In The Name Of God

THE ROLE OF SHORT LATENCY REFLEXES IN THE MOTOR CONTROL OF QUADRICEPS IN HUMANS

A Thesis Submitted For the Degree of Doctor of Philosophy in the Faculty of Medicine

by

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November 2002

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Acknowledgements

First of all, I would like to express my sincere thanks to my wife and son for all the sacrifices they have made during the last four years. Without their support I would have been unable to finish my studies so successfully.

I am grateful to the Iranian Ministry of Health and Medical Education for awarding me a scholarship.

I should also like to thank my supervisor Dr. R.H. Baxendale, most sincerely, for all his advice, support and patience throughout my studies.

These experiments would have been very difficult without the help of Mr Ian Watt. It is my pleasure to thank him for all his assistance during the last two years.

Last, but not least, I have to thank my mother and father. They have motivated and inspired me throughout my student life. Without their support I would have been unable to achieve my aims.

Dedication:

To my family

Summary

A total of 34 volunteer subjects participated in a series of experiments. These experiments were designed to investigate the characteristics and functional role of an excitatory reflex pathway linking the pretibial muscles to quadriceps (CPQ reflex). The CPQ reflex was evoked by low intensity electrical stimulation of common peroneal nerve (CPN) at the level of caput fibulae. The reflex was observed in averaged EMG of rectus femoris (RF) and vastus medialis (VM). Voluntary contraction of Q was needed to reveal the reflex and no responses were detected in the recordings from relaxed muscle. The peak to peak amplitude and area of the responses were measured in non-rectified and rectified averaged EMG.

The stability of the CPQ reflex was investigated in the first series of experiments. Nine trials were distributed across three sessions with the perceptive caution to keep the stimulating and recording conditions similar. A constant contraction (20% of maximum voluntary contraction) in quadriceps was maintained by the subjects during the tests. Constant stimulus intensity to evoke maximum reflex was applied in all trials. The result suggested that the peak-peak amplitude and the threshold of the CPQ reflex was extremely consistent with-in session and between sessions of the experiment.

Graded stimulus intensities between 0.9 and 1.5×motor threshold (MT) in tibialis anterior (TA) were applied to CPN in the second series of experiments while the quadriceps (Q) was contracted at a

level of 20% of maximum voluntary contraction (MVC). The electrical stimulation of the CPN evoked excitatory responses in all the subjects with a latency of about 30±2.1ms (mean ± 1SD). The responses were regarded significant with amplitude beyond 2 standard deviation (SD) of the mean. The mean was calculated from 30ms pre-stimulus averaged EMG. In three subjects making contractions at 20% of MVC significant CPQ reflexes were recorded with stimulation at an intensity of 0.9×MT. The extrapolation of the pooled data also suggests an electrical threshold of around 0.8×MT. This low threshold and the short latency strongly suggest the participation of group I afferent types in this reflex pathway. Maximum response was evoked by stimulus intensity of about 1.3×MT.

The changes in the reflex magnitude in different knee and hip joint positions were also investigated in another series of experiments. The knee positioning was shown to affect the reflex amplitude in all subjects. The reflex became smaller towards more flexed position of the knee joint. Two patterns of reaction were recognised among the subjects. One group showed a very significant and abrupt reduction in the magnitude of the reflex after 10°-20° of knee flexed positioning and the second group was characterised with a gradual and progressive reduction in the reflex magnitude from 10° to 50° of flexed position. The hip extended position also produced a significant attenuation of reflex magnitude compared to the flexed position however this effect was less consistent than the knee positioning in the investigated subjects.

The correlation between the reflex magnitude and the level of muscular activity in the quadriceps at both extended and flexed positions of the knee was investigated in the next series of experiments. The reflex showed a significant linear correlation to the background EMG at the extended knee position. This is probably related to the synaptic facilitation of the CPQ pathway by the central inputs. No significant changes in latency were detected by the increase in voluntary contraction. At 130° flexed position however, no correlation was found between the reflex magnitude and the level of muscular activity in Q. In fact even at muscular activity of about 40% of MVC no reflex was detected in any of the subjects at flexed position. It was concluded that this inhibitory effect interacts with the reflex at pre-motoneuronal level.

The functional role of the CPQ reflex was investigated in two other series of experiments. The pattern of changes in the reflex magnitude was studied during gait. Stimuli that could produce maximum reflex magnitude were applied in a pseudo-random sequence while the subjects were walking on a treadmill. The stimulation was applied at different time delays from heel strike, triggered by a pressure sensor at the heel. The reflex magnitude and the EMG activity in the VM, RF, TA, semitendinosus and medial gastrocnemius were measured. The reflex was at its highest magnitude shortly after heel strike. No responses were detected during the major period of gait cycle from midstance to terminal swing phase. The reflex magnitude pattern of modulation was closely correlated with the pattern of activity in the RF and VM i.e. both showed their peak shortly after heel strike and remained quiescent during the rest of gait cycle. This suggests that the CPQ reflex can provide a positive feedback input to Q motoneurone during the early stance phase of gait. This could help to stabilise the knee joint at this period to overcome the load of the body.

The nature of the areflexic period of the gait cycle was investigated in the fifth experiment. A modified knee orthosis was used to produce increased muscular activity in Q during this quiescent period. Pairs of springs were fixed into the orthosis to provide a flexor momentum to the knee joint. The muscular activity of RF and VM increased significantly throughout the gait cycle. Stimuli were applied at three instants at midstance, terminal stance and terminal swing phase. These three instants were all areflexic and EMG-silent previous to the application of the spring-loaded knee orthosis. Therefore if no inhibitory effect was affecting the reflex pathway during this areflexic period, with increase in the background EMG, the reflex was expected to reappear. The stimulation at midstance and terminal swing phase re-evoked the reflex and a positive correlation was observed between the reflex magnitude and the increase in the muscular activity in quadriceps. However, stimulation at the terminal stance phase was unable to re-evoke the CPQ reflex despite the significant increase in the background activity in Q. It was concluded that an active inhibition was imposed on the reflex pathway during this period. The critical role of the lower limb at this period is transition from stance to swing phase. This necessitates unloading of the lower limb. This unloading phenomenon is associated with knee flexion and ankle dorsiflexion to clear the foot from the ground. A strong excitatory reflex from ankle dorsiflexors to Q muscles at this period would hinder the knee flexion and the transition. It is argued that this inhibition could contribute to the unloading and transition of the lower limb to the swing phase.

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Abbreviations

- **CNS:** Central nervous system.
- **CPN:** Common peroneal nerve.
- **CPQ reflex:** the motor reflex evoked in quadriceps muscles by electrical stimulation at common peroneal nerve.
- **EMG:** Electromyogram.
- **EMG_{rms}:** Root mean square of the electromyogram.
- **GTO:** Golgi tendon organs.
- **M_{max}:** Maximum amplitude of M wave.
- **MS:** Muscle spindle.
- **MT:** Motor threshold.
- **MVC:** Maximum voluntary contraction.
- **P-P amplitude:** Peak to peak amplitude.
- **Q:** quadriceps.
- **RF:** Rectus femoris.
- **TA:** Tibialis anterior.
- **VM:** Vastus medialis.
- **SD:** Standard Deviation of Mean.
- **SEM:** Standard Error of Mean.
- **CI:** Confidence Intervals.

Chapter 1

General Introduction and Literature Review

One of the features that differentiate humans from other animals is the way they move. The bipedal stance and locomotion of humans and the skilful movements of the upper limbs are characteristics unique to humans. Little is known about the neural mechanisms involved in human movements but what is well known is that the central nervous system (CNS) and the peripheral sensory system are both needed to produce finely controlled motor activity. Different levels of the CNS could be involved in controlling the motor activity. The highest levels are mainly involved in the control of voluntary activity such as kicking a ball or picking an object from the floor. On the other hand, some motor activities are performed automatically. For example, in lifting an object from the floor, the wrist extension that accompanies the forceful grasp or the stabilising contraction in the shoulder muscles are all made involuntarily. The best known of these automatic activities are the rhythmic motor behaviours such as walking, chewing and breathing. Animal studies suggest that such rhythmic movements are created by generator circuits of neurones located in the brainstem or spinal cord (Grillner 1975). There is a general agreement that the afferent information from a variety of sources interacts with the central commands to adjust a movement to actual requirements. One way to study the involvement of afferents in these generator circuits is to study movements in patients lacking proprioceptive or central inputs.

Patients lacking proprioceptive input from their limbs are characterised by a marked degradation in the accuracy of their movements (Gordon, Ghilardi and Ghez 1995). It has been shown that this degradation is particularly severe in the multijoint movements (Sainburg, Ghilardi, Poizner and Ghez 1995). It is concluded therefore that proprioceptive information plays an important role in interjoint co-ordination during multijoint movements.

In the absence of supraspinal inputs, adult spinal-cord-injured humans are able to generate a step like oscillating motor pattern in their lower limbs (Bussel, Roby-Brami, Yakovleff, Azouvi, and Held 1988, Rosenfeld, McKay, Halter, Pollo and Dimitrijevic 1995 and Harkema, Hurley, Patel, Requejo, Dobkin and Edgerton 1997). These investigations show that the human lumbosacral spinal cord can generate step like oscillating EMG patterns when triggered and assisted by the sensory information specially those associated with weight-bearing stepping (Dietz 1998). This oscillatory pattern of activity seems to be innate however sensory inputs are necessary to trigger and also to assist these pattern generators. To achieve functional movements it is reasonable to assume that afferent information would influence the central pattern and conversely, that the central pattern generator would select the appropriate afferent information. In addition, the programmed motor response in humans can be altered by instruction or by expectation (Prochazka 1989). Voluntary commands have to interact with the spinal locomotor generator in order to change, for example, the direction of gait or to avoid an obstacle (Dietz 1997). Harkema et al (1997) showed that the mean EMG amplitude of the leg muscles was directly related to the peak load on the lower limb in each step. They concluded that the level of loading on the lower limbs provides cues that enable the human lumbosacral spinal cord to modulate its efferent output in a manner that may facilitate the generation of the stepping.

Whilst the CNS interacts with peripheral inputs to produce an appropriate movement, only a portion of this afferent information is involved. The control of human posture and gait utilises selected afferent information from a variety of sources, to modify the central motor commands. This adjusts a movement to the actual requirements. The idea that the central nervous system selects the sensory information which is appropriate to meet the requirements is well illustrated in experiments performed by Nashner (1977). In these experiments the subjects stood on a moveable platform that could be moved horizontally or tilted forwards or backwards. EMG responses obtained under various conditions for the investigation of the neural mechanisms underlying postural control. The motor responses during a toes-up platform rotation and a horizontal backward translation were compared. In both cases the triceps surae was stretched by the perturbation. The gastrocnemius stretch reflex had a compensatory role in the latter case. It was potentially destabilising in the former, as it would increase backward body sway. The response pattern recorded in both conditions was appropriate for maintaining body equilibrium. Toes-up rotation evoked a response in the tibialis anterior whereas the backward translation evoked a strong polysynaptic compensatory response in the gastrocnemius. It was suggested that the differential weighting of sensory information from the muscle stretch receptors in combination with load and pressure receptors are responsible for the observed different responses.

Based on the result of these experiments and others, the use of the sensory stimulation has become routine in the rehabilitation programme of the patients suffering from motor dysfunction. Using sensory stimulation such weight-bearing, skin stimulation and muscle stretch is believed that could help in the improvement of the motor function of these patients.

In humans stimulation of afferents from ankle muscles evokes an excitatory reflex in quadriceps motoneurones (Brooke and McIlroy 1990a, McIlroy & Brooke 1987). It is likely that this sensory information could be involved in control of motor activity in quadriceps. There is still little known about the functional role of this excitatory pathway which has only been reported in humans. The following sections in this chapter provide the general information about the sensory systems that could be involved in the control of motor activity of quadriceps.

1.1. Anatomy

1.1.1. Peroneal nerve

The sciatic nerve splits at the back of the thigh into the tibial and common peroneal nerves. The common peroneal nerve is derived from the dorsal branches of the fourth and fifth lumbar and the first and second sacral nerves. It descends obliquely along the lateral side of the popliteal fossa to the head of the fibula. It winds around the

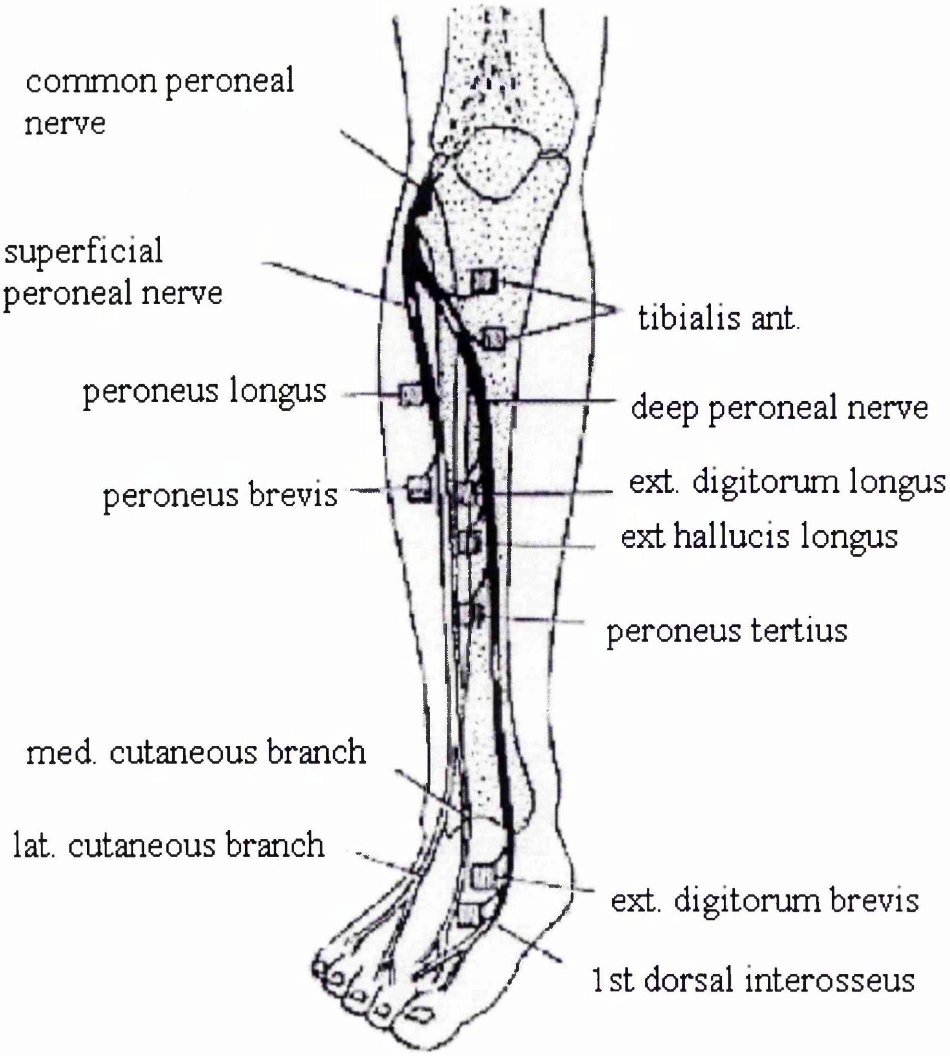

Figure 1.1. The diagram shows a schematic view of common peroneal nerve. It bifurcates distal to caput fibulae into deep and superficial peroneal branches. The muscles innervated by each of these branches can be seen in the diagram.

neck of the fibula, between the peroneus longus and the bone, where it is subcutaneous. It divides beneath the muscle into the superficial and deep peroneal nerves. Proximal to its division it gives off articular and lateral sural cutaneous nerves. A schematic view of the common peroneal nerve is shown in figure 1.1. The deep peroneal begins at the bifurcation of the common peroneal nerve, between the fibula and upper part of the peroneus longus and passes obliquely forward beneath the extensor digitorum longus to the front of the interosseous membrane. It then descends to the front of the ankle-joint, where it divides into a lateral and a medial terminal branch. In the leg, the deep peroneal nerve supplies muscular branches to the tibialis anterior, extensor digitorum longus, peroneus tertius, and extensor hallucis longus and an articular branch to the ankle-joint.
The superficial peroneal nerve supplies the peroneus longus, brevis and the skin over the greater part of the dorsum of the foot.

1.1.2. Tibialis anterior muscle

Tibialis anterior muscle is situated on the lateral side of the tibia; it is thick and fleshy above, tendinous below. It arises from the lateral condyle and upper half or two-thirds of the lateral surface of the body of the tibia and from the adjoining part of the interosseous membrane. The fibres run vertically downward, and end in a tendon, which is apparent on the anterior surface of the muscle at the lower third of the leg. It inserts into the medial surface of the first cuneiform bone, and the base of the first metatarsal bone. This muscle overlaps the deep peroneal nerve in the upper part of the leg.

Tibialis anterior is the strongest dorsiflexor of the ankle and also helps to invert and adduct the foot.

1.1.3. Quadriceps femoris muscle

The quadriceps femoris includes the four muscles on the front of the thigh. It is the great extensor muscle of the leg, forming a large fleshy mass which covers the front and sides of the femur. It is subdivided into separate portions, which have received distinctive names. One occupying the middle of the thigh, and connected above with the ilium, is rectus femoris. The other three lie in immediate connection with the body of the femur, which they cover from the trochanter to the condyles. The largest portion on the lateral side of the femur is termed the vastus lateralis; that covering the medial side, the vastus medialis; and that in front, the vastus intermedius.

The tendons of the four parts of quadriceps unite to form a single strong tendon at its distal end which inserts to the base of the patella.

1.2. Classifications of the nerve fibres

Peripheral nerves in mammals are made up of many axons of different origins and size that are bound together. The large axons are concerned primarily with proprioception, motor functions, touch and pressure while smaller axons subserve temperature, nociception and autonomic functions (Ganong 1995).

In 1943, Lloyd proposed a system of classification of muscle afferent fibres on the basis of fibre diameter. The diameters fall into four groups, which Lloyd labelled I-IV. The largest is group I that is followed by group II, III and the unmyelinated group IV. The largest group I fibres arise from primary muscle spindle endings (Ia), Golgi Tendon Organs (GTO) from a slightly smaller average diameter (Ib). Spindle secondary endings have fibres of the group II class. The afferents in cutaneous nerves are not classified by the numerical system. They share a classification with somatic and autonomic motor fibres that are originally based on the various peaks that could be identified in the compound nerve action potentials (Erlanger and Gasser 1938). Three main peaks (A, B and C) can be distinguished corresponding to fibres conducting at different velocities. Histologically, myelinated somatic axons correspond to the fastest conducting A fibre, myelinated autonomic axons to the slower conducting B fibres and unmyelinated axons to the slowest conducting C fibres. The axons which comprise the A group have a wide spectrum of fibre diameter (1-22 μm) and are originally subdivided into A_α, A_β, A_γ and A_δ in descending order of conduction velocity. In the cat, group I muscle afferents have larger diameters than the corresponding A_α fibres. As a result group I muscle afferents have the lowest threshold and fastest conduction velocities of all peripheral nerve fibres. In man, there is little difference between these two fibres. The largest muscle afferents conduction velocity is almost the same as the largest cutaneous afferents and motor efferents. Macefield et al (1989) reported that the mean conduction velocities of the lowest threshold muscle and cutaneous afferents were respectively, 74.7±6.5 m/sec and 80.3±6.7 m/sec for median nerve and 54.7±3.4 m/sec and 52.8±3.2 m/sec for the tibial nerve. Sefner and Logigan (1994) also investigated the motor and sensory conduction velocity of the isolated fibre population in human sciatic nerve. The mean conduction velocity was 57.6 m/sec for muscle afferent group Ia, 55.1 m/sec for cutaneous afferent group II, 52.4 m/sec for motoneurones and 56.3 m/sec for mixed nerve. They found a significant difference between the conduction velocity of group Ia afferents and motor axons.

Table 1.1 shows the various fibre types and the comparison of the numerical system and the letter system of classification.

1.3. Electrical stimulation

Reflexes are most easily observed and analysed when the spinal cord receives a synchronised volley of afferent input. Therefore the afferent volley is usually evoked by electrical stimulation of the peripheral nerves rather than by natural stimulation of their receptors. One result is that the threshold of the evoked reflexes can be described in terms of the intensity of the electrical stimulus.

It is possible to make a statement about the probable origin of an evoked response on the basis of the electrical threshold and latency of the response. Fortunately, in most muscle nerves, there is a fairly close relationship between electrical stimulation threshold of a fibre and the class of the relative sensory receptors (Lloyd 1943,1946).

Generally, the greater the diameter of a given nerve fibre, the lower its threshold to electrical stimulation. The largest diameter group I

Group	Origin	Fibre Type
Ia Ib	Muscle spindle, Annulo-spinal endings, Golgi tendon organs	Aα Aα
II	Muscle spindle, flower-spray ending, touch, pressure.	Aβ
III	Pain, cold and some touch receptors	Aδ
IV	Pain, temperature and other receptors	C

Table 1.1. The table shows the numerical classification of the sensory neurons. The relative lettered classes of each numerical group can be seen in the right column for comparison.

fibres are usually stimulated first, then with slightly higher threshold, the largest motor axons are stimulated. The group II afferents have higher threshold than group I afferents and motor axons.

Within any one class of afferents there are a range of thresholds. The distributions of Ia and Ib thresholds overlap and whilst there is no clear separation, it is generally accepted that the lowest threshold group Ib fibres have a slightly higher threshold than the lowest threshold Ia afferents. However, there is considerable variation between the composition of muscle nerves, even in the same species (Jack 1978).

1.4. The interneurone system

The simplest reflex arc is the monosynaptic pathway. In this unusual example the primary afferent makes direct synaptic contact with the motoneurones. The use of monosynaptic reflex arc in neurological investigations has certain disadvantages, one of which is that it cannot be completely disabled. The synaptic effects of group Ia afferents on motoneurones can be modulated by the mechanism of "presynaptic inhibition" and by changes of muscle spindle sensitivity through the fusimotor system (Matthews 1972). However, this does not completely suppress Ia synaptic action on motoneurones. In the majority of reflex pathways interneurones lie between the primary afferents and the motor neurone. This allows much more flexibility in the final effect of the reflex pathway on the motoneurones (Burke 1998). When interneurones are interposed between the primary afferent and motoneurones (non-monosynaptic pathways), three significant advantages are achieved by the nervous system. Firstly, the outcome of the effect at motoneurones can be changed. For example it is well known that Ia afferents excite the neurones on which they project, but an interposed interneurone can produce an inhibitory synaptic effect on the motoneurones when they are excited. Secondly, transmission in a non-monosynaptic reflex pathway can vary from zero to considerable amplification by virtue of the excitatory and inhibitory effects converging onto the interposed interneurones. Thirdly, other descending and ascending inputs can modulate the reflex by facilitating or inhibiting any of the synapses in the reflex pathway.

The spinal cord is now considered as a location that integrates incoming sensory information with motor commands descended from supraspinal regions. The spinal pathways of different reflexes interact extensively, often by sharing common interneurones and also supraspinal commands are mediated through interneurones in reflex pathways (Marchand-Pauvert et al 1999, Pierrot-Deseilligny 1996, Lundberg 1992)

In the spinal cord the interneurones are usually defined as nerve cells with axons which terminate relatively close to the cell body i.e. within the same spinal segment or in a nearby segment. Interneurones with axons that end at greater distances but still within the spinal cord are sometimes called propriospinal neurones.

1.5. Integration of ascending and descending inputs

Individual reflexes have usually been regarded as distinct entities, resulting from the operation of separate sections of neural system. In addition, voluntary movement was often viewed as separate and distinct from reflex actions. However, in a great number of studies on the synaptic organisation it has been shown that the spinal cord is an important site that integrates incoming sensory information with motor command signals descending from supraspinal centres (Marchand-Pauvert et al 1999, Pierrot-Deseilligny 1996, Stewart and Brooke 1993, McIlroy et al 1994). This implies two important fundamental points:

- The spinal pathways associated with different reflexes can interact extensively by sharing common interneurones.
- Control of movement by the supraspinal centres is mediated partially through interneurones in reflex pathways (Marchand-Pauvert, Pierrot-Deseilligny and Rothwell 1998 and Marchand-Pauvert, Simonetta-Moreau and Pierrot-Deseilligny 1999).

1.6. Muscle Spindles (MS)

1.6.1. Structure

-Structure

The mammalian muscle spindle consists of a bundle of specialised muscle fibres which lie in parallel within the fibres of the main extrafusal muscle. The intrafusal fibres are much shorter than fibres in the main muscle. At each end they are attached to the extrafusal fibres or to tendinous junctions. For about half of its length the spindles are contained within a thick connective tissue capsule which expands in its central zone to form a fluid-filled space, giving it its fusiform shape. There are two types of muscle fibre in each spindle, 2 or 3 nuclear bag and 4 or more nuclear chain fibres. The nuclei of the bag fibres are collected together at the spindle equator, in contrast, the chain fibres only have a single row of nuclei in the same region (Matthews 1972)

-Innervation

Large sensory neurones distribute primary endings to all muscle fibres of a spindle. These endings occupy the most central region of each fibre. Either side of them may be the secondary endings of the group II afferent fibres that terminate on only the nuclear chain fibres.

The motor supply to the spindle fibres consists of the small diameter γ neurones, which distribute their endings to the poles of the fibres. Another source of afferent fibres to the intrafusal fibres are branches of motoneurones innervating the extrafusal fibres. These shared axons are known as β axons. The actual functions of these efferents are still not clear (Matthews 1972, Ganong 1995).

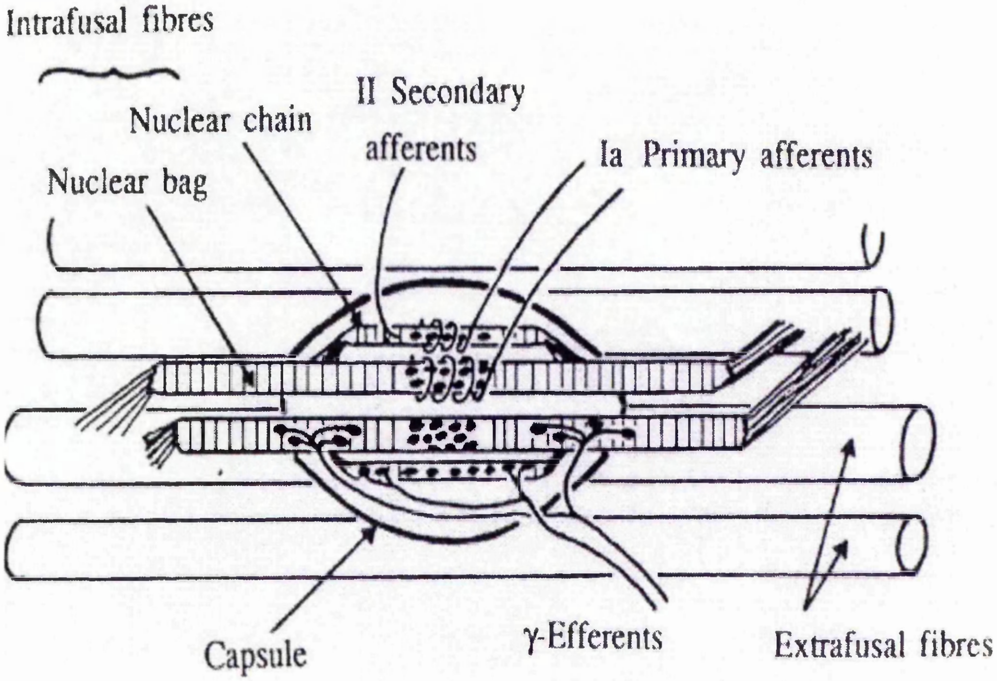

Figure 1.2. The schematic structure of a muscle spindle. The efferent innervation is shown for the lower fibres and the afferents for the upper fibres. (Modified figure from Jones & Round 1993, chapter 4)

1.6.3. Adequate stimulus for muscle spindles

It is well known that muscle spindles are receptors that signal the dynamic and static information about the muscle length to the central nervous system (Jones and Round 1993). In response to a ramp and hold stretch the firing frequency of the group Ia afferents, originating on the bag fibres, show a rapid increase during the ramp phase, but during the hold phase the frequency of firing decreases. Bag fibres can accommodate to stretch and therefore react mainly to the dynamic stretch rather than to a constant length (De Gail et al 1966, Burke et al 1976). The chain fibres however, behave like a spring and give a sustained high frequency response during the hold phase. This signal is mainly conducted through the group II afferents. There are also some Ia afferents on the chain fibres, therefore the signal in the group Ia afferents could be a mixture of the discharges from both types of the intrafusal fibres. In the other words, the group Ia fibres may signal both the dynamic and static length of the muscle.

1.6.4. Motor responses associated with muscle spindle afferents

-Group Ia afferents

The monosynaptic stretch reflex is the most basic reflex organisation in the spinal cord. David Lloyd (1943a) first showed that this reflex is generated by the fast-conducting (group Ia) afferents from muscle spindles and that the central delay for this reflex was so short that the connection between the Ia afferents and motoneurones cannot involve interneurones.

These are the only main afferent system that makes monosynaptic excitation onto motoneurones. Group II fibres also make monosynaptic connections to motoneurones (Ganong 1995). All other reflex arcs exhibit longer central delays that suggest the existence of one or more levels of interneurones are interposed in their pathways toward the motoneurones. The reciprocal projection of Ia afferents to antagonist muscles is one example of these indirect pathways. This reciprocal inhibition is a disynaptic pathway with two synaptic stages before the motoneurone. It has been shown that the reciprocal Ia inhibitory pathway is modulated by a wide variety of input systems. These input sources include Renshaw cells, ipsilateral group Ib muscle afferents and cutaneous and joint afferents as well as the descending pathways from supraspinal centres (Baldissera, Hultborn and Illert 1981). It is argued that these systems are converged onto a common interneurone system.

For a long time group Ia afferents were believed to excite only the agonist and synergist group of muscles and inhibit the antagonist groups. But it has been shown that the agonist muscles can also receive inhibitory projections from group Ia afferents. This inhibitory effect that is usually called "non-reciprocal inhibition" is conducted through interneurone/s that are shared with the group Ib from GTOs, group II muscle afferents, cutaneous and joint afferents and also supraspinal centres (Jami 1992).

-Group II afferents

It was long accepted that the monosynaptic excitation of motoneurones by Ia afferents was the main mechanism underlying the stretch reflex. Later it was found that the major response to stretching of a muscle during a voluntary contraction was a medium latency response (MLR) occurring with latency too long for a classical monosynaptic pathway. In the lower limb there are several lines of evidence showing that this MLR evoked by stretch in ankle and foot muscles is a spinal reflex originating in muscle spindle secondary endings and mediated through group II afferents (Dietz 1992, Schiepatti and Nardone 1997). This excitation from group II afferents is not confined to homonymous motoneurones. Various muscles also receive potent excitation from these afferents in cats (Lundberg, Malmgren and Schomburg 1987) and in man (Simonetta-Moreau, Marque, Marchand-Pauvert and Pierrot-Deseilligny 1999). The pattern of excitatory responses by group II muscle afferents has been investigated by Simonetta-Moreau et al (1999). It has been shown that following stimulation of the CPN and medial gastrocnemius nerve, the main excitatory responses to hamstring muscles were from group II afferents. In Q however both group I and II have strong excitatory effects. It has also been shown that in humans there was no evidence for group II inhibition of motoneurones and excitation was the only response recorded for the these afferents (Simonetta-Moreau et al 1999).

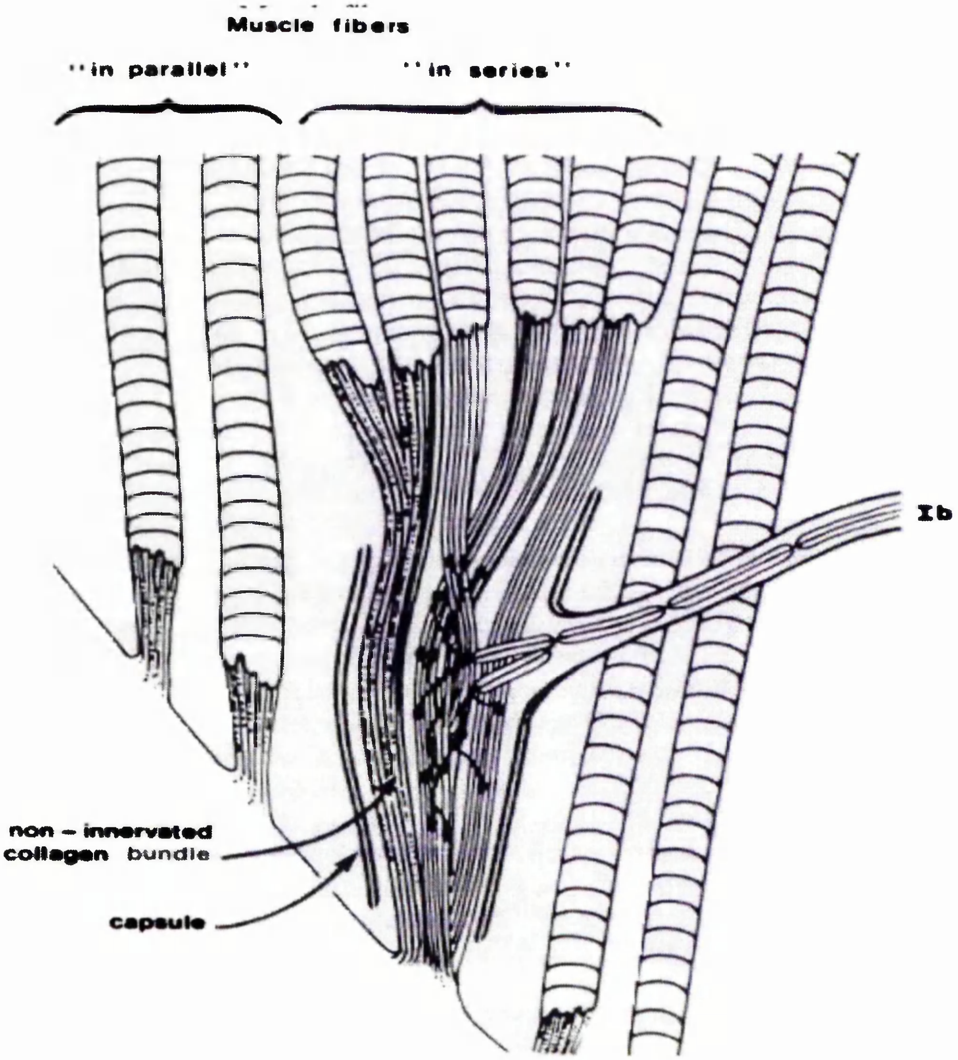

Figure 1.3. The schematic view of a Golgi tendon organ and its neural connections. The in series and in parallel muscle fibres can also be seen. (modified figure from Jami 1992)

1.7. Golgi tendon organs (GTO)

1.7.1. Structure

Tendon organs are encapsulated corpuscles innervated by large afferent fibres (Ib). Their main component is an enlarged fascicle of collagen bundles attached at one end to the individual tendons of a small fascicle of muscle fibres while the other end is in continuity with the whole muscle tendon or aponeurosis. Each receptor is thus placed "in series" with a group of muscle fibres, whereas other fibres coursing " in parallel" with the tendon organ body insert around its tendinous or aponeurotic end (figure 1.3).

The number of muscle fibres attached in series with a GTO varies in a range of 10-20 in humans (Bridgman 1970).

1.7.2. Adequate stimulus for GTO

Since the experiments of Houk & Henneman in cats (1967) and a similar study in humans (Burke, Hagbarth and Lofstedt 1978), the idea that the GTOs are receptors that monitor passive muscle stretch has been changed. The response of GTOs to the muscle stretch can hardly be considered functionally relevant because of their high threshold to muscle stretch. This high threshold of the GTO to muscle stretch provided the basis for the now obsolete idea that an emergency signal could be provided by these receptors in case of high tension developed in the muscle due to excessive stretch. It was believed that this emergency signal could help prevent the harmful over-stretch of the muscle.

Houk & Henneman (1967) pointed out that very few of the soleus GTOs they studied in cats discharged steadily in response to the stretches less than the maximum physiological length of the muscle. It has been shown that GTOs have a very poor performance as passive tension sensors (Houk, Singer and Henneman 1971).

When the isolated GTOs are studied in vitro, they respond well to the stretch applied to them. But when the muscle was stretched in situ, they appeared to be unresponsive to stretch. This has been explained by the effect of the "in parallel" connective tissues. GTOs are in parallel with most of the connective tissue within and around the muscle. The stiffness of these connective tissues is responsible for much of the passive force developed by the muscle resisting the stretch. But GTOs are weakly affected by this force. The connective tissue is pulled in parallel and not in series with the receptors. In conclusion, even though the intrinsic properties of the GTOs would allow them to work as stretch receptors, their functional properties do not include a significant sensitivity to passive muscle stretch (Jami 1992).

If consistent responses and low threshold are accepted for criteria, muscle contraction appears as the adequate stimulus for GTOs (Houk et al 1971). They demonstrated that individual GTO of cat soleus can signal the activity of single motor unit. They also concluded that the contraction of one or two in series muscle fibres should suffice to elicit the discharge of the receptors. This was later confirmed by studies on isolated GTOs in vitro (Fukami 1981).

It has also been demonstrated that a single receptor is in series with several motor units. Besides, every single motor unit was able to activate several receptors. Therefore it has been argued that contraction of each motor unit in muscles is monitored by at least one GTO (Jami 1992).

When the response of a single receptor is considered, the discharge frequency displays no clear relation to the strength of the contraction. However, the averaged frequency of the pooled discharges of the whole GTOs of a muscle was found to provide a better estimate of contractile force (Houk and Henneman 1967, Jami 1992). Despite that, the ensemble discharge of all GTOs in a muscle closely follows the course of force variations, it does not indicate the actual strength of the contraction. Instead it appears that averaged total Ib afferent traffic can well reflect the variation of force appearing at the muscle tendon (Jami 1992). This fact suggested the information supplied by GTO population in muscles essentially concern the dynamic events in force development.

1.7.3. Motor responses associated with stimulation of GTOs

Conditioning the monosynaptic reflex (H-reflex) by volleys elicited by precisely graded electrical stimulation of muscle nerves is the common method that has been used widely in humans experiments to investigate the responses of various afferent inputs on motoneurones. When motoneurones are facilitated by a conditioning volley, more motoneurone can be recruited from their subliminal fringe by the H reflex inputs. Therefore, The size of the H reflex can represent the excitability of the motoneurones.

On the assumption that group Ib fibres have slightly higher threshold than Ia fibres, the changes in the magnitude of the H-reflex conditioned by graded electrical stimulation of nerves at different intervals were recorded. These changes are plotted against the relative intervals. According to the threshold of the responses and the latencies of the changes in the H reflex magnitude, the recorded responses are attributed to a group of afferents. Since it is accepted that the group Ia afferents have the lowest threshold and the highest velocity pathway, the shortest and lowest threshold response is usually attributed to them. This is usually followed closely by another response that is believed to be from Ib afferents.

Using this method the general function and projections of the Ib spinal circuits in humans seemed similar to that in cats, including inhibition of the homonymous muscles and facilitation of antagonist muscles (Pierrot-Deseilligny, Morin, Bergego and Tankov 1981a, Pierrot-Deseilligny, Katz and Morin 1979).

-Negative force feedback regulation by GTOs

An obvious role of GTOs is to feedback information about muscle activity to the central nervous system. Jami (1992) has argued that the negative feedback (inhibition of the receptor-bearing muscles) would be useful in the control of muscle contraction. It has been suggested that this kind of negative force feedback provide an automatic control device that is turned on by an "error-signal" i.e. GTO discharges.

The difficulty in viewing the reflex circuit as a servomechanism is that this control device is gated and modulated by the descending and ascending inputs. The convergence of different peripheral and central pathways on the interneurone mediating the Ib pathways has been shown by many researchers (Lundberg, Malmgren and Schomburg 1975, Jankowska and McCrea 1983, Harrison, Jankowska and Johannisson 1983, Harrison and Jankowska 1985, Jami 1992). The effect of this convergence would be to modulate the sensitivity of this system according to the requirements. It is believed that negative force feedback tended to hold the force constant in the face of any perturbations.

-Positive force feedback regulation by GTOs

Since the 1950s it has been assumed that force feedback to the spinal cord from GTO afferents causes only reflex inhibition of the receptor-bearing muscles, whereas displacement related feedback from muscle spindles causes excitation. In both cases the reflex mechanism is equivalent to negative feedback since the changes in the sensed variable produces a muscle response that opposes the changes.

Recent evidence suggested that the GTO could also have an "positive force feedback" effect on the receptor-bearing muscles. Most of this evidence is derived from experiments on cats. Pearson and Collins (1993) have shown that Ib afferents from extensor muscles produced an excitatory response in the extensor motoneurones during locomotion. Electrical stimulation of extensor muscle nerves at group I strength during extensor phase of locomotion in cats has been shown to produce widespread enhancement of extensor activity throughout the hind limb. The extensor phase of the step cycle has also elongated after this stimulation. It has been argued that in static functions, Ib afferents generally mediate negative force feedback but in locomotion it switches to a positive feedback action. The fact that Ib afferents have widespread connections to the other muscles implies the importance of these receptors in controlling the co-ordinated activity of the muscles.

The positive force feedback pathways are mostly shown in the extensor muscles in cats (Pratt 1995). Since in the cat these muscles are all active during the load bearing activity such as walking, it is believed that positive force feedback from GTOs can contribute in load compensation.

The evidence about the positive feedback role of GTOs in humans is provided recently (Prochazka Gillard and Bennett 1997b). They stimulated the ankle and wrist muscles by feedback controlled electrical stimulation. The feedback signals were obtained from sensors monitoring the force and displacement. They found that the positive force feedback could help in load compensation. In cybernetic engineering, positive force feedback is generally equated with instability and therefore is avoided in engineering design. In linear systems, if the gain of positive feedback loop exceeds 1, instability occurs. Surprisingly it has been shown that a gain of above 1 does not cause instability in cats (Prochazka, Gillard and Bennett 1997a) and humans (Prochazka et al 1997b). It is shown that even when the loop gain was set at levels 2 or 3, the muscles under positive force feedback remained stable. The authors proposed that during muscle shortening the length-tension relationship cause a sharp reduction in force delivery. Thus even though positive feedback increases the neural derive to the muscle, the intrinsic properties of the muscle ensures stability even the force-related excitation of motoneurones is very large.

It is still not clear which muscles are controlled by the positive force feedback pathways in humans. In cats it is shown that these connections are very strong among the extensor group and enhanced during load bearing tasks (Pratt 1995). In humans, it is more complex. In different loading tasks the different group of muscles are active. During stance the knee extensors are mainly inactive but the ankle plantarflexors are active. During walking, the ankle dorsiflexors and knee extensors show synchronised activity during the loading bearing (stance) phase of the gait cycle. During running, this co-ordinated activity can be seen between the knee extensors and the ankle plantarflexors instead. Therefore, if the positive force feedback is to help in the load compensation in load bearing muscles, a more complex pathway between the muscles is expected in humans. It is also possible that these pathways may switch on/off depending on the requirements of the task.

There have been no direct studies of this idea yet. However there are some proven pathways in humans which resemble the pathways mediating these positive force feedback effects. One of these pathways, which is the main focus of the experiments described in the following chapters, is the excitatory pathway linking the pretibial muscles to the knee extensor muscles.

1.8. Excitatory pathway from ankle dorsiflexors to quadriceps (CPQ reflex)

An excitatory response in Q motoneurones (CPQ reflex) evoked by electrical stimulation of common peroneal nerve (CPN) was first described in 1978 (Bergmans, Delwaide and Gadea-Ciria). This was later supported by the study conducted by Pierrot-Deseilligny et al (1981a). Graded electrical stimulation was used for conditioning the H-reflex. Since the size of the H reflex can represent the excitability of the motoneurones, the changes in the amplitude of the H reflex was plotted against the time delays between the conditioning and the test (H reflex) stimulation. Any inhibitory or excitatory effects on motoneurones resulted from the conditioning volleys can be detected in this way. They showed that electrical stimulation at CPN resulted in an early inhibition followed by an excitatory response. On the assumption that group Ia afferents are faster than Ib afferents, they attributed the early inhibition to Ia afferents and the short latency excitation to Ib afferents.

Similar responses have been reported later using a different technique (Mao, Ashby, Wang and McCrea 1984). They used the post stimulus time histogram of firing in single Q motoneurone in their experiment. Electrical stimulation of CPN evoked facilitation in the majority (76%) of the vastus medialis motor units in their experiment.

In all of these investigations, the later excitation of the Q after stimulation of CPN was attributed to group Ib afferents. The shortest latency response, the inhibition, was attributed to the fastest afferents, the Ia fibres. The slightly longer latency excitation was attributed to the slightly slower Ib fibres.

More evidence supporting Ib afferents as the source of this excitatory response in Q were provided by the study of Brooke and McIlroy (1990a). They found that electrical stimulation of CPN before and after 20 minutes vibration at 80 Hz over the pretibial muscles did not result in a significant attenuation in the reflex magnitude. Prolonged vibration has been proved to increase the electrical threshold of group Ia axons above that of Ib afferents (Coppin et al 1970). Therefore Brooke concluded that group Ib afferents are the most likely to be responsible for this excitatory response in Q.

Whilst the great part of the literature mainly suggests that this reflex pathway is mainly composed of GTO afferents (Pierrot-Deseilligny et al 1981, Mao et al 1984, Brooke and McIlroy 1990), there is a suggestion that group Ia could also contribute. It has been shown that a short train of weak taps on the tibialis anterior tendon produced a short latency excitation of the Q H-reflex (Hultborn et al 1987). Despite the fact that muscle stretch at low amplitudes, provided by tendon tap or vibration, mainly stimulates the muscle spindles, the activation of GTO receptors has also been reported (Lundberg and Winsbury 1960). It has been shown that when muscle stretch was applied to a contracting muscle, the tendon organs become appreciably more sensitive. Tendon vibration to both contracting and non-contracting leg muscles in man has been shown to stimulate GTO receptors (Burke, Hagbarth, Lofstedt and Wallin 1976, Roll, Vedel and Ribot 1989). This means that the result of the tendon tap experiment explained earlier, not only does not contradict the contribution of GTOs but possibly suggests a parallel participation of both muscle spindle and GTO afferents in the CPQ reflex pathway. There are lines of evidence in the literature suggesting the convergence of muscle spindle and Golgi tendon organ afferents onto a shared interneurone (section 1.6.4). Therefore it would not be unusual if both group Ia and Ib afferents share in the pathway of the CPQ reflex. In fact, this parallel Ia-Ib effects are so common that in the recent studies the short latency and low threshold responses are usually referred to by a more general term of "group I" afferents.

Functionally, this possible co-contribution of the spindle and GTO afferents in this reflex pathway implies a difference between the response being evoked by stretch of the foot in a plantarflexion direction or alternatively arising from the muscle force developed in the muscle tendinous junction for the dorsiflexion of the foot. This suggests a task-dependent contribution of each of these receptors and their afferents in the motor activity of Q motoneurones through the CPQ pathway.

This low threshold excitation has been reported in all the heads of quadriceps muscle including vastus medialis (McIlroy and Brooke 1987, Brooke and McIlroy 1990a), vastus lateralis (Forget, Pantieri, Pierrot-Desielligny, Shindo and Tanaka 1989, Simoneta-Moreau et al 1999) and rectus femoris (McIlroy and Brooke 1987). The CPQ reflex is believed to have a threshold in the range of group I afferents that is below motor threshold (0.85×MT reported by Mao, Ashby, Wang and McCrea 1984 and 0.95×MT reported by Brooke and McIlroy, 1990a).

The CPQ reflex is defined as a short latency excitation. This short latency of the reflex indicates the high velocity of the afferents or/and low number of the synapses on its pathway. McIlroy and Brooke (1987) reported an average latency of 26.3ms and 33.5ms for VM and RF respectively. It has been argued that this latency is around 3ms longer than that of the monosynaptic Ia excitation (Forget et al 1989, Chaix, Marque, Meunier, Pierrot-Deseilligny and Simonetta-Moreau 1997). On the basis of this central delay it has been concluded that the pathway of the reflex should be oligosynaptic and the related interneurones are possibly located in the lumbar spinal cord.

The stimulation of the deep peroneal nerve that innervates the pretibial muscles, is shown to be the main source of the fibres responsible for the CPQ reflex. The superficial peroneal nerve, which innervates the peroneal muscles however, is shown to be ineffective in evoking an excitatory response in Q. (Forget et al 1989).

Stimulation at CPN cannot evoke any response in a relaxed Q (see section 4.4.1). It is only present when the Q is active. The magnitude of the reflex is shown to increase with an increase in the strength of activity in Q (McIlroy & Brooke 1987). This strongly suggests that the supraspinal pathways also converge onto the interneurones mediating this reflex to Q motoneurones.

It is reported that by increasing the intensity of the stimulation at CPN, a second excitation will appear with longer latency (Marque, Pierrot-Deseilligny and Simonetta-Moreau 1996). This second peak with higher threshold has latency 4-8 ms longer than the first peak. When they cooled the CPN the increase in the latency was greater for the second peak than for the first one. This indicated that the second peak is evoked by lower velocity axons than group I. They attributed this second excitation to group II afferents. It has been suggested that this group II excitation is evoked primarily from secondary muscle spindle afferents (Simonetta-Moreau et al 1999). They showed that stimulation of the skin close to caput fibulae or sural nerve did not evoke any response in Q motoneurones. This can exclude the contribution of cutaneous group II afferents to this reflex pathway, although contribution from other non-spindle group II afferents cannot be excluded.

These group II afferents are also believed to converge on the same interneurones mediating the group I excitation in the CPQ reflex pathway (Chaix et al 1997). They have shown that a significant negative correlation exists between the early group I and late group II induced facilitation of the Q motoneurones. Their conclusion was based on the fact that a large recruitment of the common interneurones by the group I volley would make them unresponsive to the following group II volley. Therefore both groups of afferents may share common interneurones.

The converging of these afferents (group Ia, Ib, II) and descending pathways onto a common interneurone system (figure 1.4) reflects the importance of this mechanism in control of Q activity. In fact, it has been suggested that these interneurones are part of the pathway that relays the cortical commands to the motoneurones of the thigh muscles (Marchand-Pauvert et al 1999). They have shown that when the transcranial magnetic stimulation (TMS) responses were conditioned by stimuli to the common peroneal nerve, they were modulated by the conditioning volley. The TMS alone produced a motor evoke potentials of 15% of M_{max} while when the CPN stimulation was coincided with the TMS an additional facilitation of maximum 30% of M_{max} on Q motoneurones. The extra facilitation was biphasic, with early and late components peaking when CPN stimulation preceded TMS by 2 and 11 ms, respectively. They concluded that the observed facilitatory interactions between cortical and peripheral volleys are consistent with interactions in a population of lumbar excitatory premotoneurones co-activated by group I and II afferents. The potency of the effects reported in this experiment reflects that a significant part of the cortical excitation to motoneurones of Q muscles is relayed via this indirect pathway. Figure 1.4 shows a schematic feature of the CPQ reflex. The possible contribution of the group Ia, II from muscle spindles and Ib from GTO is shown in this figure. The absence of monosynaptic projection between the pretibial muscles and the Q motoneurones which has been reported (Simonetta-Moreau, Pierrot-Deseilligny and Simonetta 1993, table 1), can also be seen in the figure 1.4.

Few investigations have been conducted concerning the functional role of this reflex in humans. It has been reported that the reflex magnitude increased substantially after heel strike and its magnitude was proportional to the background activity of Q during stance and stance phase of gait at 30ms after heel strike (Brooke, Collins, Boucher and McIlroy 1991).

One of the most interesting facts about the CPQ reflex is the absence of this reflex pathway in cats (Eccles, Eccles and Lundberg 1957) and in baboons (Hongo, Lundberg, Philips and Thompson 1984). This could reflect the possible relationship between this reflex pathway and the functional discrepancies between humans and these species. The unique characteristics of human locomotion could be the case. The plantigrade gait is the unique feature of human locomotion that cannot be seen in any other animal species. This reflex might be developed during the evolution from digitigrade to plantigrade locomotion in humans.

The importance of interaction between primary afferents and central pathways, particularly in the regulation of the CPQ reflex which is unique to humans makes it an interesting area for further investigation. The following chapters describe experimental investigation of the characteristics of this reflex.

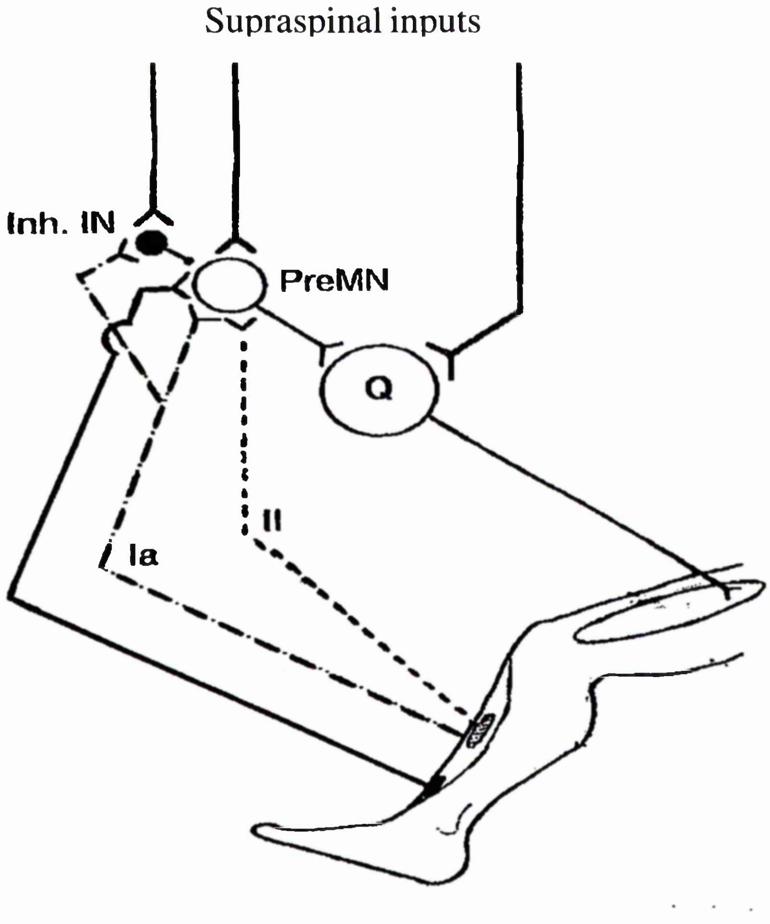

Figure1.4. Diagram showing the possible pathways that participates in the excitatory projection from the ankle dorsiflexors to quadriceps. The convergence of the supraspinal and the possible afferent pathways on the interneurone mediating this reflex can be seen in the diagram.

Chapter 2

Materials and Methods

This chapter provides details of the materials and methods that were common to all experiments. Materials and methods specific to only one experiment will be discussed in the appropriate chapter.

2.1. Subjects

Thirty four volunteer subjects aged between 17 and 47 years were recruited. 22 male and 12 female volunteers were tested. Some of them participated in more than one experiment. All were healthy asymptomatic individuals with no history of any neurological, musculoskeletal or cardiovascular problems. All volunteers were recruited from the University of Glasgow staff and students who had given informed consent to the experimental procedure. They were free to withdraw from the test at any stage. None of the subjects withdrew from any of the experiments neither did they report any kind of discomfort during the tests.

2.2. Electrical Stimulation

A constant current stimulator, DS7A (Digitimer Ltd, Welwyn Garden City, England) was used in all the experiments. Rectangular stimulus pulses of 0.2 millisecond duration were given through monopolar surface electrodes. The maximum voltage of the stimulator was set at 400 Volts. Self-adhering neurostimulation electrodes (PALS/ Nidd Valley Medical Ltd) were used in all the experiments. A photograph of the electrodes can be seen in figure 2.1.

The common peroneal nerve was stimulated by placing a round cathode, 3.2 cm in diameter, on the skin at the level of caput fibulae. A larger rectangular 5 cm×9 cm anode was placed about 2 cm distal to the cathode. The cathode was located to provide optimum stimulation of the deep peroneal nerve. This was done by exploring a range of electrode positions until a position was found where the motor threshold for the muscles innervated by the deep band was lower than the threshold for the muscles innervated by the superficial band. The muscles supplied by the deep branch are tibialis anterior, extensor digitorum, extensor hallucis longus and peroneous tertius. These muscles cause prominent dorsiflexion of the ankle. Stimulation of the superficial peroneal nerve activates the peroneous brevis and longus and causes an eversion of the foot. These two movements could be easily observed or confirmed by palpation of the tendons at the ankle. This separate stimulation of the two branches was preferred since it is suggested that afferents in the deep branch of the nerve provide the afferent limb of the reflex under investigation. In each case the site of the stimulation was chosen such that increasing

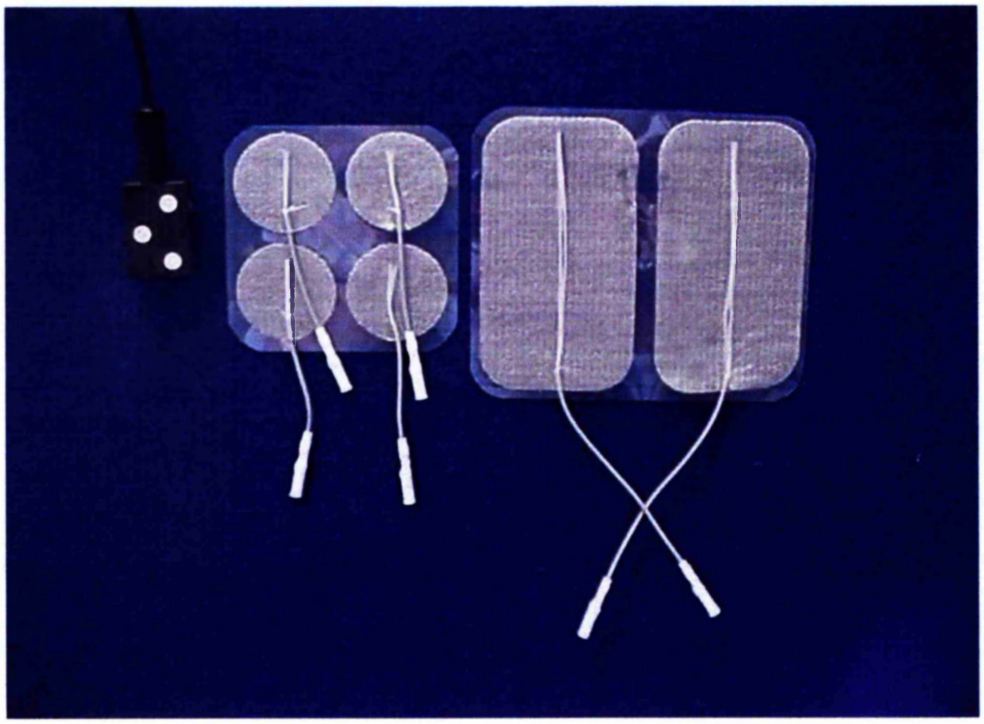

Figure 2.1. The figure shows on the right, two large indifferent electrodes (5cm×9cm), in the middle two smaller active stimulating electrodes (3.2 cm in diameter) and on the left the EMG recording electrodes.

the stimulus strength above motor threshold resulted in a steep increase in the motor response of tibialis anterior.

When the stimulus pulse excites the large diameter motor axons of the motoneurones that supply the anterior tibial muscles, an M wave is elicited. The M wave could clearly be seen in the EMG recording of the tibialis anterior muscle as the first deflection from the base line and only a few milliseconds after the stimulus artefact. Maximum M waves (M_{max}) were evoked from all subjects at different stages of the tests. This was done by increasing the stimulus intensity until the M wave reached its maximum magnitude i.e. the M wave magnitude did not increase with increases in the stimulus intensities. Stimuli at 2×motor threshold (MT) were usually able to elicit M_{max}. The M_{max} and the MT were used to standardise the intensity of the stimulus and also to check the consistency of the stimulation during the experiments. Stimulus intensities in the experiments were expressed as multiples of MT, for example 1.3×MT or as fractions of that required to elicit the M_{max}, for example 40% of M_{max}.

In most experiments the aim was to use stimulation intensities to evoke a maximum reflex magnitude at specific position of the hip and knee joint. This was at 180° position of the knee or 110° of the hip. The effect of a range of stimulus intensities on reflex magnitude is reported in the chapter 4. In general the optimum intensity for eliciting the maximum responses was 1.5×MT or strong enough to evoke M wave above 40% of M_{max} response in tibialis anterior muscles (Brooke and McIlroy 1990 and also see section 4.4.1). The current of electrical stimulation that was used for this purpose ranged between 10 and 20mA. The M wave had a threshold of between 7 and 13mA among the subjects.

During experiments the peak to peak amplitude of the M wave was continuously displayed on a storage oscilloscope. All the stored records had M wave amplitude within 5% of maximum M wave of the pre-selected amplitude. The stimulus intensity was adjusted during the tests to restore the target M wave.

The M threshold (MT) and the M_{max} were likely to change with any movement in the leg. This was because of the change of the position of the electrodes relative to the common peroneal nerve or due to movement of the muscles under the recording electrodes. Therefore, every time the position of the leg was changed, the M_{max} and the M threshold were re-measured. The intensity for the stimulation was recalculated for the new positions from the new M threshold or the new M_{max}. This ensured a consistency of the stimulation during the experiments for all the subjects.

2.2.1. Calibration of the stimulator

The stimulus intensities were expressed as multiples of the motor threshold. Consequently, it is important to know that the stimulator output is linear. This was done by recording the potential difference across a 1kΩ resistor as the stimulator delivered a range of currents. The actual current delivered was calculated using Ohm's law.

Figure 2.2 shows the data obtained. A linear correlation can be seen between the actual output and the selected one on the stimulator. This

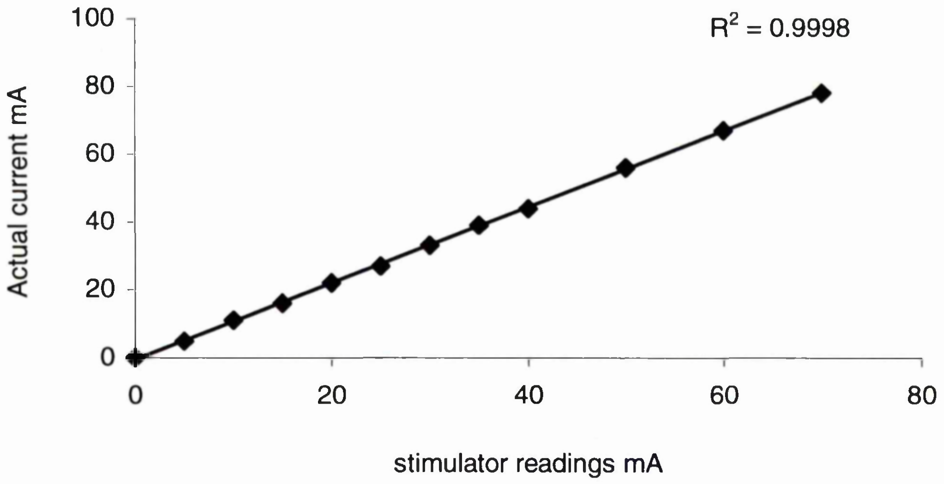

Figure 2.2. The graph shows the correlation between the readings and actual intensities of the stimuli. The obvious linear correlation reflects the reliability of the measured intensities.

means that the intensities, which have been used throughout the experiments, represent the true fractions of the motor threshold.

2.3. Electromyography Recordings

A small skin mounted pre-amplifier with integrated electrodes, measuring 7mm in diameter, was used for recording the electromyography (EMG). This recording configuration eliminated connecting wires and so movement artefacts were kept to a minimum. The EMG electrode with its integrated preamplifier can be seen in figure 2.1. The skin at the recording sites was prepared very carefully before attaching the electrodes. It was shaved and cleaned with alcohol to decrease the impedance. This ensured good signal/noise characteristics. The electrodes were placed over the belly of the target muscles, longitudinal to the predicted path of the muscle fibres. The EMG signals were amplified 1000× by AC-differential amplifier (NL104, Digitimer Ltd, Hertfordshire, England) with a band pass filtering between 10 to 3000 Hz with attenuation beyond cut-off of 40dB/decade.

Figure 2.3 shows the power spectrum of the EMG recorded from rectus femoris during 20% of maximum contraction. It can be clearly seen that the maximum frequency of the potentials was not beyond 300 Hz which means the frequencies which have been selected for the sampling rates and filtering of the EMG were very unlikely to have missed any significant frequency components.

All signals were digitised by CED 1401 Micro interface (CED Ltd, Cambridge, England) at a sampling rate of 1000 Hz and stored in a PC. Spike 2 software version 2.15 was used for processing the EMG recordings throughout the experiments.

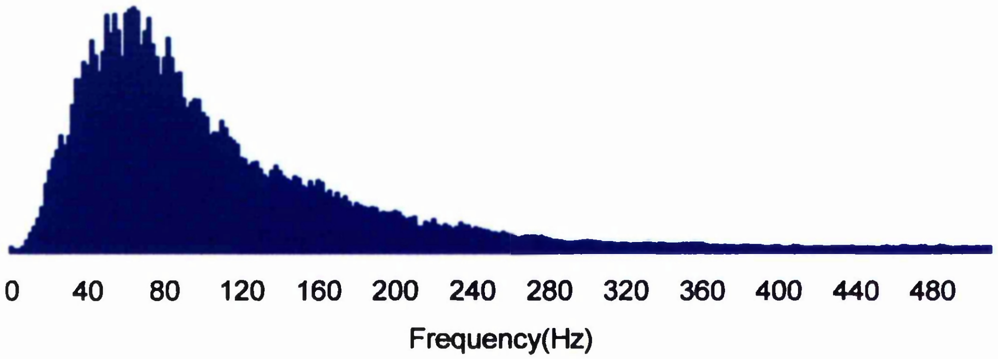

Figure 2.3. The figure shows the power spectrum of EMG recorded from rectus femoris with stimulation of 1.5×MT at common peroneal nerve without any filtration. The frequency of the captured electrical waves ranged between 10 and 300Hz.

EMG from muscles under investigation were digitised and stored continuously. The non-rectified and rectified EMG recordings were then averaged. Peri-stimulus averages of 30 to 50 samples from the digitised data were used to reveal any reflex events which were time-locked to the stimulation. The background EMG represented asynchronous activity of the motor units in the muscles during muscle contraction. The averaged EMGs were used for measuring the characteristics of the responses such as peak to peak amplitude, area, latency and duration of the reflex and also the intensity of muscle contraction at the time of the stimulation.

Figure 2.4 shows the outcome averaging of 10, 20, 30, and 40 samples. The EMG was averaged from the stimulus event points that were recorded on a separate channel. It can be seen that with increasing the number of the samples the ratio of signal to noise increases progressively and the reflex which was hardly observable at 10 repetitions becomes more prominent and statistically significant. The signal/noise ratio improves with the square root of the number of sweeps averaged. Consequently the improvement is rapid at first, e.g. 16 sweeps gives an improvement of 4 but adding an additional 20 to average 36 sweeps gives a smaller benefit as the ratio improves from 4 to 6. This improvement did not justify lengthening the periods of data capture. In addition, with increasing the number of the repetition progressively, there is the risk of muscle fatigue. Therefore the number of 30-50 samples seems to be the best compromise since it gives a reasonable signal/noise ratio without causing muscle fatigue.

However the signal/noise ratio changes with the increased number of repetition, the figure 2.4 shows that the p-p amplitude of the response is the same in all the averages of different repetitions. This reflects

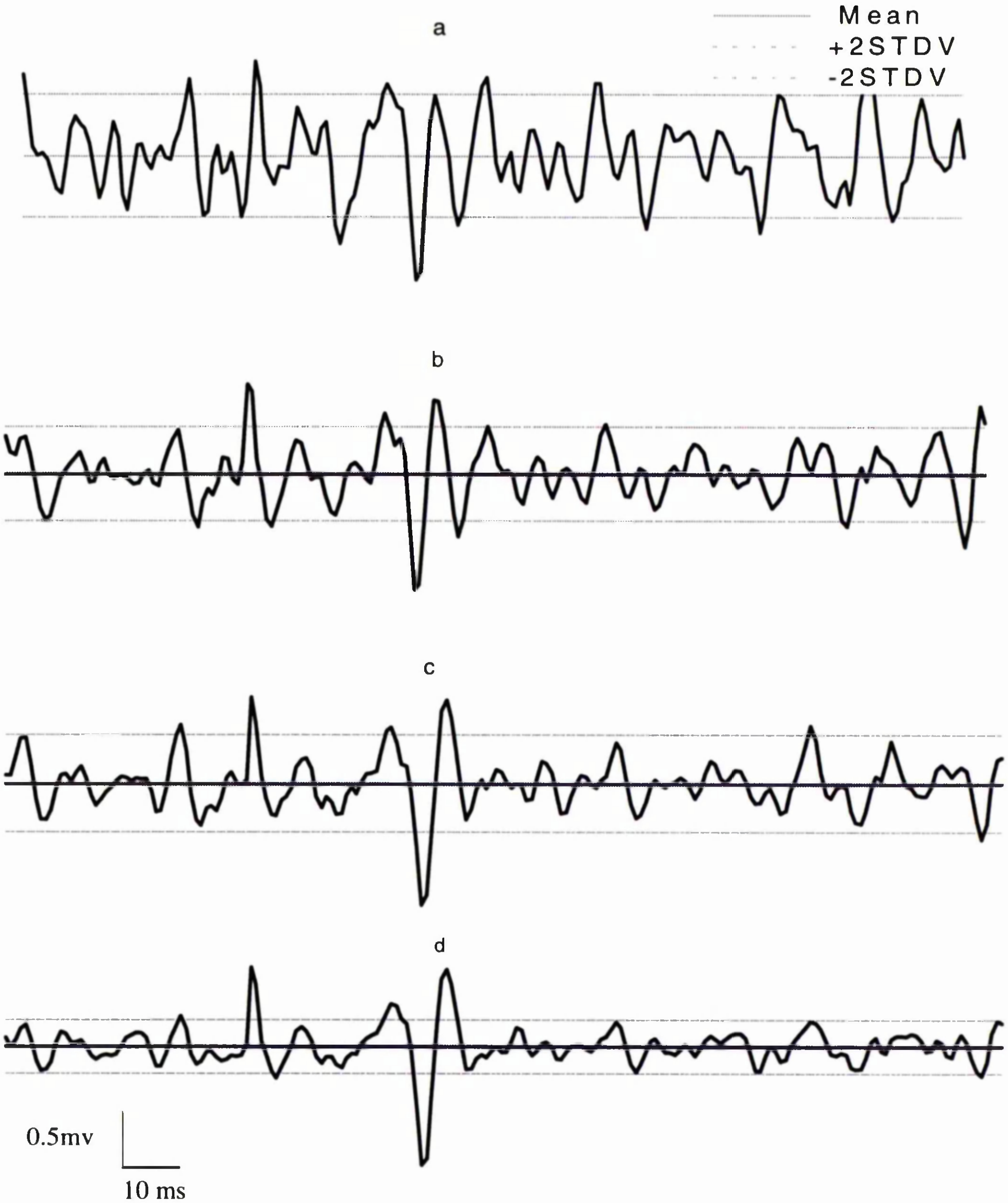

Figure 2.4. The figure shows the averaged EMG of different number of samples (a=10, b=20, c=30 and d=40). The improvement in signal/noise ratio is rapid at first but becomes less effective with higher number of samples. The band of ±2STDV clearly becomes narrower with increase in the number of averaged samples. The p-p amplitude of the reflex does not show any significant changes with increases in the number of repetitions.

that the latency and the shape of the reflex must be very constant. Otherwise, the cancellation of the positive and negative components of the response in repetitive appearance would have changed the amplitude of the reflex. This also reflects that the p-p amplitude of the CPQ reflex that is measured from averaged non-rectified EMG is a good representative of the reflex magnitude.

2.3.1. Recording Positions.

The EMG from tibialis anterior muscle was recorded 2cm lateral to the tibia and about 10-12cm distal to the patella.

Electrodes for rectus femoris muscle were placed 2cm lateral to the midline of the thigh, approximately half way between the iliac crest and the upper border of patella.

Vastus medialis EMG was recorded 3cm medial to the midline of the thigh and 10cm proximal to the patella.

2.4. Analysis

Rectified and non-rectified averaged EMG was analysed. The EMG was first rectified and then averaged to prevent any cancellation of the positive or negative components of the response. This cancellation could happen when the latency or the shape of the response changes from time to time. Since all the components of the

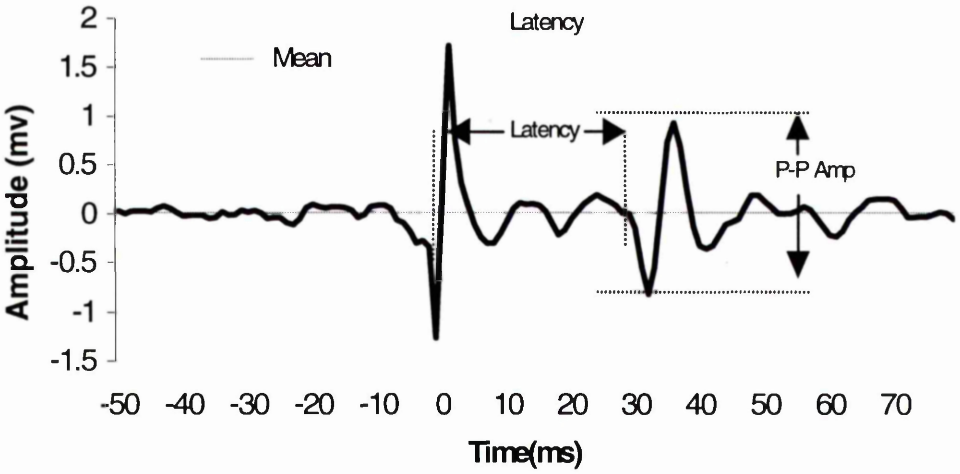

Figure 2.5. The non-rectified averaged EMG from RF muscle. The figure shows the way the p-p amplitude and the latency of the reflex were measured.

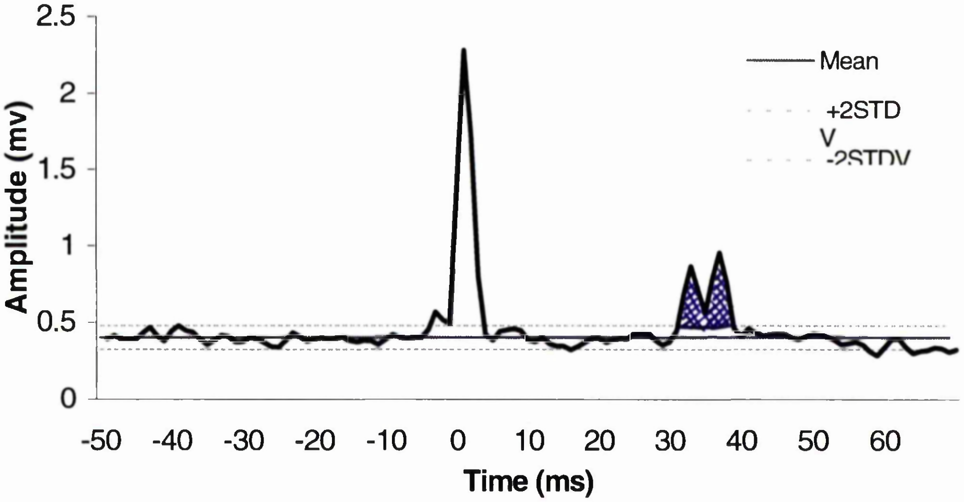

Figure 2.6. Rectified averaged EMG from RF. The EMG was rectified and then averaged for this purpose. The amplitude of the reflex was measured as the area under the rectified EMG curve above the mean EMG line. The duration of the response was measured as the time the EMG exceeded 2 SD above the mean EMG line.

EMG are positive after rectification, averaged of the rectified EMG give a better picture of the real size of the reflex.

Peak to peak amplitudes (p-p amp) were measured from non-rectified averaged EMG and expressed as millivolts or percentage of maximum voluntary contraction (MVC). The consistent shape and latency of the reflex (section 2.3 and chapter 3) ensure that the p-p amplitude of the reflex is also a good reflection of the size of the reflex. A pair of horizontal cursors was used for this measurement. This was provided by the Spike 2 software.

Latency of the responses was measured from non-rectified averaged EMG from the stimulus artefact to the point where the reflexes crossed the mean line. The mean lines were calculated from average of 50ms pre-stimulus non-rectified EMG recordings. The data was translated into a text file and saved as an Excel file. The temporal measurements were done on the Excel files (figure 2.5).

The pre-stimulus period of rectified EMG was also used to work out the 2 standard deviation of the values. Only the reflexes, which were beyond the standard deviation lines, were considered significant statistically.

The magnitude of reflexes was also expressed as the area under the rectified EMG curve. It allowed fair comparison of responses of different amplitude and duration. The area of the reflexes was measured from the section of EMG that the reflex is statistically significant. This made the measurements exclusive to only the part EMG where absolutely related to the evoked responses. The time interval where the EMG exceeded 2 standard deviation lines was selected from the largest response recorded from each subject. Since the latency of the response is mainly related to the conduction velocity of the nerves and is quite constant for each subject, the area of the rectified EMG at this time section is only related to the duration as well as the amplitude of the responses for each subject. The area of the reflexes were measured by first subtracting the rectified averaged EMG values of the above mentioned time section from the mean value and then summing up the subtraction values. This was done on an Excel spread sheet. Figure 2.6 shows the section of the rectified EMG that was used to measure the area of the responses. Since the area of just the significant part of the response was measured and used, the zero area and negative area would represent the insignificant potentials and not necessary the existence of an inhibition.

2.5. Intensity of Muscle Contraction

Intensity of quadriceps femoris contraction was measured from the intensity level of the integrated EMG. EMG was integrated by an EMG integrator module (Neurolog 703, Digitimer ltd) with a time constant of 200ms. The EMG was recorded during 3 successive maximum voluntary contractions, each of 3 seconds duration. In control experiments, contractions of known submaximal forces were made and the EMG recorded. Figure 2.7 shows the correlation between the force and the intensity of integrated EMG.

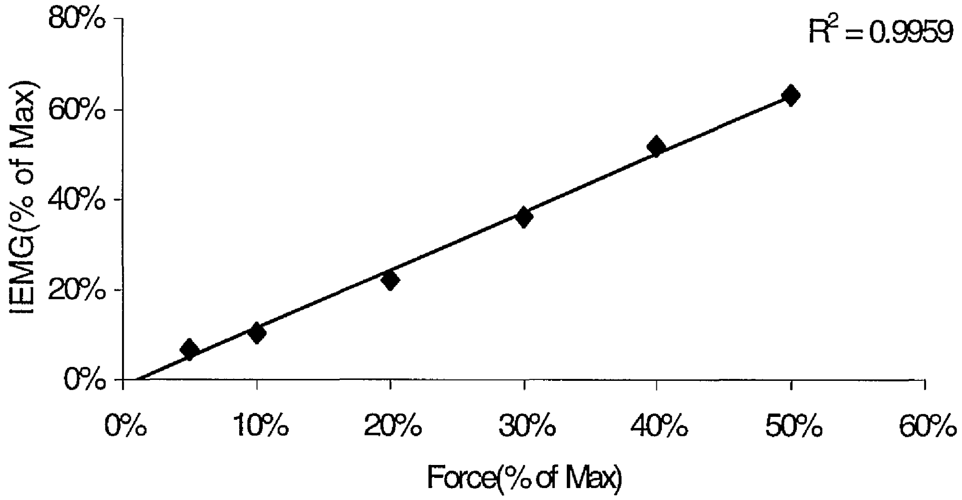

Figure 2.7. The graph shows the correlation between the integrated EMG and the force in RF in one subject.

The linear correlation between the integrated EMG and the force confirm the reliability of this method in reflecting the intensity of muscular contraction.

During the experiments in which subjects walked on the treadmill the intensity of the muscle contraction continuously changed. A different method was used for measuring the intensity of the muscle contraction. The root mean square (RMS) of 30ms section of the rectified averaged EMG around the time of the stimulation was used for this purpose. This will be described in the material and methods section in chapter 5. The MVC was also measured from average RMS of the rectified EMG during three repetitions of maximum contraction. The MVC intensity was used to standardise the contraction intensity level of muscles at the time of stimulation. The level of muscle contraction was expressed as a percentage of maximum voluntary contraction.

During the experiments in chapters 3 & 4, where a constant intensity of muscle contraction were needed, 20% of MVC was used. The level of the integrated EMG was displayed on a storage oscilloscope (figure 2.8). The sweep speed of the oscilloscope was set at high level. The integrated EMG was displayed as a line on the screen. The height of the line on the screen reflected the intensity of the integrated EMG in other words, the intensity of muscle contraction. The subjects were then asked to look at the screen during the test and they were asked to hold a constant level of contraction by keeping the height of the line at the pre-selected level.

2.6. Statistics

Reliability test was used for the first experiments concerning the stability of the CPQ reflex amplitude. An ANOVA test and pairwise comparisons, using the Bonferroni correction, were used to evaluate the significant changes of the reflexes at different joint positions. A paired t-test and correlation coefficient test was also used in different experiments. More information about the statistical analysis applied in each experiment will follow in the relevant chapters.

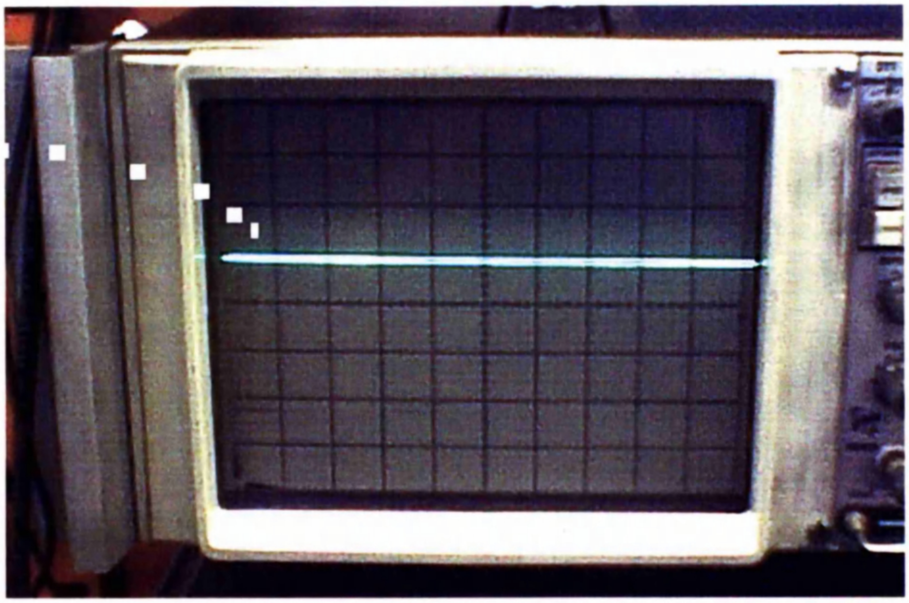

Figure 2.8. The figure shows the system used to feedback the level of muscular activity to the subject. The sweep speed of the screen was set at high level. This produced a line instead of a moving point. The height of the line reflects the intensity of the contraction in RF. The preselected height of 20% MVC was marked on the screen and the subjects was asked to maintain the high of the running line at the selected one.

Chapter 3

Consistency of the CPQ reflex

The activity of skeletal muscles is the result of the action and interactions between the central and peripheral inputs to motoneurones. These ascending and descending projections interact at the level of motoneurones or premotoneurones to produce motor activity in muscles. The basic result of these inputs in motoneurones is inhibitory or excitatory motor responses. In appropriate circumstances these can be recorded in the relevant muscles. Therefore, a method of investigating the participation and the role of these peripheral and central projections on the motor control of a given muscle is to study these motor responses.

The sensory inputs can be evoked by direct stimulation of their receptors or more conveniently by electrical stimulation of their afferent fibres (see section 1.3). The descending inputs can also be evoked by stimulating the cerebral cortex electrically or magnetically.

The H reflex is used widely for the investigation of the normal and abnormal human sensorimotor system. One of the applications of the H reflex is the assessment of the level of excitability of the motoneurone pool. Changes in the magnitude of the H reflex can be attributed to the changes in the excitability of the motoneuronal pool. This may be caused by influences of pathological conditions as in clinical studies or interaction of other neural inputs as in neurophysiological studies. All of these conclusions are based on the assumption that H reflex is a consistent and stable motor response.

Many investigations have been carried on to investigate the best method to decrease the variability of the H reflex. It has been shown that the magnitude of the H reflex in soleus is strongly related to the level of electromyographic activity in the muscle (Funase and Miles 1999). They suggested that the variability in the H reflex amplitude is due to the changes in the level of pre-activation of the motoneuronal pool during repeated trials. This variability was low when the tonic muscular activity during the trial was low (Figure 4, Funase & Miles 1999). They proposed that to obtain the most stable H reflex, tests should be done with a background of low level tonic muscular activity. The H reflex has also been shown to be more reliable during standing than lying (Ali and Sabbahi 2001, Handcock, Williams and Sullivan 2001). Sabbahi & De Luca (1981) have proposed a method to stabilise the H reflex amplitude during experiment. This included a series of conditioning stimuli at threshold level at frequency of 1 pulse/sec for 3 minutes, then lowering the stimulus frequency gradually to 0.5 pulse/sec, and finally to 0.2 pulse/sec, while at the same time reducing the stimulus intensity until an appropriate H reflex amplitude with minimum variability was obtained. They suggested this could stabilise the excitability of the recorded motoneurones and therefore the H reflex. It seems that the level of contraction is more involved in the variability of the H reflex. This is mainly because it works at the level of motoneurone. The changes in the posture however, work at presynaptic level and therefore have smaller effects. All of these efforts emphasise the importance of the stability and reliability of these motor responses in the credibility of the conclusions made in the relative studies.

Electrical stimulation over the common peroneal nerve is shown to produce a strong excitatory motor response in quadriceps muscle (CPQ reflex). This oligosynaptic pathway does not exist in cats (Eccles et al, 1957) and baboons (Hongo et al, 1984) and it appears to be unique in humans. It has also been shown that group I (Ia & Ib) and II afferent fibres and also supraspinal pathways converge on the same interneurone mediating this reflex to Q motoneurones (Marchand-Pauvert et al 1999). These facts suggest an important role for this pathway in the control of Q activity in humans. However, there is no literature describing the reliability of the CPQ reflex. The experiments described in this chapter were conducted to investigate the reliability and consistency of the CPQ reflex in a number of volunteers.

3.1. Materials and Methods

3.1.1. Subjects

Six volunteer subjects were recruited from the University of Glasgow student and staff with the average age of 22 years, height of 174cm and weight of 73kg. They had no neurological or musculoskeletal disorders. The experiment was approved by the local ethical committee.

3.1.2. Electrical stimulation

The method of stimulation has been explained in section 2.2. Single pulse stimuli were applied every 3 seconds at the level of caput fibulae. The location of the stimulating electrodes was marked using a permanent marker to assure similar situation of stimulation in the repeated trials.

Each volunteer attended three experimental sessions on different days. At the start of each session the M-threshold in TA was measured. A constant stimulus intensity of 1.5×MT in tibialis anterior (TA) was used during all recording trials.

3.1.3. Electromyography

The continuous electromyograms of rectus femoris and tibialis anterior were captured during the experiment. The technique of electromyography has been described in section 2.3. The location of the recording electrodes on rectus femoris, were marked with permanent marker which was used for all trials. This ensured that the activity of the same motor units from TA and RF was captured at all trials. The averaged non-rectified EMG from TA and RF was used for measurements of the p-p amplitudes of M wave and CPQ reflex respectively.

3.1.4. Muscular activity

The subjects were asked to hold a constant level of muscular contraction at 20% of MVC in rectus femoris during the test for the consistency of amplitude (see section 2.5). The low intensity of contraction and the short duration of the test was very unlikely to produce any fatigue. None of the subjects complained of fatigue at any time. Different levels of muscular activity in RF were used for the test of threshold consistency. Incremental levels of 5, 10, 15 and 20% of MVC were tested in ascending order in all tests. The test was stopped as soon as the reflex was observed at any of these levels. This was identified as the threshold of the CPQ reflex.

The maximum level of muscular activity in RF was measured from the integrated EMG at the start of each trial. The muscular activity was displayed online to provide a visual feedback for the subjects.

3.1.5. Experiment procedure

The experiment consisted of three sessions and each session included three trials. The interval between the three sessions was ranged between 8 hours and two days. 5 minutes recovery time was allowed between successive trials at each session. The subjects were sitting on a chair with the hip joint at 110° and the knee at 180° during the whole experiment. The control conditions were kept identical with respect to subject position, stimulus and recording configurations. At the start of each trial the maximum voluntary contraction of RF and the threshold of the M wave in TA were measured. The intensity of the stimulation and the levels of desired muscular activity were calculated accordingly.

3.1.6. Statistical analysis

The intra-individual test-retest reliability of the CPQ reflex p-p amplitude and the threshold has been analysed. A multi-correlation test was also performed and the average and the range of coefficients for the whole 9 trials were calculated. The stability of the reflex p-p amplitude is also expressed as the coefficient of variation. This is the standard deviation of the mean divided by the mean amplitude. This was used to normalise the standard deviation for differences in reflex amplitude. This was another approach to assess the stability of the reflex by measuring the amount of variations in the reflex magnitude.

3.2. Results

Electrical stimuli at the intensity of 1.5×MT evoked significant responses in all the subjects in all trials. The p-p amplitude of the responses varied among the subjects. This ranged from 0.046 mv to 0.257 mv with an average of 0.131 ± 70.5 mv in the raw EMG. The calculated values for the p-p amplitude of the CPQ reflex for all the subjects at all the trials are shown in table 3.1. The responses had an average latency of 28.5 ± 4.8 ms.

The CPQ reflex appears to be very consistent in terms of its p-p amplitude and threshold over the whole trials.

		Subject Number					
		1	2	3	4	5	6
Trials	**1**	0.204	0.095	0.221	0.050	0.134	0.102
	2	0.197	0.079	0.222	0.074	0.102	0.074
	3	0.249	0.062	0.207	0.056	0.104	0.075
	4	0.196	0.079	0.200	0.046	0.095	0.083
	5	0.194	0.109	0.237	0.074	0.109	0.089
	6	0.235	0.102	0.231	0.066	0.117	0.097
	7	0.209	0.087	0.249	0.058	0.122	0.076
	8	0.231	0.086	0.219	0.050	0.131	0.111
	9	0.190	0.063	0.257	0.058	0.138	0.097
	mean	0.211	0.085	0.227	0.059	0.117	0.089
	STDV	0.021	0.015	0.018	0.010	0.015	0.013
	Coefficient Variation	0.10	0.18	0.08	0.17	0.13	0.15

Table 3.1. The table shows the individual p-p amplitude of the CPQ reflex in the raw EMG without amplification in each trial during 20% of MVC in RF. The values are in millivolts. The mean and standard deviations of the reflex amplitude is shown at the bottom of the table. The small standard deviation in each column suggests the stability of the reflex magnitude in the trials for each subject. The small coefficient of variations (standard deviation/mean) of the reflex amplitude at the bottom row reflects minor variation of the reflex magnitude in the repeating trials.

3.2.1. The consistency of the reflex amplitude

Measurements of CPQ reflex p-p amplitude were repeated on three sessions and each session included three measurements. The reflex amplitude remained extremely stable in all nine trials and in all subjects. The reliability coefficient was calculated as the measure of stability of the reflex. The reliability coefficient is the proportion of true variability to the total obtained variability i.e. a reliability coefficient of 0.85 means that 85% of the variability in obtained scores could be said to represent true individual differences and 15% of the variability is due to random error. Measurement of reliability is based on a correlation computed between two or more events. The reliability coefficient of all the nine trials for the amplitude of the reflex was 0.994. Multiple correlation test has also been computed and is shown in Table 3.2. It is obvious that the correlation coefficients are extremely robust either for the with-in sessional or inter-sessional measurements and ranged from 0.888 to 0.998. The trial-to-trial variation in the reflex amplitude in each subject is plotted in figure 3.1. The variation in the reflex p-p amplitude was insignificant for all subjects. The coefficient of variation in reflex amplitude was 0.14 for all data and ranged from 0.08 to 0.18 in individuals.

The reflex p-p amplitude of all volunteers was compared by an ANOVA test (repeated measures) with random effects for subjects, sessions and trials. The result of the ANOVA test suggests that only the differences among the subjects reached a significant level ($p \leq 0.0001$). Neither the sessions ($p \leq 0.60$) nor the trials ($p \leq 0.16$) had significant effect on the amplitude of the reflex.

The responses had an average latency of 28.5±2.1ms. The latency remained constant for all the subjects during the experiments. No significant changes were observed in the latency of the reflexes for each subject.

3.2.2. The consistency of the EMG threshold of the CPQ reflex.

The CPQ reflex could not be elicited in a relaxed muscle. The intensity of the RF contraction was progressively increased, in steps of 5%, and the stimuli repeated until the reflex could be seen. This force was described as the force threshold.

The threshold of the CPQ reflex to the activity of RF was different in each subject. During the constant muscular contraction a normal fluctuation of less than 5% of MVC was observed. Therefore it was impossible to investigate the intervals of less than 5% of MVC. The CPQ reflex had thresholds of 5% to 10% of MVC in the subjects. The threshold of the muscular activity for the CPQ reflex was measured at each 3 sessions of experiment. Table 3.3 shows the force threshold in RF that was measured for each subject. The threshold remained absolutely consistent for each subject through the three sessions.

trials	1	2	3	4	5	6	7	8	9
1	1.000								
2	0.952	1.000							
3	0.940	0.956	1.000						
4	0.983	0.977	0.972	1.000					
5	0.956	0.984	0.914	0.972	1.000				
6	0.976	0.979	0.980	0.998	0.970	1.000			
7	0.979	0.990	0.940	0.980	0.988	0.978	1.000		
8	0.987	0.943	0.972	0.986	0.928	0.982	0.956	1.000	
9	0.962	0.952	0.888	0.939	0.945	0.926	0.972	0.999	1.000

Table 3.2. The table shows the range of the correlation coefficients over the 9 trials. The gray cells represent the intra-sessional correlation coefficients. The high correlation coefficients suggests the very high stability of the reflex magnitude in inter and intra-sessional measurements.

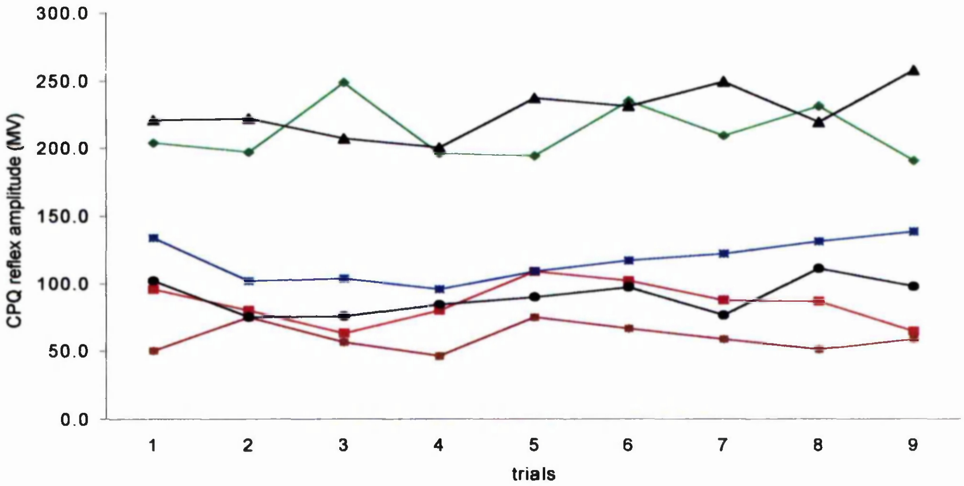

Figure 3.1.The variation of the reflex amplitude at the nine trials. The variation in the reflex magnitude is very insignificant. Each line with different colour represents one of the subjects. The stability of the reflex can be more visualised by comparing the subjects where the ones with higher magnitude remain high at all trials and so does the ones with lower magnitudes.

Sessions	Subjects					
	1	2	3	4	5	6
1	5%	10%	5%	5%	5%	10%
2	5%	10%	5%	5%	5%	10%
3	5%	10%	5%	5%	5%	10%

Table 3.3. The table shows the minimum background contraction, expressed as a percentage of MVC, necessary to reveal a CPQ reflex. Data are shown for 3 experimental sessions in 6 volunteers. In all cases the CPN was stimulated at 1.5 MT and 32 repetitions were averaged. There was no variation in force threshold between sessions.

	Subjects					
Trials	1	2	3	4	5	6
Trial 1	505	420	505	235	455	250
Trial 2	505	420	505	235	455	225
Trial 3	500	420	500	235	455	225
Trial 4	515	380	510	245	450	225
Trial 5	500	380	500	245	450	205
Trial 6	505	380	520	245	450	210
Trial 7	500	380	500	250	450	200
Trial 8	505	380	505	250	450	225
Trial 9	520	380	500	250	450	215

Table 3.4. This table shows the value of the integrated EMG recorded from RF during repeated maximum voluntary contractions in six subjects. Each value is an arbitrary measurement of the product of millivolts.milliseconds. It is accurate to 5 mv.ms The MVC level shows a very small variations over the nine trials ($r=0.99$, $p\leq0.001$).

The maximum voluntary contraction of each subject recorded at the start of each trial showed very little variation. The levels of MVC of RF at each trial can be seen in the table 3.4.

3.3. Discussion and Conclusions

The result demonstrates that, under the conditions of these experiments, the CPQ reflex displays high intra-individual reliability, i.e. it is a stable reflex. The comparisons were made for the results of sessions that were performed at different days (between-session) and also for the trials that were conducted in a same session (with-in session). The high with-in session stability of the reflex reflects the reliability of the CPQ reflex in the physiological studies which were performed in single session. These single session experiments were associated with a constant stimulation and recording situation. The between-session configuration applied in the present experiment is different from the actual conditions exists in the neurophysiological studies. Usually the location of the stimulating and recording electrodes is selected individually in each session of recording. This could result in different result than what is reached in the present experiment by exactly relocating the electrodes at similar locations. As a result, the present experiment cannot exclude the possibility of between-session variations of the reflex when the location of the electrodes was not kept similar. However, by using a constant criterion for locating the electrodes in different sessions, it is very likely to provide a reasonable consistency in the responses. This is important in the clinical neurophysiological studies when these reflexes could be used for inter-individual or day to day basis comparisons. Besides, the criteria that have been used in the present experiment in locating the electrodes would provide a very well matched situation. The stimulating electrodes were located at the point where the M wave, recorded from the TA, showed the highest sensitivity to the changes in the intensity of the stimuli. This would allow consistent electrode location even if the positions had not been marked. Alternatively, since no reflexes were elicited by stimulation of the skin at caput fibulae (section 4.4.1), a relatively large cathode can be used. This would cover the common peroneal nerve completely to make a constant stimulating condition. Small changes in the location of the larger electrode that could happen in different sessions would then have minimum effects on the recordings. Nevertheless, the importance of constant stimulating conditions underscores the higher reliability of the results provided from with-in session comparisons of the CPQ reflex compared to the between-session comparisons.

In the following chapters all the experiments included measurements that were provided from single session recordings of each subject. This means that constant stimulating and recording situations existed in all the following experiments. The extremely high within-sessional stability of the CPQ reflex support the conclusions that any changes detected in the reflex amplitude in these experiments must be of reasons other than the fluctuation of the CPQ reflex amplitude.

Chapter 4

Modulation of the CPQ reflex by knee position

4.1.Introduction, Literature Review and Aims

The motor activity in muscles is the result of the interaction between central and peripheral inputs (Dietz 1997). Afferent information from a variety of sources within the visual, vestibular and proprioceptive systems contribute toward the overall control. The present belief is that the convergence of the spinal reflex pathways and descending tracks onto common spinal interneurones could provide the site for this interaction process (Dietz 1997, Schomburg 1990).

It has been shown that motoneurones supplying the human forearm muscles receive a substantial disynaptic corticospinal excitation, which is mediated by premotoneurones located in the cervical region and act in parallel with the monosynaptic component (Marchand-Pauvert et al 1998). It seems that proximal and distal muscles receive different proportions of monosynaptic and non-monosynaptic corticospinal excitatory projections. In the monkey (Jankowska, Padel and Tanaka 1975) and in man (Brouwer and Ashby 1992) it has been shown that monosynaptic corticospinal projections are significantly smaller on motoneurones of thigh muscles than on motoneurones of more distal muscles. Therefore, one might expect an even greater part of the cortical commands to Q motoneurones to be transmitted through premotoneurones. It has also been shown that the lumbar premotoneurone system is involved in mediating part of the cortical commands to Q motoneurones (Marchand-Pauvert et al 1999). It is argued that a significant part of the cortical excitation to motoneurones of the thigh muscles in humans is relayed via these interneurones. These premotoneurones are also thought to be under influence of the group I and II afferent inputs (Marchand-Pauvert et al 1999). The very large induced extra facilitation of the motor evoked potential in Q by combined stimulation of CPN, indicates that the a great proportion of the cortical commands to Q motoneurones is relayed through interneurones co-activated by group I and II afferents from CPN.

The convergence of the spinal reflex pathways and descending tracts onto common spinal interneurones provides an appropriate site for interaction between these inputs (Dietz 1997, Schomburg 1990). This interaction is required for the modification of the motor activity to meet the demands of the external requirements. The afferent information influences the cortical inputs and the descending projections could also modulate the afferent inputs. This modulation of the peripheral inputs can be provided by the changes in their reflex gain (Jankowska 1992). The modulation of the reflex gain is not only provided by the central systems. Recently it has been found that the reflex can also be modulated by the peripheral pathways inputs. This modulation is referred to as "sensori-sensory modulation" (Brooke, Cheng, Collins, McIlroy, Misiaszek and Staines 1997). The best known example of this sensori-sensory modulation is of the H reflex in muscles of the lower limb in humans (Misiaszek, Cheng, Brooke and Steins 1998, Cheng, Brooke, Misiaszek and Staines 1995, Staines, Brooke and Misiaszek 1997a, Brooke, Cheng, Misiaszek and

Lafferty 1995). Movement-sensitive afferents of the knee joint can modulate the H reflex gain in soleus, (Brooke, McIlroy, Collins and Misiaszek 1995) tibialis anterior, (Brooke McIlroy, Miklic, Staines, Misiaszek, Peritore and Angerilli 1997) and quadriceps femoris (Dietz et al 1990). It is also believed that the central modulatory effect on the H reflex pathway is responsible for the attenuation of this reflex during locomotion (Staines, Brooke, Cheng, Misiaszek and MacKay 1997b).

It has been shown that in humans, group I and II afferents from the pretibial muscles are linked to the Q motoneurones through an excitatory, short latency pathway. The short latency of this pathway suggests that it might have an important role in motor control of Q muscles. It is an oligosynaptic pathway where the convergence of these afferents and the corticospinal projections are similar to the interneurone system described by Marchand-Pauvert et al 1999. Its functional role in motor control of the knee extensors is still under debate. The first stage would be the investigation of the characteristics of this afferent pathway and also the modulation of this reflex imposed by central or peripheral inputs. This chapter describes the experiments conducted to investigate the characteristics of the CPQ reflex and the modulation of the CPQ reflex by the changes in the position of the knee and hip joints.

4.1.1. The receptors sensitive to the joint movement

Joint movements or changes in the position stimulate receptors from different origins. These receptors are often referred to as the mechanoreceptors. These mechanoreceptors are located within the skin, in the musculotendinous unit and within the joint ligaments and capsule. Receptors in muscles (McCloskey 1987), joint capsule and ligaments (Ferrell, Gandevia and McCloskey 1987), and skin (Edin, Abbs 1991) are able to signal the movements of the joints to the CNS in humans.

A- Muscle Spindles

The structure and the innervation of the muscle spindles have been described in detail in section 1.6.1 and 1.6.2.

-The role of muscle spindles in proprioception

Joint movements are associated with stretch of a group of muscles and shortening of the antagonist group of muscles. Using a ramp and hold stretch, there is a rapid increase in the frequency of firing in the primary Ia afferents originating on the bag fibres. During the hold phase, when the spindle is at a constant length the rate of firing decreases. Bag fibres are said to accommodate to the stretch and therefore act as indicators of rate of changes (Cooper 1961).

The chain fibres behave in a more elastic fashion and give a sustained high frequency response during the hold phase (Cooper 1959). This signal is mainly from the secondary ending (group II afferents) but there are also primary afferents on the chain fibres so that the signal in the type Ia afferents may be a mixture of the responses from both types of intrafusal fibres. Since the main stimulus for the receptors is the muscle stretch these receptors are usually referred to as stretch receptors. Any movement in the body is accompanied by stretch of a group of muscles therefore it is believed that these receptors are the main ones to signal the movements (Ciscar and Roll 1998).

It is known that the changes in the spindle discharge rate initiated by the stretch of the muscle during to the movement could signal the direction and the velocity of the movement. The static information about the joint position is believed to be signalled by the nuclear bag fibres and the phasic movement of the joints is mainly included the nuclear chain fibres. Thus the primary endings respond to both changes in the length and the rate of the stretch whereas the secondary endings are just responsive to the changes in the length of the muscle (Ganong 1995).

Ciscar & Roll (1998) has argued the role of antagonist muscle receptors in coding the joint movement velocity and direction. It has been shown that in humans, the direction of a slow movement may be specified in the contrast of the spindle discharge rate, which is greater in the stretched than shortened muscle and that the velocity of this movement might be correlated with the difference between the spindle activity occurring in the agonist and antagonist muscles. This idea that the stretch receptors of both agonist and antagonist muscle groups participate in coding the joint movements is supported by other investigations (Gilhodes, Roll and Tardy-Gervert 1986, Gandevia et al 1983, Roll et al 1989).

B- Joint receptors

-Structure

Four types of endings are associated with the synovial joints of the body (Boyd 1954, McCarry 1965);

a) Free nerve endings, which are the most numerous types of joint receptors, are found throughout the connective tissue.

b) Golgi endings similar to tendon organs are found in the joint ligaments.

c) Ruffini endings are found in the joint capsule

d) Pacini-like corpuscles also have been described in the joint capsule.

There are no nerve endings on the cartilaginous surfaces of the joint or in the synovial membrane (Boyd 1954).

-Innervation

Golgi endings are innervated by large diameter group I fibres, Ruffini endings by slightly smaller group II fibres and free endings by group III/IV nerves.

-The role of joint receptors in proprioception

The majority of joint receptors show no response to joint angles in the mid-range and only fire more vigorously towards the extremes of the knee joint rotation in cats (Burgess and Clark 1969) and dogs

(Ferrell, Nade and Newbold 1986). Intracapsular anaesthesia has shown that has no significant effect on the knee kinaesthesia (Clark, Burgess, Chapin and Lipsocomb 1985). Therefore it is difficult to see the role, if any, they could play in signalling static positions of the joints. At joint positions where no stress is placed on the capsule, the receptors remain silent. It is believed that joint receptors serve to indicate extremes of joint rotation, presumably with some protective function (Gandevia and Burke 1992).

Despite their inconsistent activity through the range of movement of joints, these receptors are not excluded completely. There is evidence suggesting that some of our conscious appreciation of joint position can be provided by these receptors. Ferrell et al (1987) showed that by disengaging the tendons of the distal interphalangeal joint of the middle finger, imposed movement could still be detected, although much less accurately than usual. They also showed that injection of plasma into the joint space enhanced the proprioception and injection of local anaesthetics degraded it. On these grounds, they proposed that the discharge of joint receptors under normal conditions could produce perceived signals of joint movement that duplicate the kinaesthetic input from muscle spindle endings. It appears that their role in proprioception is dominated by the muscle stretch receptors (Ferrell et al 1987).

C- Cutaneous Mechanoreceptors

Based on the rate of adaptation to sustained stimulation and the size of the receptive field the skin receptors are divided into four main groups (Knibestol &Vallbo 1970, Knibestol 1973 and Johansson 1976); FAI (fast adapting type I) and SAI (slowly adapting type I) units have small receptive fields. These two types of receptors are very sensitive to mechanical stimulation.

FAII (fast adapting type II) and SAII (slowly adapting type II) respond to stimuli applied over a large area. They respond particularly well to the stretch of the skin and have a directional sensitivity, increasing their discharge to stretch in one direction and decreasing or not responding to stretch in the opposite direction.

-The role of cutaneous mechanoreceptors in proprioception

The role of cutaneous mechanoreceptors is well established in the perception of finger movement (Matthews 1988, Edin & Abbs 1991, Edin 1992, Collins and Prochazka 1996).

Edin & Abbs (1991) reported that a large majority of the mechanoreceptors on the back of the hand are activated by movement at nearby joints. Slowly adapting skin afferents from the dorsum of the hand display static (Edin 1992) and a dynamic (Grill and Hallet 1995) position sensitivity for movements at the metacarpophalangeal joints. Collins & Prochazka (1996) showed that electrical stimulation of the back of the hand induced movement illusion.

The fact that the main task of the fingers is associated with touching may explain the major role of these receptors in proprioception of the fingers in humans. There is less known about the role of these receptors in the other larger joints. Edin (2001) showed that all afferents from fast and slowly adapting low threshold mechanoreceptors recorded from lateral cutaneous femoral nerve responded to manually applied skin stretch. He suggested that in particular slowly adapting afferents effectively encode both static and dynamic aspects of passively imposed knee joint movements. It was concluded that receptors in the hairy skin of human could provide high-fidelity information about knee joint movements.

In summary, the relative participation of cutaneous, joint and muscle receptors in the sense of limb position depend upon the segment of body and on whether the sense of position or movement is tested.

4.1.2. Modulation of peripheral reflexes

The motor activity in the muscles is the outcome of integration of central programs and reflexes from various sources. The gain of reflexes may be altered to provide the requirements for specific tasks (Prochazka 1989). The reflex excitability can be modulated in two ways; at premotoneurone level or at postsynaptic level.

A- Modulation at motoneurone level

The modulation of peripheral reflexes could occur at the level of motoneurones by excitation or inhibition of the motoneurone membrane. This type of modulation is often characterised by a strong relationship between the level of muscular activity and the magnitude of the reflex (Capaday and Stein 1989, Matthews 1986). Capaday and Stein (1989) showed that a tonic level of postsynaptic inhibition did not affect the amplitude of the monosynaptic reflex response independently of the level of the motor output. They showed that the H reflex was abolished completely by postsynaptic inhibitory influence at rest and reappeared again at almost the same magnitude as the control values during the muscle contraction. Therefore, the level of the contraction affected the intensity of inhibition. Although this is mainly described for H reflex, based on the described physiological definition, non-monosynaptic reflexes must also follow the same rule.

B- Modulation at pre-motoneurone level

In the case of monosynaptic reflexes, this type of modulation is generally referred to as presynaptic. However, in non-monosynaptic reflexes the modulation can occur at any level before the motoneurones membrane. Therefore the term "pre-motoneurone modulation" is a better description. This modulation can be post or presynaptic in nature. It can modulate the reflex amplitude without changing the excitability of the motoneurones. Therefore, the reflex modulation can be partially or wholly independent of the contractile state of the muscle (Crenna and Frigo 1987). In other words, the reflex modulation remains the same at all levels of motor activity.

4.2. Aims

The two experiments conducted in this chapter were designed to address the following aims:

a- To investigate the general characteristics of the reflex linking the ankle dorsiflexor to the Q motoneurones.

b- To find out if knee position could modulate the reflex gain.

c- To explore the mechanisms of this modulation, the correlation between the reflex magnitude and the level of background activity shall be tested at two different knee positions.

4.3. Material and methods

4.3.1.Subjects

The experiments were carried out on 19 healthy volunteer subjects, of whom 7 were female and 12 male. 14 volunteers took part in the first series of experiments and 7 in the second experiments. Two subjects participated in both experiments. Table 4.1 shows details of the ages, heights and weights of the volunteers.

Position of the subjects

- First series of experiments

The subjects were seated in a chair with an adjustable backrest. The right hip was at 100° with the thigh strapped to the chair. The subject's right foot rested on an adjustable footplate in slight plantarflexion at 110°. The left leg hung freely. The footplate was secured to a moving crank attached to the chair. The hinge of the moving crank was adjusted to align it with the axis of rotation of the knee joint. A frame was attached to the chair and provided a solid base for fixing the moving crank at different angles. This is illustrated in figure 4.1. When appropriate, the extended position of the hip joint was achieved by laying down the backrest to the flat position.

Subjects	**Age(year)**	**Height(cm)**	**Weight(kg)**	**Gender**
1	26	167	54	f
2	21	172	74	m
3	24	169	68	f
4	23	180	85	m
5	21	195	102	m
6	21	175	76	f
7	21	173	72	f
8	47	188	80	m
9	38	185	85	m
10	30	168	60	f
11	38	185	78	m
12	38	183	92	m
13	35	175	65	m
14	22	168	58	f
15	34	171	102	m
16	38	174	76	m
17	33	170	65	m
18	32	172	74	m
19	25	162	52	f
Mean	**31**	**175**	**74**	
Stdv	**8**	**9**	**14**	

Table 4.1. The table contains information about the weight, height and ages of the subjects participated in the experiments.

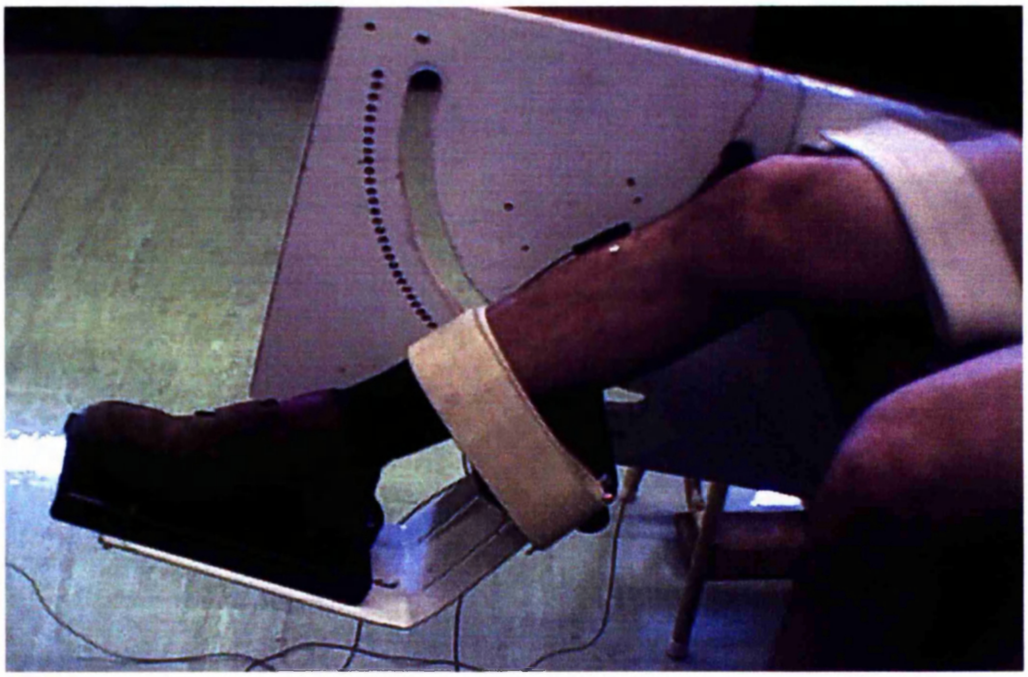

Figure 4.1. The figure shows the system that was designed to provide a range of knee positions during the experiment. The right thigh, leg and foot were secured by straps. The hinge of the crank is adjusted to align the axis of rotation of the right knee. Different positions of the knee joint were obtained by moving the crank. At each selected angle the crank was secured firmly to the board showed in the figure. The footrest and the pad behind the leg were attached to a rigid frame which was free to rotate around its attachment to the crank. This ensured a constant position of the ankle independent of the knee position.

- Second series of experiments

An isokinetic dynamometer (Kin-Com, Chattecx Corporation, Chattanooga) was used for this experiment. The subjects were seated on the chair with their hip at about 100° and the ankle left free. The right leg was secured to the rotating crank of the machine above the ankle joint by a strap. The thigh was also fixed to the chair by a strap. The seat height and position was adjusted to align with the axis of rotation of the subject's knee. The machine provided variable positions of the moving crank for the experiment. This is shown in figure 4.2.

4.3.2. Electrical Stimulation

Stimulation Intensity

Single pulses of 200μs duration were delivered through monopolar surface electrodes at 0.5Hz. The cathode was applied to the common peroneal nerve at caput fibulae.

In the first series of experiments, the threshold for evoking an M wave in TA was established by observation of the TA EMG during graded stimulation at each knee position. The stimulus intensities used during the experiment were expressed as multiples of the threshold intensity for the motor response (×MT).

In the second experiment, the maximum M wave was evoked by supra maximal stimulation of the CPN at each investigated knee position. The intensity of the stimulus was then adjusted to evoke the

Figure 4.2. The figure shows how the Kin Com dynamometer is used to investigate the correlation between the intensity of the background muscular activity and the magnitude of the reflex when the knee was in flexed and extended position.

M wave with an amplitude of above 40% of the M_{max} in TA. This is described in greater detail in section 2.2.

In both experiments, the magnitude of the M wave, recorded from TA, was used as a measure of the stimulus constancy. The peak to peak M wave amplitude was recorded and also displayed on an oscilloscope. The stimulus intensity was adjusted, if needed, to maintain a near constant amplitude.

In the first phase of the first experiments, incremental stimulation intensities of 0.1×MT from 0.9 to 1.5×MT were applied during the test. During the second phase, intensity of 1.5MT in TA was used for stimulation. This intensity was selected according to the result of the first phase, which suggested that at this intensity the maximum magnitude of the CPQ reflex was likely to be achieved.

In experiments performed to investigate the effects of cutaneous stimulation, the skin over the caput fibulae was stimulated with two rectangular electrodes measuring 5cm×9cm. The cathode was applied exactly over the area used for stimulating the CPN for each subject. The anode was placed 2 cm distal to it on the lateral side of the shin. The intensity of the stimulation was adjusted to evoke the same cutaneous sensation as the stimulation of CPN. The feedback from the subjects was used for adjusting the intensity of the stimulation.

The tibial nerve was stimulated with monopolar surface electrodes as the CPN stimulation. The cathode of 3.2cm in diameter placed at the popliteal fossa and the rectangular anode of 5cm×9cm in front of the knee. Stimulus intensity of 1.5 and 2×MT in medial gastrocnemious was delivered to the tibial nerve.

4.3.3. Electromyography Recordings

Surface EMGs were recorded from TA and RF of the right leg of the subjects in the first experiments. Vastus medialis EMG was also recorded during the second experiments. The total duration of 60 seconds was recorded for each set of test except for the contraction intensities of 30% and 40%MVC in the second experiments when the total of 40 seconds (allowing for 20 stimuli) were recorded. Figure 2.3 shows a sample of raw recordings from one of the subjects in the second series of experiments. The detail about the technique of electromyography is described in section 2.3.

4.3.4. Triggering

A period generator (NL 303, Digitimer Ltd., Hertfordshire, England) was used to produce the trigger pulses. It was adjusted to produce a trigger pulse every 2 seconds. The output of the pulse generator was used to trigger the stimulator and the oscilloscope. It also served as a synchronisation signal for the 1401. The time of the trigger was stored as an event channel and recorded in the computer along with the EMG recordings during the test. The trigger data were used for averaging the EMG recording. A sample of EMG recording is shown in figure 4.3.

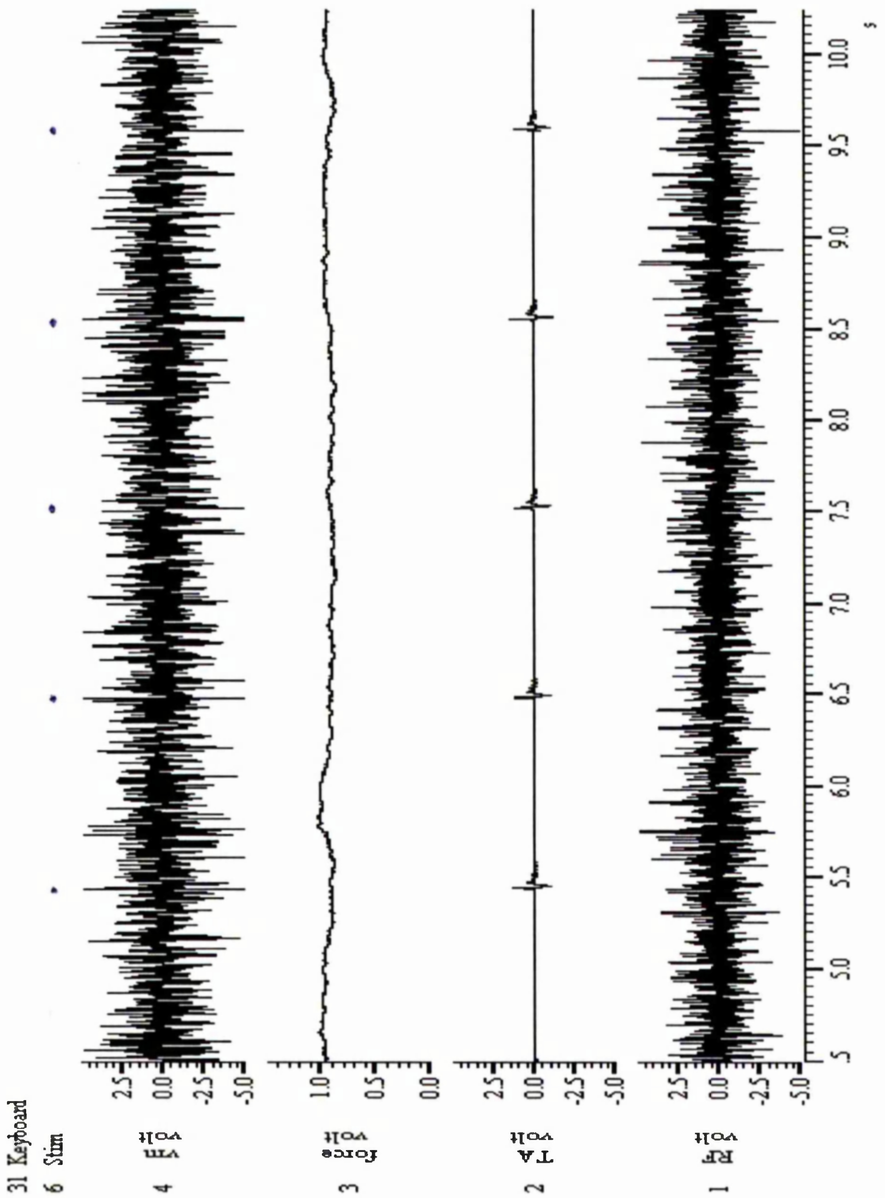

Figure 4.3. The figure shows a sample of raw data. The recording was made with the Q contracting voluntarily at 20% of MVC in RF and with the knee at 180°. Channel 3 shows the output of a NL703 (Digitimer Ltd) which integrated EMG from RF with a time constant of 200 msec.. The small variations in integrated EMG reflect a near constant level of contraction. Channel 6 (stim) shows multiple points exactly at the time of the stimulation that was used later for averaging the EMG recordings. Channels 1, 2, and 4 represent the recordings from RF, TA and VM respectively.

4.3.5. Voluntary contraction

The rectified integrated EMG was recorded during three maximum voluntary contractions for each subject. Each contraction lasted for 3 seconds. In the second series of experiments this was done in both flexed and extended positions of the knee joint. The integrated EMG of RF was used for measuring and adjusting the level of the muscle activity during the experiments. The desired level of integrated EMG was calculated and displayed on an oscilloscope in front of the subjects.

During the first series of experiments voluntary contraction of 20% of MVC was maintained by the subjects. The level for 20% of the MVC was marked on the screen to help the subjects. A short practice period was given to subjects to familiarise themselves with the task of maintaining a constant EMG. None of the subjects reported muscle fatigue or discomfort at this intensity of contraction during the tests.

During the second series of experiments different levels of EMG intensities were tested. This was done for 0%(relaxed muscle), 5%, 10%, 20%, 30%, 40% of MVC at 180° and 130° knee positions. The duration for the recording of the data at the intensities of 30% and 40% of MVC was shortened to prevent muscle fatigue. 40 seconds of recording was captured for these intensities instead of 60 seconds duration recorded for the other intensities.

4.3.6. Experimental procedure

First series of experiments

Graded stimuli were applied to the CPN with the knee joint at 180°. The intensities from 0.9×MT to 1.5×MT with intervals of 0.1×MT were used for each subject. Different knee positions were tested in the second phase of this experiment. 6 positions were tested for each subject from 180° to 130° with an interval of 10°. At each position, one minute of EMG was captured from RF muscle. The stimulus intensity of 1.5×MT was applied at all positions. The M threshold was measured at each knee position and the stimulus intensity corresponding to 1.5×MT was recalculated. This ensured consistent stimulation at all knee positions. The evoked M wave in TA displayed on an oscilloscope. Fine adjustments were made online to maintain a constant magnitude of the M wave during the test.

In another part of the experiment, carried out in another session, 10 subjects participated to explore the effect of the hip position on the reflex. Two hip positions of 110° and 180° were tested for each subject while the knee joint was fixed at 180°. The stimulus intensity of 1.5×MT was used to elicit the maximum magnitude of the reflex in RF.

During both sessions of experiment the subjects contracted the RF muscle at a constant level of 20% of MVC. The MVC was measured at first with the knee at 180° by the same method described earlier.

Second series of experiments

Different intensity levels of muscular activity at two knee positions of extended (180^o) and flexed (130^o) were tested in this experiment. Muscular activity of 0% to about 40% of MVC in RF was employed. The MVC was measured for each knee position separately. The target levels of muscular activity were marked by cursors on the screen. The subjects used these markers to adjust the level of their muscular activity to the desired level.

The stimulus intensity was adjusted to evoke an M wave in TA with an amplitude >40% of M_{max}. The M_{max} for both knee positions was measured at the start of recordings for each position. The M wave was displayed continuously on an oscilloscope to permit fine adjustment to the stimulus intensity if needed.

4.3.7. Measurement of the knee positions

Accurate measurement of the knee position was very important in the first experiments. A goniometer was used for measuring the angle of the knee. While the subject was standing a line was drawn from the greater trochanter of the femur to the lateral malleolus of the right leg. The position of the knee at 180^o was defined as the position when the line crosses anterior to the head of fibulae. At this position, two short lines were drawn on the thigh and shin of the subject. These lines were used to align the goniometer cranks later in the experiment. The centre of rotation of the knee was assumed to be the point where the two lines crossed at the lateral epicondyle of the femur. This point was used to locate the centre of the goniometer during the measurements. For each knee position investigated in the first and second series of experiments, the position of the knee was carefully measured by this method.

4.3.8. Analysis

The peak to peak amplitude and the area of the reflexes in RF were measured in the first series of experiments. The methods of these measurements are described in section 2.4. Since in this experiment the relative changes in the reflex magnitude was the main target, the magnitude of the reflex was normalised to the maximum values measured for each subject. When different intensities of stimulus were tested, the maximum amplitude and area of the response were used for normalisation. When the knee position changes were tested, the reflex measurement at 180^{0} of the knee, where it was usually at maximum, was used and the other values were expressed as the percentage of the reflex magnitude at 180^{0}. The magnitude of the reflex at the extended position of the hip was expressed as the percentage of the reflex magnitude at the flexed position where the maximum reflex was usually evoked.

In the second series of experiments only the peak to peak amplitude of the reflex in RF and VM was measured for both knee positions. When no significant reflex was detected, the peak to peak amplitude of the background EMG at the expected time for the reflex was used. The values measured in this way were standardised using the MVC the magnitude of the reflexes was expressed as the percentage of the MVC.

4.3.9. Statistics

An ANOVA test was used to explore the significance of changes in the reflex magnitude at different knee and hip positions. Pairwise comparisons between the reflex magnitude at all knee positions were done using the Bonferroni test. Difference between the mean was considered significant at a level of $p \leq 0.05$.

In the second series of experiments the correlation co-efficient between the p-p amplitude of the reflex and the intensity of the background EMG was calculated.

4.4. Results

4.4.1. First series of experiments

The effect of increasing the stimulus intensity on the reflex magnitude

Stimulation of CPN at caput fibulae at intensities from 0.9 to 1.5×MT resulted in incremental changes in the reflex magnitude recorded from RF. Figure 4.4 (A) shows the averaged rectified EMG at all the stimulation intensities in one of the volunteers. This was recorded with RF contracted at 20% of MVC. Stimuli between 1-1.3×MT still show clear CPQ reflexes with significant amplitude. The alignment of traces also suggests that a small CPQ reflex is developing at 0.9×MT however it is not statistically significant.

The stimulation at 1.5×MT was unable to produce a significant reflex in relaxed RF. Figure 4.4 (B) shows the averaged rectified EMG in relaxed RF with the stimulus intensity of 1.5×MT applied to the CPN. It can be clearly seen that in the relaxed RF no response is elicited compared to the very significant one when the muscle was contracted at 20% of MVC.

The responses had a biphasic shape with an averaged latency of 29.4ms ± 2.2ms (mean ± 1SD) and average duration of 15.7 ± 2.1ms. The peak to peak amplitude of the recorded reflexes at stimulus

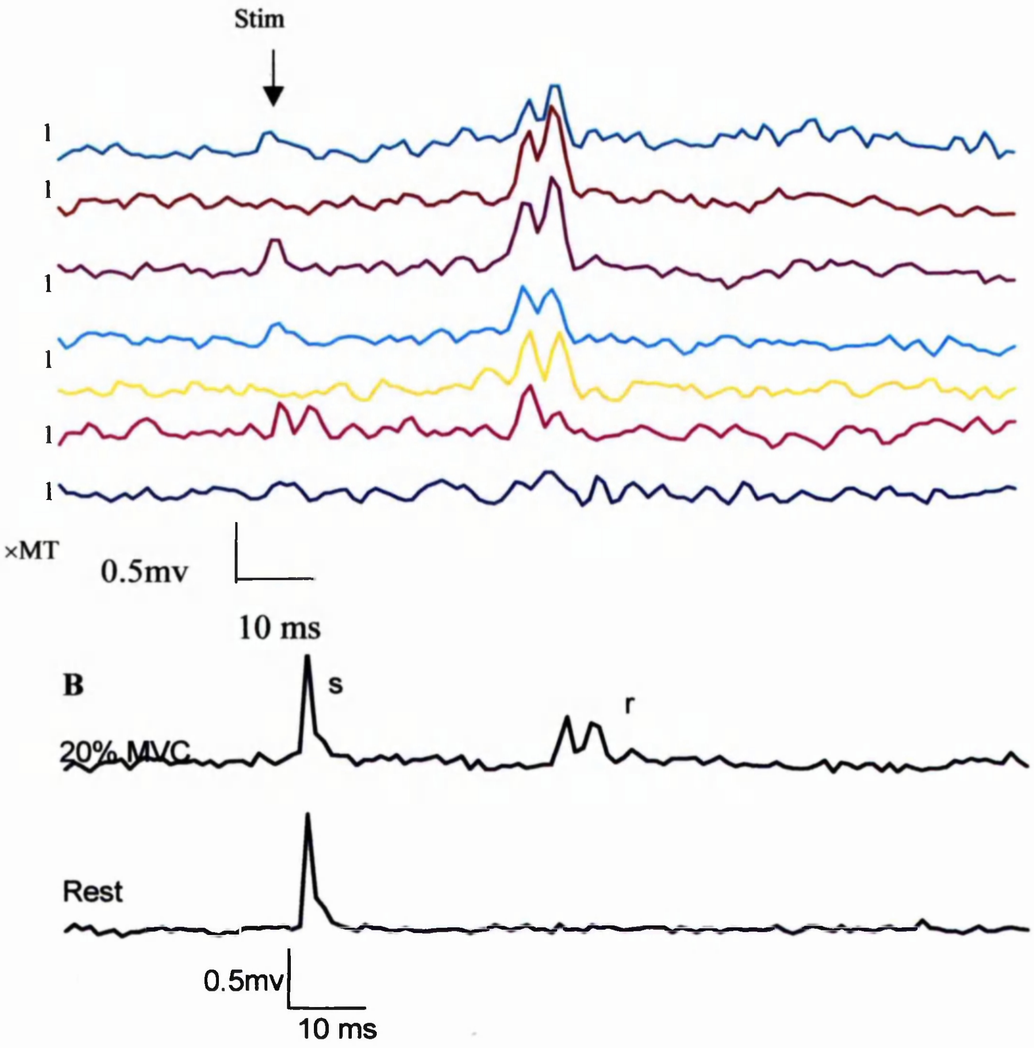

Figure 4.4. The correlation between the magnitude of CPQ reflex and the intensity of electrical stimulation of one volunteer is shown in figure A. In this case the magnitude of the CPQ reflex reached its maximum magnitude at around 1.3×MT. No significant increases can be seen in the magnitude at higher intensities in this subject. This happened at intensities between 1.3-1.5×MT in the other subjects. In some cases the amplitude of the reflex decreased at higher intensities. Figure B shows the rectified averaged (30 responses) EMG of RF during the contraction at 20% of MVC and rest in different subject. The CPN was stimulated at 1.5×MT in both cases. No reflex (r) is evoked when the muscle was relaxed. This suggests a strong excitatory effect of the supraspinal projections on the CPQ reflex.

intensity of 1.5×MT ranged from 0.61 to 4.5mV. The threshold of the reflex occurred at currents of 0.9-1.2×MT in TA. In three subjects a significant reflex was elicited with electrical stimulus at an intensity of 0.9×MT.

As the intensity of stimulation was increased up to 1.5×MT, the peak-peak amplitude and the area of the reflexes increased. The relationship between the reflex area/amplitude and the stimulus intensity is shown in figure 4.5. It can be seen that the correlation is almost linear at the lower stimulus intensities up to 1.3×MT for both reflex area and amplitude. The reflex magnitude reaches its highest mean level between 1.3 to 1.5×MT. In this figure the reflex area and p-p amplitude was expressed as percentage of maximum value recorded for each subject. The result is consistent with that reported by Brooke & McIlroy (1990a).

The extrapolation of the regression line, fitted to the lower stimulus intensities up to 1.3×MT, suggests that stimulation intensity below 0.9×MT could elicit the reflex.

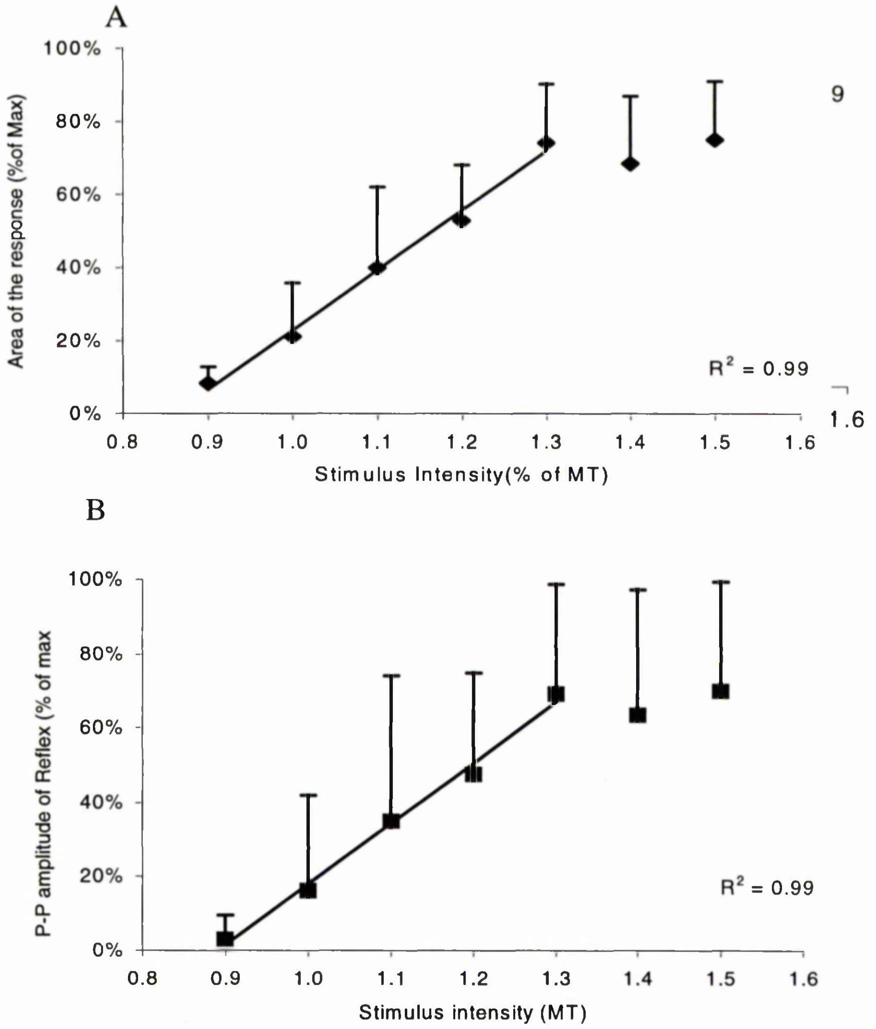

Figure 4.5. The pooled reflex area (A) and p-p amplitude (B) of 14 subjects evoked at different stimulus intensities. The maximum responses were observed at different intensities of stimulation from 1.3 -1.5×MT and in some cases a slight decrease in the size of the reflex was seen. Therefore, the pooled data at intensities of 1.3 - 1.5×MT shows a lower values than 100% that is expected. The reflex area and amplitude show a linear increase up to 1.3×MT of stimulus intensity. The extrapolation of the trend line of this linear section suggests the threshold for the afferents responsible for the reflex is below 0.9×MT. This threshold is in the range of group I afferents. The error bars represent the standard deviations at each stimulus intensity.

The effect of knee position on the reflex magnitude

The peak to peak amplitude and area of the reflexes in RF were measured at different knee positions. An identical procedure was followed at each position. The threshold for stimulation of TA motor fibres was established at each position. The stimulus intensity was adjusted at 1.5×MT to evoke a maximum reflex magnitude as illustrated in figure 4.5.

Experiments were performed in 14 volunteers. The magnitude of the reflex was maximum at 180° in all but two cases. In these two volunteers the reflex was slightly larger at 170° compared to 180°. The reflex was reduced in amplitude when the knee was held in progressively more flexed positions. Figure 4.6 shows samples of non-rectified averaged EMG at all the investigated knee positions. The reflex magnitude reduces with flexion of the knee joint. In eight of fourteen subjects, the reflex was not elicited at positions more flexed than 160°. In the other subjects the reflex magnitude showed a more gradual reduction towards more flexed positions. The pooled values of reflex area at all knee positions for both suggested groups can be seen in the figure 4.7a. It is clear that the reflex magnitude is reduced abruptly after 10° of knee flexion (filled circle) in the first

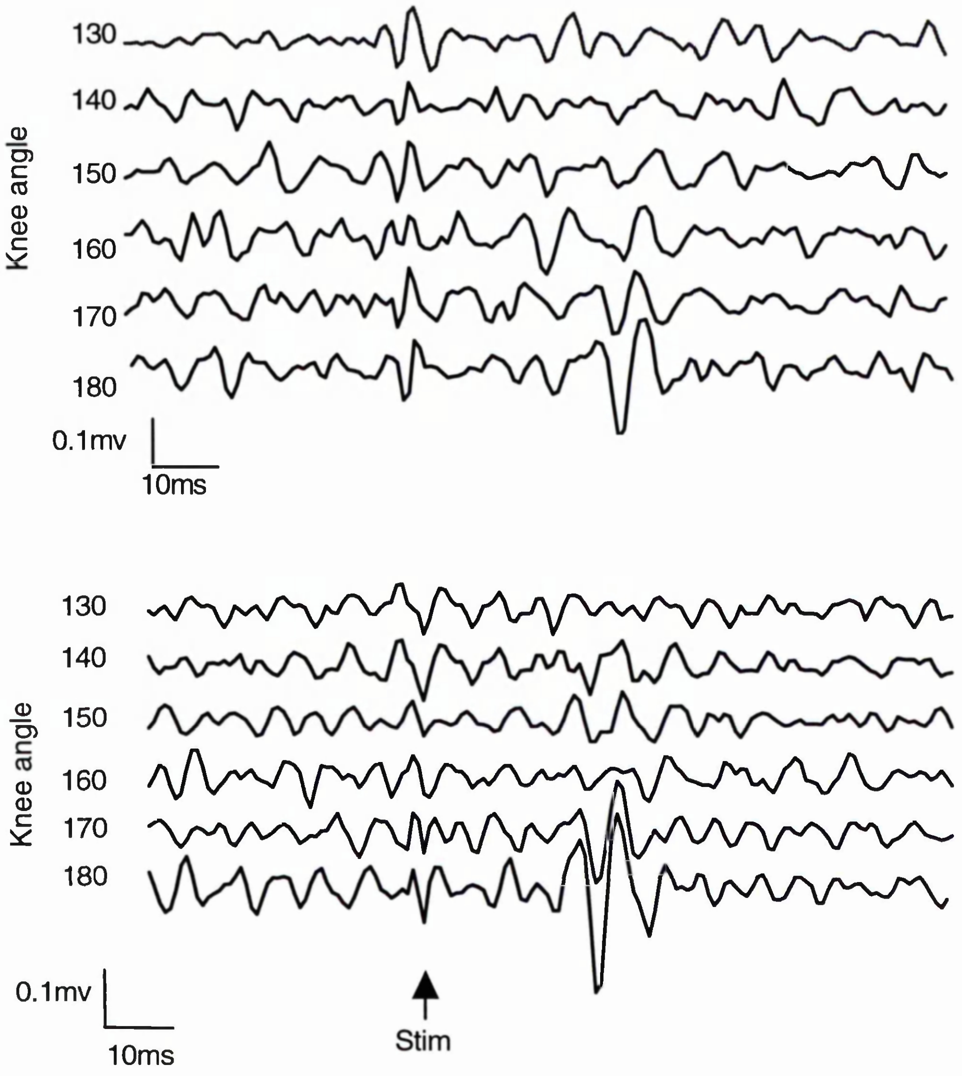

Figure 4.6. The non-rectified EMG of RF at different knee angles in two subjects. It can be seen that the maximum magnitude of the reflex is elicited at the fully extended position of the knee joint. At more flexed position the reflex magnitude is attenuated. The intensity of the stimulation was at 1.5×MT at all knee positions.

In the upper example, only the reflex at 180^{o} exceeded 2 SD above the mean. In the lower case, the reflexes at 170^{o} and 180^{o} exceeded 2sd above the mean.

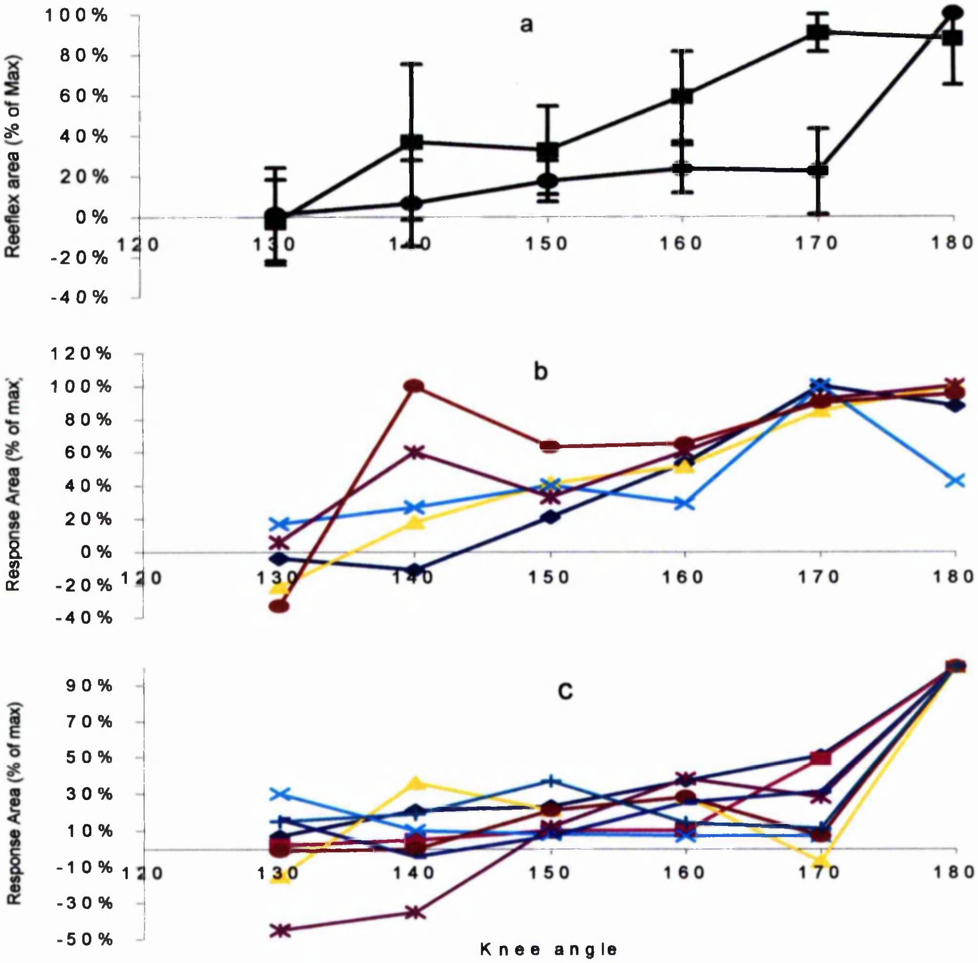

Figure 4.7. The figure shows the magnitude of the CPQ reflex at a range of knee positions.

Panel A shows mean data for two groups of response. In one case, filled squares, the reflex is progressively smaller at more flexed positions. Five of volunteers showed this pattern. In the other case, filled circles, the reflex is sharply reduced by flexion of 10° and then shows little further change. Nine volunteers showed this pattern.

Panel B shows the individual responses of these with progressive modulation.

Panel C shows the individual responses of these with sharp reduction on flexion.

As explained in section 2.4 the negative value in one of the subjects (purple) does not necessary reflects existence of an inhibition.

Group while the other group (filled square) shows a gradual reduction in the reflex magnitude after 10°-20° of flexion.

The pooled data for all the subjects can be seen in figure 4.8. The substantial attenuation of reflex magnitude at the first 10° of flexion follows by a gradual and linear reduction. The comparison of the area and amplitude of the CPQ reflex in all the knee positions showed a significant changes when tested by an ANOVA test ($p \leq 0.0001$). Table 4.2 shows the pairwise comparisons between all the knee positions. The differences in the reflex magnitude between 180° and other knee positions were highly significant ($p \leq 0.005$-0.0002). However, the attenuation of the reflex magnitude at other two positions elsewhere in the range, was smaller and often not statistically significant. This became significant statistically, if the mean values of every 20° or 30° of knee flexion position were compared.

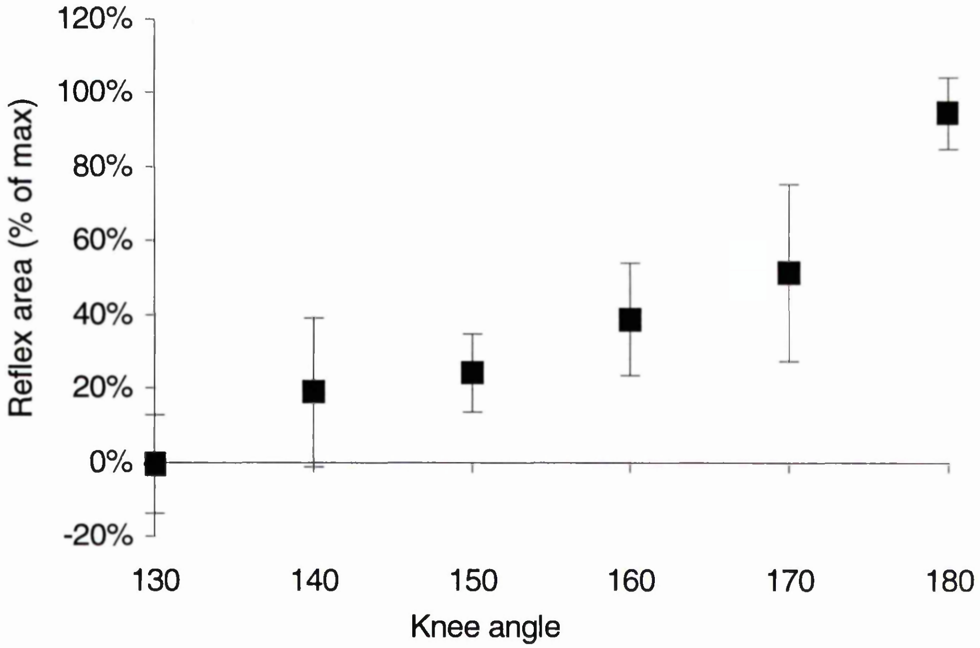

Figure 4.8. The mean reflex area of all 14 subjects at different knee angles. The reflex shows an incremental attenuation at flexed positions of the knee joint. The area of the reflex is maximum at 180°. No reflex elicited at 130° of knee flexed position. It is between 180 and 170 of flexion that significant and maximum attenuation is seen ($p \leq 0.006$). The error bars represent the standard deviations.

Contrast	Difference	95% CI		
180 v 170	43%	13% to	73%	(significant)
180 v 160	56%	26% to	86%	(significant)
180 v 150	71%	41% to	100%	(significant)
180 v 140	75%	45% to	105%	(significant)
180 v 130	95%	65% to	125%	(significant)
170 v 160	13%	-17% to	42%	
170 v 150	28%	-3% to	57%	
170 v 140	32%	2% to	62%	(significant)
170 v 130	52%	22% to	82%	(significant)
160 v 150	15%	-15% to	45%	
160 v 140	19%	-11% to	49%	
160 v 130	39%	9% to	69%	(significant)
150 v 140	4%	-26% to	34%	
150 v 130	24%	-6% to	54%	
140 v 130	20%	-10% to	50%	

Table 4.2. The table shows the pairwise comparisons between the area of the CPQ reflexes at different knee positions. The table shows data from 14 subjects. In each subject the largest CPQ reflex is normalised to 100%. Other reflexes are expressed relative to this. The differences column shows the difference in means reflex size at two angles. The third column shows the confidence intervals of the differences. Comparisons are made using an ANOVA with Bonferroni corrections. Significance level is 0.05. The first 10^{0} of knee flexion produced the most significant attenuation of the reflex magnitude. This becomes less significant toward more flexed positions of the knee joint.

The effect of hip positions in the reflex magnitude

The magnitude of the CPQ reflex in RF was also investigated at two positions of the hip. Ten subjects participated in this experiment. At a flexed hip position (110°) all of the subjects had a significant reflex in RF. At the extended position of the hip (180°) 4 of the subjects showed statistically significant inhibition in the reflex magnitude ($p \leq 0.05$ for the area and $p \leq 0.02$ for the p-p amplitude of the CPQ reflex). Four others showed a small but insignificant reduction and two showed no changes in the reflex magnitude at all. However, the pooled data of all 10 subjects suggest significant inhibition in the reflex after extension of the hip joint ($p \leq 0.01$ for mean p-p amplitude and $p \leq 0.008$ for mean reflex area). The average inhibition in the reflex p-p amplitude was 34%±10% (± SEM) and for the area of the reflex it was 57%±10% of the reflex values in the flexed position of the hip.

Cutaneous and tibial nerve stimulation

In all experiments the CPN was stimulated transcutaneously. It was possible that excitation of receptors in skin over the nerve might have contributed to short latency reflex in the RF. To investigate this possibility, the same area of the skin over the caput fibulae was stimulated with a larger electrode. The intensity of stimulation was adjusted to match the sensation evoked earlier. This did not evoke an M wave in TA. The skin stimulation was not able to evoke responses in the RF in any of the subjects.

The stimulation of 1.5×MT was unlikely to spread to the antagonist muscles or tibial nerve. However, to investigate their contribution in the production of the reflex in RF, the tibial nerve was stimulated at 1.5 and 2×MT for soleus. With these intensities of stimulus, no response was detected in RF in any of the subjects.

4.4.2. Second series of experiments

The correlation between the intensity of the background activity in Q and the magnitude of the reflex in flexed and extended positions of the knee joint was investigated in seven volunteers.

The relationship between the intensity of muscular activity and the reflex magnitude

The experiment included measurement of the reflex p-p amplitude at flexed and extended positions of the knee joint. Several intensities of background muscular activity were tested at each knee position while identical stimulus intensity was applied to the CPN.

- At extended position of the knee joint

Figure 4.9 shows the changes in the reflex p-p amplitude with increases in the intensity of the background EMG in RF. No reflexes were recorded in any of the subjects when RF was relaxed. The reflex appears at some contraction level between 5 to 20% of MVC.

It was not possible to test higher intensity muscular contraction because of muscle fatigue causing changes in the background EMG.

The reflex magnitude increased proportionally with increases in muscular activity. It appears that the early linear correlation between the reflex magnitude and the motor activity reaches a maximum at some points between 30% and 40% of MVC. The pooled p-p amplitude of the reflex at all the investigated intensities of muscular activity is shown in figure 4.10.

- At the flexed knee position

It was not possible to elicit the reflex in any of the subjects when the knee was held in the flexed position (figure 4.9). Even with muscular contraction of about 40% of MVC it was still impossible to evoke significant reflex. Figure 4.10 shows the pooled data from all the subjects. Since no reflex was detected at flexed position of the knee, the values represented for the p-p amplitude of the reflex are the p-p amplitude of the EMG at the time where the reflex was expected for each subject. The positive values of reflex p-p amplitude in the figure 4.10a at higher intensity of the muscular activity, does not reflect the

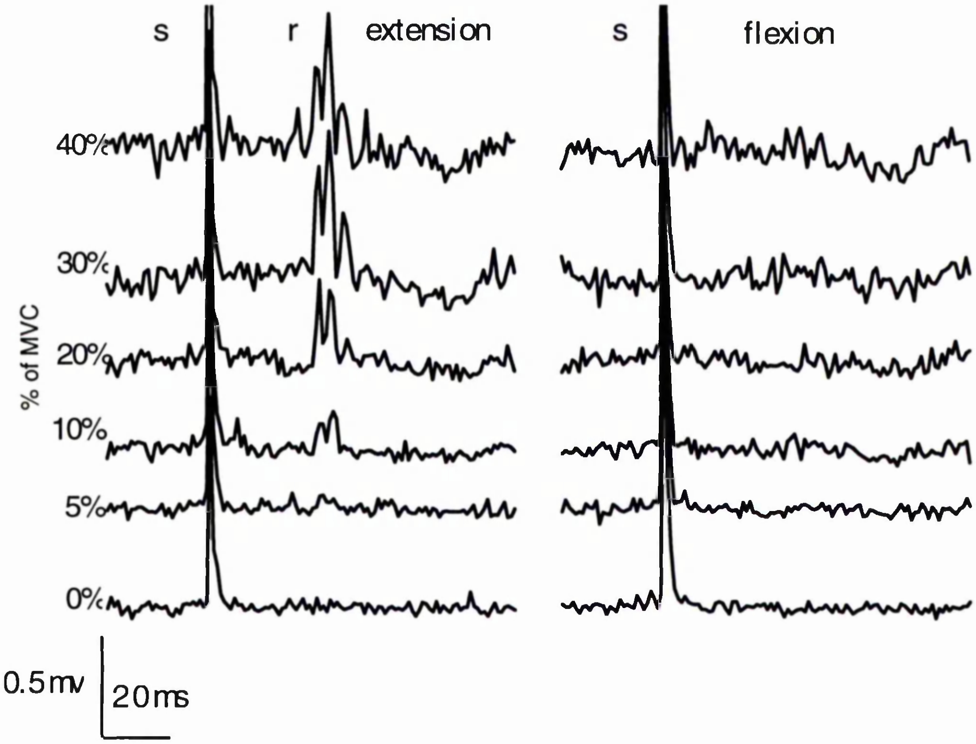

Figure 4.9. The rectified averaged EMG recorded from RF at flexed and extended position of the knee and at different level of muscular activity in one of the volunteers. The CPQ reflex showed a positive correlation to the increased in the intensity of activity in RF when the knee joint was extended. At flexed position of the knee joint, however the responses was not evoked at any of the investigated intensities. A small inhibition can be seen at a latency of around 65ms in this case with an area of 12% of MVC. This was detected only in this subject. Interestingly this week inhibition was not inhibited by the flexion position of the knee joint, as it remained almost unchanged between 20% and 40% of MVC at both knee positions. (s= stimulus, r= reflex).

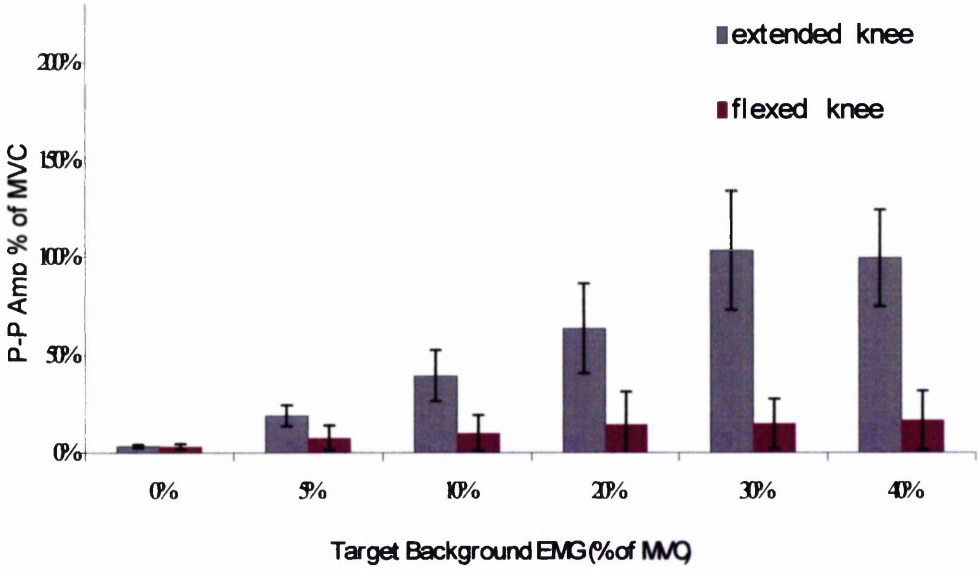

Figure 4.10. The pooled p-p amplitude of the reflex at different level of muscular activity, at flexed and extended position of the knee joint. The reflex magnitude shows a positive correlation with the increased muscular activity in the extended position of the knee but no correlation can be seen in the flexed position.

reflex magnitude, but instead they represent the increase in the background magnitude with increase in the motor activity. Therefore, in the flexed position, no correlation exists between the reflex magnitude and the level of motor activity in the RF or VM.

The consistency of the stimulation

The p-p amplitude of M wave in TA was measured for all the intensities of muscular activity and for both knee positions. Tibialis anterior was at rest during the experiment. The values for this were expressed as percentage of MVC at each knee positions. Figure 4.11 shows the pooled M wave amplitude in TA at both knee positions. This remained nearly at constant magnitude and above the limit of 40% of M_{max} in both investigated knee positions.

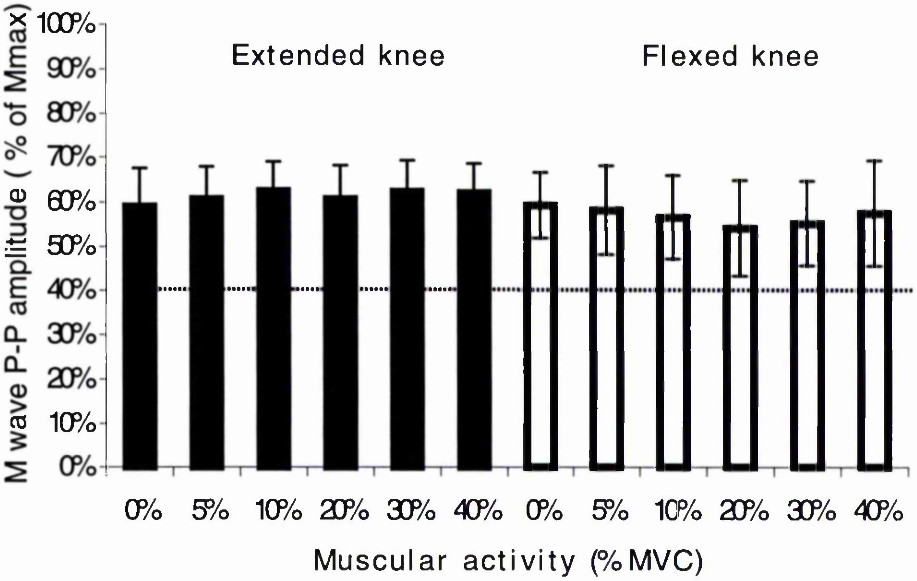

Figure 4.11. The pooled M wave peak to peak amplitude at extended (left) and flexed (right) positions of the knee joint at different intensity of muscular activity. The error bars show the 95% confidence interval for the mean values.

4.5. Discussion and conclusions

4.5.1. The nature of the afferents responsible

The results show that low intensity electrical stimulation at caput fibulae was able to elicit a short latency reflex in RF. The average latency of the reflexes was 29.4ms in RF. This is similar to what has been reported by the other investigators such as McIlroy and Brooke (1987) who has reported average latencies of 26.3 and 33.5ms for the CPQ reflex in VM and RF respectively.

Extrapolation of the data in figure 4.5 suggests that the threshold of the afferents responsible for this reflex must be about 0.8×MT in TA. In addition to this, three of the subjects showed a significant reflex with stimulation at 0.9×MT. This strongly suggests that the afferent responsible for this reflex must be low threshold and fast conducting afferents. Group I afferents best fit these characteristics.

The stimuli applied at caput fibulae in this experiment could also activate skin receptors under the electrodes. Although the latency of the CPQ reflex is beyond the latency expected by the slow cutaneous afferents, the possible contribution of these afferents were investigated. Pure cutaneous stimulation mimicking the cutaneous sensation produced by CPN stimulation was unable to evoke any response in Q (Chaix et al 1997, Forget et al 1989). Therefore it is unlikely that cutaneous afferents could provide strong excitation at Q motoneurones sufficient to elicit the large reflexes observed during this experiment.

However the direct involvement of the cutaneous afferents in the CPQ reflex is very unlikely, it has been shown that stimulation of specific skin fields can produce excitatory effects on the transmission of some spinal pathways to a given motoneurone pool (Pierrot-Deseilligny 1996, Pierrot-Deseilligny, Bergego and Katz 1982). Therefore it is possible that afferents originating from skin fields of particular relevance in stance and gait i.e. foot sole and toes, which were not explored here, may have an excitatory effect on the transmission of the CPQ reflex.

Stimulus intensities of above 2×MT at caput fibulae have been shown to evoke double excitatory responses in Q muscles (Simonetta-Moreau et al 1999, Marchand-Pauvert 2002). The shorter latency response had a lower threshold and was attributed to group I and the later higher threshold one with latency of about 43ms was attributed to group II afferents. Stimulus intensity of 1.5×MT is unable to activate group II afferents in CPN. It has been shown that these afferents have threshold of about 2.1 times that of group I afferents (Simonetta-Moreau et al 1999). Therefore with the stimulation intensity used in this experiment and the short latency of the reflexes, it is unlikely that group II afferents can make a major contribution.

The stimulation of 1.5×MT is also very unlikely to spread to the antagonist plantar flexor muscles or to the tibial nerve in the popliteal fossa. This remote possibility was investigated by stimulating the tibial nerve with intensity of 1.5 –2 × MT of the soleus muscle. This never evoked responses in RF in any of the subject. This result is consistent with the result reported by McIlroy and Brooke (1987).

The overall conclusion is that group I afferents in CPN are the major afferents responsible for eliciting the reflex in RF. As explained in section 1.8, afferents from GTOs and muscle spindles primary and secondary afferents converge in this reflex pathway. It is believed that all these afferents converge onto a common interneurone on their pathway to Q motoneurones (Chaix et al 1997, Marchand-Pauvert et al 1999). Functionally, this implies a difference between the response being evoked by stretch of the foot in a plantarflexion direction or alternatively arising from muscle force developed in the musclo-tendinous junction for the dorsiflexors of the foot. Because of the different mechanical stimulus needed to initiate the discharges in each of these receptors, it is reasonable to assume that their contribution in evoking the CPQ reflex or the control of Q activity is "task-dependent".

4.5.2. The pathway of the reflex

The excitation reflects a prominent facilitation of the RF motoneurone pool since it is observed directly in the electromyogram. The sharp onset and the short latency of the reflex suggest that the excitation is not mediated through a long chain of interneurones but through an oligosynaptic pathway. McIlroy and Brooke (1987) argued that with the afferent and efferent conduction velocity of 67 and 57m/sec (Fukushima, Yamashita and Shinada 1982) respectively, the predicted central latency of the CPN-induced excitation of Q motoneurones was estimated to be 3-3.7ms longer than that of the monosynaptic Ia excitation. Almost the same central latency was also reported by Chaix et al (1997). They concluded that the pathway of this reflex is most likely to be oligosynaptic. The interneurones mediating the reflex must receive a strong descending excitation since the relaxed muscle never showed any reflex even at 1.5×MT.

In cats, propriospinal neurones located rostrally to motoneurones relay the central commands to the target motoneurones (Edgley and Jankowska 1987a). They have documented the existence of a group of short propriospinal neurones, located in the intermediate zone/ventral horn of mid lumbar segments which project to motoneurones located more caudally. These interneurones have also been shown to receive inputs from group II and I afferents (Edgley and Jankowska 1987b) and from descending tracts (Davis & Edgley 1994). The existence of such lumbar premotoneurone system in the human has been shown recently (Marchand-Pauvert et al 1999). They have shown that the supraspinal tracts and group Ia, II and Ib afferents from pretibial muscles, converge onto a same interneurone. They have argued that these interneurones are part of the lumbar premotoneurone system that relays a great proportion of the descending commands to the thigh muscle motoneurones.

4.5.3. The modulation of the reflex by the knee movement

The result of the experiment shows that the reflex gain was modulated with changes in the knee position. Flexion of the knee resulted in a substantial attenuation of the reflex in RF.

It has been shown that the reflex magnitude is positively correlated to two main factors ; stimulus intensity (figure 4.5) and the intensity of muscular activity (figure 4.9). Any changes in these two factors leads to changes in the reflex magnitude. Either of these factors could be responsible for the attenuation of the reflex in the present experiment. The stimulus intensity was constantly monitored on line and adjusted, if needed. The M wave evoked by stimulus intensity of 1.5×MT was measured peak to peak. During the recording at each joint position, the M wave magnitude remained at near constant level. The M threshold for each knee position was measured separately and the intensity of the stimulation was adjusted accordingly. Therefore, any changes in the position of the electrodes that might have occurred with changes in the position of the knee joint, was compensated by readjusting the stimulus intensity from the M threshold measured for that position.

Changes in the background level of muscular activity in also unlikely to be responsible for the reflex attenuation. During the experiment the subjects made voluntary contraction of RF at 20% of MVC. This avoids fatigue when combined with the short duration of contraction used in the present experiment.

The level of muscular activation could change at different knee positions. In this case a constant percentage of MVC would not reflect the same fraction of the absolute maximum at all the knee positions. The literature does not provide any evidence to suggest that knee flexion could increase the maximum electrical activity of Q motoneurone pool. In addition, result of the second series of experiments, in the present study, also showed that the MVC did not change significantly with the knee flexion.

Overall, it is reasonable to conclude that the sensory discharge, which arises as a consequence of the knee movement, led to the movement-dependent modulation of this reflex during flexion of the knee.

The afferents responsible for the modulation

The gain of a reflex can be altered strongly by the convergence onto its pathway (Prochazka 1989, Watson 1992). In these experiments, it appears that the inhibition of the excitatory pathway from the ankle dorsiflexors to RF arises mainly from some component of the somatosensory receptor array activated as a consequence of changes in the knee position and/or the hip position.

Position and movement of the joints can be signalled by the discharges from receptors within the joint capsule or ligaments (Ferrell et al 1987), skin (Edin 1992, Collins & Prochazka 1996) or muscle spindles (Gilhodes et al 1986, Gandevia, Lesley, McCloskey and Potter 1983, Roll et al 1989). Any or all of these could be responsible for the inhibition of the reflex in RF occurred by flexion of the knee joint.

The vestibular or the visual system are very unlikely to have any role in this inhibitory modulation since the position of the head and the visual inputs remained unchanged at all knee positions investigated.

Numerous studies have investigated the role of joint receptors in proprioception. These receptors have been shown to discharge mainly at the extremes of the knee joint rotation (Burgess and Clark 1969, Ferrell et al 1986). In human finger joints these receptors appear to be involved in position sense when the muscle stretch receptors are not available (Ferrell et al 1987). For the knee joint, the current view is that most joint receptors remain silent through the natural ranges of movement. The inhibition in the CPQ reflex occurred at a flexed position of the knee joint where the joint receptors are mainly quiet, therefore it is unlikely that these receptors could have a major role in the movement-dependent modulation of the reflex. Stimulation of collateral ligaments of the knee joint in humans (Kim, Rosen, Brander and Buchanan 1995) and the knee joint capsule in cats (Baxendale, Ferrell and Wood 1988) are shown to have an excitatory effect on the Q motoneurones. It is possible that these receptors could have an excitatory effect on the reflex at the fully extended position of the knee, when they are highly active. However there is no evidence in the present experiment to support this idea.

Information from the skin mechanoreceptors is shown to be important for proprioception in human hand and finger joints (Edin 1992). Edin (2001) has also shown that receptors in the human hairy skin can provide information about the knee joint position and movement. Despite this sensory role, stimulation of the terminal cutaneous branch of the femoral nerve which produced a sensation irradiating toward patella, and also stimulation of the small sciatic nerve, which produced sensations irradiating toward the popliteal fossa, are not able to evoke any depression of Ib excitatory effect from CPN to Q motoneurones (Pierrot-Deseilligny, Bergego, Katz and Morin 1981b). This area of the skin is most likely to have role in perception of the knee movement and position (Edin 2001). On these grounds, it is unlikely that the skin mechanoreceptors have a major role in the attenuation of the reflex with knee flexion.

The role of muscle spindles in proprioception is well described in the literature. Flexion of the knee results in stretch of the quadriceps muscles. The role of knee movement in the modulation of other short latency reflex in the lower limb is well documented in the literature. The H reflex has been shown to be inhibited substantially during flexion of the knee joint in activities such as stepping (Brooke et al 1991), walking (Brooke et al 1991, Capaday and Stein 1986) running (Capaday and Stein 1987) and pedalling (Brooke, McIlroy and Collins 1992, Brooke, Misiaszek and Cheng 1993, McIlroy et al 1992). It has been shown that removing the populations of mechanoreceptors of the knee joint in cats could not remove the inhibitory effect on the H reflex in the small muscles of the foot until the muscle mechanoreceptors of the quadriceps muscle group were deactivated (Misiaszek Barcley and Brooke 1995). They concluded that muscle mechanoreceptors of Q provide the major inhibitory inputs to the H reflex pathways when the knee is flexed. Different studies in humans, using different and more indirect methods, also support this idea that Q muscle spindles are the most responsible for the inhibition of the H reflex in the leg muscles (Cheng et al 1995, Staines et al 1997a,b).

The present experiment does not provide any evidence about the origin of the afferents responsible for the observed inhibition of the reflex. However, on the basis of exclusion of skin and joint mechanoreceptors and the positive information in the literature, it would be plausible that stretch receptors of Q muscles could have a major role in the observed gain modulation of the CPQ reflex during knee flexion. More investigation is needed to address the origin of the afferent responsible for the gain modulation of this short latency reflex by the knee movement.

The result of the present experiment does not agree with that reported by Brooke and McIlroy (1990). They found no correlation between the movement in the leg during pedalling and the reflex magnitude. Instead they concluded that the modulation coincided with the ongoing contraction level in Q muscle. It is not certain why they were not able to detect the movement-related modulation of the reflex, but there are some possible explanations for this:

a) It is not clear what the position of the knee was when the stimulation was applied to CPN. The height of saddle usually is adjusted to provide a semiflexed position in the knee joint when the pedal crank is at the bottom of its cycle. Therefore it appears that they might never have tested the reflex with the knee fully extended. The result of the present experiment shows that the major inhibition of the reflex happened at the early ranges of the knee flexion from full extended position. This could explain why they have missed to record any modulatory effect in their experiment.

b) The reaction to the knee movement among the subjects investigated in the present experiment was clearly inconsistent. This suggests that in order to reveal the actual movement modulatory effect of the knee, the number of the subjects as well as the sequence of knee positions tested should be reasonably large. The number of the subjects (4) in their study and the tested knee positions was comparatively small.

The different reactions to the knee movement

The movement–related modulation observed in the present experiment had different characteristics among the subjects. The pooled data from all the subjects in figure 4.8 could be misleading. It seems that the abrupt modulation during the first 10-20 degree of knee flexion might have different origin from the later more gradual modulation. However, if the data from each subject are considered individually, two patterns of modulation could be found among them. The first major group shows a very substantial inhibition at the first 10-20 degree of flexion. The second group shows a gradual attenuation of the reflex magnitude.

This different reaction to changed knee position could simply be because of the normal variation in the sensitivity of the responsible modulatory system to the knee movement. This could have also resulted from either different sensitivity of the receptors to the knee movement or different strength of the convergence on the CPQ reflex pathway.

4.5.4. The effect of the hip position on the reflex magnitude

Extension of the hip joint resulted in significant inhibition of the CPQ reflex in RF muscle. However this inhibition was less consistent than that produced by knee flexion. In fewer than half of the subjects investigated the reflex was inhibited substantially with hip extension. This might reflect a weaker convergence of sensory inputs from afferents sensitive to hip position than that from the knee joint or simply a weaker sensory inputs triggered by hip extension. Whilst knee flexion can stretch both mono and biarticular parts of Q muscles, hip extension can just stretch the biarticular part of Q i.e. RF. Knee flexion can therefore provide stronger sensory inputs than hip extension. The difference between the effect of knee and hip positions on the CPQ reflex could be the result of this mechanical difference. Alternatively this might be because of different range of movement or sensory discharge provoked by the hip positions employed in the present experiment. Overall, it is clear that the hip movement is a less powerful source of inhibition than knee movement.

4.5.5. The effect of intensity of motor activity on the reflex

Reflex excitability can be modulated in two ways. It can be reduced postsynaptically which leads to reduced reflex excitability. Alternatively, the input can cause changes at premotoneurone level. The correlation between the magnitude of the reflex and the intensity of the muscular activity can reveal the nature of mechanisms involved in the modulation of the reflex. In postsynaptic inhibition a strong correlation often exists (Matthews 1986) but in premotoneuronal inhibition, the reflex modulates partially or wholly independent of the contractile state of the muscle (Crenna & Frigo 1987, Ruegg 1989).

At the flexed position of the knee joint, where a strong inhibition is imposed on the reflex pathway, incremental intensity of the muscular activity could not reproduce the reflex (figure 4.9, 4.10). This dissociation between the reflex and the muscular activity strongly suggests that a premotoneuronal inhibition was involved. In addition, if the inhibition were postsynaptic, the excitability of the motoneurone pool should decrease. This would have decreased the maximum recruitment capacity of the motoneurone pool (Capaday & Stein 1989). This would have led to decrease in the intensity of maximum EMG activity in related muscles. It was not observed in the present experiment.

The overall conclusion must be that the knee flexion modulates the CPQ reflex mainly at premotoneuronal level. Since it is likely that the descending commands converging on this pathway are also relayed through this interneurone system to the Q motoneurones, the site of the movement-induced inhibition must be earlier, before the convergence with of the descending pathway. Otherwise, the result would be the same as the postsynaptic inhibition on the motoneurones i.e. the reflex magnitude would reappear and increased with the increased in the motor activity level.

At extended positions of the knee, where no inhibition on the reflex pathway was expected, a strong correlation was observed between the intensity of the motor activity and the reflex magnitude. This is very similar to the " automatic gain compensation" introduced by Matthews (1986) for the stretch reflex.

Although the result from the present experiments provides indications of the potential functional significance of the pathway, interpretation of such significance is still limited by the way in which the afferents were activated. In this study, electrical stimulation was used to activate the afferents of the reflex pathway. As a result, the magnitude of the response reflects synchronous afferent discharge. Such electrical stimulation could lead to spatial recruitment that might exceed the maximum magnitude of response possible from natural state of recruitment. Thus the present responses might not represent adequately those evoked by natural discharge of the appropriate receptors.

4.5.6. Functional significance of modulation of CPQ reflex

The strong CPQ reflex at extended positions of the knee has implications for the role of this reflex pathway in human stance and locomotion. The reflex links the afferents from the ankle dorsiflexors to the motoneurone of the knee extensor muscles. Therefore the pathway is active when the ankle dorsiflexor receptors are stimulated. This could result in a "positive feedback" effect on to the knee extensor motoneurone pool. The positive feedback effect from the ankle muscle afferents to Q muscles could help in providing the stability of the knee joint.

The CPQ reflex could be triggered by the stimulation of the muscle spindles or the GTOs in the ankle dorsiflexors. As discussed earlier the proportional participation of each of these afferents that construct this reflex pathway depends on the type and the strength of the stimuli on the ankle muscles. These different stimuli could be provided at different functional tasks.

In human gait, the peak of activity in ankle dorsiflexors happens close to heel strike (Dubo et al 1976) where the sudden loading of the lower limb happens. This may indicates the possible role of loading on the activity of the CPQ pathway. This peak of activity in dorsiflexors coincides with the peak of activity of Q muscles. Since the contraction is the adequate stimulus for the GTOs a major activation from the group Ib fibres is likely at this time. This may reflect the positive force feedback from ankle dorsiflexor GTOs to Q motoneurones. The CPQ reflex could re-enforce the activity of the Q which is needed during the stance phase to cope with the load of the body. The role of GTOs as load receptors (Pearson et al 1995) may indicate a load compensatory effect from ankle dorsiflexors to Q.

During standing, any backward sway will result in a sudden stretch of the dorsiflexor muscles which could stimulate muscle spindles. The imposed imbalance is followed by a reflexive contraction in Q to resume the balance. It is possible that the spindles group Ia or/and II afferents from ankle dorsiflexors can be involved in this excitatory effect through the CPQ projection to Q.

The functional significance of the reflex attenuation after flexion of the knee or hip joints in not clear. The reflex seems to co-ordinate the activity of the ankle dorsiflexors and knee extensors during dynamic tasks. The reflex inhibition that occurs after knee flexion, could break this positive link between these two groups of muscles allowing or facilitating isolated activity of ankle dorsiflexors when the Q activation is unnecessary. During walking, the positive force feedback from group Ib afferents from ankle dorsiflexors to the knee extensors would help with load compensation during the early stance phase but for the transition from stance to swing phase this positive load effect should be removed. This would help the unloading of the leg, which is necessary for the transition. The ankle dorsiflexion coincides with knee flexion to lift the leg from the ground. An uninhibited CPQ reflex during this period would hinder the knee flexion and therefore the transition to swing phase.

The following experiments in the next chapter were designed to provide the information about the potential functional role of this neural pathway during locomotion in humans. The existence and the functional role of the reflex inhibition are also addressed in the next chapter.

Chapter 5

Modulation of the CPQ reflex during gait in humans

5.1. Introduction

5.1.1. Literature reviews

Analysis of human gait first became possible towards the end of 19th century with the development of photographic recording of running movements (Marey 1894). The technique for recording electrophysiological responses during locomotion was developed and demonstrated first in cats (Engberg and Lundberg 1969). The technique was then improved and was used to analyse human locomotion. However, very few studies have been conducted concerning human locomotion. One difficulty in studying human locomotion is that the control mechanism can only be investigated by indirect methods. For example, latencies and the electrical thresholds must be used to make inferences about the nature of the pathways responsible for the reflexes. Therefore, the human data has largely been interpreted with regard to animal experiments. There are clearly some common features between the pattern of activity and the underlying neuronal mechanisms during quadripedal locomotion in cats and that seen during bipedal gait in humans however, distinct differences exist.

The heel-to-toe sequence of movement during stance phase is a unique feature of human plantigrade gait. This requires a distinctive pattern of co-ordination among the muscles of the leg from that is seen in digitigrades.

The CPQ reflex may be an example of the distinctive specialisation of the plantigrade gait. The literature suggests that this reflex is unique to humans. It does not exist in quadrupeds like cats (Eccles et al 1957) or digitigrades like baboons (Hongo et al 1984). It is likely that this reflex could be significant in the motor control of the leg muscles, particularly quadriceps, during gait in humans.

Irrespective of the conditions under which gait is investigated, the neural pattern evoked during a particular task is always directed toward maintaining the body's centre of mass on the base of support (Dietz. 1998, Dietz and Duyson 2000). The small base of support during stance and locomotion in human is also another distinctive feature, which demands a more complex control mechanism than that used by quadrupeds. One consequence of this is that the selection of afferent inputs by central mechanisms must correspond to the requirements for body stabilisation

In summary the distinctive characteristics of human locomotion necessitates that the pattern of neural control must be different from that of the quadrupeds.

5.1.2. Kinematics of the human gait

Human gait can be characterised by the repetitive events occur during each gait cycle. A gait cycle is defined as the time interval between two successive occurrences of one of the repetitive events of walking. It is convenient to use the instant of heel strike as the initial event of gait cycle. Each gait cycle is divided into two phases, stance and swing. Stance phase is the period when the foot is in contact with the ground and swing phase is the period that the foot is moving forward in the air. The stance phase usually lasts about 60% of the gait cycle and the swing phase about 40%. However, this varies with the speed of walking, the swing phase becoming proportionally longer as the speed increases (Murray 1967). The phases and subphases of the gait cycle are shown in figure 5.1. The stance phase can be subdivided into 4 sub-phases (Rose and Gamble 1994):

a) Loading response: Starts from heel strike until the time when the other foot lifted from the floor (toe-off of the opposite foot).

b) Midstance: starts from the toe off of the opposite foot until the body positioned directly over the stance foot.

c) Terminal stance: starts from the end of midstance until the heel strike of the opposite foot.

d) Preswing: starts from the heel strike of the opposite foot until the foot lifted from the floor.

It can be seen that during gait there are two periods when both feet are in contact with floor. This is called double stance that includes about 22% of gait cycle (Whittle 1996). Double stance is the characteristics of walking. With increases in the speed of walking the duration of double stance become shorter until it is substituted with double swing which is characteristics of running.

The swing phase is also subdivided into three sub-phases:

a) Initial swing: starts from the start of the swing phase until the time when the knee is in its maximum flexion during gait.

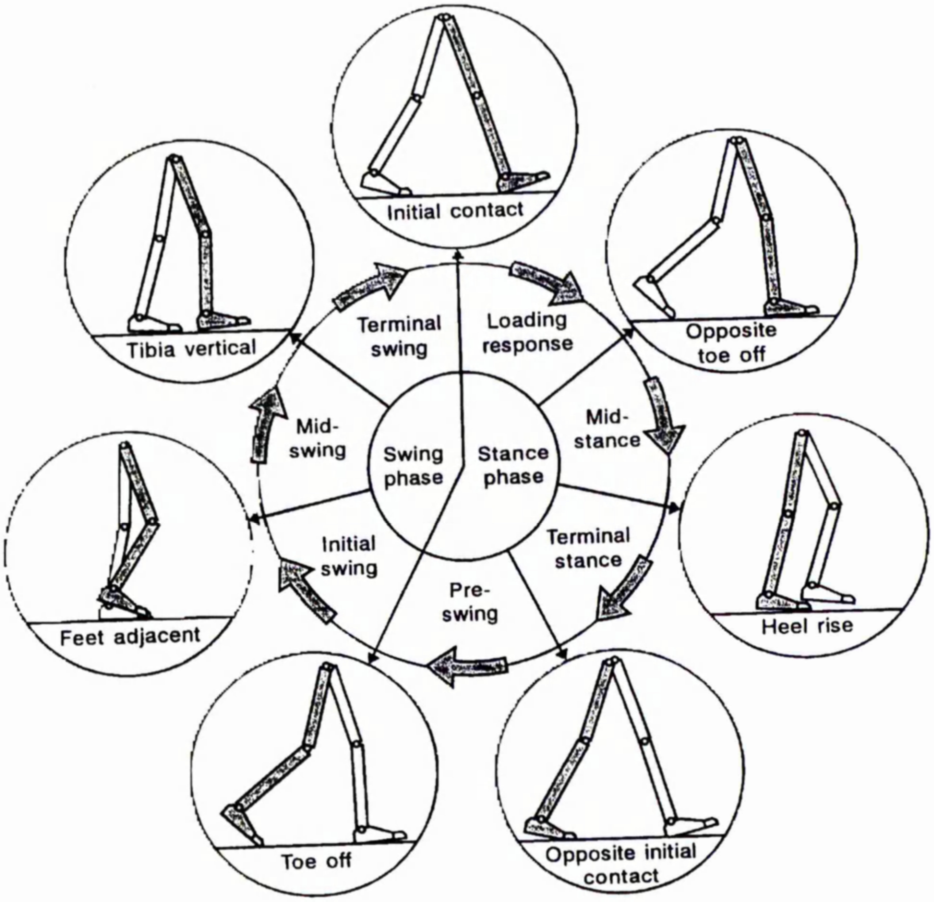

Figure 5.1. The phases and subphases of gait cycle. The positions of the right leg during a single gait cycle can be seen (shaded leg), (Modified figure from "Gait Analysis, second edition, Whittle M.W., 1996).

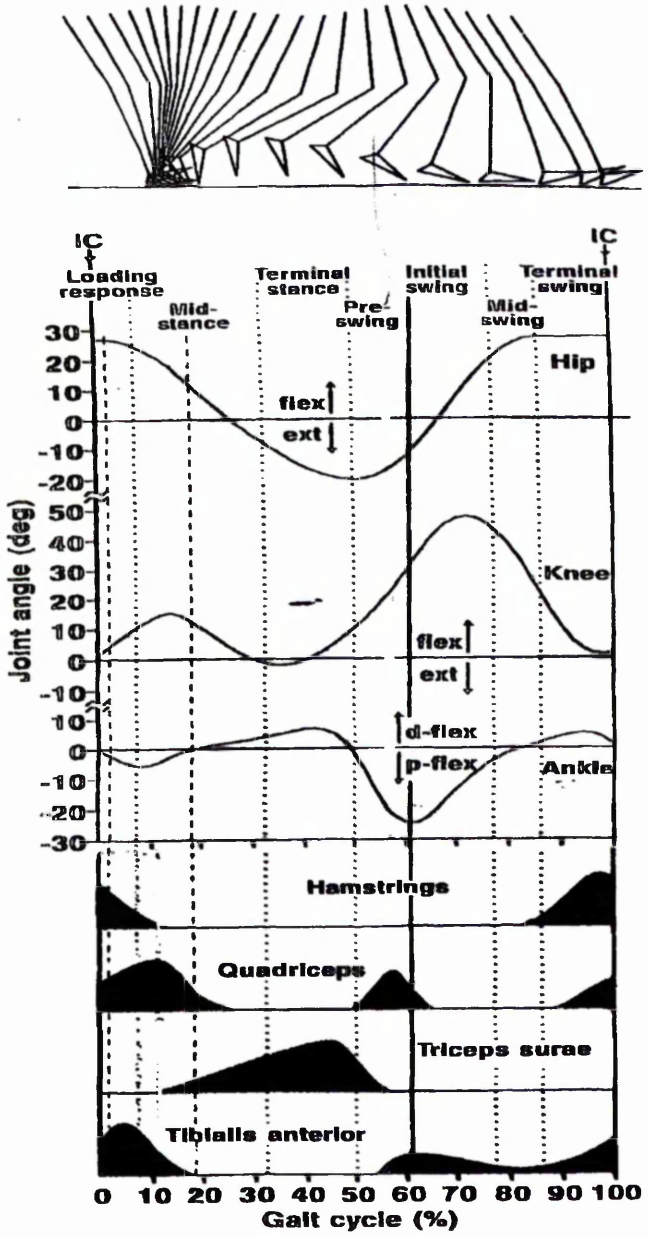

Figure 5.2. The cyclic movement in hip, knee and ankle joints (top) and the typical activity of major muscle groups (bottom) during the gait cycle of 1100ms duration and speed of 4.7km/h (modified figure from "Gait Analysis, second edition, Whittle M.W., 1996).

b) Midswing: starts from the end of initial swing until the time when the leg is vertical to the ground.

c) Terminal swing: starts from the end of midswing until before the next heel strike.

A cyclic pattern of movements in the joint and activity in the muscles of the leg occurs in each cycle. Figure 5.2 shows the pattern of muscular activity and joints movement during each gait cycle in a normal 22-year-old female. The individual measurements reported for this subject in figure 5.2 do not always correspond to average values, because of the normal variability between individuals, although they are all with in normal range.

5.1.3. Neural control of gait

Movement such as locomotion is determined by the strength of activation of the muscles in the lower limbs as well as the intrinsic muscle properties. The EMG activity recorded from the leg muscles reflects the action and interaction between central programs and afferent inputs from various sources (Dietz 1997). Any changes in the neuronal or biomechanical systems may lead to pathological movement disorders.

Central Programming

The motor program for human gait has been defined in two ways:

- Communications in the central nervous system that are based on past experiences and that can generate postural adjustments and movement (Brooks 1979).
- A set of muscle commands that are structured before a movement sequence begins and that allows entire sequence to be carried out uninfluenced by the peripheral feedback (Keele 1968).

With respect the first definition, programs are not based totally on the past experiences but are also partly innate. Step like movements are present at birth and can be initiated spontaneously or triggered by peripheral stimuli. A central origin of these movements is implied as the EMG bursts precede the actual mechanical events (Forssberg 1986). Stepping also occurs in anencephalic children which suggests that a spinal mechanism co-ordinates the movement. The central programme generates a complex and widespread pattern of muscle activation triggered by external or internal events.

With regard to the second definition of central programming, it is known that programmed movements can be influenced by sensory inputs in some circumstances (Brooks 1979). Although rhythmic alternating leg movements are co-ordinated by a central generator, the infant is unable to maintain body equilibrium. These children lack the appropriate afferent input and integration of the programmed leg muscle EMG pattern which is needed to achieve modulation and adaptation to the actual needs.

Therefore, to achieve functional movement it is reasonable to assume that afferent information would influence the central pattern and consequently, that the central pattern generator would select the appropriate afferent information (Dietz 1997). The convergence of spinal pathways and descending tracts on to common spinal interneurones appears to be the rule, implying that the interneurones play an integrative role (Schomburg 1990). Voluntary commands also have to interact with the spinal locomotion generator in order to change the direction of gait or avoid an obstacle.

Both spinal locomotor centres and the reflex mechanism are under control of the brainstem and supra spinal motor centres (Dietz 1997). This is shown in figure 5.3.

Peripheral reflex mechanisms

Several studies have demonstrated that the contribution of afferent inputs to the regulation of locomotion is significant (Dietz 1998, Dietz and Duyson 2000, Sanes, Mauritz, Dalakas and Evarts 1985, Gollhofer, Schmidtbleicher and Dietz 1984, Taylor et al 2000). Feedback information from muscles, joints and associated tissues via the proprioceptive reflex system is required to adjust the motor programs to irregularities of the ground during walking or to respond if the leg encounters resistance. These proprioceptive inputs modulate muscle EMG activity in the leg during gait.

Group Ia afferents are the best known for their modulation by presynaptic inhibition during gait. Several investigations using indirect methods addressed the presynaptic inhibition of group Ia afferents during gait (Capaday and Stein 1986,1987, Cheng et al 1995). The modulation of group Ia reflexes during gait revealed a

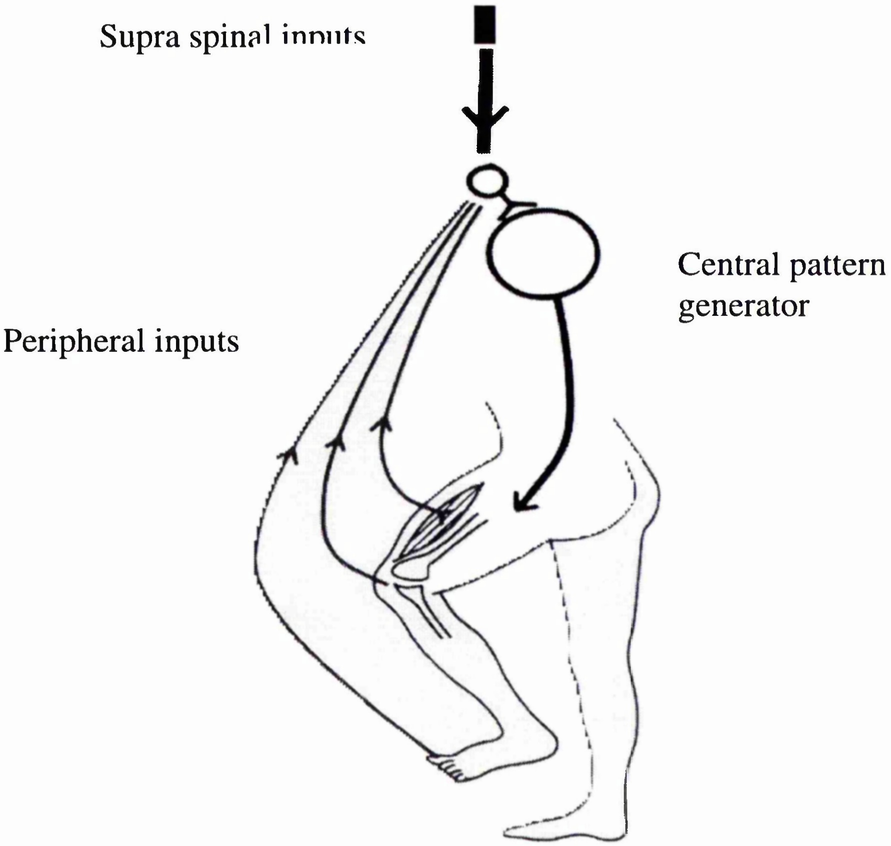

Figure 5.3. Schematic drawing of the neuronal mechanisms involved in human gait. Leg muscles become activated by a programmed pattern generated within spinal interneuronal circuits. This pattern is modulated by a multi-sensory afferent input which adapts the pattern to the actual requirements. Both the programmed pattern and the reflex mechanisms are under supraspinal control (modified figure from Jankowska and Lundberg 1981).

new aspect of the peripheral contribution in motor control of gait. Ia afferent pathways are able to modulate other reflexes. Ia inputs from the knee and hip muscles have been shown to inhibit the H reflex in soleus (Brooke et al 1992,1995, McIlroy et al 1992) and TA (Brooke et al 1997) during locomotion. This modulation of reflex gain might take place on common interneurones where convergence of descending tracts and several different afferent pathways occurs (Baldissera et al 1981). For spinal motor systems, premotoneuronal inhibition provides a way to modulate the relative contribution of afferents to a given reflex response.

During locomotion, the amplitude of the soleus/gastrocnemius H reflex is modulated throughout the entire step cycle. Maximum facilitation occurs at the end of the stance phase and maximum inhibition occurs during the swing phase and the beginning of the stance phase (Capaday & Stein 1989, Crenna and Frigo 1987). However, throughout the entire step cycle, the amplitude of the H reflex is considerably smaller than that during standing (Capaday & Stein 1986,1987).

Two functional implications of modulation of group Ia afferent input during gait have been suggested. Firstly, facilitation of the gastrocnemius/soleus stretch reflex at the end of the stance phase contributes towards the compensation for ground irregularities and assists during the push-off phase (Capaday & Stein 1987, Sinkjaer, Anderson and Larsen 1996). Secondly, the depression of leg extensor Ia input during the swing phase, prevents the occurrence of an extensor stretch reflex during ankle dorsiflexion (Capaday & Stein 1986).

The group I (and II) afferents from the ankle dorsiflexors have a strong short latency excitatory effect on the Q motoneurones (Brooke and McIlroy 1990a, McIlroy et al 1986, Marque et al 1996, Simonetta-Moreau et al 1999). This projection is oligosynoptic and the interneurones in this pathway are a site for convergence of supraspinal pathways. The current view of the pathway of this reflex is explained in section 1.8. There is no information about the role of this excitatory reflex in the control of activity of Q muscles during gait. The only investigation conducted addressing the role of this reflex during gait was performed by Brooke and McIlroy (1990). They concluded that the reflex magnitude during gait is correlated to the intensity of the background EMG in the Q muscles. This conclusion is based on testing at only one instant of the gait cycle shortly, 30ms after heel strike. This study could not address the actual role and importance of this excitatory reflex, linking the ankle dorsiflexors to the knee extensor muscles, in motor control of Q muscles. The pattern of the modulation for this reflex during gait, which is yet unknown, could reveal the actual contribution of this neural pathways during human gait.

5.2. Aims

The two experiments in this chapter follows two aims:

1) To find out that how the magnitude of CPQ reflex changes during gait. In other words, to investigate the pattern of modulation of this reflex during gait.

2) If the reflex is modulated, to investigate the causes of the modulation at different phases of the gait cycle.

5.3. Material and Methods

5.3.1. Subjects

The experiments included 2 studies of 10 volunteer subjects. Seven male and 3 females were tested. Seven volunteers participated in each study. 5 volunteers took part in both studies. The age of the volunteers ranged from 21 to 47 years. None of the subjects had any history of neuromuscular injury or systemic disease.

5.3.2. Electrical stimulation

Stimulation intensity

Stimulus current was applied to the common peroneal nerve at caput fibulae. During gait, ankle dorsiflexor muscles show variable intensity of activity at different phases of the gait. As a result it was inappropriate to measure the M threshold during gait. Alternatively, the M_{max} was used instead as the criteria to adjust the intensity for the stimulation. Stimulus of an intensity adequate to evoke M wave of above 40% of M_{max} in tibialis anterior is capable of evoking maximum reflex magnitude in the knee extensor muscles (Brooke & McIlroy 1990b). The intensity of the stimulus during both studies was adjusted accordingly. The M_{max} peak to peak amplitude was also used to standardise the intensity of the stimuli among the subjects. The evoked M wave amplitude was expressed as percentage of the M_{max} for each subject.

The M_{max} was measured as the average of ten waves evoked by supra maximal stimulation. The stimulation was applied at several points during the gait cycle in both experiments. The delay for the stimulation was set from the heel strike.

The relative position of the electrodes and the common peroneal nerve is likely to change during gait. The M_{max} was therefore measured separately for all the new stimulation latencies. This ensured constant stimulation conditions during the experiments. Intensity of the stimulation was adjusted to evoke an M wave with amplitude of above 40% of the M_{max} at each delay. The tibialis anterior EMG was displayed on a computer during the tests. Further adjustment was done as necessary during the test to ensure that the M wave amplitude was constant at 40% M_{max}.

5.3.3. Electromyographic recordings

Surface EMGs were recorded from tibialis anterior, vastus medialis, rectus femoris, semitendinosus and medial gastrocnemius of the right leg of all subjects in the first study. During the experiment with knee orthosis only tibialis anterior, vastus medialis and rectus femoris electromyograms were recorded. In both experiments each trial consisted of 3-5 minutes continuous EMG recording during which 40 stimuli were applied in a pseudo-random sequences.

Figure 5.4. The figure shows subjects during the experiment. All the wires were gathered and secured with a belt. The length of the cable was long enough to allow enough freedom of movement and to prevent any strain on the electrodes during walking. The EMG electrodes are attached at the appropriate sites. The stimulating electrodes can be seen at the lateral side of leg at the level of caput fibulae. The goniometers are attached to the ankle and the knee joint by using a double-sided sticky tape. Pressure switches are secured to the heel and the level of the metatarsal heads of the shoe.

All the wires connected to the subject's leg were organised into a bundle using a soft belt. This avoided any restriction of movements. The length of the wires was long enough to provide at least 0.5m movement, forward and backward, during walking on the treadmill (Powerjog, Sport Engineering Ltd, Birmingham, England). The way the volunteers were prepared for the experiments can be seen in figure 5.4.

5.3.4. Triggering

Two small pressure switches (1cm×2cm), which did not interfere with normal gait, were located on the heel and at the level of metatarsophalangeal joints on the sole of the right shoe. The switches were secured in place by strong adhesive tape.

The position of the switches was selected in order to identify the start and the end of the stance phase of gait. At each heel strike the switch closed and a 12 volt electrical potential continued until the foot lifted clear of the ground. Therefore the timing of the switch closing and opening reflected the heel strike and the start of the swing phase respectively. The closing potential was used to trigger a delay module, the oscilloscope and also provided a digital input to the computer. The trigger pulse passed through a digital delay width module (NL 401, Digitimer Ltd, Hertfordshire, England). Different delays were set from the heel strike by this module. The output of this module was used to trigger the stimulator and also recorded as a digital input event in the computer during the test. The delay of the stimulator from the heel strike was measured on line to confirm the accuracy of the adjustment.

A hand switch was also included in the trigger circuit. This provided further control of the triggering during the test by opening and closing the trigger circuit. This prevented habituation to the stimulation. The trigger was applied every 2-5 strides in a pseudo-random sequence.

5.3.5. Modified knee orthosis

During gait, quadriceps femoris EMG activity started near the end of terminal swing phase and continued to mid stance phase (see section 5.1.1). During the remainder of the gait cycle they were nearly silent. In order to increase the knee extensor muscle activity during this silent period, a specific knee orthosis (fig 5.5) was modified. By adding 1 or 2 pairs of springs, each added a 50N load, to the knee brace, a variable flexion moment was applied to the knee joint. This increased the intensity and the duration of quadriceps muscle activity during gait. The subjects were encouraged to walk as normally as possible with the knee orthosis. The speed of the treadmill was the same for all three configurations therefore similar step duration was expected at all the times. No significant changes in the step duration was observed.

Three different configurations of the knee orthosis were tested for each subject:

a) without springs
b) with one pairs of springs
c) with two pairs of springs

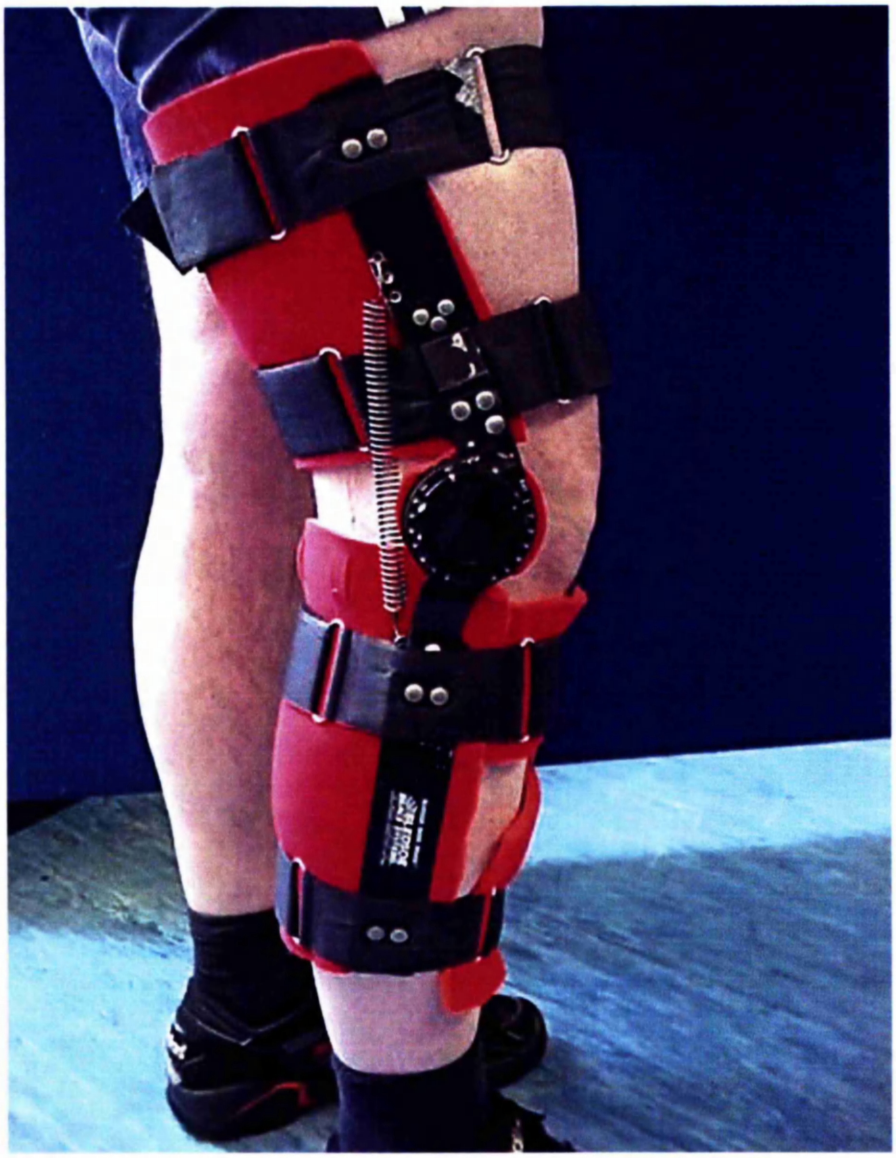

Figure 5.5. The figure shows the modified orthosis with a pair of springs fixed behind the knee hinge. This provided a flexor moment around the knee joint that increased the activity of quadriceps muscle throughout the gait cycle.

These configurations provided three levels of flexion moment and proportionally three levels of quadriceps muscle EMG activities. The orthosis was fitted tightly to the subject's knee so that the axis of the hinges on the brace coincided with the imaginary knee axis crossing the condyles of the femur. The correct position of the orthosis was confirmed by getting a resistance-free and full range of knee flexion for each subject.

5.3.6. Goniometers

Two single axis electrogoniometers (Biometrics Ltd, Cwmfelinfach, Gwent) were used to detect the movement of the knee and the ankle during gait. The goniometers were sensitive to the movement in one plane. Any relative movement between the arms of the goniometer changed its output voltage proportional to the movement applied. The output voltage was amplified, digitised by a CED micro1401 interface and recorded in the computer during the test. This output voltage was translated into actual joint range of movement using the correlation equation for each goniometer. This is described in the next section.

The arms of the goniometers were secured in place with sticky tape. The alignment and location of the goniometer arms were selected carefully so that the movements of the knee and the ankle happened in the plain of the sensitivity of the goniometers. Both goniometers were stuck to the medial side of the relative joints.

These goniometers were used to analyse the relative movements in the joints during gait. They were less accurate for measuring the absolute positions of the joints at every instant of gait.

Calibration of the goniometers

Calibration tests were done for both goniometers to translate the voltage output into the angle changes of the movement. Several lines at intervals of 10 degree were drawn on a card. The arms of the goniometers were placed along the lines at different angles and the output of the goniometers was recorded for each angle. The correlation between the output currents of the goniometers and the range of the rotations of the goniometer arms was shown in figure 5.6 for both goniometers. It is clear that both goniometers have linear correlation with joint positions, therefore the correlation equation for both goniometers would be accurate for translating the output current values into actual angle values. To do this the goniometer output voltage at selected instants of the gait was measured and transformed into angle values using the equations. The difference between the angle values represented the relative movement that happened between the selected instants of gait.

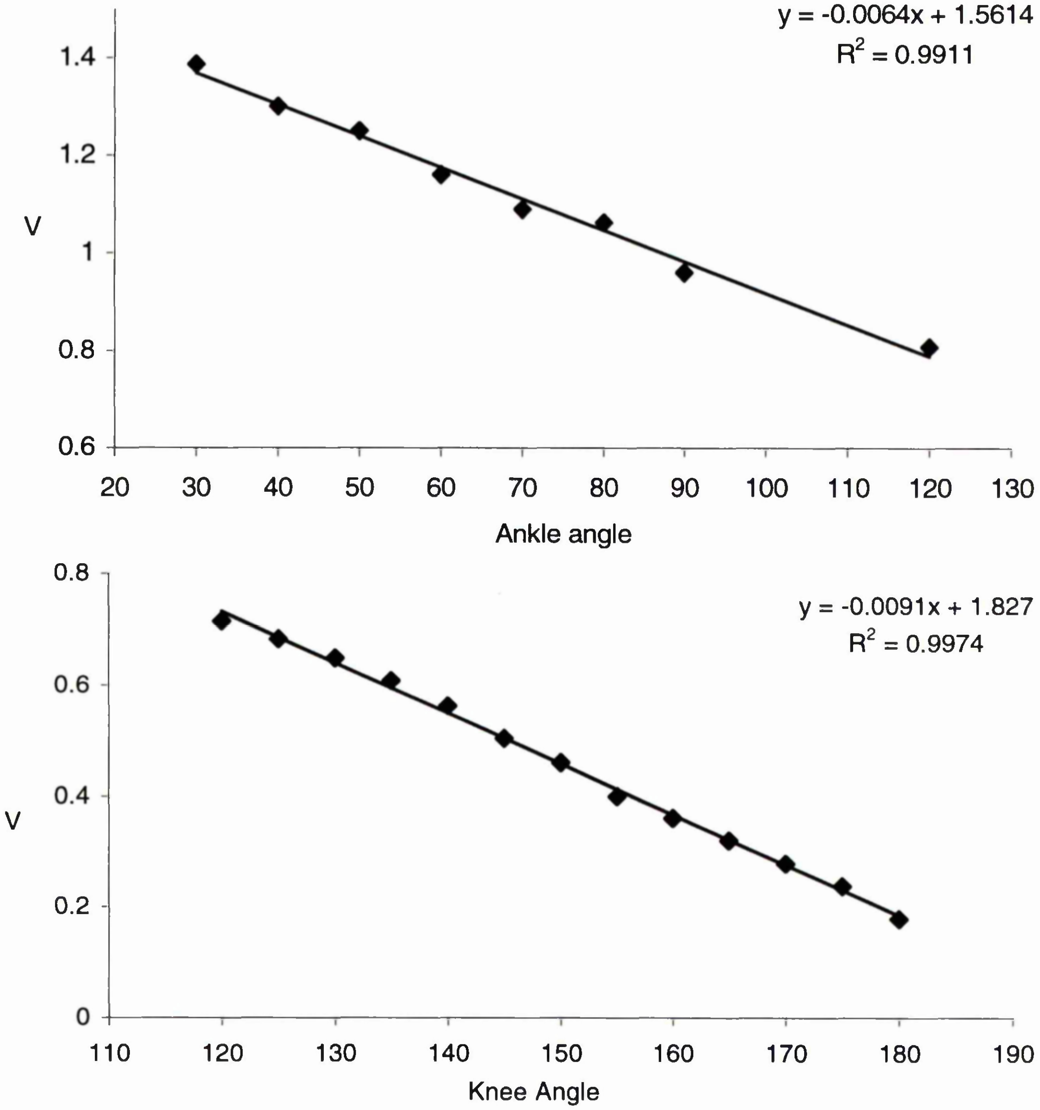

Figure 5.6. The calibration graphs for the ankle goniometer (top) and the knee goniometer (bottom). Both graphs show a clear linear correlation between the output of the goniometer and the actual angle. The equation of these correlation graphs can therefore be used to calculate the actual range of movement in both joints. 180° at the bottom graph and 90° in the top graph represent the full extension and the neutral position in the knee and ankle joint respectively.

5.3.7. Experimental procedure

Pattern of modulation during gait

The experiment started with about 5 minutes of walking until the subjects felt at ease on the treadmill. The speed of the treadmill was set to a value at which the subjects felt comfortable. The range of the speed was from 3.5 to 4.5 kilometres/hour. This resulted in average gait cycle duration of 1165ms with standard deviation of 50ms in all the investigated subjects. Figure 4.3 shows a sample of recording during the experiment.

The stimulation was applied every 3-5 strides in a pseudo-random sequence. Sets of recordings were done with stimulation at different latencies from the heel strike. Since the duration of the gait among the subjects was similar, stimulation happened at similar points in the gait cycle with all preselected latencies.

Delays of 0, 50, 100, 150, 200, 300, 500, 700, 900, 1000, 1100ms after heel strike were selected. At the start of each set of recording the M_{max} was recorded and measured in tibialis anterior muscle. The intensity of the stimulation was adjusted accordingly to evoke M wave of 40% of the M_{max} amplitude. Three maximum voluntary contractions of quadriceps femoris of 3 seconds duration each were also recorded at the start of the experiment. The MVC intensity was used later for normalisation of the peak to peak amplitude of the reflexes and the intensity of the muscle EMG activity at each instant of stimulation.

A control recording was done without stimulation where from the intensity of the EMG activity of the muscles at each stimulus delay was measured for analysis.

Experiment with knee orthosis

This experiment was designed to investigate periods of the gait cycle when no reflexes could be elicited. During this areflexic period the Q EMG was also silent. The magnitude of the reflex is known to be correlated to the intensity of muscular activity (section 1.8). This experiment was performed to investigate if increases in the muscular activity of Q during this period could evoke the reflex. A modified knee orthosis was designed and used for this purpose.

Enough habituation periods were provided for each subject wearing the knee orthosis, until the subject felt comfortable walking on the treadmill. The speed of the treadmill was adjusted at a comfortable value. This was ranged between 3.5 and 4.5 kilometre/hour. Once the speed was selected it was used in all the trials for that subject.

Three contraction intensities of quadriceps femoris were obtained during areflexic period of gait by using the modified knee orthosis. This can be seen in figure 5.13. Three stimulation delays were applied for each subjects and for each knee brace configurations; without spring, with one pairs and two pairs of springs. The latencies was adjusted individually to occur during these periods of gait:

- during mid stance
- during the transition from stance to swing
- during the terminal swing phase

The fine adjustment of the stimulation timing for each subject was made individually to set the stimulation near the peak of activity of rectus femoris at these three periods. These were at about 300ms, 700ms and 1100ms after heel strike.

Like the first experiments, a control recording was done for each knee brace configuration. M_{max} and the maximum voluntary contraction were also recorded the same way as the first series of experiments. Specimen data obtained during treadmill walking is shown in figure 4.3.

5.3.8. Data analysis

Pattern of modulation during gait

- Muscular activity during gait

The rectified EMG from rectus femoris, vastus medialis, tibialis anterior, medial gastrocnemius and semitendinosus were analysed by averaging 40 gait cycles. In this and the next experiment, the instant of heel strike was used to trigger the averaging of the EMG recordings. Therefore, the time 0ms in all the averaged EMG represents the instant of heel strike.

- Pattern of reflex modulation during gait

The peak to peak amplitude of the reflexes at each stimulus delay of stimulation was measured for all the investigated muscles. The non-rectified average of 40 EMG samples was used for this purpose.

The peak to peak amplitude was expressed as percentage of the EMG during MVC for each subjects.

- Intensity of muscular contraction

This MVC was calculated from the averaged root mean square electromyogram (EMG_{rms}) of three maximum contractions at the start of each experiment for each subject. This was done only for knee extensor muscles. The EMG_{rms} of 10-second rest period before the maximum contraction was measured in the same way. This was set as an offset to compensate for the background EMG. The EMG_{rms} of the rest period was subtracted from the EMG_{rms} of the MVC and the EMG_{rms} measured at different intervals during gait cycle.

The RMS of the maximum EMG activity of a muscle represents a lower value than the maximum p-p amplitude that can be measured. For example in a sinusoidal wave the RMS equals $(\sqrt{2})^{-1}$ multiplies the peak amplitude. The normalised values of the reflex represented as percentage of MVC could therefore show values above 100% of MVC in extreme cases. This does not reflect a higher level of excitation than the maximum capacity of the motor neurone pool.

The intensity of muscle EMG activity was calculated by averaging the RMS of 30ms period post-stimulus. Three randomly picked post-stimulus periods from raw control EMG were used for this purpose. For example for the stimulation delay of 300ms, the average of three randomly chosen periods between 300ms and 330ms after heel strike from raw EMG was calculated. This period is selected because the volley from the common peroneal afferents reaches the quadriceps motoneurones at about the middle of this period. The intensity of the muscle activity at the instant of the stimulation is therefore very well represented in this way.

The figure 5.7 shows that linear correlation exists between the RMS of the raw EMG of RF and the force exerted by the knee extensors. This confirms the reliability of RMS values in showing the actual intensity of muscle activity as a fraction of MVC intensity. The EMG intensity for the knee extensor muscles was expressed as percentage of MVC during both experiments.

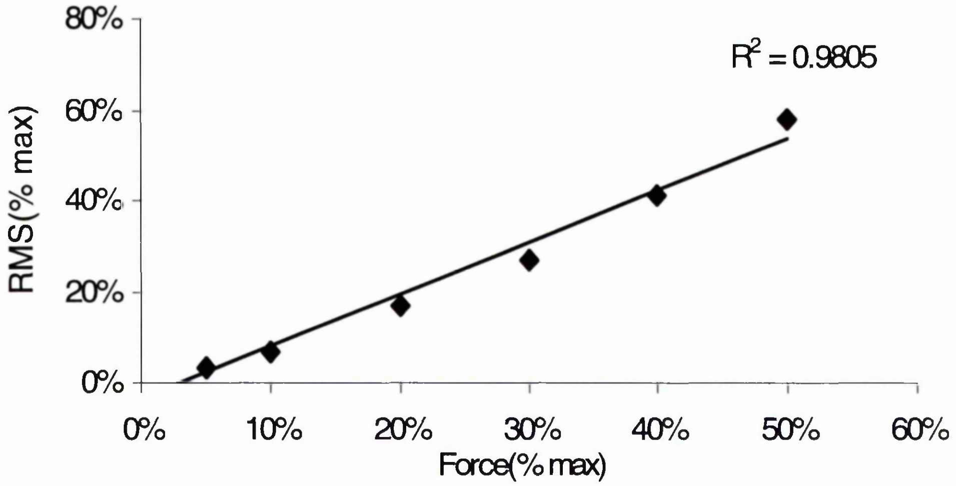

Figure 5.7. The graph shows the correlation between the EMG_{rms} of non-rectified EMG and force. A linear correlation exists between the two variables. This suggests the reliability of EMG_{rms} to estimate the intensity of muscular activity.

- Knee and Ankle Movement

The goniometer signals were used to calculate the range of movement of the knee and ankle during gait (fig 5.6). 40 samples of knee and ankle recordings were averaged from the heel strike for this purpose.

The flexion and extension range of movement during gait was measured for both joints for each subject. The average ranges of relative movement and the confidence interval for them were calculated accordingly.

- M Wave Measurement

The non-rectified tibialis anterior EMG was analysed. The M wave was measured peak to peak. The M_{max} peak to peak amplitude in TA was measured from the non-rectified EMG recording with supra maximum stimulation. 10 samples of EMG were averaged from the stimulation digital event data. The M_{max} was measured for all latencies separately. The amplitude of the M wave at each stimulus delay, was expressed as percentage of the M_{max} measured for that specific stimulus delay. This confirmed the consistency of the stimulation at all the latencies.

Experiment with knee orthosis

- Muscular Activity

Non-rectified EMG from vastus medialis, rectus femoris and tibialis anterior were analysed. Stimulation delays were selected from a trial recording done with 2 pairs of springs to the knee orthosis. These latencies were selected according to the criteria explained in section

5.3.7. Forty gait cycles were captured and averaged for control recording for each knee orthosis configurations.

The intensity of muscular activity in vastus medialis and rectus femoris at the time of the stimulation was analysed in the same way as described for the first series of experiments. The M_{max} was also measured separately for all three latencies by the same method.

The magnitude of the reflex evoked by the stimulation was measured peak to peak from average of 40 non-rectified EMG samples. This was done for every three latencies and orthosis configurations. In summary the whole samples captured from each subjects included:

- control recordings for each knee orthosis configurations
- trial recording with 2 pairs of springs added to the knee orthosis
- M_{max} recordings for each knee orthosis configurations
- EMG samples at each stimulus delay and for each knee orthosis configurations

- M Wave Measurement

The M_{max} for all three selected latencies was measured peak to peak from the averaged non-rectified tibialis anterior EMG from supra maximal stimulation trial. The M wave magnitude which represent the intensity of the stimulation was measured from the average of 40 non-rectified EMG samples in tibialis anterior. The peak to peak amplitude of the M wave at any stimulus delay was expressed as percentage of the M_{max} magnitude at that stimulus delay.

- Knee and Ankle Movements

The movement of the knee and ankle were analysed exactly the same way as the first series of experiments. This was done from the control recording captured for each orthosis configuration.

5.4. Results

5.4.1. Pattern of modulation during gait

Pattern of muscular activity during gait

The muscles of the lower limb showed a cyclic pattern of activity during gait. The following paragraphs will address the pattern of activity in these muscles. In all the following sections the timings would be clarified by percentage of the gait cycle where they happened. All the data is extracted from the average of 40 gait cycles.

- Quadriceps femoris

RF and VM had a very similar pattern of EMG activity. The pattern of activity of both muscles during gait is shown in figure 5.8. Both muscles were active from terminal swing to midstance. RF contraction starts from about 75% and VM starts from about 87% of gait cycle. This is the beginning of terminal swing phase. The peak of activity for RF and VM happens early after heel strike at about 4% of gait cycle for RF & VM. The peak of RF activity ranged from 13% to 39% of MVC with the average of 19%. Vastus medialis peak contraction intensity ranged from 17% to 40% and with a mean of 25%. EMG activity dropped slowly to its lowest level at mean 25% of gait cycle for VM and 17% for RF. This was at about the midstance period.

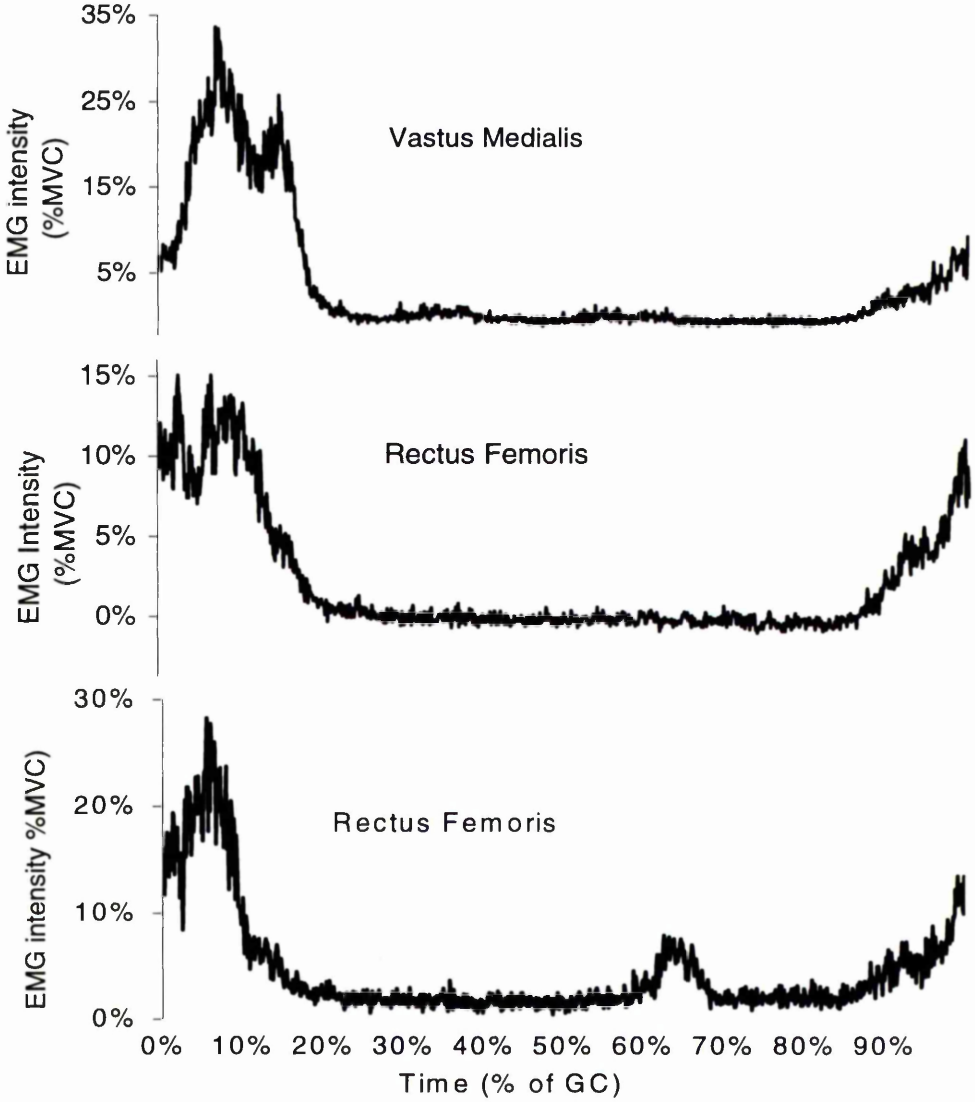

Figure 5.8. The rectified averaged EMG of VM and RF during gait cycle. Each gait cycle starts at heel strike and ends just before the next heel strike of the same foot. "0" on the time scale defines the instant of the heel strike. The figure at the bottom shows activity of RF in one of the subjects with a second peak during the transition period. This was observed in half of the investigated subjects.

In 4 out of 8 subjects investigated in this experiment, RF showed a second peak of activity at the end of the stance phase. The bottom panel in figure 5.8 shows this. It happened between 55% and 70% of gait cycle. This second peak was of lower intensity than the early stance peak ranged from 4% to 8% and the peak intensity of 6% of MVC in average. This was not detected in the VM recordings.

Figures 5.9 shows the pooled intensity of activity for RF and VM during gait from all the investigated subjects. The 95% of confidence interval for the mean background EMG at each instant of the gait cycle can also be seen.

- Semitendinosus and Gastrocnemius

Figure 5.10 shows the EMG activity of semitendinosus and medial gastrocnemious during gait. Semitendinosus showed two peaks of activity. The first peak was before heel strike during the terminal swing followed by smaller one, which was started at early swing phase and continued until the terminal swing. Medial gastrocnemius muscle showed also two peaks of activity during gait. The first larger one was during midstance to terminal stance and followed by a lower intensity peak during midswing phase. It is almost silent at the heel strike.

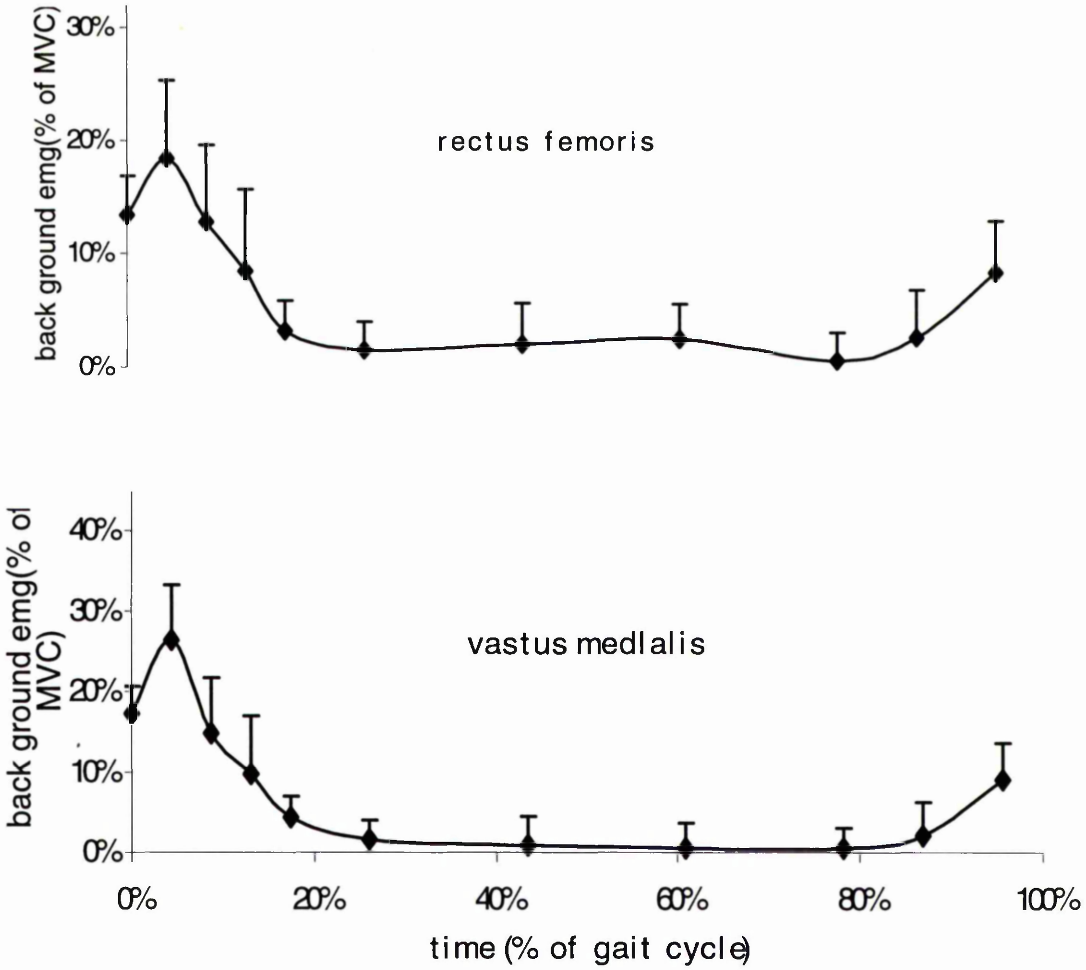

Figure 5.9. The figures show the pooled intensity of the EMG for VM and RF during gait cycle (N=7). The 95% of confidence intervals for the mean are added to the graph. The pattern of activity in both muscles is almost similar. The major activity occurred at early stance phase while during the rest of gait cycle both muscles remained almost silent. A slight increase in activity of RF can be seen for a short period from late stance to early swing phase. This is the result of a small second peak of activity that was observed in 4 subjects during this period. This was not observed in VM.

- Tibialis anterior

The pattern of tibialis anterior activity is shown in figure 5.10. This muscle had a burst of activity started shortly before heel strike. Its peak occurred at about heel strike. Its activity dropped steeply to almost rest level after the early stance phase at about 5% of gait cycle and remained silent during the remaining stance phase. Another peak of activity but of lower intensity started at the start of the swing phase. It remained active at low intensity during the swing phase until the next heel strike.

The changes in the magnitude of the CPQ reflex during gait

Electrical stimulation, at an intensity which elicits an M wave of 40% of M_{max} in TA, was applied to common peroneal nerve at different latencies from the heel strike. The responses in all muscles under investigation were analysed.

Short latency reflexes only appeared in the knee extensor muscles. No other responses, inhibitory or excitatory were detected in the other muscles.

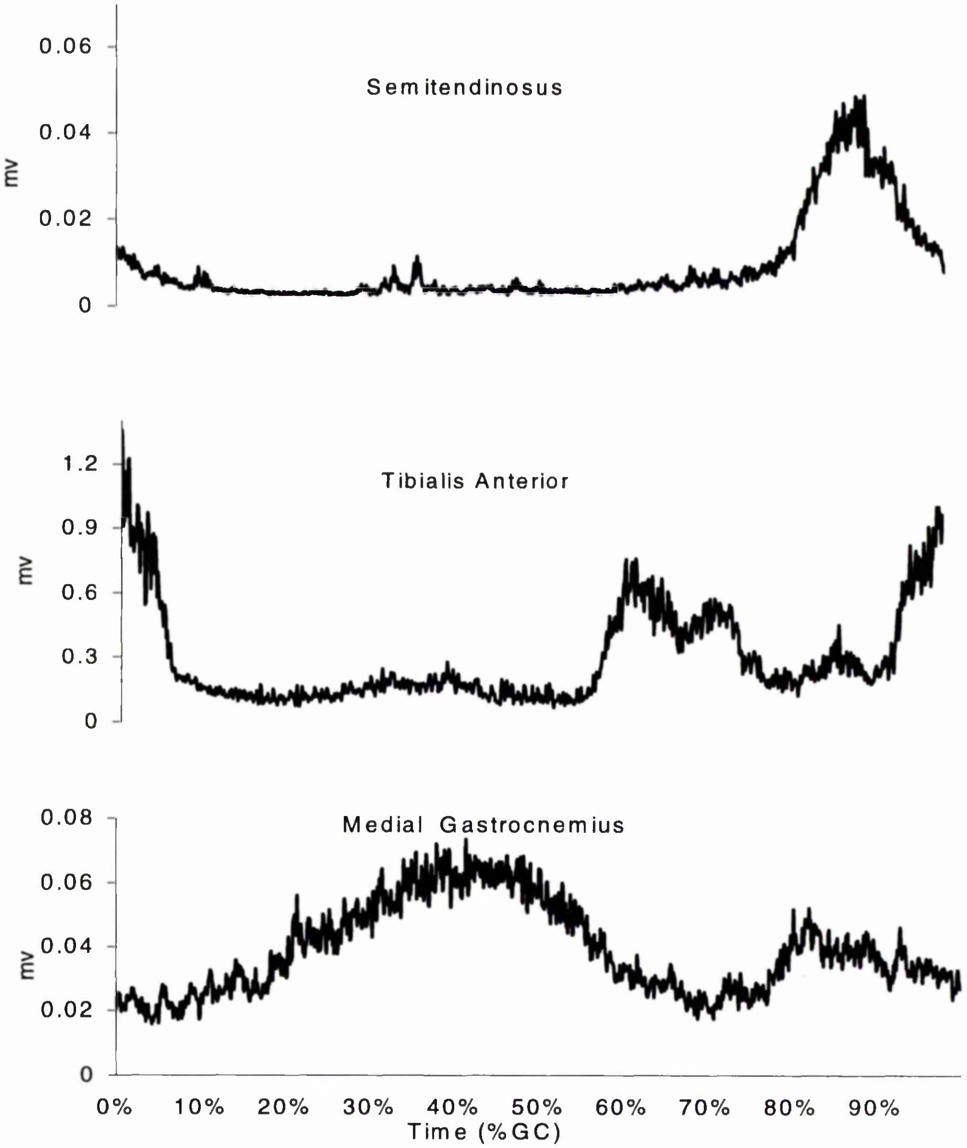

Figure 5.10. The figure shows the rectified averaged EMG of ST, MGC and TA during gait cycle. TA and MG show an opposite pattern of activity during gait i.e. when one is active the other is silent. Semitendinosus showed its highest activity during the late swing phase and remained almost silent during the whole stance and early swing phase.

The peak to peak amplitude of the reflex in VM and RF changed during gait. The reflex was at its maximum magnitude between the terminal swing and early stance phase. Figure 5.11 shows the pattern of changes in reflex magnitude in both muscles. A similar pattern was observed from both muscles during gait. It can be seen that the magnitude of the reflex reaches its maximum early after heel strike. The peak intensity of the reflex at this period was 70% MVC for RF and 121% of MVC for VM. The magnitude of the reflex then decreases gradually to an areflexic state which lasts until the terminal swing phase. The reflex appears again during terminal swing (at 80% and 75% of gait cycle for VM and RF). It increases towards its peak at heel strike. The figure also shows the 95% of confidence intervals for the mean intensity of the reflex. The large interval during the early stance phase reflects the wide range of reflex intensity among the subjects.

Changes in evoked M wave magnitude during gait

The peak to peak amplitude of the M wave, expressed as percentage of M_{max}, is shown in figure 5.11. The 95% confidence interval of the mean M wave amplitude was also added into the graph.

Stimulation at an intensity capable of evoking M waves of above 40% of M_{max}, are known to elicit a maximum reflex. It was very important

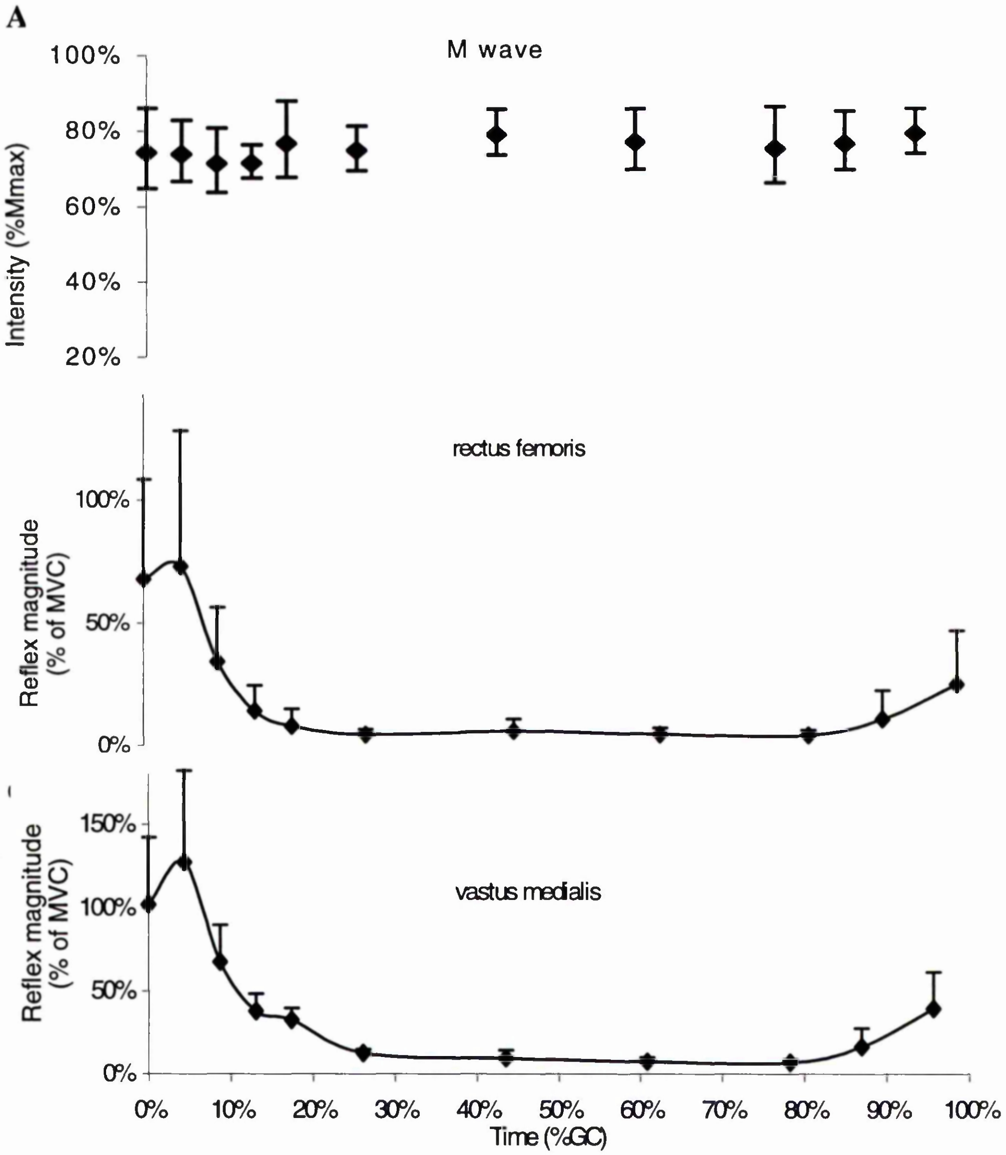

Figure 5.11. Panel A shows the mean amplitude of the M waves recorded in TA during the gait cycle. There are no significant changes and the values are above 40% of M_{max}. Panel B shows the mean amplitude of the CPQ reflex in RF during the gait cycle. Panel C shows the mean amplitude of the CPQ reflex in VM during gait. The reflex was largest during the early stance phase in VM and RF. During the rest of gait cycle both muscles remained areflexic.

that the M wave should always exceed 40% of M_{max}. It can be seen in figure 5.11 that the M wave magnitude never dropped below the 40% of M_{max} limit. It remained clearly constant during the tests at all the stimulation latencies. This confirmed the consistency of the stimulation during the experiment.

Knee and ankle movement during gait

Figure 5.12 shows the pattern of movement for both joints. At heel strike the knee is nearly in full extension. After heel strike the knee joint flexes slightly by about 3 degrees on average (arrow 1). This small flexion happens early in the stance phase at about 12% of gait cycle. A larger knee flexion, mean 22^{o} (SD of 7.6^{o}), started at preswing and reached its peak during the early swing phase (arrow 2). It started at mean 48% and reached its peak at 80% of gait cycle on average.

The pattern of the ankle movement during gait can be seen in figure 5.12. The ankle moves toward plantar flexion exactly at heel strike (arrow 3) and reaches its peak at mean 9% of gait cycle. An average of 2 degrees of plantar flexion happened at this period. The movement of the ankle changes to dorsiflexion which reaches its maximum of 7 degree at 50% of gait cycle. The ankle moves again toward plantarflexion (arrow 4) and reaches its maximum range of 19 degree at 65% of gait in average. A sudden dorsiflexion movement (arrow 5) follows the peak of plantar flexion. The ankle moves gradually in direction of dorsiflexion until the next heel strike where again it moves toward plantar flexion.

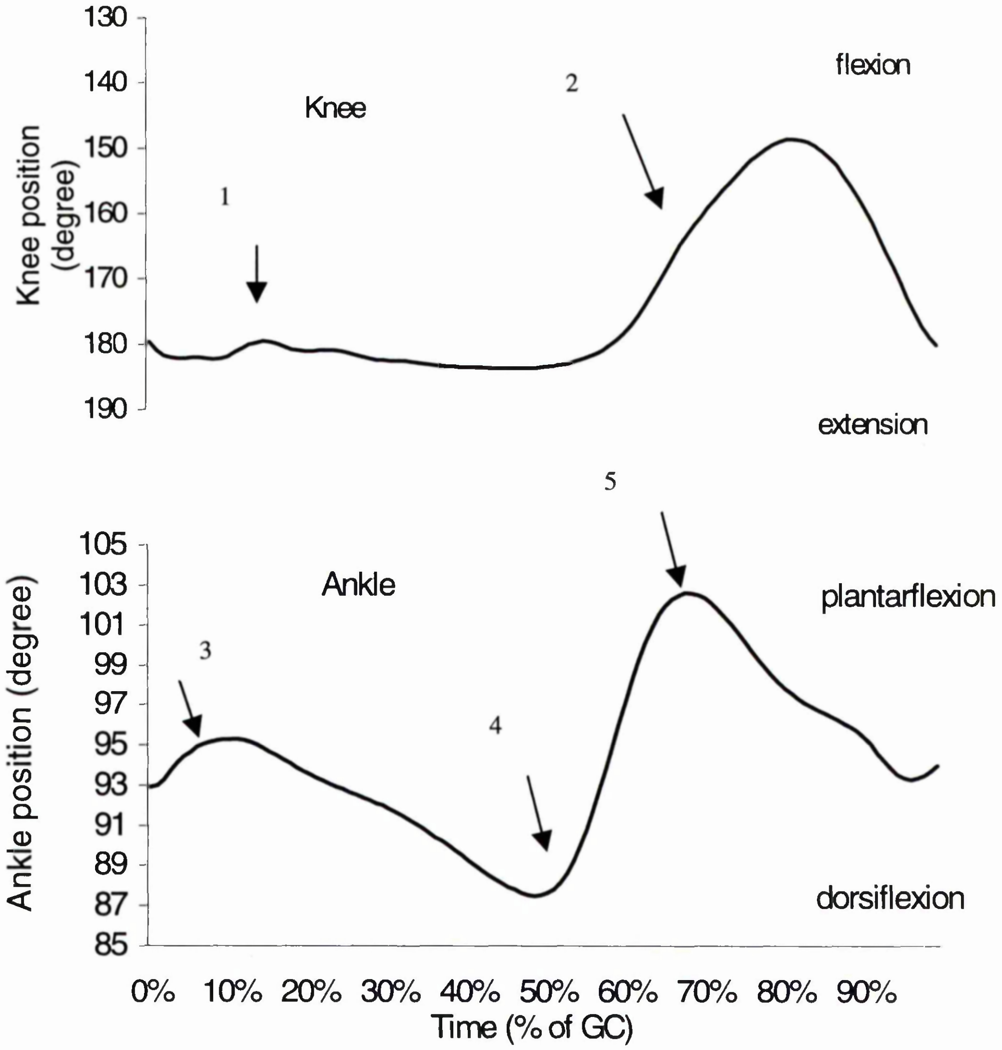

Figure 5.12. The pattern of movement in the knee (top) and ankle (bottom) during gait in one of the subjects. The knee joint showed two peaks of flexion. One shortly after heel strike which was very small and the second larger one during the terminal stance to midswing phase. The heel strike occurs at 0% of the gait cycle. The goniometers output was sampled at 100 Hz. Arrows 1& 2 show two peaks of knee flexion at the start of stance and swing phase respectively. Arrows 3and 4 show two peaks of plantarflexion at the start and the end of stance phase respectively. Arrow 4 shows the sudden dorsiflexion that starts at the beginning of swing phase.

5.4.2. Experiment with knee orthosis

Changes in muscular activity

Figure 5.13 shows a sample of averaged rectified EMG for RF and VM. Three types of gait are illustrated; normal and with the orthesis loaded by one or two springs. The EMG recordings for the three configurations of the knee orthosis and springs are shown for comparison. The springs obviously increase the intensity of activity in both muscles. The pattern of the muscular reaction was very similar in all the subjects. The knee extensors showed an increase in the peak of activity just after heel strike. The contraction of RF and VM at this point also lasted longer. The duration and the intensity of the muscle activity at this period further increased with the addition of the second pair of the springs.

The most prominent change in muscular activity happened at the transition period from stance to swing phase. At this period RF and VM reacted with increases in their activity. During normal gait only half of the subjects showed low level activity at this period. The activity of RF and VM also started earlier during the swing phase.

These three levels of muscular activity provided chances to explore the correlation between the reflex magnitude and the intensity of the muscle activity during the areflexic period of knee extensors.

The arrows in the figure 5.13 show three points of the gait cycle. These three points are at stance, stance to swing transition and swing periods. They lie at about 25%, 65% and 90% of gait cycle respectively. Comparisons between the intensity of muscular contraction (EMG_{RMS}) produced at the three configurations showed a significant increase at all three stimulation delays ($p \leq 0.006$, $p \leq 0.003$ and $p \leq 0.005$ in midstance, transition and terminal swing respectively). The CPQ reflex could not be elicited in RF and VM at these latencies during normal gait. This is clearly shown in figure 5.11. The delay of the electrical stimulation was set to coincide with these points of increased muscular activity.

A summary of average increases in the RF and VM activity at each period and with the three orthosis configurations is presented in table 5.1 and figure 5.14. It can be seen that at all the selected points the intensity of muscular activity was changed almost with the same quantity.

Modulation of the reflex

Electrical stimulation was applied to the common peroneal nerve at latencies of about 25%, 65% and 90% of gait cycle. The points were adjusted individually according to the reaction of the muscles to the applied external resistance provided by the knee orthosis. These points were selected so that the stimulation coincides with the periods of increased muscular activity. Figure 5.15 is a sample of averaged non-rectified EMG recordings in RF for all the three stimulation latencies. The reactions of the Q at these three periods were different and will be discussed in separate paragraphs below.

Springs	Rectus femoris			Vastus medialis		
	Midstance	Terminal stance	Terminal swing	Midstance	Terminal stance	Terminal swing
0 pairs	1%	2%	3%	2%	3%	5%
1 pairs	8%	5%	8%	17%	7%	11%
2 pairs	19%	17%	19%	30%	20%	25%

Table 5.1. The average changes in the level of activity in rectus femoris and vastus medialis, expressed as a percentage of MVC, recorded in seven subjects using the three configurations of the knee orthosis. The muscular activity is increased during all three selected periods of gait.

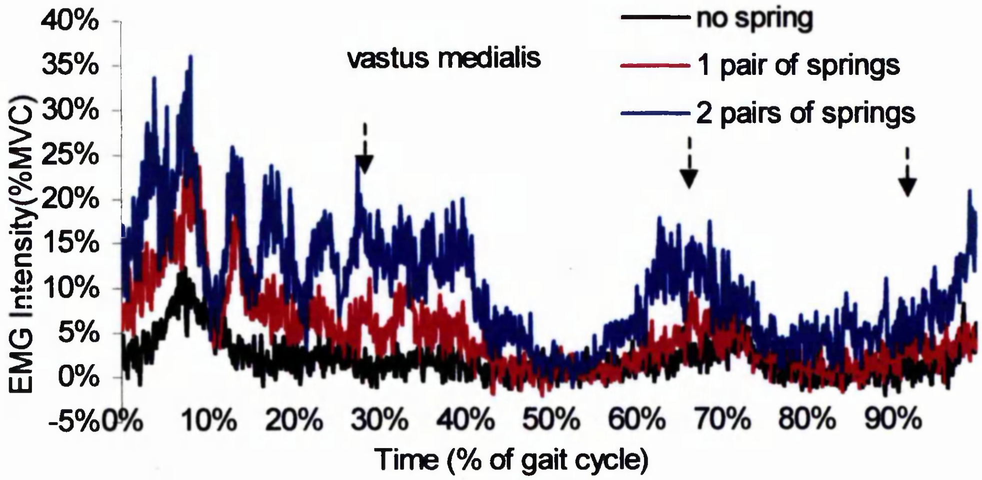

Figure 5.13. The figure shows the changes in the EMG activity in VM after adding 1 and 2 pair of springs (50N each) to the knee orthosis. The arrows show the points selected for the stimulation in this subject.

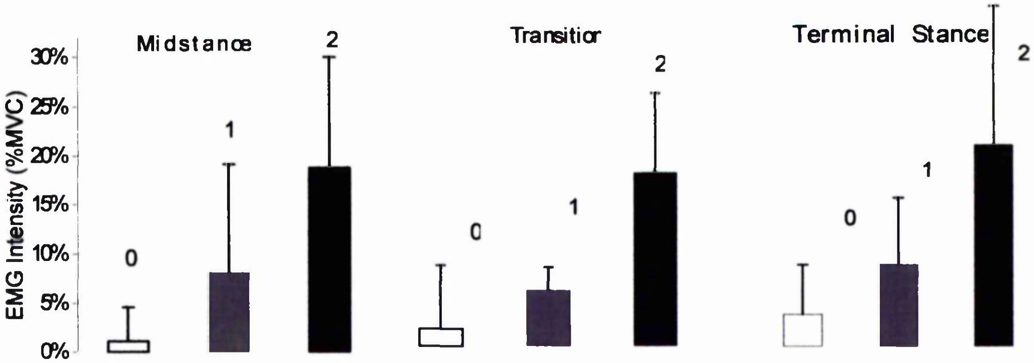

Figure 5.14. The pooled intensity of the background EMG in RF gained with the three configurations (0, 1 and 2 pairs of springs) of the orthosis at the three selected stimulation latencies (N=7). The increased in the background activity was significant at all three stimulation delays ($p<0.006$). The error bars represent the 95% confidence intervals.

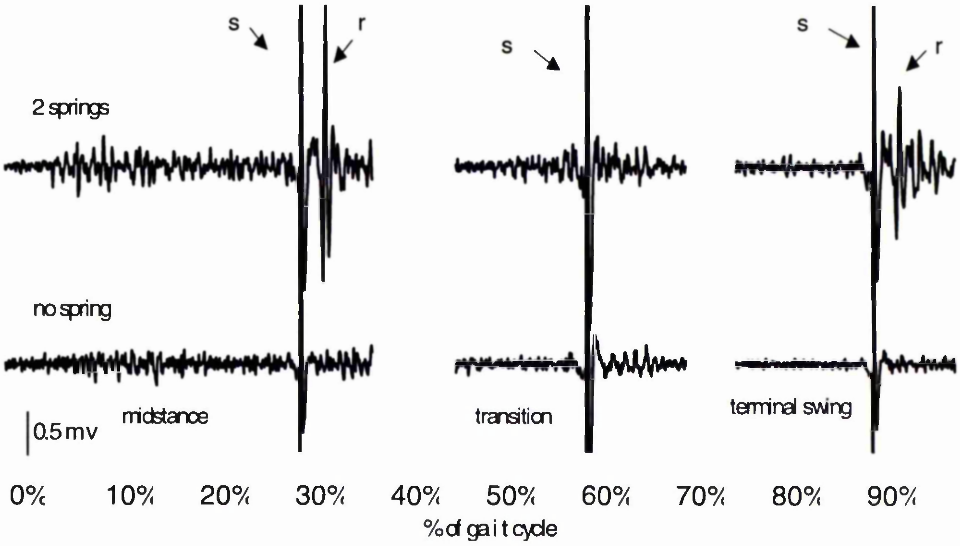

Figure 5.15.the non-rectified averaged EMG of RF during the stimulation at three latencies from heel strike. The top row shows the recordings with 2 springs added to the knee orthosis. The bottom row shows the recordings with the orthosis worn but without any spring. The increase in the background EMG is clear at the time of stimulation for all three latencies. (s= stimulus, r= response)

- During midstance

The reflex magnitude in RF and VM increased along with the increase in the muscular activity. Figure 5.16 shows a sample of EMG recording for VM and RF in one subject. It can be seen that with increase in the background EMG activity obtained by adding springs to the knee orthosis, the magnitude of the reflex increased proportionally. The average increase in the magnitude of the reflex during this period can be seen in figure 5.17. With 2 pairs of springs loading to the knee orthosis, the magnitude of the reflex reached to the average value of 76% and 95% of MVC in RF and VM respectively.

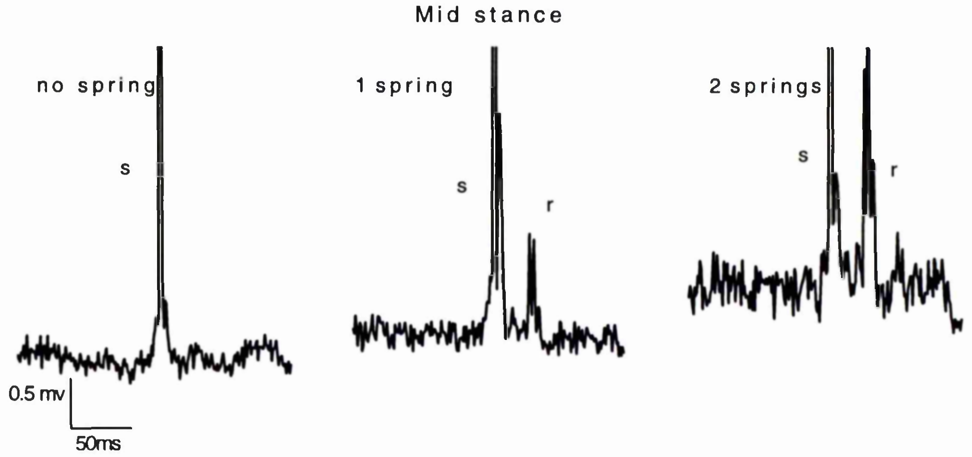

Figure 5.16. The figure shows the average of 40 samples from rectified EMG of RF in one of the volunteers. Only the section of the EMG during midstance is shown. The reflex is not elicited during unloaded gait (right panel). As the background EMG is increased, by addition of the springs to the orthesis, a clear reflex appears that grows larger with the increases in the background EMG.

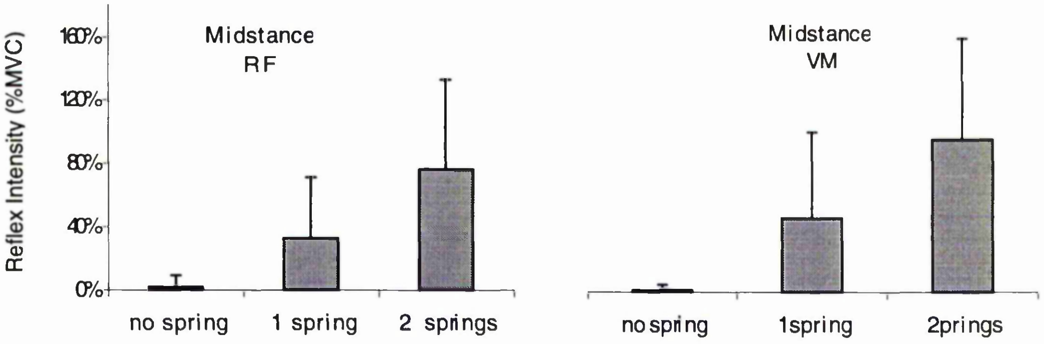

Figure 5.17. The reflex magnitude for VM (right) and RF (left) during midstance stimulation with all three orthosis configurations (N=7). The reflex reappears with the increase in the background EMG and increases with it significantly (ANOVA test, $p \leq 0.015$). The error bars represent the 95% CI.

- During the transition from stance to swing

During this period, even with increased background activity, a CPQ reflex could not be elicited. All the subjects remained areflexic during this period despite significant increase in the EMG activity. Average increase of 17% of MVC in the muscular activity occurred during this period that was above the threshold needed for the reflex. The effect of background activity in Q and the magnitude of the reflex is described in section 4.4.2. Figure 5.18 shows a rectified averaged EMG of one subject with stimulation during this period and with the three different orthosis configurations. The averaged magnitude of the responses is shown in the figure 5.19. The values in the graph are the amplitude of the rectified EMG at the expected time of the reflex.

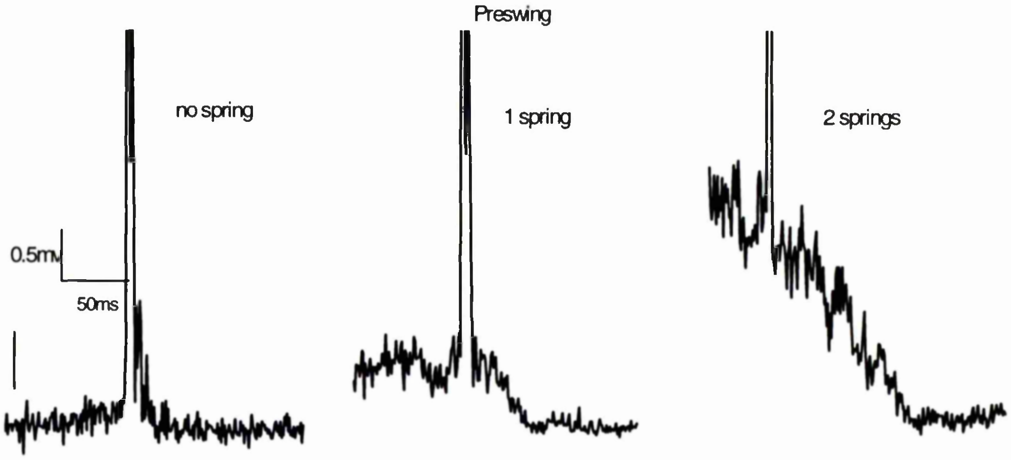

Figure 5.18. The figure shows sections of the average rectified EMG around the transition from stance to swing phase in RF in one subject. 40 samples were averaged. Each of the three sections shows the averaged EMG recorded from gait tests with knee orthesis loaded at different levels. The increased background EMG was achieved by adding 2 pairs springs to the knee orthesis. It can be clearly seen that the reflex could not be elicited even with significant increase in the background EMG.

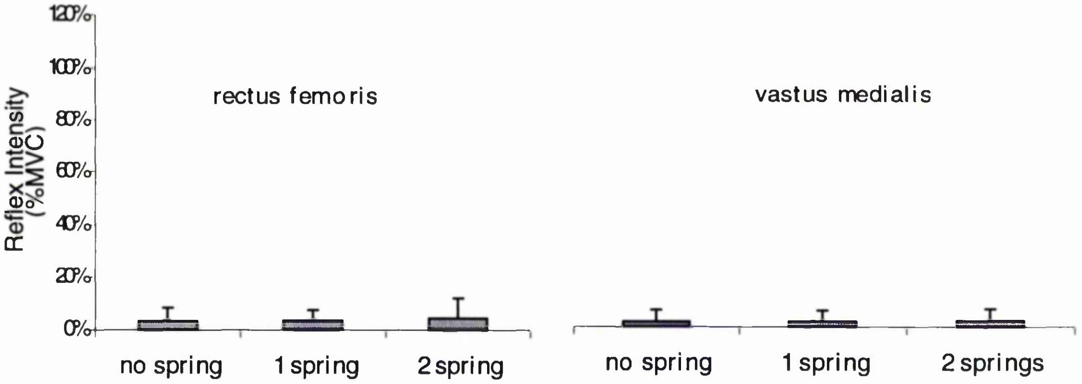

Figure 5.19. The figure shows the pooled magnitude of the reflex during the stimulation at the transition period. No reflex was detected during this period with the application of the knee orthesis ($p \geq 0.9$). The values in the graph represent the peak to peak amplitude of the EMG at the expected time of the reflex (N=7). The error bars represent the 95% CI.

- During terminal swing

During this period the CPQ reflex was absent when there was no background activity. It appeared and increased in magnitude with increased in the intensity of the background EMG. This is shown in figure 5.20. The average magnitude of the reflex during this period can be seen in the figure 5.21.

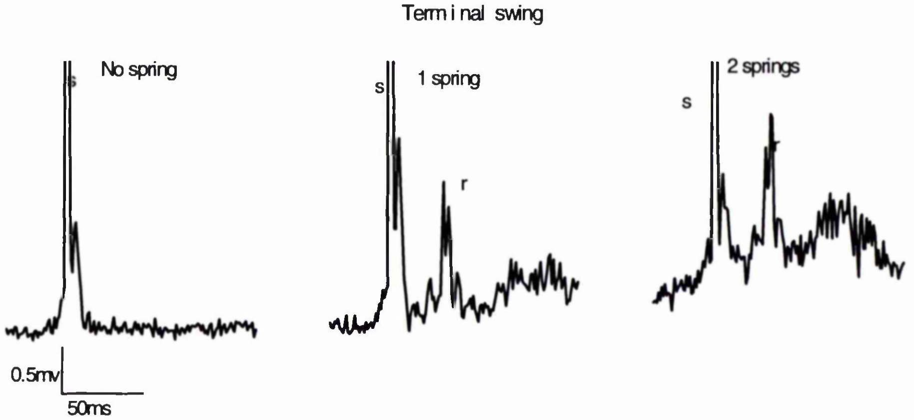

Figure 5.20. The figure shows the CPQ reflex in the averaged (40 samples) rectified EMG at terminal swing phase in one subject. Three intensities of background EMG, shown in separate panels, achieved by adding springs to a knee orthosis worn by the subjects during gait. It can be clearly seen that with increases in the background activity the magnitude of the reflex increases significantly.

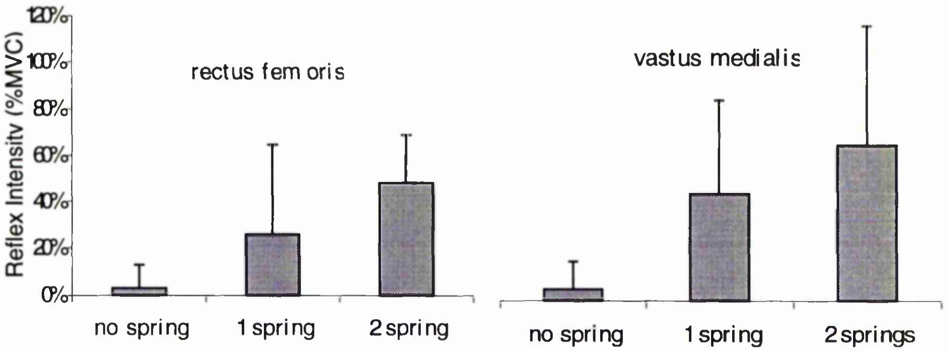

Figure 5.21. The figure shows the pooled magnitude of the reflex during terminal swing phase for VM (right) and RF (left) (N=7). The magnitude of the reflex increases proportionally to increases in the intensity of the background EMG ($p \leq 0.04$). The error bars represent the 95% CI.

The M wave magnitude during the experiment

The electrical stimulation at each point of the gait cycle with all the configurations of the knee orthosis elicited M waves in TA that were consistently above 40% of M_{max}. Figure 5.22 shows the pooled M wave amplitude and the 95% of confidence intervals for the mean at all the three points used for stimulation.

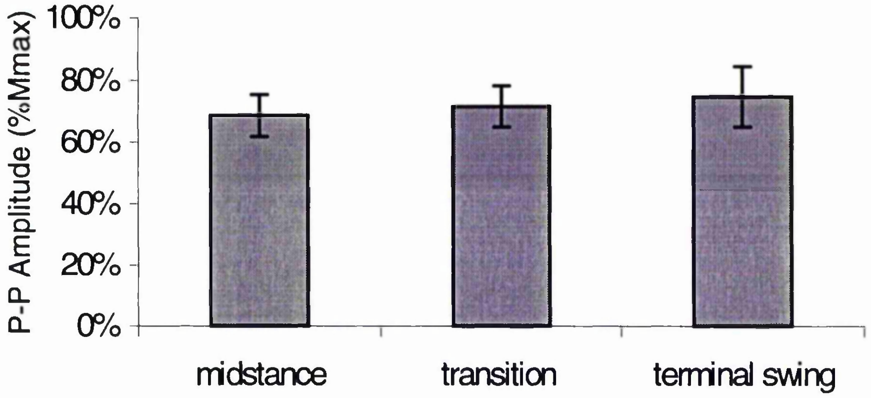

Figure 5.22. The figure shows the peak to peak amplitude of the M wave that was measured at each point and presented as percentage of the M max. It can be seen that the amplitude of the M wave never dropped below the 40% of M_{max} and remained almost constant during the experiment.

5.5. Discussion and Conclusion

5.5.1. The pattern of modulation of CPQ reflex during gait

Stimulation of CPN at different points in the gait cycle evokes short latency reflexes of different magnitudes in vastus medialis and rectus femoris. The reflex was at its highest magnitude shortly after heel strike. During most of gait cycle from midstance to terminal swing no reflexes could be elicited. It is known that descending inputs have an excitatory effect on this pathway. Indeed, a minimum descending input is needed for the appearance of the reflex. The strength of these descending inputs on this pathway is reflected as the intensity of the muscular activity in the quadriceps muscles. The threshold muscular activity for this reflex is very low. In fact with EMG activity of less than 10% of MVC significant reflexes are to be expected. This was described in section 4.4.2. The result shown in chapter 4 shows that the CPQ reflex amplitude increases with increasing quadriceps activity up to 40% of MVC.

During gait, the activity of the VM and RF muscles reaches the peak of about 20% of MVC after heel strike. By comparing the pattern of changes in the reflex magnitude and the intensity of EMG activity during gait a strong correlation can be seen. Figure 5.23 clearly shows the linear correlation between these two factors during gait cycle. This is very similar to the automatic gain compensation for the

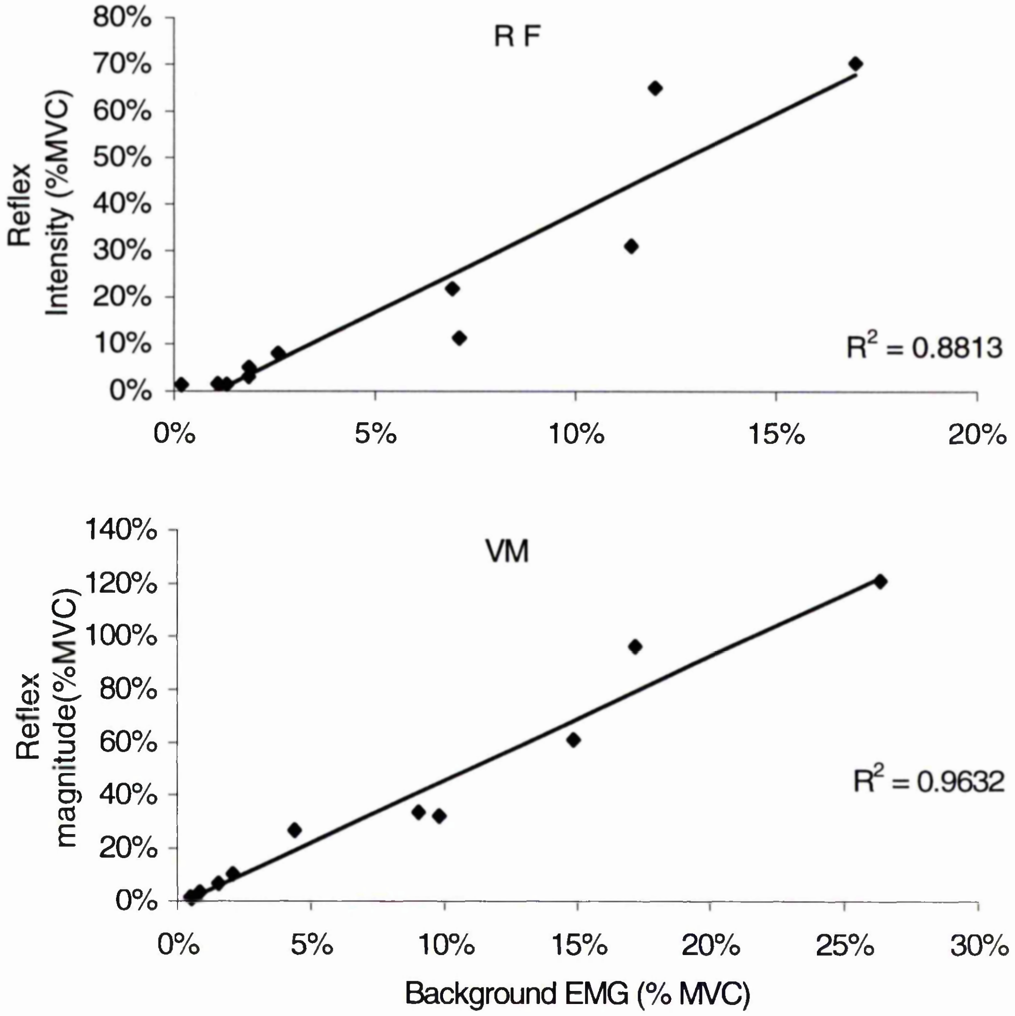

Figure 5.23. The correlation between the magnitude of the CPQ reflex and the intensity of the background EMG in VM (bottom) and RF (top) during the whole gait cycle. A clear positive correlation can be seen in both muscles ($p \leq 0.001$ for VM and $p \leq 0.007$ for RF) however, most of the points in the figures have values very close to zero. These points represent the relatively long period of the gait cycle when both muscles were silent.

monosynaptic stretch reflex described by Matthews in 1986. As the background force increases so does the number and the frequency of the active motoneurones available to be modulated by a given input.

Careful attention to the figure 5.23 reveals that the most of the points on the regression line are positioned near zero. This is because during the greater period of the gait the background EMG and the reflex are at near zero values. If the changes in the background activity in VM and RF are responsible for the gain modulation of the CPQ reflex during gait, it would be expected that increasing the background EMG activity during this long quiescent period would cause the reflex to reappear.

Half of the subjects investigated in this experiment showed some EMG activity during the transition period from stance to swing phase in RF. This has also been reported in other investigations (Dubo, Peat, Winter, Quanbury, Hobson, Steinke and Reimer 1976). In 11 out of 20 normal subjects they investigated, a small second peak of EMG activity in quadriceps happened during this transition period from stance to swing phase. The intensity of the background activity at this period was as high as 8% of MVC. This is above the threshold the reflex is shown in chapter 4. In spite of adequate background activity no reflexes were detected during this period. This raises doubts about the actual nature of the reflex modulation during this areflexic period. In fact, for this group of subjects, the correlation between the reflex magnitude and the intensity of background EMG is very weak during this period of gait.

The relationship between muscular activity and reflex magnitude is clear and strong during the early stance period. But it is not clear whether the absence of this excitatory effect is a result of simple disfacilitation or an active inhibition during the period of Q quiescence.

Brooke and McIlroy (1990) investigated the changes in the short latency reflexes during gait in humans. They investigated the changes of the CPQ reflex at 30ms after heel strike during gait cycle. They showed that the CPQ reflex magnitude increased with increasing background EMG activity in Q. Considering that they have just studied one point of gait cycle, their conclusion can not be extended to the whole gait cycle. Their conclusion however, suggests the positive correlation between the reflex magnitude and the background intensity during the early stance phase.

One might wonder if the CPQ reflex is actively inhibited during the areflexic period of gait? This was investigated in the experiment with knee orthosis. The spring-loaded orthosis increased the activity in RF and VM during the period of gait when they usually are silent.

The figure 5.14 clearly shows that the knee orthosis was able to increase the background EMG in VM and RF during the quiescent period of gait. The increase was much higher than the force threshold for the reflex in all three phases tested. Therefore if no inhibition is present, it was expected that stimulation would evoke reflexes with intensities proportional to the intensity of background EMG.

Figures 5.24 shows the VM and RF responses to electrical stimulation at three different periods of the gait cycle. Electrical stimulation at midstance period, elicited reflexes which increase in magnitude in proportion to the background EMG. This was similar to early stance phase. It seems that the reflex pathway remains open for activation during the stance phase. This is consistent with the necessity of stability and balance for the lower limb during stance phase of gait.

The same reaction to the intensity of the background activity is observed during the terminal swing phase.

The most significant differences occur during the late stance to early swing phase, during which the leg is in transition from stance to swing phase. At this period, despite significant increases in the background EMG, no reflexes were detected in VM and RF. This is shown in figure 5.24. The lack of a significant response could not be a simple response to disfacilitation, since the increase in the background EMG during this period was almost the same as the other two periods of gait investigated (figure 5.14).

It may be concluded that an inhibitory effect is present at this period. The idea that the excitatory reflex is inhibited during the transition period of the gait cycle suggests a more complex role for the CPQ reflex.

The inhibitory response in hamstring muscles, reported by Brooke and McIlroy (1989), was not observed in semitendinosus with stimulation at CPN during gait. Neither did medial gastrocnemious show any excitatory or inhibitory responses. Likewise CPQ reflex, a minimum activity in hamstring is needed to reveal this inhibition. Insufficient background activity could not be the reason for the absence of this inhibitory response in semitendinosus. It is active at during the terminal swing and early stance phase of gait (figure5.10). It is plausible that the inhibitory pathway from CPN to hamstring muscle is not active during gait. The activity of hamstrings during this period helps the stability of the knee through co-contraction with quadriceps muscle. Therefore, the inhibition of these muscles could significantly affect the stability of the knee.

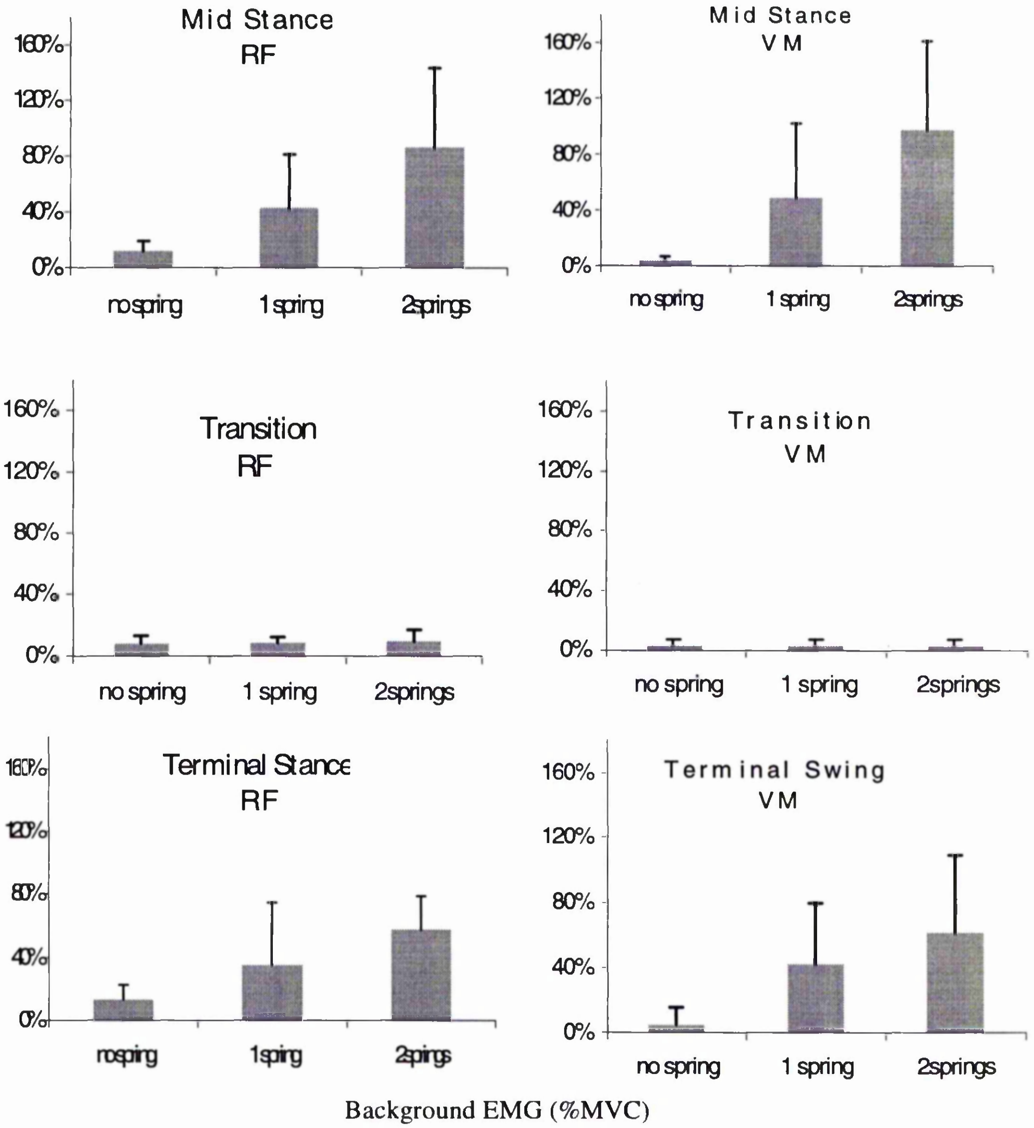

Figure 5.24. The correlation between the pooled reflex magnitude and the background EMG intensity for VM (right) and RF (left) at the three latencies used for the stimulation (N=7). No correlation can be seen during the transition period from stance to swing phase for VM and RF. During stance and terminal swing the correlation is strong and linear. The error bars represent the 95% CI.

5.5.2. A possible source of the inhibition at the transition period

This investigation does not provide direct evidence about the origin of the afferents involved in the inhibition of the CPQ reflex observed during the transition period. However, indirect evidence can be obtained.

The knee joint movement appears to show a correlation with the inhibition seen in the reflex. The results in chapter 4 suggest that flexion of the knee joint by 10 to 20 degrees is capable of inhibiting the reflex significantly and the reflex was at its maximum magnitude at the extended position of the knee. The pattern of knee movement during gait is very consistent with the pattern of modulation of the reflex. During the stance phase the knee joint is near full extension. The reflex must have its maximum potential for activation during this period. The result of the experiment with the knee orthosis supports this idea. This positive correlation between the knee joint position and the reflex excitability could also be seen in the terminal swing phase where the knee is again extended and the reflex can be elicited if the background activity is strong enough.

The only period when the knee flexes rapidly and significantly during gait is from the preswing phase to the midswing phase. An average of 22° of flexion was observed in these experiments. This was sufficient to produce a strong inhibition as described in chapter 4. This period of maximum flexion movement of the knee was when the maximum inhibition in the reflex was detected. This suggests that the receptors signalling the static and/or dynamic position of the knee joint could have a role, at least partly, in the inhibition recorded during the transition period.

It is not known that which receptors might be involved in this inhibition. Skin receptors, joint receptors and quadriceps muscle spindles are stimulated by knee flexion. The nature of the afferents input was discussed earlier in section 4.5.3. It was suggested that the stretch receptors of Q and to a lesser extent the hip flexors are the most likely sources for the inhibition of the CPQ reflex.

That the hip joint position could help the transition from stance to swing phase has been proposed for a long time. Grillner and Rossignol (1978) have shown that preventing hip extension in one hind leg in cat terminated stepping movement in that leg without influencing the movement of contra lateral leg. Only when the hip was allowed to extend beyond a critical angle did stepping resume. It has been reported that stretching or vibrating a hip flexor muscle during the stance phase leads to an earlier onset of swing in walking decerebrate cats (Hiebert, Whelan, Prochazka and Pearson 1996). The receptors signalling hip extension are probably the primary and secondary endings of muscle spindles in the hip flexor muscles (Kriellaars, Brownstone, Noga and Jordan 1994). These results are all obtained from animal experiments and extrapolation to humans must be done with caution. It is possible that the movement of the leg during gait could be employed to regulate the activity of the muscles.

The hip joint movement during gait was not recorded in these experiments but the normal pattern of hip movement suggests that it could participate in the inhibition of the CPQ reflex during the transition period. The hip joint is in a flexed position at heel strike and it moves gradually toward its neutral position by the end of the midstance. The leg reaches its maximally extended position at the end of the stance phase where the inhibition of the CPQ reflex happens. There is no direct evidence for the contribution of the hip flexor receptors. However, the correlation between the hip position and the result of the experiments on cats, suggest that the stretch receptors of the hip flexors could help the transition from stance to swing during gait in humans by boosting the inhibition of the CPQ reflex.

This active and strong inhibition of the reflex can suggest a functional role during the transition from stance to swing phase. During the transition period the ankle dorsiflexors showed a peak of activity. This helps the foot to clear from the ground and to start the swing phase of gait. This is accompanied by knee flexion which is also necessary for this transition. In half of the investigated subjects a second but smaller peak of Q contraction was detected during the transition period. An active CPQ reflex during the transition period could result in increased Q activity. This could seriously hinder the flexion of the knee joint that is necessary for the clearance of the foot from the ground and start of the swing phase. Inhibition of CPQ reflex however, would help the transition from stance to swing by preventing of any co-contraction of ankle dorsiflexors and knee extensors.

It is plausible that the distortion of this reflex pathway could be a possible reason for abnormal Q activity featured in some movement disorders.

Chapter 6

General Conclusions

The experiments described in this thesis show that stimulation of group I afferents from ankle dorsiflexor muscles can produce an excitation of quadriceps motoneurones. This reflex pathway appears to be specific to humans and has a major contribution to the motor control of the knee extensor muscles. Different aspects of this projection were investigated in a series of experiments.

The characteristics of the CPQ reflex are very stable. The with-in session and between session reliability of the reflex magnitude and threshold is extremely robust (r=0.88-0.98). In the other words, the reflex characteristics remain consistent for each person. This is particularly clear for with-in session measurements where constant stimulating and recording situations were ensured. However the stability can also be maintained between sessions providing that similar criteria are followed for locating the stimulating and recording electrode. All the comparisons in the experiments described in this thesis were performed from the data collected within a single session basis. Therefore, it is possible to be confident of the results.

The CPQ reflex is elicited by low threshold afferents excited by stimulation less than 0.9×MT in TA. It has relatively short latency of about 30ms. Maximum amplitude of the reflex was achieved at about 1.3×MT.

The CPQ reflex obviously has a threshold in the range of group I fibres. The short latency of the reflex also indicates the high velocity of the afferents responsible for this reflex which is also in the range of group I afferents. The group II muscle afferent has also been shown to involve in this reflex pathway, however the intensity of the stimulation used in all the present experiments was bellow the threshold of 2.1×MT that has been suggested for the group II fibres (Simonetta-Moreau et al 1999).

The group I afferents from pretibial muscles arise from Golgi tendon organs (Ib) or from muscle spindles (Ia). Since both of these types of fibre have almost the same electrical threshold and velocity, the latency and the threshold of the CPQ reflex could not help to distinguish between them. In the experiments reported in chapter 5, it is more likely that group Ib afferents are responsible for the excitatory effect on Q. The contraction of ankle dorsiflexors could stimulate a large number of GTO afferents. The synchronised and co-ordinated contraction of ankle dorsiflexors and Q during early stance phase of gait coincides with the only period of gait when the CPQ reflex could be evoked. This indicates that the Q activity could be re-enforced by the activated GTOs which are stimulated by the simultaneously contracted ankle dorsiflexors.

The intensity of the contraction in Q had a significant effect on the magnitude of the reflex. No reflexes were evoked when the muscle was relaxed. A minimum intensity of about 5% of background EMG in the quadriceps muscles was necessary to activate the reflex pathway. In fact, it is probable that the descending commands are largely relayed through the interneurones mediating the CPQ reflex to Q motoneurones

The CPQ reflex was elicited at different knee and hip positions. Constant stimulation was applied in all the investigated positions. This was provided by using the intensities to produce M waves with amplitudes of the same fractions of the M_{max} in TA. Besides, since the experiment was based on the with-in session comparisons of the reflex magnitude, the reflex was highly likely to be very stable. Therefore any changes in the reflex magnitude at different joint positions could be attributed to other factors except the changes in the recording, stimulation or automatic fluctuation of the reflex magnitude.

The reflex showed a significant attenuation when the knee and the hip were positioned at flexed and extended positions respectively. The inhibition produced at flexed position of the knee was so strong that even increased quadriceps activity as high as 40% of MVC could not restore the response in any subject. It is likely that the afferents from quadriceps muscle spindles, stretched by changes in the position of the knee or hip, are responsible for this substantial inhibitory effect. In addition, the dissociation between the reflex magnitude and the level of background activity in Q in the flexed position of knee is a reason to believe that this inhibitory projection could interfere with the reflex at pre-motoneuronal level.

The functional role of the CPQ reflex was investigated while the subjects were walking on a treadmill at constant velocity. During gait all the subjects showed similar pattern of changes in the magnitude of the CPQ reflex. The reflex could be elicited at the very end of the swing phase and reached its peak shortly after heel strike. The period from midstance to terminal swing phase was absolutely areflexic. The level of activity in RF and VM also showed a similar pattern of changes with their peak shortly after heel strike. Ankle dorsiflexors produced two peaks, one at the heel strike and the smaller one during the terminal stance to mid-swing phase. The coincident peak of activity in the Q, the pretibial muscles and the reflex during the stance phase suggest the possible positive feedback effect from pretibial muscle receptors onto the activity of Q during this load-bearing period of gait. The co-ordinated activation of ankle dorsiflexors and knee extensors during the early stance phase is major difference between the plantigrade type of locomotion in humans and digitigrade locomotion in animals. The absence of this reflex pathway in cats and baboons and the strength of it in humans suggests that this reflex could indicate the specific requirements of plantigrades compared to the digitigrades. The co-ordinated activation of pretibial muscles and quadriceps is necessary for the initial heel contact of the foot in plantigrade locomotion. The CPQ reflex could provide and help this co-ordination and also enforce the Q activity during the early stance phase of gait in humans.

During the stance phase the reflex magnitude displayed a positive correlation to the level of activity in Q. This suggests that the changes in the magnitude of the reflex during gait could be related to the changes in the level of descending inputs, which was shown to have an excitatory effect on the reflex pathway. This conclusion seems true for the early stance phase when Q is active. However this conclusion cannot be exclusive to the areflexic period of gait cycle where Q is almost silent. The nature of reflex modulation during this areflexic period was investigated by increasing the activity of Q during this period. If the reflex pathway were just under the influence of the descending inputs throughout the gait, increased Q activity during the areflexic period would expect to restore the reflex. The increased activity of the Q was achieved by using a spring-loaded knee orthosis. Three periods of gait cycle, where the muscle was active but no reflex had been elicited, were chosen for the investigation. The reflex magnitude showed a strong positive correlation with the level of background EMG during midstance and terminal swing phase. However the reaction of the reflex during transition period was completely different. The significant increase in Q activity during this period was not able to re-evoke any responses. This strongly suggested an active inhibition of the CPQ reflex during this period.

The knee joint showed a pattern of movement during gait with its maximum range of flexion started from terminal stance to the mid-swing phase. This was the time when the active inhibition of CPQ reflex also appeared. This was consistent with the result of the experiment described in chapter 4 which showed that the flexed position of knee is able to produce a substantial inhibition of the reflex.

6.1. Functional significance

6.1.1. During stance phase

Different types of muscle afferent, group Ia, Ib, II all appear to converge in the CPQ reflex pathway. The difference in the adequate stimulus needed for each of these afferents and their receptors implies that the proportion of their contribution in the activity of this reflex pathway is very likely to be task-dependent.

The CPQ reflex is very active during the early stance phase of gait. At this period an eccentric activation of the ankle dorsiflexors is followed by a peak of activity in the Q muscles. This eccentric type of contraction is a very strong stimulus for the GTOs. The muscle spindles will also be stimulated at the same time. However there are some reasons to believe that their contribution in the CPQ reflex during this period is very weak.

- There is a very small range of plantarflexion, during the early stance phase. Although the muscle spindles are very sensitive to small changes in the muscle length, the strength of their afferent input is correlated with the amount of muscle stretch. The small change in the pretibial muscle length is not likely to be a strong stimulus for the muscle spindles. The strong contraction of these muscles may very well be a powerful stimulus for the GTOs.
- The ankle movement starts later than the peak of activity in the ankle dorsiflexors and often later than the peak of activity in Q. Therefore it is unlikely that muscle spindle discharges could have a strong role in the production of the CPQ reflex at early stance phase. On the other hand, the co-ordinate peak of activity in ankle dorsiflexors and the Q muscles during stance phase of gait could indicate a major role for group Ib afferents.

These two factors indirectly suggest that the Golgi tendon organs of ankle dorsiflexors is more likely to be involved in this excitatory effect to the quadriceps motoneurones during this period. This is consistent with the needs of load compensation during stance phase of gait.

Upright human stance and gait is an unstable equilibrium condition which requires a continuous regulation in order to hold the body's centre of mass over the small support i.e. the feet. Afferent inputs from visual (Pfaltz 1985) and stretch reflex (Diener, Dichgangs, Guschlbauer and Mau 1984, Dietz, Quintern and Sillem 1987) systems are known to be involved in the control of stance and gait. However, as demonstrated during both in space (Clement, Gurfinkel, Lestienne, Lipshits and Popov 1984) and during immersion (Dietz, Horstmann, Trippel and Gollhofer 1989) experiments these sensory systems can not provide information about the influence of gravity on upright stance and gait. Afferent inputs from "gravity dependent" receptors are required to indicate the projection of the body's centre of mass within the base of support. The load receptors, which are proposed to provide this information, are Golgi tendon organs (Dietz 1992).

Pearson & Duysens (1976) extended the classical findings of Sherrington (1910) which showed that force feedback to the spinal cord from tendon organ afferents caused reflex inhibition of the receptor-bearing muscles. They proposed a significant positive force feedback effect for Golgi tendon organs. The experiments revealed that extensor group Ib afferents produce excitatory responses in the load-bearing muscles during gait. The fact that the positive force feedback has been only studied in the extensor group comes from the fact that in cats, the antigravity muscles are extensors. However in humans this classification is different. The ankle plantar flexors in animals are very active from the first instant contact to the ground. In humans the equivalent muscles are the ankle dorsiflexors. In fact, the unique feature of the human gait is the heel to toe gait. The strong activity of the ankle dorsiflexors during the early stance phase of the gait implies a load-bearing role for this group of muscles. It would therefore reasonable to expect that the Golgi tendon organs of this group of muscle could also produce a positive force feedback effect on the other load-bearing muscles during the stance phase, specially the early stance phase.

The stimulation of group I fibres at common peroneal nerve is shown to have a strong excitatory effect on Q muscles during the early stance phase. This coincides with the peak of activity in both Q and ankle dorsiflexors muscles. It is very likely that the strong activation of Golgi receptors in pretibial muscles have a positive force feedback effect on Q muscles during this period.

6.1.2. During transition from stance to swing

Transition from stance to swing is in fact transition from a load bearing to an unloaded situation of the leg. Unloading of the leg seems to be a necessity for this transition. The knee joint flexion and the ankle joint dorsiflexion at this time allow the leg to lift from the ground. The strong positive force feedback between the ankle dorsiflexors and Q muscles could be an obstacle for the knee flexion at this time. If the activation of the ankle dorsiflexors could produce the same excitatory response in the Q muscles, the knee flexion, which is necessary for the transition would be hindered. Thus activity of this neural pathway would be a problem for transition from stance to swing. The result of the experiments in this chapter showed that this excitatory link is strongly inhibited during this period. This is probably originated from the stretch receptors of the knee extensors and/or the hip flexors. The inhibition of this reflex seems to be a critical feature for the transition from stance to swing in human gait.

6.2. Future plans

Abnormal activity in Q is a part of motor dysfunction that can be seen in some neurological diseases, such as strokes and Parkinson's disease. Investigation of the characteristics of the CPQ reflex could reveal more of the nature of these sensori-motor malfunctions.

Data in chapter 4 of this thesis show that proprioceptive inputs can modulate the CPQ reflex in the knee extensors. This reflex modulation supports integration of different sensory pathways in the motor control of the knee extensors during functional activities such as gait. It is worth investigating the possibility of the distortion in this reflex in clinical cases which show abnormal Q activity.

The pattern of modulation of the CPQ reflex during gait also suggests the important role that this reflex could have in the stability of the lower limb during the stance phase and the initiation of the swing phase. Weak CPQ reflexes during stance phase could possibly lead to instability of the knee. Alternatively, CPQ reflex hyperactivity could result in problems in limb unloading and the initiation of the swing phase. This could be investigated in patients suffering from gait related disorders.

Appendix 1

Modulation of the low threshold reflexes in human lower limbs by changes in knee position.

Presented in the "3rd World Congress in Neurological Rehabilitation,
Venice, April 2002.

Abstract

In man, stimulation of group I afferents in the common peroneal nerve evokes non-monosynaptic excitation of quadriceps (Fournier *et al* 1986). This is attributed to Ib afferents Brooke *et al* (1990) acting through an oligosynaptic pathway. This abstract describes experiments performed to investigate the effect of the knee joint position on these reflexes. Experiments were performed in 14 volunteers. The protocol was approved by the local Research Ethics Committee. Single pulses of 200 microseconds duration were delivered to the common peroneal nerve at 1.3-1.5×motor threshold for tibialis anterior. The responses were recorded in the averaged EMG of rectus femoris during ongoing contractions at 20% of maximum. The average latency and duration of the responses was 29.4 ± 2 and 15.7 ± 2 milliseconds respectively. Reflexes were elicited at intervals of 10° between 180° and 130°. The mean magnitude and area of the response showed a very significant drop ($P \leq 0.005$) between 180° and 170° followed by a more gradual decrease at more flexed positions. At 130° of flexion, no response was detected in any of the subjects

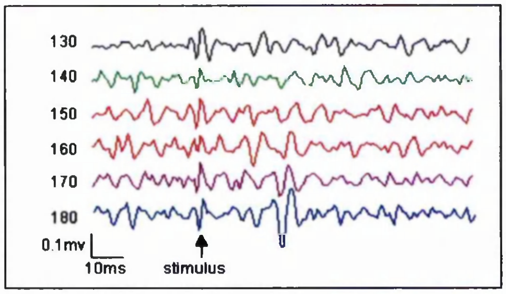

Figure 1.
A series of reflexes elicited in the averaged EMG of rectus femoris by stimulation of the common peroneal nerve at 1.3x motor threshold. Reflexes were elicited at a series of knee positions between 130° and 180°. The reflex is present only near full extension

The modulation of the reflex gain by knee position may be of functional significance during gait since the strongest effects occur when the knee is extended, that is in the position at about heel strike.

Brooke JD. Mcllroy WE, (1990) EEG & Clin. Neurophysiol., 75: 401-409
Fournier E et al (1986) J Physiol, 377: 143-169

Appendix 2

Inhibition of Ib Reflexes in Quadriceps During Gait in Humans.

Presented in the "XIV congress of International Society of Electrophysiology and Kinesiology".
June 2002, Vien.

Abstract

In man, stimulation of Ib afferents in the common peroneal nerve evokes non-monosynaptic excitation of quadriceps (Q) (Fournier et al 1986). Experiments were performed on 10 volunteers to investigate the modulation of this reflex during gait. Single pulses of 200microsecs duration were delivered to the common peroneal nerve at points in the gait cycle during treadmill walking. Stimuli produced M waves above 40% of M_{max} in tibialis anterior. The reflexes were recorded in the averaged EMG of rectus femoris (RF) and vastus medialis (VM). The reflex was at its highest magnitude shortly after heel strike as Q showed its maximum activity. During most period of gait cycle from midstance to terminal swing no reflexes was observed. Q was silent during this period. This reflex modulation is strongly correlated to the pattern of motor activity of the Q during gait (figure 1).

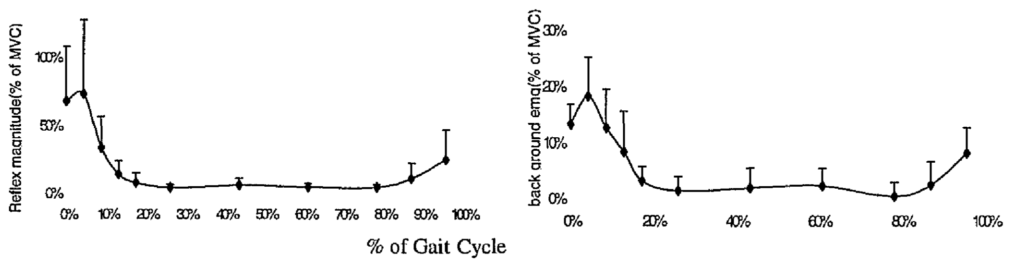

Figure 1, the pattern of modulation of the reflex and the motor activity of RF during gait.

The reflex could not be elicited between mid stance and late swing phases. This may be the result of inhibition of the reflex pathways or it may be due to lack of muscle activity. We were able to encourage the VM and RF muscles to contract with different intensities during their quiescent period of gait by using a modified knee orthesis. Springs were used to provide a knee flexion moment. This increased the intensity and duration of RF and VM activity. It was expected that stimulation would evoke reflexes with intensity proportional to the intensity of background EMG, if no active inhibition was encountered.

Electrical stimulation at midstance and the terminal swing phase elicited reflexes which grew larger with increased background EMG. The most significant discrepancy appeared between late stance to early swing phase. Despite significant background EMG in VM and RF no reflexes was elicited. This is seen in figure 2. No correlation was found between the reflex magnitude and the muscular level of activity during this period. The increase in the background EMG during this period was almost the same as the other two periods of the gait.

It was concluded that an active inhibition was imposed on this reflex during the transition period from stance to swing. This inhibition seems to be a critical feature for the transition from stance to swing during gait in humans.

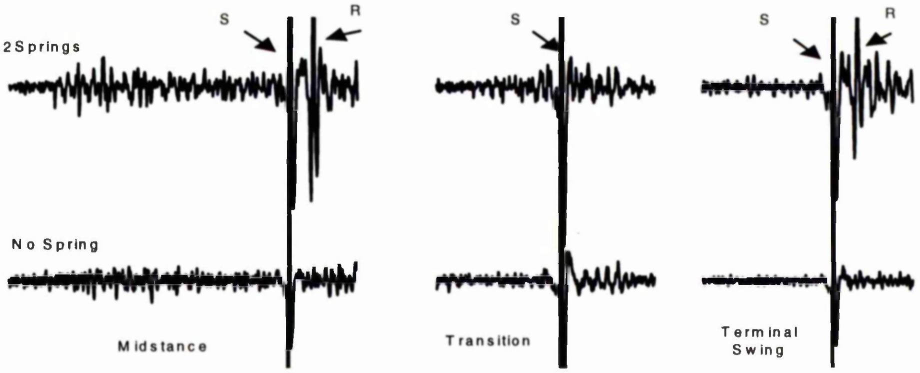

Figure 2, the averaged non-rectified EMG of RF in one of the subjects wearing the knee orthosis, without springs (bottom) and with two pairs of springs (top) added to it. No response was evoked during the transition period with increases in the background EMG in RF.

Fournier E et al (1986) J Physiol, 377: 143-169

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