaves the gain attenuation intact (Brooke *et al.*, 1996b), indicating that the special senses are little involved in the movement-induced modulation.

The passive movement effect is not a function of the pattern of movement alone, as at 10 rpm little gain change occurs when the range of motion is severely curtailed by use of a very short pedal crank (approximately 2.3 cm) (Cheng *et al.*, 1995a). However, that velocity of movement can still produce gain attenuation. This is seen when the velocity is held constant but the range of movement is restored, by returning to a longer pedal crank, e.g. of 18.9 cm. In addition, the effect on the reflex pathway is still observable if the shank alone is rotated about the knee joint, or if the thigh alone is rotated about the hip (Brooke *et al.*, 1993, Misiaszek *et al.*, 1996b). Given the lack of effect from special senses, these results suggest that a somatosensory receptor group(s), activated as a consequence of either type of isolated movement, initiates the reduction in gain.

2.3.1.1. *The receptor which initiates the down-regulation*

The primary endings of the spindles of the monoarticular extensor muscles of the hip and knee are major initiating sources for the down-regulation of the soleus H reflex with passive movement. [We do not know what role is played by the spindles in ankle muscles. We can observe up to 50% decreases in H reflexes when passive movement occurs around the ankle alone (Brooke *et al.*, 1996b). However, homosynaptic depression may account for such changes (Hultborn *et al.*, 1996).] The evidence for a role played by spindles in muscles at hip and knee comes from four different experimental techniques, involving (1) the phasing of the reflex over the movement cycle; (2) the effect of equivalent rates of stretch of these extensor muscles; (3) the effect of tap of the tendon of such a muscle; and (4) selective removal of groups of somatosensory receptors of the canine hind limb. (For the delimitation to monoarticular muscles, see Section 2.3.2.4, re: biarticular muscles.)

Figure 3 shows that over the full cycle of slow passive movement the reflex magnitude is at a minimum at the point of fullest flexion of the leg (Cheng *et al.*, 1995a) (180° on the abscissa). This is similar to active movement (see Fig. 2), where the reflex is most depressed in the phase when the leg is flexing. For both types of movement, there is release of the inhibition as the leg movement enters the extension phase. Note that the posture of the leg ("static" line) also modulates the gain of the pathway. In this figure, and also in Fig. 2, the stability of the M waves is also noteworthy, as it provides a biocalibration of the constancy of the stimulus intensity applied to the large diameter afferent fibres. Maximal attenuation of the soleus H reflex still occurs at the fullest flexion elicited, when the passive movement is restricted to rotation of the shank about the knee or the thigh about the hip (Brooke *et al.*, 1993). From such data on the movement phase, it can be inferred that the attenuation-initiating somatosensory receptors are activated during leg flexion, discharge maximally by full flexion and stop discharging, or are offset by other effects, as the leg starts to extend. There are a number of somatosensory receptors that might be associated with discharge in that phase of the movement. Prominent among these are the stretch receptors of the extensor muscles of the hip and knee.

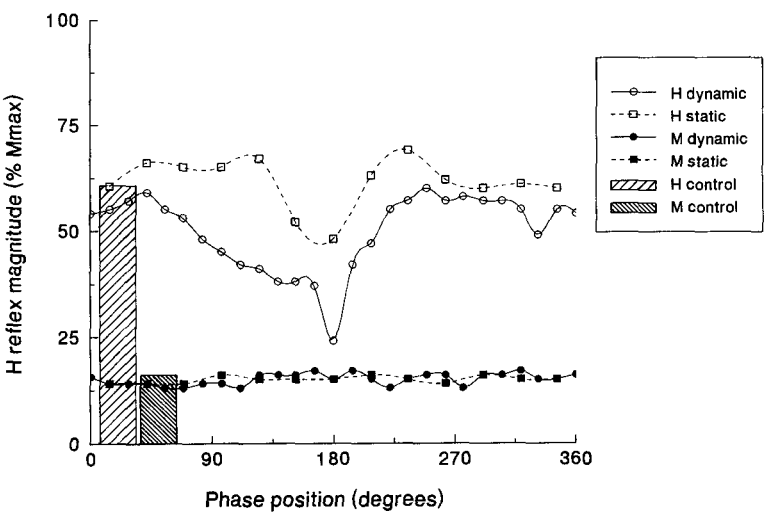

Fig. 3. Magnitude of soleus mean H reflexes ($n = 4$ subjects) across the cycle of passive pedalling movement, with the leg static or moving (dynamic) at 10 rpm, with pedal crank lengths of 16.4–18.9 cm to achieve the same leg joint angular displacements for each subject. Note that 0° represents the most extended position for the leg. (Data from Cheng *et al.*, 1995a.)

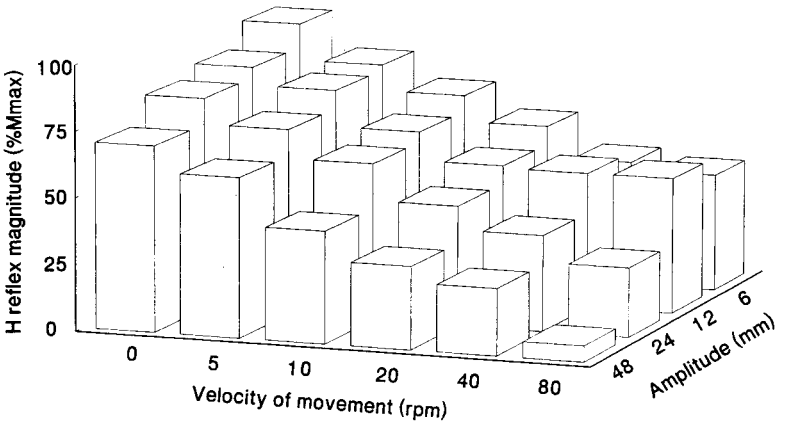

Fig. 4. Magnitude of soleus mean H reflexes ($n = 4$) with different combinations of rate and range (displayed as the amplitude of stretch of the vastii muscle calculated biomechanically) of passive movement of the leg. Conditions across the diagonals share the same estimated rate of stretch of the hip and knee extensor muscles. (Data from Cheng *et al.*, 1995a.)

The primary stretch receptors of muscle spindles are particularly sensitive to the rate of stretch they receive whereas secondary endings are particularly sensitive to the range or amount of stretch. One could, therefore, evaluate the possible contributions from primary or secondary endings by selectively manipulating the rate and/or amplitude of stretch (Cheng *et al.*, 1995a). A biomechanical model of the monoarticular knee extensor muscles was used to define states of movement kinematics that provided equivalent rates of stretch of that muscle group. Thus, large rates of movement were combined with small ranges, and vice versa. Mean H reflex magnitudes for these equivalent rates of stretch are shown horizontally across the diagonals of Fig. 4. That data shown in Fig. 4 strongly support the hypothesis that the receptor initiating the attenuation (a) is driven by the rate of stretch of the knee extensor muscles; and (b) discharges through a fairly simple transformation to lead to the pathway attenuation (Cheng *et al.*, 1995a). As can be seen, in all except two of the 18 comparisons between means on the same horizontal diagonals, the hypothesis was supported, there being no statistical difference in the degree of attenuation for equivalent rates of stretch. Of course, the figure also shows the strong relationship between attenuation and either rate of movement or range of movement.

If the soleus H reflex is attenuated because primary endings of muscle spindles discharge in extensors of the knee, a quadriceps tendon tap should attenuate the reflex. This was demonstrated to be the case (Cheng *et al.*, 1995b). The onset latency of the attenuation was appropriate for Ia afferent transmission to elicit presynaptic inhibition. The accompanying observation of short latency stretch reflexes in quadriceps implied that Ia fibres were activated in the femoral nerve. The reflex attenuation lasted for seconds (see Section 2.3.1.4 for review of such long-lasting effects).

These three sources of evidence, implicating muscle spindle receptors in attenuation of the H reflex, were supported by data from an experiment which isolated the muscle mechanoreceptors during rotation of the shank about the knee in the anaesthetized dog. Figure 5 shows that the absence of cutaneous or joint receptor discharge from the leg had no significant effect on the gain attenuation during shank

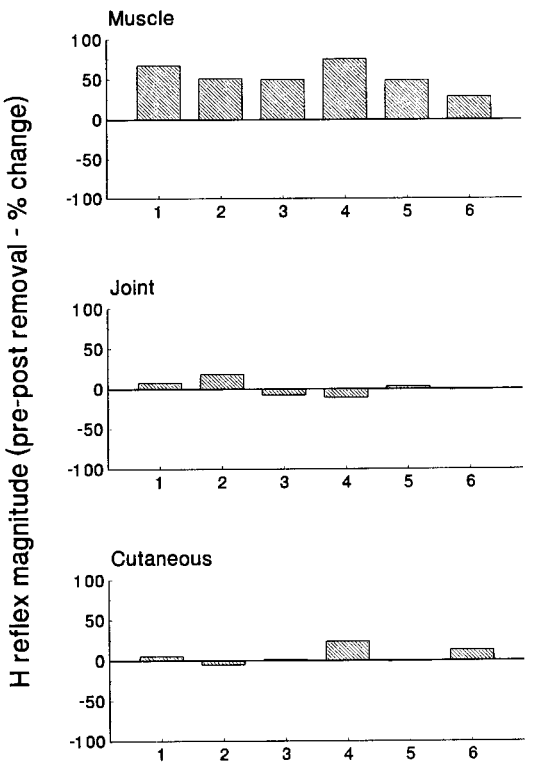

Fig. 5. Average change in mean magnitude of H reflex in the second interosseus muscle of six dogs (1–6 on abscissa) during passive continuously alternating flexion–extension movement of the shank about the knee, following deletion of cutaneous receptors of the leg, knee joint receptors or knee extensor muscle mechanoreceptors. The only statistically significant change, loss of movement-induced attenuation, occurred with the removal of the muscle mechanoreceptors ($p < 0.05$). (Data from Misiaszek, 1995.)

movement (the numbers on the abscissa denote individual dogs). In contrast, removal of inputs from the quadriceps muscle receptors always led to the removal of the gain attenuation. Recently, it has been demonstrated that sinusoidal stretches applied to the isolated quadriceps muscle yield phase-dependent attenuation of the soleus H reflex in the acute decerebrate cat. The attenuation is greatest when quadriceps is being stretched, i.e. lengthening (Misiaszek, unpublished data).

It is noteworthy that study of PAD, a marker often used to indicate presynaptic inhibition, supports this conclusion about receptor source. The Ia afferents showing the highest dynamic change in frequency with stretch experienced the largest PAD, heteronymously elicited (Enriquez and Rudomin, 1994). These Ia afferents served muscle spindle bag1 receptors. This may mean for the human work presently reported, that afferents serving dynamic change of stretch in quadriceps produce strong PAD in such afferents serving other muscles of the leg, such as soleus, tibialis anterior and abductor hallucis.

2.3.1.2. *Inhibitory basis for the down-regulation*

Presynaptic inhibition appears to play a major role in the reflex attenuation arising from the muscle mechanoreceptor discharge consequent to passive movement. This conclusion was reached with the study of passive stepping (Brooke *et al.*, 1995a) and also the study of passive pedalling (Misiaszek *et al.*, 1995b). Subjects maintained a tonic contraction of the soleus muscle during passive movement, which was maintained across the different phase positions, and the reflex magnitudes obtained were compared with those where the contraction was maintained and the limb was at rest. The intention was to use the contraction to stabilize the membrane potentials of the motoneuronal pool for soleus, i.e. to minimize the effect of other postsynaptic effects. When this condition was tested, it was found that passive movement of the leg still induced reflex attenuation. Accordingly, this reflex change was inferred to result from inhibition occurring before the motoneuronal synapse. The interpretation then can be made that presynaptic inhibition had occurred. Caution in interpretation is needed, as the introduction of a tonic contraction is tacitly assumed not to alter significantly the other synaptic currents on the motoneuronal membrane. If these currents also change, they may be responsible for altered recruitment gain (Kernell and Hultborn, 1990). This and other underlying assumptions in the tonic contraction paradigm cause one to be cautious about such an interpretation, as discussed in Section 2.2.2, even though it is the best explanation currently available.

A presumed presynaptic inhibitory effect also has been observed in the H reflex of the contracted tibialis anterior muscle, an ankle dorsiflexor (Brooke *et al.*, 1996c). This complements the report of attenuation induced in this pathway just after heel strike in active walking (Brooke *et al.*, 1991a). With tonic contraction of that muscle at 15% maximum voluntary contraction (MVC), attenuation was induced by passive pedalling movement of the whole leg at movement rates of 20 and 60 rpm. The mean percentage attenuation of the reflex from posturally matched seated control values was 19%, less than the 35% reduction seen in soleus with tonic contraction. Also, the reflex in tibialis anterior recruits a much smaller percentage of the total motoneuronal pool, thus the reduction in terms of $\%M_{max}$ was small, on average being 5%.

The conclusion that presynaptic inhibition contributes to the H reflex attenuation observed with human leg movement, active or passive, is compatible with studies conducted on other animals. During fictive locomotion in the cat, PAD is maximal at full flexion of the leg (Bayev, 1980; Duenas and Rudomin, 1988; Duenas *et al.*, 1990). This modulation (Gossard *et al.*, 1991; Sillar, 1991) and the enhancement of PAD with locomotion (Duenas and Rudomin, 1988; Duenas *et al.*, 1990) is expressed as presynaptic modulation of motoneuronal EPSPs elicited by stimulation of large diameter afferents (Hishinuma and Yamaguchi, 1989). The PAD also is modulated to the swimming rhythm of the lamprey (Alford *et al.*, 1991). Consistent with the previous suggestion that muscle spindles are an initiating source for the inhibition is the observation that very effective initiation of PAD occurs in the cat as a consequence of muscle mechanoreceptor discharge (Jankowska, 1992).

The data reviewed do not rule out a contribution to the reflex attenuation from postsynaptic inhibition. Indeed, there is evidence that last-order PAD interneurons can elicit both pre- and postsynaptic effects (Curtis and Lodge, 1982; Rudomin *et al.*, 1987). However, the data imply strongly that there is a premotoneuronal contribution to the H reflex attenuation with movement.

2.3.1.3. *Route from initiating receptor to inhibitory site*

There is a spinal route from the extensor muscle mechanoreceptors to the segmental presynaptic inhibitory interneurons which down-regulate the H reflex. This is seen most obviously in the acutely spinalized dog, when movement of the shank about the knee joint still elicits attenuation of the H reflex in the second interosseus muscle (Misiaszek *et al.*, 1996a). It is seen also in human subjects with clinically complete spinal lesions (located in the range T7–C4), where attenuation of soleus H reflexes occurs with passive pedalling movement of the legs (Brooke *et al.*, 1995b). Further evidence for a spinal route from receptor to pathway attenuation was provided in a study of change in reflex magnitude when passive movement started at times that were unpredictable for the subjects (Brooke *et al.*, 1995b). The initial force applied as movement commenced was used as a signal immediately to initiate data collection, and elicit the stimulus after a variable delay. A spinal route was indicated by the brief latency of 50 msec from movement initiation to the first statistically significant depression of H reflex magnitude in soleus. In confirmation of these data from the various experiments, when a tap was applied to the quadriceps tendon (Section 2.3.1.3), the attenuation of soleus H reflexes was statistically significant after 36 msec, a latency appropriate for spinal transmission (Cheng *et al.*, 1995b).

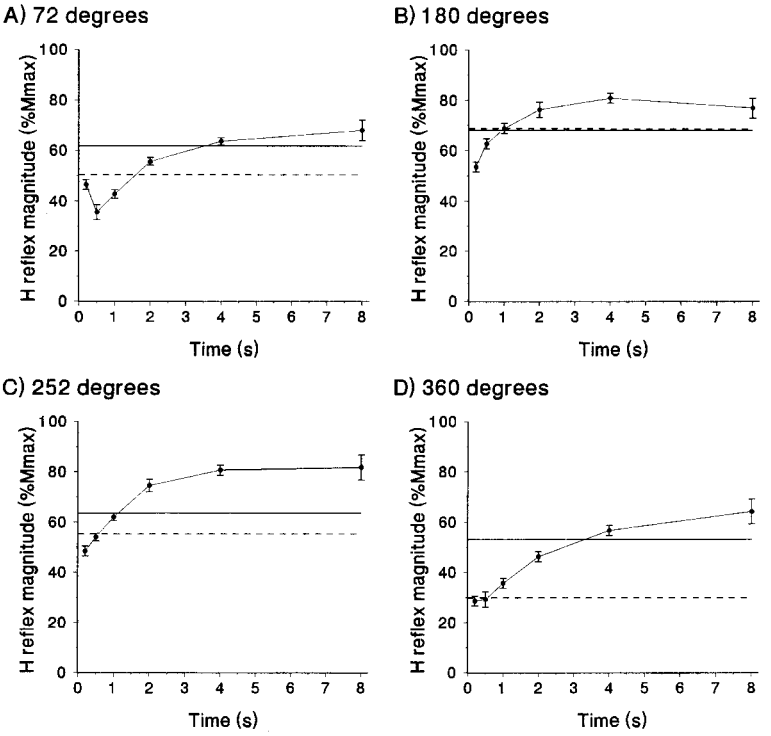

Fig. 6. Mean magnitudes of soleus H reflexes ($n = 4$) (solid line, filled squares) after passive movement of the single leg stops at four different positions past top-dead centre (0° = the position in which the knee was most fully flexed). (A) Leg stopped at 72° past the fully flexed knee position. (B) 180°. (C) 252°. (D) 360° (or 0°). Error bars are one standard error. Mean stationary control amplitude, solid line, and mean control amplitude during movement at that position, dotted line. (Data from Misiaszek *et al.*, 1995b.)

2.3.1.4. *Long-lasting effects after conditioning stops*

When passive movement stops, the soleus H reflex magnitude does not return immediately to pre-movement, control values. Even after a duration anticipated to be sufficient for the decay of long-lasting presynaptic inhibition (200–400 msec) (Eccles, 1964), the reflex is still depressed. As Fig. 6 shows, up to 4 sec can elapse after movement cessation, before the control value is achieved (Misiaszek *et al.*, 1995b). The extent and duration of the post-movement attenuation relates to the position at which the movement stops. Stopping with the knee at its most flexed point (360°), when the attenuation during movement is greatest (dashed line), results in the most profound effect. Least effect occurs when the knee is at its most extended position (180°) and attenuation during movement does not occur. Such a long-lasting effect also occurs following a tap on the quadriceps tendon, where it can extend up to 8 sec (Cheng *et al.*, 1995b). The basis for this long duration of attenuation is not clear. Perhaps it is the result of a local modulatory substance or sustained by descending control. Such long-lasting effects occur following slow stretch of the soleus muscle and have been attributed to homosynaptic depression (Nielsen *et al.*, 1993). As this infers transmitter depletion due to the stretch (Hultborn *et al.*, 1996), it is not the explanation for the effects presently reported, as the latter conditioning occurs through heteronymous not homonymous connections. It is reported that, in a spastic patient using 1 sec trains of electrical stimulation to the common peroneal nerve in order to assist walking, there is concomitant depression of H reflex magnitudes for at least 1 sec post-stimulus (Stein *et al.*, 1993), i.e. beyond the time course of a few hundred milliseconds expected for presynaptic inhibition from cutaneous stimulation. The inhibition following passive movement may share common elements with the inhibition observed when contraction ceases in the autogenic muscle (Schieppati and Crenna, 1984). That study invoked a central descending origin for the inhibition. Such may be the case for the cessation of contraction and cessation of passive movement. A caution is that, in the latter study of contraction release, quadriceps was contracted as well as soleus. This raises the possibility of the inhibitory drive arising from quadriceps muscle spindles then extending into the period of relaxation of the soleus muscle.

The basis for these long-lasting effects is worthy of further research. Also requiring further study is the final facilitation observed following the long-lasting inhibition after movement ceases or after tendon tap. This facilitation, as late as 4–8 sec post-cessation of movement, is statistically significant (Misiaszek *et al.*, 1995b). Its origin is not clear. It seems unlikely that it is post-inhibitory rebound of motoneuronal discharge (Aoki and Yamamura, 1980; Calabrese *et al.*, 1989; Getting, 1989). The long-lasting attenuation of the reflex is evident even when the

subject maintains a tonic contraction of soleus. Post-inhibitory rebound would likely be subsequent to a prolonged hyperpolarization of the motoneuronal pool, i.e. postsynaptic inhibition. Alternatively, it may result from a change in descending control initiated by movement cessation. Certainly such control powerfully facilitates the agonist H reflex before movement starts (see Section 2.4).

2.3.2. *Contralateral Movement*

With movement of the contralateral leg, there occurs also conditioning of H reflexes in the other leg, when it is stationary. As in the work described above, the contralateral ankle was immobilized. When the contralateral leg is moved actively by the person, the soleus H reflexes in the stationary one are modulated in phase with the active leg (McIlroy *et al.*, 1992), as Fig. 7(A) shows, although the attenuation is not as profound as that seen in the moving leg. When the contralateral leg is moved passively, Fig. 7(B) shows that soleus H reflexes in the stationary one are attenuated, but not phase-modulated (Cheng *et al.*, 1996). This conclusion persists when rotation occurs about the single contralateral joints of knee or hip, with the other two joints of the leg immobilized [Fig. 7(C) and (D)] (Misiaszek *et al.*, 1996b). The phase modulation still does not appear, if the velocity of movement is changed, higher or lower. Investigation has been made exploring these "crossed effects", with regard to neural route to the attenuating site, initiating receptor source(s), type of inhibition, and central processing.

2.3.2.1. *Neural route to attenuating site*

Attenuation of the soleus H reflex with passive movement of the contralateral leg occurs in human quadriplegics with clinically complete lesions (Brooke *et al.*, 1995b). Thus, it is likely that the conditioning is proceeding through spinal paths which are caudal to the lesion. This is supported by recent research on the acutely spinalized, anaesthetized dog (Misiaszek *et al.*, 1996a). In the intact dog, reflexes in second interosseus muscle contralateral to the movement are attenuated. With spinalization, the contralateral attenuation remains. The degree of attenuation is similar in spinalized and intact dogs. These experiments on humans and dogs suggest that it is very likely that a spinal route is taken for the contralateral inhibition of human soleus H reflexes, just as for ipsilateral modulation.

2.3.2.2. *The receptor which initiates the down-regulation*

With passive contralateral movement, the attenuation in the soleus reflex of the stationary leg strongly depends on the velocity of the movement. Figure 8 shows this dependence with data on individual

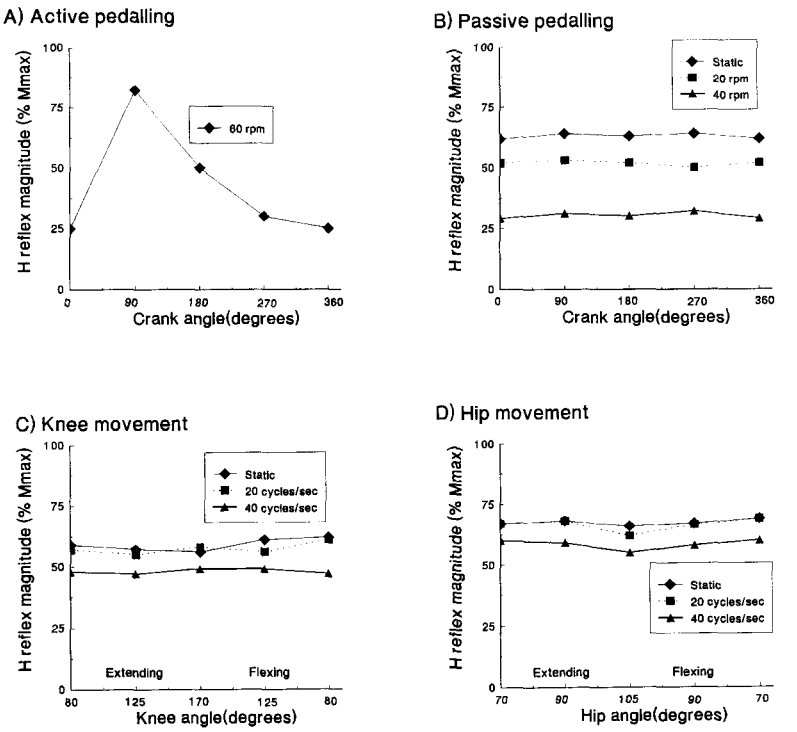

Fig. 7. Contralateral movement attenuates human soleus H reflexes in the stationary, opposite leg. (A) Magnitude of such reflexes with active movement of the contralateral leg over the pedal cycle at 60 rpm (0° represents the position when the knee is most fully flexed). (B) Passive movement of the contralateral leg at 20 and 40 rpm. (C) Passive movement of the contralateral shank about the knee at two velocities. (D) Passive movement of the contralateral thigh about the hip at two velocities. (Data from McIlroy *et al.*, 1992; Cheng *et al.*, 1996; Misiaszek *et al.*, 1996b; Misiaszek *et al.*, 1996b, respectively.)

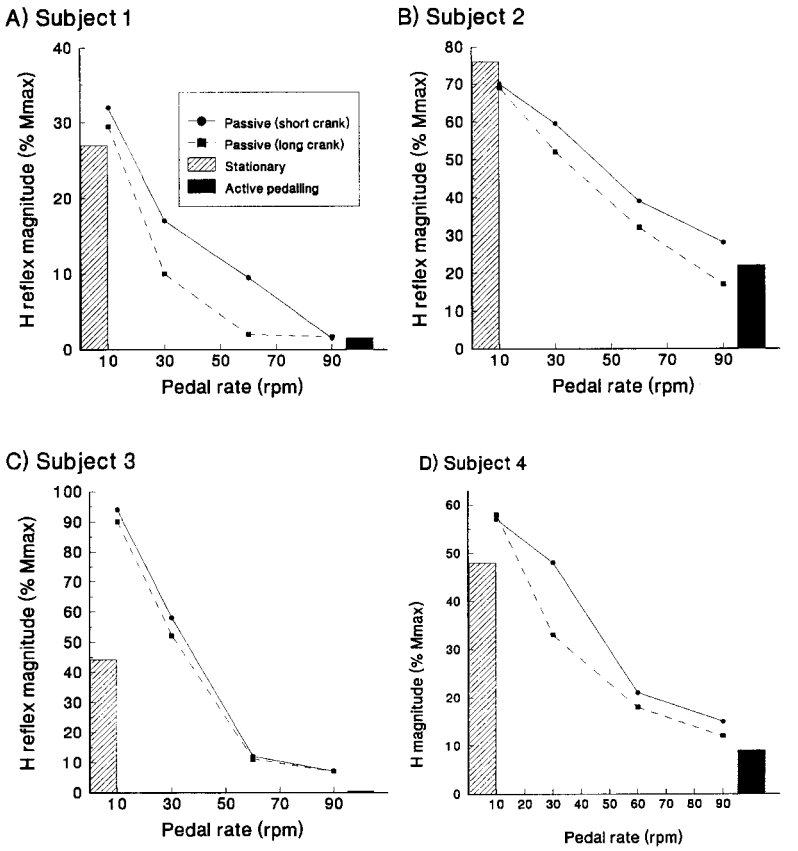

Fig. 8. Dependence of attenuation of the soleus H reflex of the stationary test leg on the velocity of movement of the contralateral leg; S1–S4, individual subjects. Data were obtained when the knee of the moving leg was passing through its most flexed position. Data are shown also for static control (left-hand bar) and for passive pedalling movement of the test leg at 60 rpm (right-hand bar). (Data from Brooke *et al.*, 1994.)

subjects (Brooke *et al.*, 1994). Very similar results arise for the reflex in the passively moving leg, although the effect is more powerful (compare the bar to the left for the test leg moved at 60 rpm, with the value for that leg when the opposite limb was moved at a pedal rate of 60 rpm (Collins *et al.*, 1993a). The positive relationship of reflex attenuation to velocity of the contralateral movement continues to be seen with measurement across the cycle of movement, as Fig. 7(B) illustrates (Cheng *et al.*, 1996; Misiaszek *et al.*, 1995d). This relationship continues to be the case with rotation about the contralateral hip or knee joints individually [Fig. 7(C) and (D)] (Misiaszek *et al.*, 1996b). Velocity dependence is one criterion implicating muscle spindles as the conditioning receptors. The inference from the present velocity dependence is that the somatosensory receptor initiating the contralateral attenuation is the muscle spindle.

2.3.2.3. *Inhibitory basis for the down-regulation*

There is limited information about the nature of the attenuation arising from the contralateral movement. Tonic contraction of the autogenic muscle on the stationary side has shown that the reflex attenuation on that side is still present (Cheng *et al.*, 1996). This suggests that a mechanism operates before the soleus motoneuronal pool. More research is needed to determine if this mechanism is presynaptic inhibition. Because this is a crossed effect, there are likely to be internuncial synapses between the initiating somatosensory receptor and the postsynaptic motoneuronal membrane, with the opportunity for postsynaptic effects to come to bear on the interneuronal membranes.

2.3.2.4. *Basis for the more complex processing of the contralateral projection*

The data from contralateral effects are not amenable to as simple an explanation as those from ipsilateral effects. Puzzling is the difference in susceptibility to modulation over the movement cycle, comparing active or passive effects on the pathways for the moved leg, versus these active or passive effects onto the stationary leg. One question is: "Why does the pathway for the stationary side, during active movement of the other leg, modulate in phase with that moved leg?". The answer appears to be: "Because that is the modulation of firing of the contralateral somatosensory receptor". Interestingly,

however, the modulation of the soleus H reflexes in the test limb during active movement of that limb is antiphase to the contralateral limb. It may be possible that the inhibitory influence arising from the moving contralateral limb, clearly seen when the test limb is stationary, is itself down-regulated during active movement of the test limb. Alternatively, it may be that the contralateral and ipsilateral effects combine to produce the pattern observed with both legs actively moving. The net result would be attenuation over the whole movement cycle and a wave of modulation the amplitude of which has been damped by the less strong antiphase effect.

When passive movement elicits contralateral attenuation, there is the question: "Why does the reflex on the moving limb show phase modulation with passive movement, yet the attenuated reflex in the opposite, stationary leg does not?". It is not that the conditioning was too strong to reveal modulation [see Fig. 7(B)–(D)]. It was speculated that removal of phasing could reflect the activation of some phase-modulated somatosensory receptor which was in antiphase with the muscle spindle discharge from the extensor muscles of contralateral hip and knee, and which could attenuate the contralateral path. Unfortunately, the likely candidates, receptors in accessible flexors of the hip and knee, proved not to be the source of such discharge (Chapman *et al.*, 1991; Misiaszek *et al.*, 1996b). [Indeed, manipulation of the lengths of those muscles had little effect on contralateral gain modulation induced by passive movement.] Further, insensitivity of the contralateral effect to movement phase does not seem to rest on conditioning from the special senses, as it occurs in spinal humans (Brooke *et al.*, 1995b) and anaesthetized dogs, intact and spinal (Misiaszek *et al.*, 1996a). It appears that the absence of phase modulation of reflex activity from the contralateral side comes from some additional spinal interneuronal processing which is more complex than that required to account for the ipsilateral effect.

2.4. Centrifugal Influences with Movement

Increases in H reflexes *before* movements in which the autogenic muscle is the agonist, and decreases when it is the antagonist, are well known. The effects are held to involve release or increase, respectively, in presynaptic inhibition (Ruegg, 1989; Ruegg *et al.*, 1990). Task requirements of accuracy through kinesthetic information do not change those pre-movement modulations (Collins *et al.*, 1993b). It is possible, though, to observe the descending effects integrated with presynaptic inhibition elicited peripherally through stimulation of the nerve to the antagonist. For the agonist, this can result in reduced reflex magnitude, reflecting reduction of the release of presynaptic inhibition by the descending command that is part of the movement initiation (Stewart and Brooke, 1993). Also, when a visual stimulus is used to elicit a forward step, H reflex gain in soleus begins to attenuate before EMG activity (McIlroy *et al.*, 1994). This implies a descending origin for that gain modulation.

There are a number of reports of centrifugally induced attenuations of H reflex amplitudes in soleus muscle during movement. Subjects asked to walk on an elevated beam reveal further attenuation of gain, compared to walking on the ground. The authors felt that the changes which occurred in the kinematics of the gait did not account for the additional attenuation, and attributed it to descending influences (Llewellyn *et al.*, 1990). It has been reported also that H reflex magnitudes are attenuated when rock-climbing (Bennett *et al.*, 1993). They are reported also to be attenuated during a one-legged stork stand when deprived of vision or when the support surface is unstable (Hoffman and Koceja, 1995). Proposed descending effects on presynaptic inhibitory interneurons were suggested in the latter study, on the basis of the lack of correlation between the attenuation and the ongoing EMG. (That study only controlled stimulus intensity through a constant stimulus current probe and not through M wave monitoring.)

Differential effects that can be attributed to descending influences were observed in two instances of movement leading to touch-down from a height (Dyhre-Poulsen *et al.*, 1991). There was little activity in soleus before touch-down from hopping and H reflex gain was high. In contrast, both soleus and tibialis anterior were activated prior to landing from a downward jump, presumably reflecting descending control (possibly arising in preparation for landing and/or from vestibulospinal influences), and H reflex gain was low. The combination of descending control and H reflex gain were seen to transform the muscles from a spring unit, to a damping one for voluntary landing in the downward jump.

Soleus H reflex gain attenuates as an early response to voluntary ballistic rotation of the head to the contralateral side (Anson and Kasai, 1995). There is a quiet period in the ongoing soleus EMG at that time. As this attenuation precedes the EMG activity evoked in the neck muscle studied, the gain change was attributed to "pre-innervation", i.e. descending effects.

There is evidence for a centrifugally induced increase in H reflex gain during passive movement. When increasing percentages of a maximum voluntary contraction are delivered to the autogenic contralateral muscle, it appears that there is concomitant descending inhibition of spinal, perhaps presynaptic, inhibitory interneurons, as the conditioning effect of ipsilateral movement diminishes as the descending volley increases (Cheng *et al.*, 1996). This interpretation is supported by the evidence in the cat that action potentials elicited from motor cortex and from red nucleus can inhibit the presynaptic inhibition exerted on Ia terminals by Ia afferents (Lundberg and Vyklicky, 1963; Hongo *et al.*, 1972). Also, it has been shown in humans that transcranial magnetic stimulation alleviates the H reflex attenuation induced by vibration, the timing of this descending conditioning suggesting a release of presynaptic inhibition (Valls-Sole *et al.*, 1994).

There is also the possibility of affective state altering monosynaptic reflex transmission. Stretch reflex magnitudes are increased when stimulus occurrence is linked with the presentation of pictures of high affect content, pleasant or unpleasant (Bonnet *et al.*, 1995). Whether this operates directly within the

system of the group I afferent to alpha motoneuronal membrane or indirectly through the gamma motoneuronal system or via local metabolic influences is not known. It is not clear what principles govern these various centrifugal, descending influences on sensory transmission, nor is it clear whether sensory triggers elicit the influence in some cases. The human neural bases merit further research.

There are chronic centrifugal influences which condition the magnitude of H and stretch reflexes over weeks and months (Evatt *et al.*, 1989; Wolpaw and Carp, 1993; Segal and Wolf, 1994). Learning in the spinal cord is suggested. As noted above, these are outside the purview of the present report.

2.5. Functional Interpretations of Movement-Induced Modulation of H Reflex Gain

It is likely that the gain attenuation induced by extensor muscle spindle activation applies to active movement as well as passive, for both will cause such receptors to discharge. Its contribution to the gain attenuation could last over the whole movement cycle of natural active movement. At a natural walking cadence of 120 steps/min, the presynaptic inhibition set up during the flexion phase of leg movement could extend over the 500 msec of the extension phase. Also, there is Ia discharge from quadriceps spindles over much of the cycle in cat locomotion (Loeb and Hoffer, 1985), likely reflecting modulation of fusimotor drive (Prochazka *et al.*, 1977a; Taylor *et al.*, 1985). This fits well with the data of Capaday and Stein, 1987a), who demonstrated that during running, despite increased excitability of the motoneuronal pool, the soleus H reflex during the stance phase was of lower magnitude compared to walking. It is expected that, during running, the spindle discharge from quadriceps will increase during the stance phase. The further decrease in reflex gain perhaps reflects this. The modulation over phases of the movement may, in contrast, arise from centrifugal sources of control, this modulation playing on a ground of attenuation from the centripetal conditioning. Perhaps this descending input terminates attenuation which, on the basis of the data after passive movement, would otherwise last much longer. If this is the case, one would like to identify specifically how this is achieved.

Most interpretations of functional significance have addressed the modulation of gain seen in soleus H reflexes while walking, and when comparing stable stance to walking. The stretch reflex component of the soleus response to brief pulses of perturbation is modulated in humans (Stein and Kearney, 1995) and in decerebrate cats, with activated ankle muscles (De Serres *et al.*, 1996). The soleus stretch reflex is powerful. Passive rotational pulses, as small as 1–2°, elicit autogenic responses greater than 20% MVC. The gain, however, is highly nonlinear for different pulse characteristics or levels of ongoing contraction (Stein and Kearney, 1995). This reflex can be elicited during normal bipedal walking, when it can reach an EMG magnitude of 30–60% of the ongoing activity seen in soleus (Yang *et al.*, 1991b). Similar to the H reflex, this stretch reflex is modulated during walking (Yang *et al.*, 1991b). If two dorsiflexion stretches are applied in close temporal proximity, there is a task-specific effect on recovery of the stretch reflex for the second perturbation. The recovery is much faster during standing compared with sitting (Gollhofer and Rapp, 1993). Note, however, that background soleus EMG levels, hence muscle stiffness, were not stated to be matched in the latter study. It does appear that the results on H reflex modulation are likely to be functionally extended to the stretch reflex.

From this first section of the review, it is clear that many factors act to attenuate the gain of the soleus H reflex and therefore have the potential to contribute to gain control during walking (possibly mediated through neural networks associated with pattern generation). These factors include: (1) the posture of the limb acts through discharge of extensor muscle spindles; (2) movement-induced discharge of those spindles is a powerful down-regulator; (3) contraction of the antagonist, tibialis anterior, depresses the soleus H reflex; (4) stimulation of large diameter afferents in the nerve to the antagonist, the common peroneal, inhibits the reflex; (5) the contralateral moving leg contributes to the inhibition; (6) descending effects contribute to the changes in gain.

As in much of the nervous system of mammals, there appears to be substantial redundancy in the control of H reflex gain attenuation. This has been interpreted as over-insurance, to control the power of the reflex in soleus. It may be that functionally the gain of the soleus H, and by extension stretch, reflex is high in stable posture so that it can contribute automatically to the maintenance of that posture. The induction of small responses of that reflex, subthreshold for conscious awareness, provide support for this view during quiet stance (Fitzpatrick *et al.*, 1992). Under this hypothesis, the leg movement is of low amplitude in stance and only when the movement exceeds that amplitude at the start of walking, does the reflex gain fall. Certainly, within 200 msec after active walking begins, the gain is down (Edamura *et al.*, 1991), as it is within 50 msec of starting passive pedalling movement (Brooke *et al.*, 1995b).

It has been assumed until recently that, although the Ia pathway to the muscle is attenuated, the Ia pathway to the brain will remain open so that the brain is apprised of what is happening to the legs. There are concerns about this hypothesis, however, and the data are reviewed in Section 4. It is appropriate first to turn to another major category of reflexes observed in human leg muscles.

3. MODULATION OF GAIN OF CUTANEOUS REFLEXES OF THE LEG

3.1. Methodology

In addition to the factors affecting the H reflex and denoted in Fig. 1(B), for the longer latency reflexes arising from cutaneous afferents there must be additional potential for convergence at pre- and postsynaptic sites on the chain of interneurons leading to the motoneuron (Baldissera *et al.*, 1981). This chain may engage with complex centres of

processing signals, such as those associated with pattern generation in the spinal cord or brain. This additional potential for sites of reflex modulation also increases the potential for confounding the interpretation of experimental results through the intrusion of unanticipated and unidentified convergences.

Study has been made of electrical stimulation of the purely cutaneous sural nerve, with stimulation site at the lateral malleolus of the ankle (Duysens *et al.*, 1990), the tibial nerve with stimulation at the medial malleolus (Yang and Stein, 1990), stimulation of the superficial peroneal nerve at the dorsum of the ankle (Zehr *et al.*, 1996) and stimulation of the digital nerve with cuff electrodes on the toe (Belanger and Patla, 1984; Brooke *et al.*, 1991b). Differing reflex EMGs can result, as reported in Section 3.2. Responses have been observed in biceps femoris, semitendinosus, rectus femoris, the vastii, medial gastrocnemius, lateral gastrocnemius, soleus, tibialis anterior and peroneus brevis muscles. Usually, the muscles have to be active for a response to be observed. When a number of muscles are studied simultaneously, care is required to avoid cross-talk/volume conductance. Differences in latencies, waveforms, phasic modulation or between subjects help to confirm that such confounding has not occurred.

In addition to varying sites, different stimulation parameters also have been used. For non-nociceptive responses, trains of stimuli have been used with different numbers of pulses (P) durations (D) and interstimulus intervals (ISI), e.g. 3 P of 0.3 msec D with ISI of 10 msec (De Serres *et al.*, 1995), and 5 P of 1.0 msec D with ISI of 4 msec (Duysens *et al.*, 1990). The effect of different stimuli on nociceptive responses is reported (Meinck *et al.*, 1985). The common practice is to measure latencies from the start of the first pulse.

Biocalibration of stimulus intensity can be more of a problem than with the H reflex. With study of a mixed nerve such as the tibial nerve at the ankle, use can still be made of the M wave (e.g. in abductor hallucis) as a reflection of stimulus stability applied to the cutaneous afferents. However, for a purely cutaneous nerve, researchers have relied on the perceptual threshold (PT), as an indicator of stimulus constancy. This threshold is the first perception of stimulus current, at the local skin site. The stimulus then is delivered as a proportion of the voltage or current required for that stimulus at PT. A constant stimulus current is felt to occur at PT. With this technique, it is usual to make periodic confirmations of the constancy of voltage or current values for PT as the experiment progresses. Even with such care, PT potentially introduces variation into the experiment. A particular problem is that PT usually is only established at rest. One is not able to use the assessment of PT during the movement, as perception can vary when the magnitude of the evoked biopotential varies as a consequence of movement (Angel and Malenka, 1982; Duysens *et al.*, 1995).

To obtain reflex responses, it is usually necessary for the target muscle (the muscle from which reflex responses are being measured) to be active. Not all studies have reported care in ensuring that other muscles are not active, in addition to the target one. That deficiency leaves open the possibility of evoked heteronymous proprioceptive drive contributing to the expression of the reflex. Reflex EMG activity of the whole muscle commonly is observed. Single motor unit reflex activity has been reported and the technical difficulties of this procedure addressed for movement studies (De Serres *et al.*, 1995). Responses also have been observed in the reflex kinematics of the leg (Duysens *et al.*, 1992; Zehr *et al.*, 1996).

An additional distinction between cutaneous and H reflexes is that cutaneous reflexes are less well synchronized and are often far more difficult to detect from traces of single trials. As a result, analysis of cutaneous reflex responses typically requires integration of full-wave rectified, conditioned and averaged EMG responses. This integration occurs, in different studies, over differing time intervals. It is also common for the average conditioned and integrated EMG of an unstimulated set of samples to be deducted from such an average for samples with stimulation, resulting in "subtracted trials". When doing so, reported examples of the raw data are helpful.

The literature shows variations in the parameter(s) derived to analyse changes in the longer latency cutaneous reflexes as a consequence of movement. The EMG data have been compared for fixed time intervals following stimulation (Yang and Stein, 1990; Tax *et al.*, 1995). The magnitudes of one or more components of the EMG complex of the reflex have been compared across conditions, sometimes with little specific concern reported for variations in the temporal characteristics of the component between trials or subjects. A recent suggestion is to integrate the area of reflex EMG for 150 msec post stimulus, the ACRE 150 (Zehr *et al.*, 1995). While this approach simplifies interpretation, by averaging the effects of all excitation and inhibition, it loses detail of the specific temporal and spatial characteristics that may be of neurophysiological significance. Accordingly, it may be best used as an addition to other parameters. Goniometric measurements of changes in angle of leg joint segments have been used to infer the function of the reflexes (Duysens *et al.*, 1992). They have been used also to assess function defined as a connection between reflex kinematics and the proposed needs of ongoing gait patterns (Zehr *et al.*, 1996).

3.2. Control Reflexes at Rest

Two historical views of responses to stimulation of cutaneous nerves were that they represented a flexor withdrawal reflex (Sherrington, 1910) and, later, that they represented a more complex array of cutaneomuscular responses associated with excitation from skin sites overlaying the target muscle and inhibition from sites over antagonist muscles (Hagbarth, 1960). Recent studies support the view that the responses are complex, and also that reciprocal activation can occur, but simple functional concepts of withdrawal or reciprocal action are incomplete interpretations. Responses are observed (see Sections 3.2 and 3.3, also Figs 9,11) which do not lie in either category.

Reflexes evoked at longer latency than H reflexes, and often from purely cutaneous nerves, modulate in

magnitude over a cycle of human leg movement such as walking (Duysens *et al.*, 1990; Yang and Stein, 1990; De Serres *et al.*, 1995) or pedalling (Belanger and Patla, 1984; Brown and Kukulka, 1993). The morphology of such reflexes is more complex than that of H reflexes. Typically an early response can occur, P1, usually < 65 msec, a P2 response often occurs, usually from 70–120 msec, and later responses also occur. There is a difference between responses to nociceptive versus non-nociceptive stimulation. (Note that the present review does not cover the substantial literature on cutaneous and flexor reflex effects during movement in animals other than humans. It also maintains its focus on the human leg and does not cover upper limb responses.)

There is no single pattern which describes the "control" situation, the response of a human leg muscle to cutaneous stimulation with the limb stationary. "What then, are the various patterns of early responses for the different muscles, against which to judge the changes brought about by movement?" Before an answer, some qualifiers are necessary. There is individual variation between subjects and between studies. There also can be variation within muscles, and within single units, when fine wire electrodes have been used during movement. So, our current attempt to expose the main patterns seen, of necessity does not address much of this variability.

We have tried to see order in substantial variation existing in the studies of non-nociceptive responses, and have drawn from many papers (namely Yang and Stein, 1990; Burke *et al.*, 1991; Duysens *et al.*, 1990, 1991, 1992, 1993, 1994; Aniss *et al.*, 1992; Kukulka, 1994; De Serres *et al.*, 1995; Tax *et al.*, 1995). Figure 9 was constructed from these recent studies, to indicate the patterns of early responses in various muscles (abbreviated to initials, clarified in the figure caption). The figure describes P1 and P2 (Duysens *et al.*, 1993) excitatory (+) and inhibitory

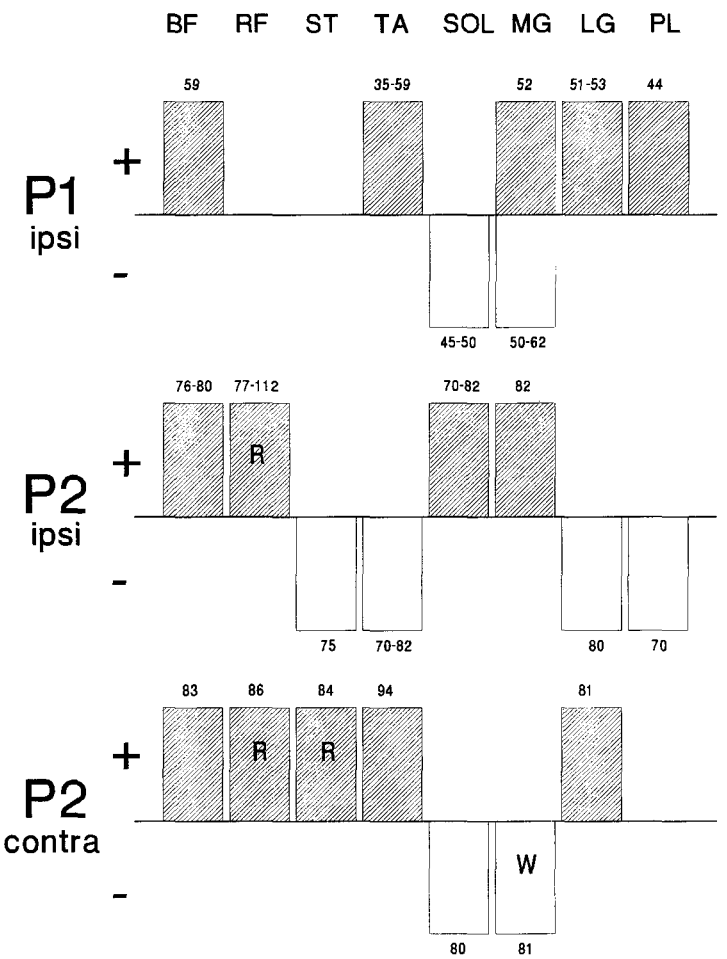

Fig. 9. Literature summary of early (P1) and middle (P2), excitatory (+) and inhibitory (−) responses to trains of non-noxious stimuli applied to cutaneous afferents (sural or tibial nerves), with latencies (msec) denoted by the numbers. Responses ipsilateral to the stimulation (ipsi) were in subjects supine, sat or stood, except for two muscles which involved running (R) subjects. Contralateral data (contra) are marked as appropriate, when it was necessary to use running or walking (W) conditions. Muscles surveyed are shown by the columns for the following abbreviations: BF, biceps femoris; RF, rectus femoris; ST, semitendinosus; TA, tibialis anterior; SOL, soleus; MG, gastrocnemius medialis; LG, gastrocnemius lateralis; PL, peroneus longus.

(−) responses obtained from sural or tibial nerve stimulation at the ankle, with the latencies enumerated. The ipsilateral responses all come from subjects who were supine, sat or stood, with the exception of ST and RF P2, which are from running (R). There were no data from static states for P1 contralateral, nor for three of the seven contralateral P2 responses; because of this absence, P2 contralateral data are included for RF and ST during running and MG during walking (W). The figure shows that there is variation in reflex response between muscles, when the limb is static. From the figure, and from the underlying studies, the following points are made:

1. P1 responses are often reported as weak and inconsistent.
2. For muscles across the ankle joint, P1 ipsilateral most often is the reciprocal sign of the P2 which follows, ipsilaterally or contralaterally.
3. For contralateral muscles across the ankle, those P2 responses reported are reciprocal to P2 ipsilateral.
4. For two of the three muscles spanning the hip and knee joints, excitation continues from P1 over P2 latencies.
5. Response patterns are reported to be reproducible when subjects are retested.

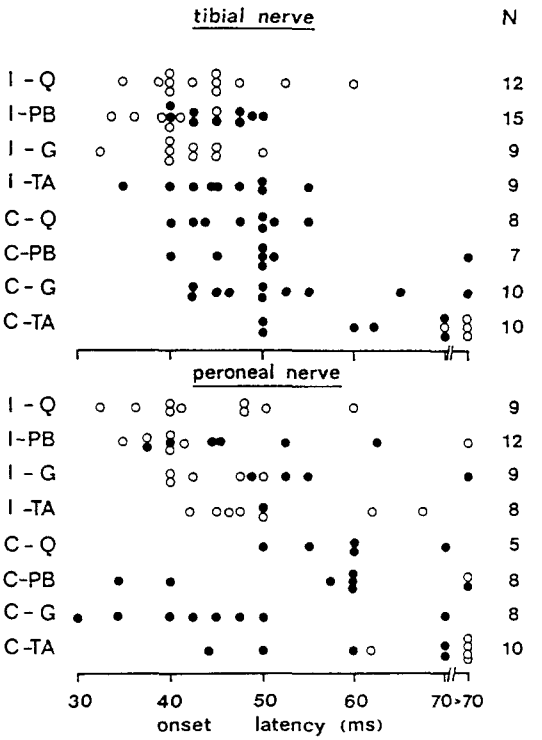

Fig. 10. Onset latencies and sign of responses for a range of ipsilateral (I) and contralateral (C) muscles, following noxious stimulation of tibial or peroneal nerves in humans. For any muscle, individual points, which are filled when inhibitory and open when excitatory, are from different subjects. Muscle abbreviations: Q, quadriceps vastus lateralis; PB, posterior biceps; G, gastrocnemius; TA, tibialis anterior. (From Meinck *et al.*, 1981 with permission.)

Single unit studies in general support these conclusions, and the overall pattern of results in Fig. 9, although the latencies are shorter (Aniss *et al.*, 1992; Kukulka, 1994; De Serres *et al.*, 1995).

Higher, *nociceptive*, levels of stimulation at the ankle elicit responses starting at 30–70 msec. A diagram showing the onset latencies (i.e. P1) and sign of responses for a range of ipsilateral and contralateral muscles, with between subject variation, is shown in Fig. 10 (from Meinck *et al.*, 1981). Recent studies with subjects at rest show P1 and P2 latencies as inhibition then excitation, for soleus (45 and 85 msec, respectively), biceps femoris (71 and 126 msec, respectively) and rectus femoris (84 and 97 msec, respectively), and excitation then inhibition for tibialis anterior (57 and 85 msec, respectively) (Brown and Kukulka, 1993; Anderson *et al.*, 1995).

3.3. Active Movement of the Legs

3.3.1. *Phenomena and Suggested Functions*

Figure 9 describes the considerable variation seen in the responses of muscles to electrical stimulation of cutaneous afferents in the stationary limb. It is not surprising, therefore, that the addition of active movement of the limb makes interpretation complex. There is a kaleidoscope of results arising from different tasks, different stimulus modes and sites, different target muscles and different latencies post-stimulation. Such variation may well reflect the set of functional constraints associated with the demands of upright balance and bipedal gait (see Section 3.4). From this variation, we have extracted some common elements.

Noxious levels of stimulation during leg movement often result in suppression of the inhibitory P2 responses seen with such stimulation at rest (see Section 3.2) and their replacement with excitation. The amplitudes of the excitatory P2 responses can modulate according to the phase of the background EMG (Belanger and Patla, 1984; Crenna and Frigo, 1984; Anderson *et al.*, 1995). However, exceptions to this link to background EMG are reported (Belanger and Patla, 1984; Anderson *et al.*, 1995).

The patterns of P2 responses to noxious stimuli during movement are presently characterized by muscle. (We have not attempted to express the responses after deduction of the specific response of each muscle at rest, as the required control data are often not available.)

1. In biceps femoris and vastus lateralis, P2 responses are excitatory in both swing and stance phases (Crenna and Frigo, 1984; Belanger and Patla, 1984; Duysens *et al.*, 1993). These excitatory reflexes either side of the knee will stabilize it, avoiding collapse of the leg on contact with a noxious environmental obstacle. (This will be the functional effect of response to electrical stimulation. Whether it occurs with natural stimulation is still an open question. This qualifier applies currently to all functional interpretations of gain changes in electrically activated pathways.)
2. In tibialis anterior, excitation tends to occur throughout the phases of walking (Belanger and

Patla, 1984; Duysens *et al.*, 1990; Brown and Kukulka, 1993). [Note, however, that sural nerve stimulation at > 2.5 PT leads to inhibition during swing in running (Duysens *et al.*, 1992) and no response during stance (Duysens *et al.*, 1990, Duysens *et al.*, 1992).] During swing, the excitatory reflex will withdraw the foot from a noxious environmental obstacle and during stance will maintain a dorsiflexed ankle appropriate for weight-bearing (McIlroy, 1990).

3. In soleus and medial gastrocnemius muscles, stimulation of sural or tibial nerves during walking mainly elicits inhibition. During swing there may simply be no response. (Duysens *et al.*, 1992; Brown and Kukulka, 1993). [However, strong stimulation of the digital nerves during swing and early stance can result in excitation (Belanger and Patla, 1984).] The inhibition seen in these plantar flexors functionally will act as the reciprocal to the excitation seen in tibialis anterior.

For contralateral muscles, data could not be found to complement those reported above for the ipsilateral muscles.

Non-noxious stimulation during movement has been more extensively studied than noxious. Between supine and the small movements of standing, little change occurs in the cutaneous reflex EMG (Aniss *et al.*, 1992). It is noteworthy that the latter authors do comment on their earlier studies, showing that cutaneous stimulation appears to alter the discharge of gamma motoneurons when subjects stand, but not when they are supine (Aniss *et al.*, 1990). The main effects reported during gait are seen at P2 latencies. They are summarized in Fig. 11, which shows the change in reflex activity for different muscles, comparing static versus gait (Duysens *et al.*, 1990, 1991, 1992, 1993; Yang and Stein, 1990; De Serres *et al.*, 1995; Tax *et al.*, 1995). Some common elements emerge from the data in Fig. 11.

1. The dominant theme is ipsilateral facilitation. One interpretation of this has been that discharge of cutaneous receptors of the foot contributes to normal activation of the muscles during the gait cycle. However, there are some studies which do not support this conclusion. Anaesthesia of the plantar surface of the human foot little alters the pattern of responses to perturbation of voluntary extension of the leg against a tonic flexor force (McIlroy, 1990). Also such anaesthesia of the foot of the cat does not alter the EMG activity for normal locomotion (Engberg, 1964) or for landing from falls (Prochazka *et al.*, 1977b). It is not clear to what extent the cutaneous signal, which may be the default trigger, is replaced by other somatosensory signals in such an experimental manipulation. In conducting the first study (McIlroy, 1990), we observed that the anaesthesia initially severely compromised one-legged stance with the eyes closed, but after from five to 10 attempts subjects became much more adept at maintaining the posture. This suggests the replacement of one signal by another.

2. Modulation of the ipsilateral responses to the

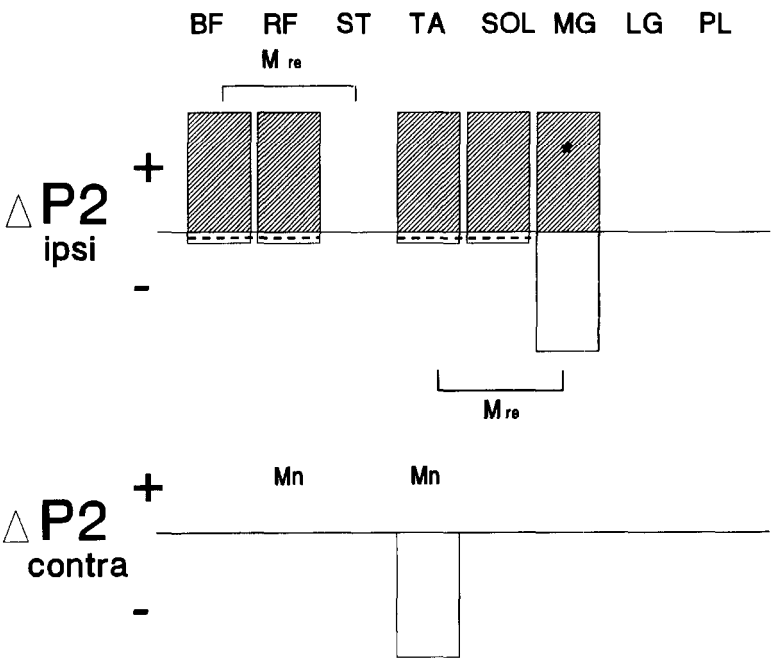

Fig. 11. Literature summary of change in P2 response, as facilitation (+) or suppression (−) to non-noxious cutaneous stimulation (sural or tibial nerves), from static to gait conditions (muscle abbreviations as in Fig. 9). Reversal within a muscle, to suppression in late swing, shown by dotted line. Phase-modulated reciprocal actions between muscles shown by Mre and square bracket. Modulation not reciprocal and not in phase with the ongoing EMG, shown as Mn. Symbol * indicates that some subjects showed facilitation. For P1 responses in ipsilateral ST and for P2 responses in contralateral RF, no stationary data are available, thus no value is shown for the change from the static control state.

phase of the movement cycle of the leg is seen in two ways.

(a) Firstly, there is suppression during the late swing phase. This is seen in four muscles, tibialis anterior, soleus, rectus femoris and biceps femoris. Three separate motor units were assessed in tibialis anterior and the reflex reversal was observed in each of the three (De Serres *et al.*, 1995). This suggests that parallel excitatory and inhibitory pathways exist from the cutaneous afferents to the motoneurons, with the events of locomotion containing a key to switch between the two routes.

(b) Note that the "reversals" in these four muscles may not be of the same type. In tibialis anterior, it appears that the P2 inhibition seen in the static limb is overridden by excitation in the gait cycle, except for a brief period of inhibition seen in late swing. For the other three muscles, excitation seen with the limb static is also seen during gait, with the exception of the brief inhibition in late swing. Perhaps this inhibition occurring in these four muscles in late swing ensures that central commands for foot strike cannot be automatically altered through environmental stimuli that elicit cutaneous reflexes.

(c) The second type of ipsilateral modulation is the reciprocal activation across different phase points between tibialis anterior and medial gastrocnemius and also between biceps femoris and semitendinosus. It has been suggested that the antagonistic reflex activation in the hamstrings during the stance phase furthers the ongoing cadence of the locomotor cycle (Tax *et al.*, 1995).

3. The magnitudes of reflexes do not strictly co-vary with the ongoing EMG activity in the target muscle. This suggests that premotoneuronal events play a role.

4. Ipsilateral and contralateral responses appear to be controlled separately. Excitatory contralateral reflexes are reported for biceps femoris, semitendinosus, rectus femoris and soleus, with inhibitory ones for tibialis anterior and medial gastrocnemius (Duysens *et al.*, 1991; Tax *et al.*, 1995). Figure 11 shows that, for contralateral reflexes, there are few static control data from which to express the changes to which that figure attends. The phasing of the contralateral reflex tends to follow the target leg, not the stimulated one (Tax *et al.*, 1995). This implies complex processing of the reflex action potentials which proceed contralaterally.

5. The static posture of the leg, mimicking that over the gait cycle, does not significantly alter cutaneous reflex magnitudes. This has been taken to suggest that the modulation with movement is not arising primarily from discharge of joint receptors.

6. The changes in P2 activation during gait usually occur without significant changes in latencies.

The study of other animals is not the focus of this review. However, it must be noted that complexity of responses to stimulation of cutaneous afferents also is observed in the cat (Pratt *et al.*, 1991; Forsberg, 1979). As in the studies on humans, there are differences in responses between muscles, within muscles, between tasks, between stimulation sites and between intensities of stimulation.

3.3.2. *Neural Route to EMG Modulations*

A spinal oligosynaptic path is suggested by the brief latencies of the earliest responses. This conclusion was arrived at with single motor unit recording of inhibition in triceps surae at a latency of 40 msec following sural nerve stimulation (Kukulka, 1994) and at latencies from 42 to 44 msec in a variety of dorsi and plantarflexor muscles following stimulation of sural and tibial nerves at rest (Aniss *et al.*, 1992). This spinal route likely accounts for the other P1 responses. Interpretation of the route for subsequent responses, such as for P2 at 70–120 msec, or longer responses, cannot be simply inferred from the latencies. This is because triggered reactions dependent on the brain's prior awareness of forthcoming stimulation are reported with latencies of 65–70 msec for response of tibialis anterior and vastus medialis to foot perturbation (McIlroy and Brooke, 1986), and similar latencies of 60–70 msec in arm muscles with forearm perturbation (Crago *et al.*, 1976). Calculation of latencies for pathways leading to and returning from the cerebral cortex produce values starting as low as 80–90 msec (Burke *et al.*, 1991; Aniss *et al.*, 1992). Loop pathways to the brain stem likely have lower latencies. The occurrence of conditioned voluntary reaction times at 110 msec in rectus femoris during human gait (Wetzel and Gorman, 1986) further encourages caution against automatically assuming that latencies of 70–120 msec reflect spinal routes. At the other end of the latency scale, patients with complete spinal lesions provided what likely were spinal responses with latencies from 100 msec up to several hundred milliseconds (Roby-Brami and Bussel, 1987). It appears that these late effects arose from activity in inhibitory pathways that were activated in parallel with those transmitting a long-lasting excitatory reflex (Roby-Brami and Bussel, 1992). As a result of these constraints, it has to be accepted that responses at 65 msec or more may arise from supraspinal, propriospinal or oligosynaptic spinal routing. There is a need for experiments clarifying the neural routes for P2 and longer responses.

3.3.3. *Initiating Sources for Modulations*

There is a research opportunity to uncover the initiating sources for the modulations of the amplitudes of cutaneously evoked reflexes during movement. The matter is not clear presently, for either nociceptive or non-nociceptive conditions. Facilitation of the target muscle by the background EMG for locomotion may be a component. However, a number of studies comment on the failure of the reflex magnitude to follow strictly the phasing of the ongoing EMG. From this it has been inferred that one means of modulation occurs at a premotoneuronal level. What initiates that premotoneuronal control is not clear. It has been suggested that the modulation may be coupled to the actions of central pattern generators for locomotion. It may be that the changes in pathway activity over the gait

cycle reflect the generator opening alternative routes to the motoneurons as a component of the total pattern-generating enterprise (Duysens *et al.*, 1992). There is little direct evidence for this as yet, beyond (a) the experiments demonstrating the existence of such generators in mammals and other animals; and (b) the failure of the reflex changes to track the ongoing EMG in locomoting humans.

Modulation from proprioceptor drive as a consequence of movement has been little explored. It has been concluded in a number of studies that the static posture of the limb contributes little to the modulation patterns seen with movement. Drive from kinesthetic receptors needs to be explored through passive movement, which also allows controlled variation of the cutaneous drive from the skin. There is an early report that passive movement in patients with complete clinical lesions of the spinal cord leads to facilitation of responses to noxious levels of stimulation in the leg (Dimitrijevic and Nathan, 1968). Most enhancement occurs when the movement of the limb segment is opposite to the direction in which the cutaneous receptor field stimulus would have made the limb move. In addition to kinesthetic receptor drive, there is a need for studies of vestibular drive onto these pathways, given that balance is a continuous challenge for the system during walking and running. A further research opportunity is to explore the role of drive descending from the cerebrum, both voluntary and involuntary. For example, the effect of fear of falling, changes in attention or visual deprivation during upright stance, may act as potential initiating sources for modulating these reflex paths.

There appears to be the opportunity, almost the necessity, to combine further investigation of the electrically evoked cutaneous reflexes with behavioural studies of (1) enhancement or reduction of the availability of cutaneous receptor drive during movement; (2) the kinematic effects of natural stimulation of the dermatomes served by the cutaneous nerves that, in the presently reviewed work, were electrically stimulated; (3) the full pattern of locomotor events in relation to the kinematic consequences of the cutaneous reflexes; and (4) biomechanical evidence of the control of balance and stepping. The present review cannot extend to that field. Yet, functionally interpreting the electrically induced responses has to seem somewhat cavalier when it is not validated against more macroscopic views.

3.4. Synthesis of Functional Interpretations of Movement-induced Modulation of Cutaneous Reflex Gain

In the absence of studies specifically investigating the originating sources for modulations of cutaneously evoked reflexes, functional interpretations rest on speculation from the results of the studies of active movement. Some speculations were made in Section 3.3.1 on responses in specific muscles, or sets of muscles. This section briefly attempts a broader view.

The nociceptive reflexes appear to act as phase-dependent protective responses (Crenna and Frigo, 1984; Belanger and Patla, 1984). During stance, the knee is stabilized by co-contraction and the reflex activity at the ankle is mainly directed at avoiding perturbation of the foot on which balance rests. During swing, the knee continues to be stabilized and the foot is withdrawn by excitation of dorsiflexor muscles coupled with plantar muscle inhibition. The basic principle may be to maximize the trade-off between avoiding the source of the strong stimulus and preserving both balance and the rhythm of locomotion.

The non-nociceptive responses may, like the noxious ones, reflect equilibration between the two factors of the behavioural goal and the response to cutaneous stimulation which could elicit withdrawal if not constrained. A third factor to take into account is the naturally occurring discharge from skin receptors during bipedal gait. Thus, some of the non-nociceptive responses seen during gait may be enhancement of part of the natural neural pattern for locomotion, not simply protection of that locomotion.

4. MODULATION OF THE GAIN OF SCALP-RECORDED SOMATOSENSORY EVOKED POTENTIALS (SEPS) FROM STIMULATION IN THE LEG

4.1. Methodology

The review continues to focus on leg movement in healthy humans. It now extends to scalp-recorded potentials evoked from the brain, as they are also conditioned during movement. The remainder of the present review uses the abbreviation "SEP" to denote the first potential recorded from cortical sites, unless otherwise noted. The magnitude of the SEP arising from the initial reception of stimuli at primary sensory cortex (S1) from single square wave pulse stimulation of nerves in the leg, is of the order of 1–10 μV. That of the ongoing background electroencephalographic (EEG) activity is of the order of 10–100 μV. Basic procedures for obtaining and extracting the signal from the "noise" are described (Chiappa, 1983), as is advice for measurements in "hostile" environments (Gevins *et al.*, 1994). Limb movement constitutes "hostile" in recording SEPs. Controlling experimental confounding is important, including removing environmental intrusions, EMG intrusions from eye and postural muscles, and electrical fields over the recording area.

The M waves or multiples of perceptual threshold to stimulation are used to biocalibrate stimulus strength. The stimulus threshold for SEPs is lower than that for H reflexes, with maximal SEPs occurring when the responsible muscle afferent volley is less than 50% of its maximum (Gandevia *et al.*, 1982). To maximize afferent transmission, a short stimulus pulse width, e.g. 0.5 msec, is often used. The SEPs evoked from the leg have maximum amplitudes overlying S1 at Cz′, 2 cm caudal to Cz, in accordance

with the International 10–20 system for EEG electrode placement (Homan *et al.*, 1987).

It is very difficult to separate by scalp topography the SEPs from different legs, as the receptive zones lie along the border of the longitudinal fissure, deep within the central sulcus. Area 3a is a primary receptive region for action potentials originating in muscle afferents. Areas 3b and 1 receive primarily information from cutaneous afferents, while area 2 receives a convergent input from both muscle and joint afferents (Kaas, 1983). The SEP is an average of the firing of many cells and is extracted from the ongoing EEG activity by its constant temporal relationship to the delivered stimulus. The biophysics of negative and positive going phases of the EEG as points of synchronized passage of membrane potentials relative to the position of the recording electrodes, has been reviewed (Gloor, 1985).

A band pass filter of 1–100 Hz is adequate for acquisition of SEP signals, with sampling at 1000 Hz, and amplification of 40 000–200 000. A 10-point running average displayed online during collection is helpful in confirming adequate acquisition. With averages from 40 samples, we obtain 95% confidence intervals for means of approximately $\pm 0.17\ \mu V$ from measurements at rest and approximately $\pm 0.77\ \mu V$ during passive pedalling of the leg when the subject is sat with the trunk and head supported. Algorithms are available to enhance signal recognition. These offer the opportunity to reduce collected sample sizes (Nishida *et al.*, 1993; Schürmann *et al.*, 1995).

The SEPs are identified within nominal windows, such as "P32", close to 32 msec latency after the stimulus, or as temporally ordered positive and negative deflections, e.g. P1, N1, P2, etc. (Regan, 1989). Descriptive statistics then are reported for specific measured latencies. Although some reports give SEP magnitudes from isoelectric line to peak of wave, it is more common in movement studies to give peak to peak values, e.g. "P1–N1".

Initial cortical SEPs evoked from tibial nerve are held to arise from muscle afferents (Macefield *et al.*, 1989), the longer central conduction times for cutaneous afferent transmission leading to mean latency increases of approximately 4 msec from sural compared with tibial nerve stimulation at the ankle (Vogel *et al.*, 1986). In the progression from muscle afferents of the leg to the S1 receptive cells, there is considerable opportunity for pre- and postsynaptic modulation of the signal at the synapses with Clarke's column cells of the dorsal spinocerebellar tract, with the dorsal column nucleus Z cell synapses approached by Clarke's column collaterals, at synapses with ventro-posterior thalamic neurons, and at the S1 cell itself, deep in the central sulcus for the leg (for this routing specifically for the main transmission of muscle afferents from the human leg, vs traditional dorsal column projections, see Brodal, 1981). Experimental intrusions, arising externally or internally in the CNS, may cause unanticipated change in signal transmission through any of these sites. As a result, there is need for strict experimental control of the surroundings and the subject's central state including: allocation of attention, degree of preparedness, ongoing motor states and state of arousal.

4.2. Active Movement of the Leg(s)

4.2.1. *The SEP Gating and Requirement for Accuracy from Kinesthesis*

4.2.1.1. *During movement*

In most studies, SEPs are elicited from single, square wave pulses of stimulation in the ipsilateral leg, the leg that is moved. The SEP from tibial nerve stimulation is gated when the soleus muscle is contracted (Cohen and Starr, 1985), when the shank is actively flexed about the knee (Cohen and Starr, 1987) and when subjects actively pedal a cycle ergometer (Brooke *et al.*, 1996b), compared with sitting with the leg muscles relaxed. The SEPs also are gated from sural nerve stimulation, when subjects actively pedal (Brooke *et al.*, 1996b). This gating can be so profound as to inhibit the SEP completely, or at least reduce it so that it cannot be distinguished from the recording system noise.

A study has been made of SEPs from a train of stimuli to the sural nerve. In this case, the first cortical SEP occurs with a longer latency (around 51–62 msec) than that seen with single pulses (around 34 msec) and the P50–N80 magnitude is comparatively very large, being in the order of 15–50 μV at rest (Duysens *et al.*, 1995). This SEP also is gated when subjects walk, the attenuation being phased over the gait cycle. The attenuation is stronger immediately following foot contact rather than late in the immediately preceding swing phase (Altenmüller *et al.*, 1995; Duysens *et al.*, 1995).

The attenuation of SEPs when subjects are active is partially alleviated when there is a demand for movement accuracy requiring kinesthesis (Staines *et al.*, 1994; Staines *et al.*, 1996a). Subjects deprived of visual information were required to move the left foot about the ankle in order to track the experimentally induced passive movement of the right foot, the target, about the ankle. In such conditions, the position of the target foot should be conveyed to the subject through plantar and dorsiflexor muscle spindle discharge (McCloskey *et al.*, 1983; Refshauge and Fitzpatrick, 1995), with the most rapid transmission being from primary receptor endings through Ia afferents. This position information channel was probed by test pulses to the tibial nerve of that target (right) leg, with the SEP magnitudes reflecting the pathway gain. SEP magnitudes were depressed by passive (right foot) movement alone. This depression did not occur when the subject actively tracked that movement using the left foot.

The passive movement of the right foot was the same in both conditions, in terms of root mean square amplitude and frequency power spectrum. Thus, accuracy directed at utilizing muscle spindle information in the test pulse channel resulted in a reduction of the SEP gain attenuation for evoked potentials derived from excitation of muscle spindle afferents. Given the common peripheral conditions of movement, this indicates a central source for centrifugally proceeding modulation of the ascending somatosensory transmission. It is noteworthy that, while the ascending sensory information (expressed as an SEP) was released from inhibition during the tracking task, the peripheral expression of the same

test pulse (H reflex) did not differ between the tracking and non-tracking task conditions.

4.2.1.2. *Before movement*

In a forewarned reaction time task, subjects receive a warning signal and then later, often after a 1 sec delay, receive a response signal which is followed, after a reaction time, by the agonist EMG activity (Brunia, 1993). The response signal can be for accurate movement. In a recent study, the required accuracy was to track the passively moved foot with the other foot in the absence of vision, the start of that passive movement being the response signal. In such a design, the SEP gain is significantly reduced over the warning and response periods in the leg which will be active. However, in the target leg, the gain is maintained higher, at the control levels, in the warning period. As no movement has taken place, centripetal influences do not apply and the gain modulations can be associated with centrifugal conditioning, likely from brain activity. The need for kinesthetic information is associated with the channel for that information being kept open (Staines *et al.*, 1996a). However, gain changes for kinesthetic accuracy again appear to be selective for the ascending path to the brain, as the gain of the H reflex is not altered when similar kinesthetic requirements are imposed (Collins *et al.*, 1993b; Staines *et al.*, 1996a; see also Section 2.4).

4.2.1.3. *Long-lasting effect after movement stops*

Unlike the clear evidence for long-lasting attenuation on H reflexes (Section 2.3.1.4), there is no information about the status of SEP gain from the legs when movement has stopped. It is intriguing, though, to note that SEPs from the upper limb show depressed gain for at least 500 msec after movement has stopped (Angel *et al.*, 1986). The SEPs were evoked by a tactile stimulus to the fingertip during and after rapid movement of the thumb.

4.3. Passive Movement of the Leg(s)

4.3.1. *The SEPs Compared to Active Movement*

The SEPs from either tibial nerve or from sural nerve stimulation are depressed during active pedalling movement. They are depressed equally when the movement is induced passively. Thus, the descending control required for pedalling does not alter the attenuation (Brooke *et al.*, 1996b). As the velocity of movement, passive or active, increases, the attenuation of SEP gain increases (Rauch *et al.*, 1985; Staines *et al.*, 1996b, 1996c). Because of this velocity dependence, a role has been explored for rapidly adapting muscle receptors acting as the initiators of the gain regulation.

4.3.2. *The Receptor Which Initiates SEP Down-Regulation in Passive Movement*

As discharge of spindle receptors in leg extensor muscles initiates down-regulation of H reflexes in soleus, it is reasonable to explore a role for such conditioning for the SEPs ascending from stimulation of the tibial nerve at the knee. Support for this view occurred recently, in an experiment studying the change of SEP magnitude at different points in the cycle of passive leg movement. Most attenuation was found to occur in the phase when the leg was most flexed (Staines *et al.*, 1996d). As this is when the extensor muscles are most stretched, their receptors were implicated. It was subsequently hypothesized, and found, that equivalent rates of stretch of the extensor muscles of hip and knee, from markedly different combinations of range and velocity of passive pedalling movement of the one leg, led to equivalent amounts of attenuation of the SEP (Staines *et al.*, 1996b, Staines *et al.*, 1996c). The dependence of the biopotential magnitude on the rate of stretch was very similar for SEPs and H reflexes. Thus, the muscle spindle receptor again emerged as an important source which initiates regulation of a sensory path and its target neuron, in this case a source for centripetally proceeding conditioning of potentials recorded at the scalp.

4.3.3. *Route and Inhibitory Basis for SEP Down-Regulation*

Passive movement attenuates SEPs evoked from the leg. Neither the neural route nor the nature of the depression of SEPs evoked from the leg are clear at this time. One is tempted to speculate on a brief distal route for the conditioning, i.e. through the spinal circuits, as occurs for the H reflex. The only available evidence on SEPs from the leg supports this view. Measurement of lumbar potentials in SEPs proceeding to cortical levels showed attenuation, as did the scalp potentials, with vibration of the Achilles tendon (Cohen and Starr, 1985). Such vibration would strongly activate the spindles in triceps surae muscle, and likely also activated spindles in other muscles of the leg. It appears that this spindle discharge leads to inhibition of afferent transmission prior to the potentials recorded over the lumbar cord. The matter of the site of attenuation is ready for investigation. So, also, is clarification of the type of attenuation developed. Is it occlusion at one of the relays and/or at the cerebral receptive cells? Is it pre- or postsynaptic inhibition and, if it is inhibition, at what point is this centripetally proceeding conditioning applied?

5. A SIGNIFICANT ROLE FOR THE MUSCLE SPINDLE: CONDITIONING OF PATHS FROM SOMATOSENSORY RECEPTORS

The muscle spindles play significant roles in modulating the gains of both tibial nerve elicited SEPs and soleus H reflexes. (It is not known what role proprioceptors play in the modulation of cutaneous reflexes.) Centripetal conditioning occurs at spinal levels for H reflexes, and possibly occurs at spinal levels for SEPs. The originating source appears to be the extensor muscle spindles across the hip and knee. Figure 12 is a tentative attempt to summarize the current view of the neural paths involved in this centripetal conditioning. For the sake of clarity, the

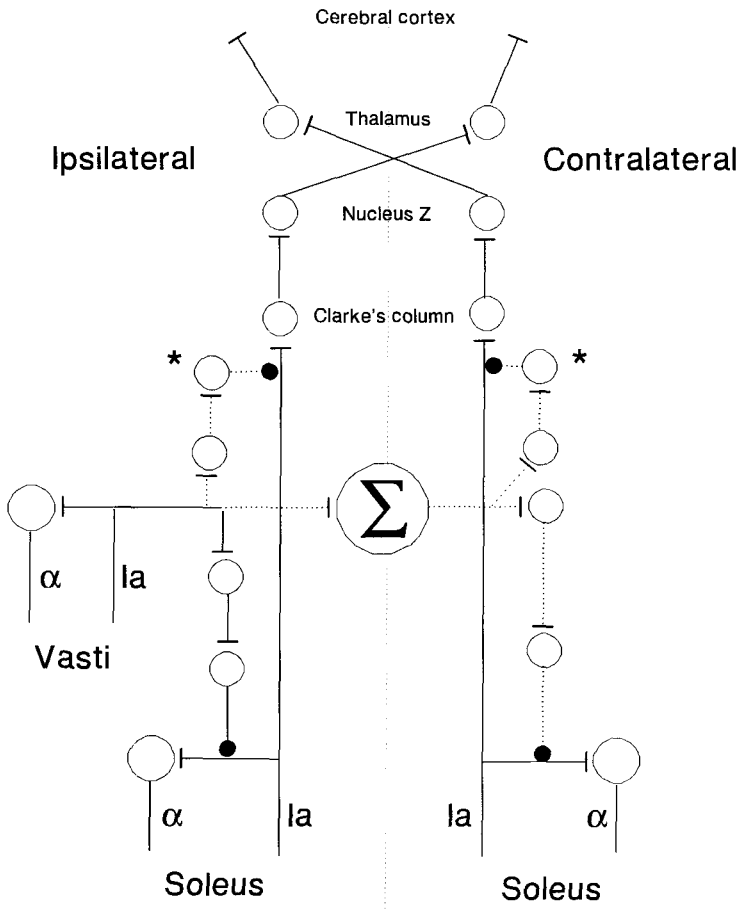

Fig. 12. Tentative neural path diagram suggesting a basis for the powerful attenuation of H reflexes and SEPs from the leg, with movement of a leg. More security of inference is shown by solid lines. Symbol * shows least secure, see text for discussion. Abbreviations are vasti–vastii muscles and soleus–soleus muscle. Symbol Σ symbolizes complex processing in the spinal cord. The flow onto H and SEP paths from vastii could have been replicated for the hip extensor muscle gluteus maximus, but was omitted for clarity.

replication of the knee extensor (vastii)-induced effects by the hip extensor muscle gluteus maximus is omitted. We restrain the conditioning sources to the uniarticular muscles because of the insignificant effect on soleus H reflexes when altering the stretch of the biarticular muscles of hip and knee (Section 2.3.2.4). A more complex transformation is indicated for the effects induced on contralateral soleus by ipsilateral movement, because of the loss of phase modulation that occurs. There are indications that the effects on soleus could also be shown for other muscles, such as tibialis anterior and abductor hallucis, but these have been omitted. This is not simply for clarity but also because careful evaluation of receptor source, type of inhibition and neural route has not been made for muscles other than soleus in humans. Chains of presynaptic inhibitory neurons are shown as pairs (we have no idea how many are involved, but more than one) which terminate axonally. The site of conditioning of the ascending path is suggested as the Ia terminals synapsing with Clarke's column cells. This is particularly tentative as the evidence is limited to the report of reduced lumbar potentials with conditions that attenuate the SEP from tibial nerve. The site presently suggested would reflect spinal events, as appears to occur for the H reflex. When the full neural diagram is known for humans, it may well be that many heteronymous conditioning paths will be shown, with multiple conditioning converging from them onto the paths from somatosensory receptors.

Muscle spindle discharge also appears to be the initiating source for the brain-induced *centrifugally* proceeding modulation of SEPs from the leg. When centrifugal conditioning of SEPs occurred during movement, the determination of the position of the foot and thus its accuracy of movement likely rested on spindle discharge. (Memory traces of spindle discharge defining the latest position of the foot likely provide one basis for brain plans preparing for accuracy of movement.) Thus those traces, together with preparation of the ascending path for the transmission of impulses originating in muscle spindles, appear to set the gain of the SEP prior to movement. We suggest that there is a principle, taking these results together from centripetal and centrifugal conditioning, namely, that a primary role for muscle spindles is to condition the transmission in

somatosensory pathways. This underpins the global concept — somatosensory paths are gated by movement. The effect may occur through oligosynaptic routes or through more complex control centres which lead to complex transformations from the original signal. Observation of the potent influence seen during passive movement may reflect the default for movement-mediated control on primary afferent flow.

The basic function of this conditioning of sensory paths by discharge in other sensory receptors may be to control the density of flow onto target neurons. We hypothesize that the strong convergence from large diameter primary afferents onto relay and, subsequently, cerebral receptive cells in primary sensorimotor cortex (Weisendanger and Miles, 1982; Lemon, 1988; Wall, 1988) would render those target neurons comparatively insensitive to the modulatory effects of subthreshold potentials from other sources of convergence, if attenuation was not the default condition. A similar argument can be made for the dense convergence of large diameter afferents onto motoneurons (Mendell and Henneman, 1971). In upright quiet stance, this strong convergence may contribute to maintaining anteroposterior stability through the soleus stretch reflex. During more extensive movement of the legs, such as walking or running, the afferent flow is constrained, enabling feed-forward from locomotor centres to control motoneuronal discharge and increase that afferent flow only at functionally appropriate points in the cycle of movement. Thus, modulation of both spinal and ascending paths may be to control the density of transmission so as to leave the target neurons patent for modulation by other inputs. Default down-regulation between primary afferent groups appears to avoid disabling the sensitivity of the target neuron. Testing this speculation may prove an attractive modelling opportunity.

Coincidental with the preparation of the review, two recent papers lead to the conclusion that change in muscle fascicle length was "a variable of significance to the central nervous system" (Refshauge *et al.*, 1995). Further, for the purpose of detecting change in the position of the limb, "the population response of spindles is likely to be the effective sensory input" (Refshauge and Fitzpatrick, 1995). We embrace that view, feeling that imposed rate of stretch, leading to specific rates of discharge of muscle spindles, conditions sensory pathways and is read by the brain for accuracy of performance, leading to modulation of ascending SEPs.

We do not know how generalizable is the principle of movement modulation of afferent flow, nor the specificity of the role of muscle spindles as initiators of sensori-sensory conditioning. For the present, this conditioning has only been demonstrated for muscle spindle discharge in close functional proximity to the test pathway. Some studies on the upper limb appear to indicate that only sensory fields within the moving segment are gated by the movement (Cohen and Starr, 1987)). However, there do appear to be some differences in the extent of modulation seen between the movement of the lower limbs as compared to the upper limbs. For example, the absence of profound contralateral modulation from movement in the upper limb and the modest or inconclusive changes arising from passive movements in the upper limb are clearly different from results presently described from the lower limb. It is necessary to know whether this conditioning may extend between the arms and legs or over other sensory modalities. It will be necessary also to determine the task specific modulations of this sensori-sensory conditioning which is identified so strongly during passive movements.

6. CONCLUDING REMARKS

Gain control of afferent activity from sensory receptor discharge in movement is a widespread phenomenon in the animal kingdom, occurring in vertebrates and invertebrates (Watson, 1992; Burrows and Matheson, 1994; Wolf and Burrows, 1995). In vertebrates it is reported in cats (Akazawa *et al.*, 1982; Gossard *et al.*, 1991), dogs (Misiaszek *et al.*, 1995a) and lamprey (Sillar, 1991; Alford *et al.*, 1991). The present paper reviews evidence supporting its occurrence in moving humans. Being studies made on humans, the evidence is indirect, by necessity. Evidence from other animal studies, necessarily intrusive and involving conditions distorted from the natural state, supports the conclusions from this work on humans. Considerable progress has been made within the present topic over the past few years. There is still lack of understanding in a number of places and we have tried to identify these areas throughout this review.

It is now appropriate to return to the view held at the end of the Introduction. Clearly, the task characteristics and the ongoing and changing state of the CNS together define the status of transmission in sensory pathways, hence the status of reflex expression and information available to the brain. The task and the CNS state will determine what gain modulation occurs, what the initiating source is and over what pathways the modulatory influence travels. Understanding these factors, and how they interplay, will lead us toward understanding the function of these modulations in free field behaviours and help us develop general motor control principles. Presently, the understanding about transmission from primary afferents leads us to distrust any model of motor control that assumes such transmission is immutable, or assumes that it provides a point signal used as a constant criterion by the CNS in the placement of the limb (see discussion in McCloskey and Prochazka, 1994). Rather, the primary afferent discharge appears to be subjected to constantly shifting access into the CNS, as conditions change within the brain, the spinal cord and the sensed external world.

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