DOCTORAATSPROEFSCHRIFT

Faculteit Geneeskunde

Neurophysiological and Anatomical Aspects of Cutaneomuscular reflexes in some muscles of the human lower leg

Neurofysiologische en Anatomische aspecten van Huid-Spier-Reflexen in spieren van het onderbeen van de mens

Proefschrift voorgelegd tot het behalen van de graad van
Doctor in de Medische Wetenschappen

STEPHAN HAUGLUSTAINE

Promotoren : Prof. dr. K.J. van Zwieten
Prof. dr. J. Duysens

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According to the guidelines of the Limburgs Universitair Centrum, a copy of this publication has been filed in the Royal Library Albert I, Brussels, as publication D/2000/2451/124

To my wife, Kristien

To my children,

Adelien, Sander and Hanne.

CONTENTS

1. GENERAL INTRODUCTION

Organisms have a nervous system to observe the environment and to react to it with an adequate behavior. To achieve this dual task the nervous system can be viewed as an integrator that analyzes the sensory information which it receives by its sensory pathways and as a generator that sends command signals along its motor pathways to muscles and other effectors.

A very important behavior is locomotion. The last three decades a lot of investigation about the neural control of locomotion has been done. To generate seemingly simple and automated movements the central nervous system has to produce specific patterns of motor neuron impulses, resulting in coordinated muscle activity of synergistic agonists and antagonists. Apart from the generation of locomotion there has to be a continuous control on it, so that it can be adjusted to expected and unexpected external factors.

Brown (1911) suggested the existence of a spinal locomotor center, after investigation of cats with a transected spinal cord and cut dorsal roots. Such spinal cats still showed rhythmic alternating contractions of flexors and extensors.

In humans clinical and experimental findings suggest also the existence of a spinal locomotor center, called central pattern generator (see Duysens et al. 1998 for review). Nowadays the theories of such a spinal center are accepted, however, the understanding of the control mechanisms on this center stays an important challenge in modern neuroscience. Roughly, one can say that locomotion is programmed in the spinal locomotor centers which are reciprocally influenced by supraspinal and peripheral feedback mechanisms.

This thesis wants to highlight some new ideas about the cutaneous peripheral feedback mechanisms in humans during locomotion. It will give some information about the sensor (input) and motor part (output) of cutaneomuscular reflexes of the lower limb. Centrally the input will be processed according to the demands. In this thesis the importance of the task-dependency and the phase-dependency provided by the cutaneomuscular reflexes is studied.

Finally, some anatomical data are presented to clarify the kind of output of cutaneomuscular responses seen in the heads of the gastrocnemius muscles.

1.1. Spinal organisation of motor function: Central Pattern Generator (CPG)

Muscles are innervated from spinal cord motoneurons that are located in the ventral horn. The cytoarchitectural arrangement of the motoneurons is a topographical one with respect to the target musculature.

For locomotion the term central pattern generator (CPG) refers to a group of motoneurons and interneurons that after stimulation is responsible for creating a stereotypic kind of motor pattern.

The idea of a CPG is suggested by experiments on **animals**, especially cats. In the beginning of the twentieth century Brown (1911) saw that after transection of the spinal cord and the entering dorsal roots cats still showed coordinated alternating muscle activity in ankle flexors and extensors. He suggested that there was a spinal locomotion center divided in two different halves for extensors and flexors. The de-afferentiation done by Brown (1911) was not total because today it is known that some of the afferent fibers enter the dorsal cord in the ventral roots. However, the importance of those afferent fibers for locomotion seems very unlikely (Grillner and Zangger 1984; Coggeshall 1980).

In the beginning of the sixties there was a growing interest for localization of neural cells that can trigger coordinated behavior. Wiersma and Ikeda (1964) showed that experimental activation of one single interneuron by the crayfish could elicit a type of coordinated behavior. They termed such an interneuron a command neuron. The synaptic output of such a command cell seemed to be extremely complex and highly organized. It was suggested that a small collection of command interneurons could be responsible for natural behavior. Two types of command neurons can be distinguished: 'trigger' command cells (Willows and Hoyle 1969) can elicit a motor output that lasts longer than the stimulus itself while 'gate' command cells have to be continually activated to maintain the evoked behavior. The latter ones can activate motor systems involved in posture and phasic motor systems involved in locomotion and other movements (Kennedy et al. 1967; Davis and Kennedy 1972; Bowerman and Larimer 1974).

In tetrapod vertebrates activation of one single neuron is not sufficient to produce a coordinated motor output, however a group of cells can act if it has a command function. For example in the cat, stimulation of the white matter of the spinal cord could elicit stepping (Sherrington 1910; Grillner and Zangger 1974; Grillner 1976) and scratching movements (Deliagina et al. 1975). After electrical stimulation of a particular brainstem site below the transection by a 'mesencephalic' cat quadruple stepping could be evoked. Dependent of the intensity of stimulation different locomotion patterns could be produced, for example stepping, trotting, and galloping. The 'mesencephalic' cat is a decerebrated cat obtained after transection of the brainstem at the level between higher and lower colliculus. After curarization (this is the use of muscular relaxants) and extensive denervation in order to eliminate the afferent input completely, rhythmic activity output was recorded at the efferent nerves in the ventral roots. This rhythmic output was well organized between agonist and antagonists of the limbs. This form of fictive locomotion pointed the importance of local spinal neural networks in generating rhythmic output.

In the mid-sixties the group of Lundberg (Jankowska et al. 1957) discovered a spinal network with the same characteristics suggested by Brown (1911) that was sensitive to intravenous (I.V.) l-DOPA (1-β-3,4-Dihydroxyphenylanaline) administration. They observed acute spinal cat preparations becoming active after a flexor reflex afferents (FRA) train stimulation following the I.V. administration. They saw long latency and long-lasting reflex discharges. When ipsi- and contralateral stimulus trains were combined at an appropriate delay, the interneurons of flexor and extensor pathways mutually inhibited each other producing the efferent effects postulated by Browns half-center hypothesis (1911). After potentiation with the mono-amino-oxidase inhibitor (MAO-inhibitor) Nialamide (Lundberg 1979) short periods of alternating activity in flexor and extensor nerves could be elicited after a single train of FRA stimuli. This is similar to the fictive locomotion that could be produced during continuous afferent stimulation in the spinal cat with an optimal noradrenergic drive (Grillner and Zangger 1979).

The idea of a spinal CPG can be implemented in several ways. The first alternative is a CPG for each kind of movement that controls all limbs. This means that different CPG's will be activated during walking, running and galloping responsible for the basic coordination of the limb movements needed to pose this basic locomotor activity. A second alternative is a limb coupled CPG. In this case different locomotor activities result from different interactions between these CPG's.

Experiments support the second alternative. After low spinal transection of cats walking on a split belt treadmill the interlimb coordination between the hindlimbs could be adjusted to the two different velocities of the separated belts. After eliminating afferent feedback (Grillner and Zangger 1979) the possibility of separate limb control was not affected, suggesting a program for separate limb control. Further, Grillner (1976, 1981) proposed that not only each limb, but each joint and each synergistic muscle group acting around a joint, could be controlled by a unit burst generator. The unit burst generators could be coupled in phase, out of phase or with a variable phase giving rise to various behaviors. Getting (1989) who made a comparative analysis of invertebrate central pattern generators, suggested a theory about building blocks in the CNS. Each motor pattern is the result of assembling those building blocks in unlimited possible combinations. Attempts to identify how such building blocks can be assembled to generate different stereotypic patterns in cats were done by Gelfand et al. (1988). They made a comparison between locomotion and a scratching movement and observed that there is are lot of similarities in alternation between flexor and extensor phase, but the extensor phase is obviously shorter during scratching. Further the rhythm of scratching is higher and the activity of the hindlimbs is different; being in flexion for scratching and being in extension for locomotion.

These unit burst generators themselves can be build up out of various building blocks of membrane, synaptic and network properties that can be controlled by various transmitters released by segmental and suprasegmental axonal inputs.

Experiments during the last decades in addition to clinical observations give some evidence for existence of a **human** CPG (for review see Duysens et al. 1998):

Luys (1893) described very old observations made until then by other observers during decapitation of animals and humans in death executions. They saw that some rhythmic flexor reflexes and even coordinated movements could be elicited by skin contact after decapitation. Similarly Hanna and Frank (1995) reported alternating leg movements in patients during the periods immediately before and after brain death.

In the first half of the twentieth century Lhermite (1919) and Kuhn (1950) reported about of rhythmic involuntary movements generated by the spinal cord lacking supraspinal input.

Bussel and co-workers (1988) saw in patients with a complete spinal cord lesion rhythmic contractions of the trunk and the extensors of the legs which could be induced, stopped and modulated by peripheral stimulation of the FRA. His colleagues did already describe that in patients with clinically complete spinal cord section FRA stimulation revealed the same motor patterns which were seen after I.V. administration of l-DOPA in cats (Roby-Brami an Bussel 1987).

In patients with incomplete lesions of the spinal cord rhythmic alternating flexor and extensor activity is more common. Calancie et al. (1994) reported about a patient who after one week of severe locomotor training displayed stepping-like movements when he was positioned in a supine position with extended hips. Furthermore in incompletely spinal cord injury (SCI) it is still unclear whether the supraspinal centers do generate locomotion or whether they control the locomotion generated by a CPG.

Sleep-related periodic leg movements (SRPLM) are stereotyped, periodic, repetitive movements involving one or both legs that appear mostly in healthy subjects over 30 years old. Yokota et al. (1991) described those SRPLM in patients with SCI suggesting that SCI could permit the expression of a spinal generator by desinhibiting it. The SRPLM were also present in patients with total spinal cord lesion suggesting that this phenomenon is related to spinal automatisms.

After spinal cord stimulation in persons with a complete spinal cord lesion, myoclonic stepping with reciprocal activity of the symmetric muscles could be obtained. This phenomenon suggests the existence of the CPG in humans.

In a weightless simulator constant stimulation of proprioceptive afferents of the suspended leg could elicit cyclical hip and knee movements in both legs (Selionov et al. 1997; Kazennikov et al. 1997). This CPG activity was initiated and sustained as long as the stimulation lasted. This experiment supports the view that the basic rhythm of locomotion can be elicited involuntary in humans.

During the prenatal phase ultrasound imaging shows presence of coordinated movements as kicking, swallowing and yawning. These movements are closely similar to those seen in the newborn infant. An externally supported infant makes step-like movements with the legs showing complex inter- and intralimb coordinated muscle activity. Thelen and co-workers (1987) suggested that mature walking may evolve from the newborn stereotyped movement pattern. Roby-Brami and Bussel (1987) described stepping movements in anencephalic newborns.

Taking into account all these remarks, the evidence of a CPG-like structure at the spinal level in humans is very great. Knowledge of this CPG may be of great importance in the follow-up, treatment and revalidation of patients with SCI.

Duysens et al. (1996) compared the phase-dependency of cutaneous reflexes during forward and backward walking and saw that there was a reversal of the reflexes caused by a possible reverse of the total motor program of walking. Previous work already showed the mirror trajectory images of forward and backward walking suggesting different phase coupling of the same unit bursts (Perell et al. 1993; Vilensky et al. 1987; Winter 1989). In analogy with cats during walking and scratching (see Gelfand et al. 1988), probably in humans the same neuronal network is used for both forward and backward walking, but the programmed sub-units of this motoric movements are activated in an other sequence (Duysens et al. 1996). Further research has to be done to prove whether the theory about 'assembling building blocks' of Getting (1989) can be implemented on humans.

1.2. Afferent control of locomotion

Locomotion is the product of a locomotor system where the central pattern generator is centrally positioned. The motoric behavior is the result of integration of the motor program with the reciprocal peripheral and supraspinal influences. To assure a stable gait a certain amount of feedback is necessary, as is evident from observations on de-afferented cats, in which gait was affected as compared to intact cats (Grillner 1981; Rossignol et al. 1988). This section of the introduction will focus on the peripheral feedback existing of proprio- and exteroceptive afferent information. As known from basic neurophysiology proprioceptors detect stimuli generated by the system itself while exteroceptors detect external stimuli that impinge on the system. The information provided by exteroceptors and proprioceptors enables the system to organize a rapid response to a perturbation, to determine limb position and to differentiate between self-generated and imposed movements.

1.2.1 Proprioceptive control

Sherrington (1910) saw that thoracal lifting of spinal cats and dogs did induce extension and air-stepping of the hindlimbs. After removal of the skin and thus the exteroceptors the behavior sustained. It was suggested that the proprioceptors of the hip were responsible for the air-stepping reflex. Later experiments on cats (Grillner and Rossignol 1978; Pearson and Rossignol 1991; Hiebert et al. 1996) did support this idea of proprioceptive control.

The modulation of the stretch reflexes is phase-dependent during locomotion. This is well studied in humans during walking, running, stepping, hopping and pedalling (Garret et al. 1981; Capaday and Stein 1986, 1987; Crenna and Frigo 1987; Brooke et al.1991, 1995; Moritani et al. 1990; Boorman et al. 1993; Llewellyn et al. 1990; Bennet et al. 1993; Van de

Crommert et al. 1996) and also in different muscles as soleus, gastrocnemius, biceps femoris, tibialis anterior and quadriceps femoris.

For the H-reflex (Hoffmann 1934; see also Schieppati 1987 for review), an artifically elicited response, this phase-dependent modulation is not similar during different motor tasks (Capaday and Stein 1987) but strongly influenced by the requirements of executed motor task (Dietz and Noth 1978; Dyhre-Poulsen et al. 1991). Motion-related sensory receptor discharge was thought to be important for this modulation (Brooke 1993), but very recent experiments by Schneider et al. (2000) do not support this hypothesis.

Other investigations have also demonstrated that afferents from the skin affect the H-reflex (Hugon 1973; Pierrot-Deseilligny et al. 1973, 1981).

1.2.2. Cutaneous (exteroceptive) control: Cutaneomuscular reflex responses (CMR)

In the beginning of the study of the cutaneous reflexes two elementary descriptions of those reflexes were made: Sherrington (1910) saw that after stimulation of nociceptive cutaneous receptors a flexor withdrawal reflex occurred. It was a coordinated flexion of the whole stimulated limb. It was Hagbarth (1960) in the early sixties who completed the description of this reflex response as a more complex array of cutaneomuscular responses associated with excitation from skin sites overlaying the target muscle and inhibition from sites over antagonistic muscles.

The importance of afferent information during locomotion is shown by Jankowska et al. (1967a) in **cats** after I.V. L-DOPA administration. The suggested spinal network became active after FRA stimulation preceded by the L-DOPA administration. After alternating ipsi- and contralateral stimulation they could induce fictive locomotion.

Other experiments showed the possibility of motor output without afferent information, but pointed also to the importance of peripheral feedback for normal locomotion, since elimination has a great impact on the fine tuning of the locomotor pattern (Grillner 1981; Rossignol et al. 1988).

To clear out the mechanism of feedback with cutaneous afferent information during locomotion Hultborn and Illert (1991) did propose the FRA Hypothesis. The hypothesis suggests that the command signal activates interneurons in one of the several alternative pathways of the FRA. The movement that is caused by the motoneuronal discharge activates itself different types of receptors, some of witch belong to the FRA (surrounding skin). The movement itself gives thus an important inflow in the FRA, channeled into the path that is already activated by the CNS because transmission in the other paths already is inhibited. In this manner the movement gives a strong selective positive reinforcement of the activity in the interneural pathway defined by the CNS. This means also that the FRA has also alternative paths that can be facilitated which explains the observations that in some spinal cats contradictory results are seen after FRA stimulation.

Cutaneous afferents innervating the skin of the distal hindlimb of the cat are in a good position to monitor limb loading. For example when trains of electrical pulses of weak intensity were applied to the skin area innervated by the sural nerve the extensor burst during the stance phase was prolonged and the onset of the following flexion phase was delayed (Duysens and Pearson 1976). A possible explanation for this phenomenon is that load-related cutaneous input from the foot can inhibit the pre-motor center for the generation of flexion during the swing phase. The spinal origin of the inhibitory effect of the cutaneous afferents on the flexor half centre was shown by Conway et al. (1994). After termination of a period of cutaneous stimulation a post-inhibitory rebound with late flexor discharges was seen (Jankowska et al. 1967).

Jankowska et al. (1967b) did identify interneurons in the lateral part of layer VII of the spinal cord of the cat that were activated by ipsilateral and inhibited by contralateral FRA stimulation. They suggested their possible importance as rhythm generator for the alternating activity between flexors and extensors which is the same for all muscles within a single limb. The synaptic input of those interneurons stays a challenge to discover.

Most previous studies about cutaneoumuscular reflexes on **humans** employed nociceptive stimuli (Belanger and Patla 1984, 1987; Crenna and Frigo 1984), but during the last decades cutaneous reflexes after non-nociceptive stimuli are of basic interest in modern neuroscience. The present study is focussed on the cutaneous reflexes after non-nociceptive stimuli.

The morphology and latency of cutaneous reflexes are more complex than that of H-reflexes: In the leg of humans, an early response (P1) ipsilateral can occur, usually earlier than 65 ms after nerve stimulation, followed by a mid-latency response (P2) with onset 70-120 ms after stimulation appearing in both legs. Later responses (P3) also occur but are less studied until now.

In their review article Brooke and co-workers (1997) enumerate some characteristics of cutaneous reflexes based on many papers (Yang and Stein 1990; Burke et al. 1991; Duysens et al. 1990, 1991, 1992, 1993, 1994; Aniss et al. 1992; Kukulka 1994; De Serres et al. 1995; Tax et al. 1995):

- P1 responses are often weak and inconsistent.
- For muscles around the ankle joint, P1 ipsilateral most often is the reciprocal sign of the P2 which follows, ipsilaterally or contralaterally.
- For contralateral muscles across the ankle, those P2 responses reported are

identical to P2 ipsilateral.

- For two of the three muscles spanning the hip and knee joints, excitation continues from P1 over P2 latencies.
- Response patterns are reported to be reproducible when subjects are retested.

The neural route of the cutaneous reflex arc is not clear yet. For the P1 responses a spinal oligosynaptic path is suggested by the short latency of the response. This conclusion is based on single motor unit recordings (Aniss et al. 1992; Kukulka 1994). For the P2 responses the neural pathway is more complicated and not fully understood. The used pathway can not be inferred from the latency of occurrence because there are known reactions dependent on the brain's prior awareness reported with latencies of 60-70 ms (McIlroy and Brooke 1986). Loop pathways to the brainstem likely have shorter latencies. Another argument against automatically assuming a latency of 70-120 ms as a spinal latency is the occurrence of conditioned voluntary reactions times at 110 ms in the rectus femoris muscle during human gait (Wetzel and Gorman 1986). In contrast, Roby-Brami and Bussel (1987) describe responses with latencies from 100 ms up to several hundred milliseconds in patients with complete SCI. So it is concluded that responses at 65 ms or more may arise from supraspinal, propriospinal and oligosynaptic spinal pathways and that the description of the neural route of P2 responses stays an experimental challenge. Very recently Pijnappels et al. (1998) and Nielsen et al. (1997) did study the cortical facilitation of cutaneous reflexes in tibialis anterior and biceps femoris muscle. They saw that the discharge properties of TA motor units following combined electrical sural and transcortical magnetic stimulation was larger than the algebraic sum of the discharge probability following each of the two stimuli separately during isometric contraction (Nielsen et al. 1997) and walking (Pijnappels et al. 1998). Direct electrical cortical stimulation had no facilitating effect (Nielsen et al. 1997).

1.3. Contribution of this study

A reflex arc can be divided in three parts:

- Input: there is a stimulus that elicits the reflex (sensory part)
- Processing: there is a processing of information that influences the reflex (phase-dependency and task-dependency)
- Output: the result of the reflex (motor part)

1.3.1. The sensory part of the CMR

Experiments on cats pointed the importance of stimulation site for the resulting cutaneomuscular reflex after cutaneous stimulation. Ellaway et al.(1997) showed the cutaneous afferent influence on the discharge of γ-motoneurons in the triceps surae of the decerebrated spinal cat. Mechanical stimulation of discrete areas of skin within the sural nerve field caused facilitation or inhibition of individual γ-motoneurons supplying the gastrocnemius and soleus muscles. Sometimes a γ-motoneuron facilitated after stimulation at one site could be inhibited after stimulation at another location.

In humans, Van Whezel et al. (1997) and Zehr et al. (1997) did some experiments in which the three major lower limb cutaneous nerves (sural, superficial peroneal and tibial nerves) were stimulated with non-noxious intensities. They compared the reflex activity of different lower limb muscles after stimulation of those three nerves and they concluded that the stimulation site is very important for the resulting muscle activity. Zehr at al. (1998)

showed that the responses to sural nerve stimulation during swing resulted in a withdrawal of the foot from the localisation of the stimulus, with a net result of avoiding a destabilizing stumble.

Van Whezel et al. (1997) and Zehr et al. (1997) stimulated the cutaneous nerves with surface electrodes on sites where the nerves pass near to the surface of the skin. The stimulated nerve fibers come from a broad skin area (sole, dorsum of the foot and toes) and the reflex responses are a result of reflex responses from all those nerve fibers. In this study some experiments with ring stimulation of the second and fourth toe are done to know whether the size and the modulation of the responses following this digital nerve stimulation are comparable with those seen after proximal total cutaneous nerve stimulation.

For H-reflexes it is known that motion-related sensory receptor discharge plays an important role for the H-reflex modulation during locomotion in humans (Brooke et al. 1997). This sensory-related modulation of cutaneous reflexes is not seen during a passive cycling movement tested by the same author (Brooke et al. 1999). It is not known what the importance is of movement related feedback for the modulation of cutaneous nerve reflexes. In this study the modulation of cutaneous nerve reflexes during limping, as a form of restricted gait with reduced movement related afferent input, was studied and compared with normal walking and running.

Very recently Schneider et al. (2000) could not corroborate the idea of motion-related modulation of H-reflexes and made the hypothesis of different pathways for the modulation of H-reflexes and cutaneous reflexes questionable.

1.3.2. Processing of the CMR

1.3.2.1. Phase-dependency of CMR

In humans a phase-dependent and task-dependent modulation of the cutaneous reflexes during locomotion is seen. The pattern of responses in ipsilateral and contralateral muscles cannot be explained on the basis of an automatic gain control (Matthews 1986), which would set the gain of the reflex simply on the locomotor background EMG activity, but rather on the basis of a premotoneuronal gain control (Duysens et al. 1992, 1993, 1996). Rossignol (1996) describes in his review concerning the neural control of stereotypic limb movements that there are three levels at which the phasic modulation of spinal reflexes during locomotion can occur: motoneuronal, interneuronal and presynaptic levels:

- Since no conductance changes could be observed in motoneurons during the fictive cycle, it was concluded that the increase in postsynaptic potential (PSP) amplitude after cutaneous stimulation, during the depolarizing phase of the motoneurons, is caused by a premotoneuronal mechanism.
- Since excitatory postsynaptic potentials (EPSP's) can be as large as 40%, it is possible that the membrane depolarization of the motoneurons may also participate in the modulation of the reflex responses.
- The excitability of a number of interneurons is controlled directly by the CPG to ensure the balance between maintaining the progression and organizing appropriate corrective responses needed to adapt it to the real environment.
- Reflex modulation can also occur by changing the excitability of the afferent terminals at the presynaptic levels. This was postulated because it was seen that H-reflex amplitudes did change during stance, walking and running however the EMG output was the same.

In this study the phase-dependency of CMR during hopping and limping is studied. Phase-dependency during walking and running is well known in humans (Yang and Stein 1990; Duysens et al. 1990-1996; Tax et al. 1995; Van Wezel et al. 1997; Zehr et al. 1997, 1998). But is there still a phase-dependent modulation of the reflexes during reduced gait (limping) and in phase-locomotion (hopping)?

CMR after ringstimulation of the toes is already studied in different steady-state tasks with changing background activity (Gibbs et al. 1995), but phase-dependency of CMR after ringstimulation during continuous movement as during walking has not been studied yet.

1.3.2.2. Task-dependency of CMR

From experiments on H-reflexes (Stein and Capaday 1988; Simonsen and Dyhre-Poulsen 1999; Edamura et al. 1991) it is known that there are differences in reflex activity during walking and running.

After cutaneous stimulation a facilitation of P2 responses was described in several studies both during running (Duysens et al. 1992, 1993; Tax et al. 1995) and walking (De Serres et al. 1995; Duysens et al. 1990-1992). It is proposed that this enhancement of P2 responses prior to the onset of the swing phase reflects an opening of pathways which could assist or exaggerate flexion in the ensuing swing phase (see also Duysens and Loeb 1980; Duysens et al. 1992).

At the end of the swing phase during walking a reflex reversal of TA and BF is seen (Tax et al. 1995). In the present thesis cutaneous stimulation experiments during hopping, an in-phase locomotor task, are done. And during the limping experiments the altering of the phase-dependent modulation of the cutaneous reflexes is studied. The phase-dependency of the cutaneous reflexes during this executed motor task is compared with the modulation during normal walking and running.

1.3.3. The motor part of the CMR

Zehr et al. (1998) studied the sural nerve reflexes in tibialis anterior (TA), soleus (SOL), lateral (LG) and medial (MG) gastrocnemius, vastus lateralis (VL) and biceps femoris (BF) during walking and made some assumptions about their function. They concluded that the resulting EMG and kinematic responses suggest that cutaneous reflexes stabilize human gait against external perturbations encountered during swing.

However BF and ST are synergists during normal locomotion their phase-dependent modulation after sural nerve stimulation differs (Tax et al. 1995). The reflex synergy is basically different from the locomotor synergy. Tax and co-workers (1995) therefore suggest that the cutaneous feedback from the sural nerve does more than merely providing assistance for the background locomotor task.

In cats stimulation of low threshold cutaneous afferents in the sural nerve can give rise to excitatory responses in motoneurones of the triceps surae . However, the different parts of this muscle group are not equally involved in these reflexes. MG motoneurones innervating fast twitch muscle units, show more sural nerve evoked EPSPs than slow Sol units (Burke et al. 1970, 1973).

We extrapolated this idea to the gastrocnemius muscle of humans and studied the CMR in both heads during different tasks (walking, running and hopping) and after stimulation of different nerves (sural nerve versus mixed nerve stimulation of the tibial and superficial peroneal nerves). During normal locomotion both heads are synergists for flexion of the ankle.

Duysens et al. (1994) already showed some difference between the CMR of MG and LG and suggested some functional meaning of this difference. In the anatomical section of this thesis those two heads of the gastrocnemius muscle are studied in extenso and some hypothetical ideas are worked out about a possible function of the gastrocnemius muscle outside the sagittal plane. The hypothesis made by Zehr et al. (1997) about avoiding destabilizing stumbles possibly can be transposed to two heads of the same muscle and even more to the function of different neuromuscular compartments within one muscle entity.

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2. CUTANEOMUSCULAR REFLEXES OF THE LOWER LIMB AFTER RINGSTIMULATION OF THE TOES DURING WALKING.

2.1. Abstract

- For cutaneomuscular reflexes (CMR) in the leg the contribution of the toes has been investigated only under static conditions while the role of these digital reflexes during gait is unknown.
- In nine adult human, reflexes from rectus femoris (RF), biceps femoris (BF), medial head of gastrocnemius (GM), lateral head of gastrocnemius (LG), tibialis anterior (TA), extensor hallucis brevis (EHB), extensor hallucis longus (EHL) and flexor hallucis brevis (FHB) were measured following electrical stimulation through ring electrodes around the second and fourth toe (innervated by the superficial peroneal and tibial nerve). Since these reflexes may be important for gait, they were recorded while the subjects were walking on a treadmill with a speed of 4 km h^{-1}.
- The phase-dependent modulation of the mid-latency (P2) responses is described. Except MG and LG all lower limb muscles studied showed significant facilitatory responses during the stance swing transition. RF and TA are also facilitated during most of the stance phase while FHB is facilitated during the total swing period.
- Both MG and LG are suppressed during the stance phase. It is unknown whether this also applies for more proximal stimulation of tibial or peroneal nerves but it is clearly different from the results on sural nerve stimulation where MG shows facilitatory and LG suppressive responses during the stance phase.
- For most muscles the reflexes are consistent across the population. However, for TA

there are two groups of subjects with respectively facilitation and suppression of TA activity at the end of the swing phase.

- Since the size and the modulation of the responses following digital nerve stimulation are similar to those seen after more proximal stimulation of the peroneal and tibial nerve it can be concluded that digital afferents contribute significantly to the previously observed responses. In addition, the present data show that toe muscles are involved in this type of reflexes as well.

2.2. Introduction

In recent years the evidence for task dependent modulation of cutaneomuscular reflexes (CMR) has been growing. For fingers, stimulation with ring electrodes was used by the group of Stephens (Caccia et al. 1973; Buller et al. 1980, Garnett & Stephens 1980; Jenner & Stephens 1982; Issler & Stephens 1983, Evans et al. 1989, 1990; Gibbs et al. 1995). They found that the amplitudes of the E1 and E2 responses change as muscles participate in different tasks (Evans et al. 1989, 1990; Harrison & Stephens 1989). Similarly for the toes, Gibbs et al. (1995) found task dependency. They compared the CMR in several lower leg muscles during voluntary contraction at 10-20 % of the maximum EMG level when lying down and during normal postural activity. However, so far toe stimulation has not been studied during locomotion. Studies which have used stimulation of nerves to the foot rather than to the toes have already indicated that cutaneous reflexes are facilitated in locomotor tasks (Duysens et al. 1995; Nielsen et al. 1997). Furthermore for these foot nerves it is well-established that there is a strong phase-dependent modulation of these reflexes during the step cycle (E1 and E2 are often termed P1 and P2 in that case; Yang and Stein, 1980; Duysens et al; 1990-1996; Tax et al. 1995; Van Wezel et al. 1997; Zehr et al. 1998a, 1998b). The effects differed for different nerves ('local sign'). Van Wezel et al. (1997) and Zehr et el. (1998a, 1998b) studied the cutaneous reflexes after sural, peroneal and tibial stimulation and found that some features of the modulation (such as the suppressive responses in ankle dorsiflexors at end swing) were similar for all nerves, while other features differed (strong facilitatory responses in the same muscles at end stance only after sural and peroneal but not after tibial nerve stimulation). The contribution of the toe afferents to these responses is not known. Hence a study of the reflexes following toe stimulation during gait is needed to throw light, not only on the dependency of such responses on gait, but also on their phase-dependency. Furthermore, some foot stimuli evoke very different effects in muscles which are mostly synergists. For example, medial and lateral gastrocnemius (MG and LG) react quite differently after sural stimulation during locomotion tasks (Duysens et al. 1995b; Hauglustaine et al. 1998a). During the stance phase, the MG shows facilitatory and LG suppressive responses. It is suggested that the resulting toe-out torque is important as a reaction to stimulation at the lateral (sural) site of the foot. To understand the importance of this stimulus localisation in this differential activation of both heads of the gastrocnemius muscle, the activity of both heads after stimulation of the digital nerves of the second and fourth toe is studied. It was hypothesised that there would be no differential effects in that case since stimulation is near the midline of the foot and rotation outside the sagittal plane is not appropriate.

2.3. Methods

2.3.1. Experimental set-up

A group of 9 normal subjects (3 female and 6 male) aged between 22 and 41 participated in this study of cutaneomuscular reflexes during walking. The experiments were carried out in conformity with the declaration of Helsinki for experiments on humans. All subjects had given informed consent and had no known history of neurological or motor disorder. They were asked to walk on the treadmill with a speed of 4 km/h while wearing a safety-harness which was fastened to the ceiling. Before starting the experiment the subjects were adjusted to the experimental situation. Between these training periods, during quiet standing, the perception threshold (PT) was determined psychophysically by gradually increasing and decreasing the stimulus amplitude in at least three series. The attainment of a constant PT was an indication for stable stimulation conditions and therefore a prerequisite for starting the main experiment. All subjects reached a stable PT within 30 to 60 minutes. No data were sampled in this period.

Foot contact with the split-belt treadmill was detected with two built-in force plates. Bipolar EMG activity was recorded in the leg ipsilateral to the stimulation site by means of surface electrodes over rectus femoris (RF), biceps femoris (BF), tibialis anterior (TA), medial gastrocnemius (MG), lateral gastrocnemius (LG), extensor hallucis longus (EHL), extensor hallucis brevis (EHB) and flexor hallucis brevis (FHB) muscles. Proper positioning of the electrodes over the particular muscle bellies was verified by means of cross-talk tests and by visual inspection during a short running period. The stimulation electrodes were two ring electrodes (type E/D S-K Medelec Ltd.) of which one was positioned around second toe and the other around the fourth (Rowlandson and Stephens

1985). The electrical stimulus consisted of 5 rectangular pulses of 1ms given over a period of 21 ms. A custom-made constant voltage stimulator provided the desired stimulus amplitude.

2.3.2. Computerized stimulation properties and data gaining

The electrical stimuli were varied with respect to the timing of presentation in the movement cycle. Ipsilateral footfall on the belt during the walking experiment served as reference points of time in the movement cycle. Detection of this ground contact could trigger the computer to release a stimulus after a certain delay which is a multiplication of a sixteenth of the movement cycle time. The stimulus intensity was two times the perception threshold (2xPT). There were 16 stimulus conditions (timing) for each experiment. Every stimulus was presented 10 times for each condition in the main experiment. An equal number of controls was sampled. Hence each experiment yielded 320 trials. The successive stimulus presentations were separated with an ad random interval of 2 to 5 s, which corresponded to at least two cycles of unperturbed movement.

Regarding the stability of this cutaneous stimulation, one could expect movement induced instabilities. Stable stimulation depends both of the constancy of the applied current and the constancy of the current to the stimulated nerve. Conform to former studies (Duysens et al. 1990-1993, 1995; Tax et al. 1995) the applied current was measured between the onset of stimulation and the following 50 ms and did never deviate significantly at any given phase from the mean across all phases during the walking experiment reported here.

Hence ring electrodes did not differ in this respect from the previously used methods (Duysens et al. 1990, 1993). Similarly, in the upper limb the sensory volley elicited by ring stimulation of the digital nerves did not change significantly during various motor tasks

(Evans et al. 1989).

The experimental data were sampled by a computer system after amplification and low- and high-pass filtering. The storing on hard disk of each trial started 100 ms prior to stimulation and lasted for 1600 ms.

2.3.3. Data analysis

The EMG analysis started with a procedure for the detection of reflex responses. First, the 10 trials of each stimulus condition were averaged. For each stimulus phase this resulted in one average 'reflex' trial and one 'average' control trial. The average control trials were subtracted from the corresponding average reflex trials to obtain the 'pure' reflex responses (Belanger and Patla 1987; Yang and Stein 1990; Duysens et al. 1991). The subtraction technique allowed both facilitatory and suppressive responses to be measured.

The time window for the reflex peaks was set by visual inspection (time resolution 2ms) as described in earlier studies (Yang and Stein 1990; Duysens et al. 1991; Hauglustaine et al. 1998a). The mean EMG values within the window were calculated for the average reflex, control and the corresponding subtracted trials. The resulting data underwent both an amplitude and a time normalisation procedure so that a proper intersubject comparison could be made. For the amplitude normalisation, the EMG data were scaled for each muscle to the maximum control value in the step cycle. For the normalisation of the time axis, the step cycle was subdivided into 16 equal intervals (phases). Phase 1 is for all subjects the beginning of the stance phase of the ipsilateral leg during the walking movement.

The significance of the difference ($p \leq 0.05$) between the control and reflex activity was tested with a Student's paired t test.

2.4. Results

In the arm the cutaneomuscular reflex (CMR) responses have three identifiable early components comprising an initial short latency increase (about 50 ms after stimulation) in EMG activity, the E1 component, followed by a decrease, the I1 component, followed by a second increase (about 80 ms after stimulation), the E2 component (Caccia et al. 1973; Stephens & Usherwood 1976). In the leg, similar responses are seen but they are referred to as P1 and P2 (Duysens et al. 1990), conform to definitions in the cat (Duysens & Loeb 1980). Figure 2.1. shows a rough 'pure' reflex EMG pattern of the BF muscle of one subject after cutaneous stimulation of the digital nerves of the second and the fourth toe. As shown in the methods section the 'pure' reflex is obtained after subtracting the averaged control EMG activity from the averaged EMG activity after stimulation. A phase-dependent modulation of the P2 (equivalent of E2; Jenner & Stephens 1982) component is seen.
In this study eight muscles of the lower limb are studied; RF and BF as biarticular muscles of the upper leg, MG and LG as plantar flexors of the ankle, TA as dorsal flexor of the ankle, EHL and EHB as extensors and FHB as flexor of the first toe.

2.4.1. Biarticular muscles of the upper leg

As biarticular muscles of the upper leg the phase-dependent modulation of the P2-response of RF and BF are studied. In figure 2.2. the population (n=9) average of the control and reflex activity of both biarticular muscles is plotted. For BF (see fig. 2.2., bottom) a strong facilitation is seen near stance swing transition (phase 8) and the beginning of the swing phase (significant at phase 11). For RF (see fig. 2.2., top) significant facilitations are seen during the first half of the stance phase (phase 1-4), at stance swing transition (phase 9) and near the end of the swing phase (phase 14 and 16).

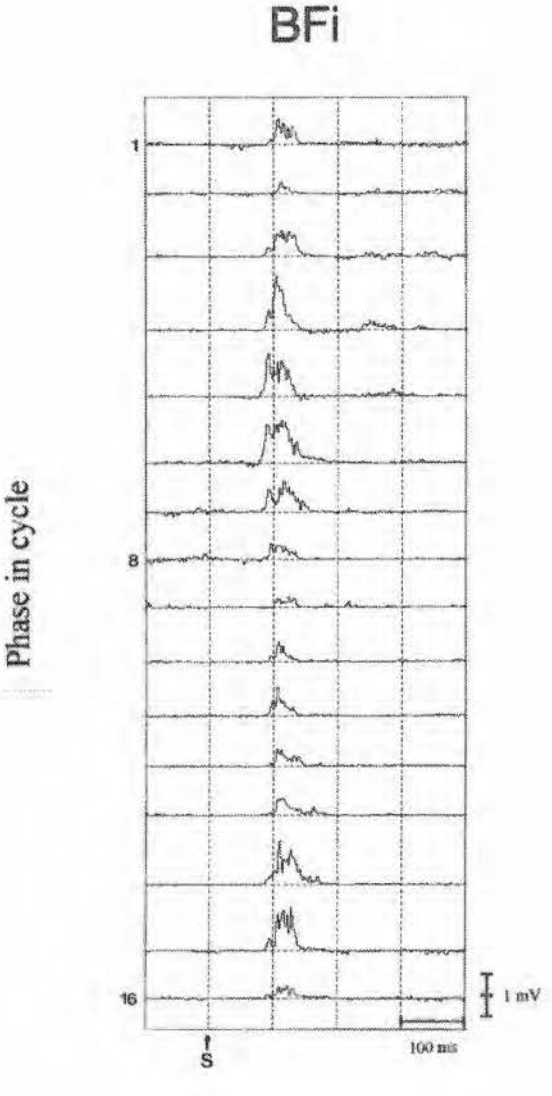


Figure 2.1. 'Pure' reflex activity (reflex minus control activity) of the ipsilateral BF of one subject after stimulation of the digital nerves of the second and fourth toe at 2 x PT during sixteen different phases of the step cycle of the walking movement. S with arrow indicates the time of stimulation. About 80 ms after stimulation the phase-dependent 'pure' reflex response is shown.

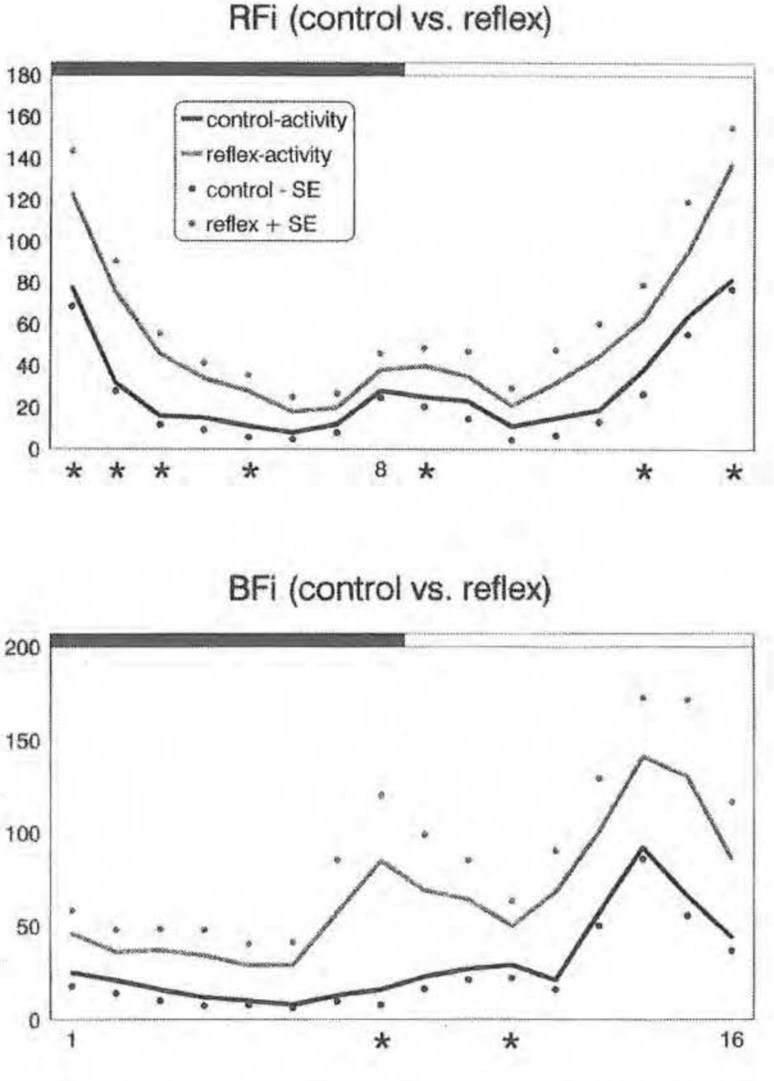


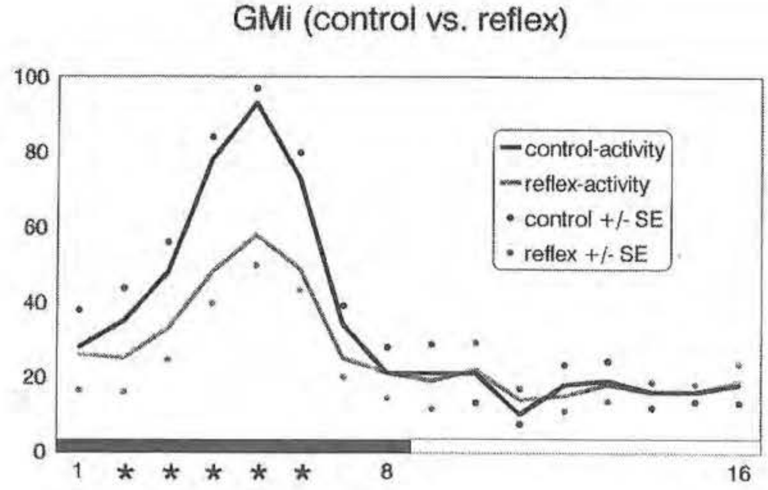
Figure 2.2. Plot of the mean control and reflex activity of RF (A) and BF (B) of the whole population (n=9) during the walking movement. For both figures: black line = control activity; grey line = reflex activity. The phases with a significant difference between control and reflex activity are indicated with an asterisk ($p \leq 0.05$ after a Student's paired *t* test). Horizontal bars: stance phase with ground contact = black; swing phase = white.

2.4.2. Plantar flexors of the ankle

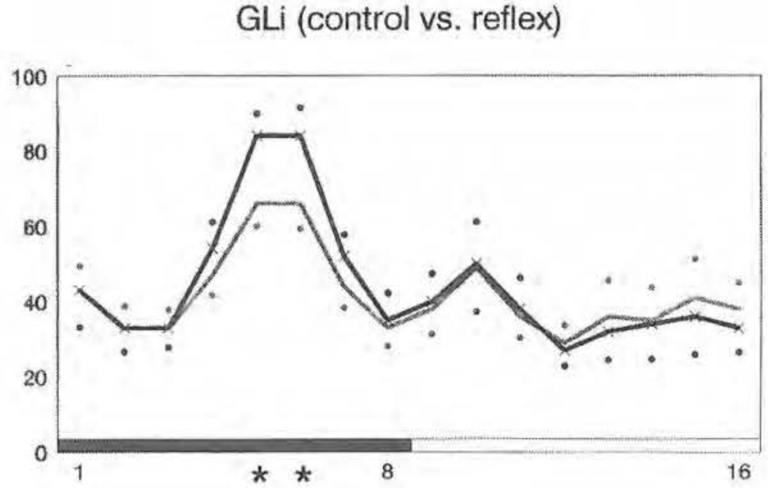
As plantar flexors of the ankle the two muscular heads of the gastrocnemius muscle are studied. As shown in figure 2.3. the phase-dependent modulation of the reflex activity of both heads is similar. A suppression of the muscular activity is seen during the stance period while during the rest of the step cycle the reflex activity follows very strictly the envelope of the background activity. In GM (fig. 2.3., top) the suppression of the muscular activity (phases 2-6) is more pronounced than in GL (fig. 2.3., bottom; phases 5-6).

2.4.3. Dorsal flexor of the ankle

As dorsal flexor of the ankle the TA is studied. After cutaneous stimulation of the digital nerves of the second and fourth toe TA shows strong reflex activity (fig. 2.4., top). In the population two groups of responders can be determined. Six subjects showed strong facilitations of the TA activity while the three other subjects showed suppressions. In figure 2.4., beneath the population figure the pure reflex response of two subjects is plotted. TA of Subject 4 shows suppressive responses during the swing phase (phase 8-16) while TA of subject 9 gets facilitated during the whole step cycle. This difference in reflex response during the swing phase of the two groups of responders causes the lack of significance during the greatest part of the swing phase for the whole population (see fig. 2.4., top).



GMi (control vs. reflex)



GLi (control vs. reflex)

Figure 2.3. Plot of the mean control and reflex activity of GM (A) and GL (B) of the whole population (n=9) during the walking movement. For the legends see figure 2.2.

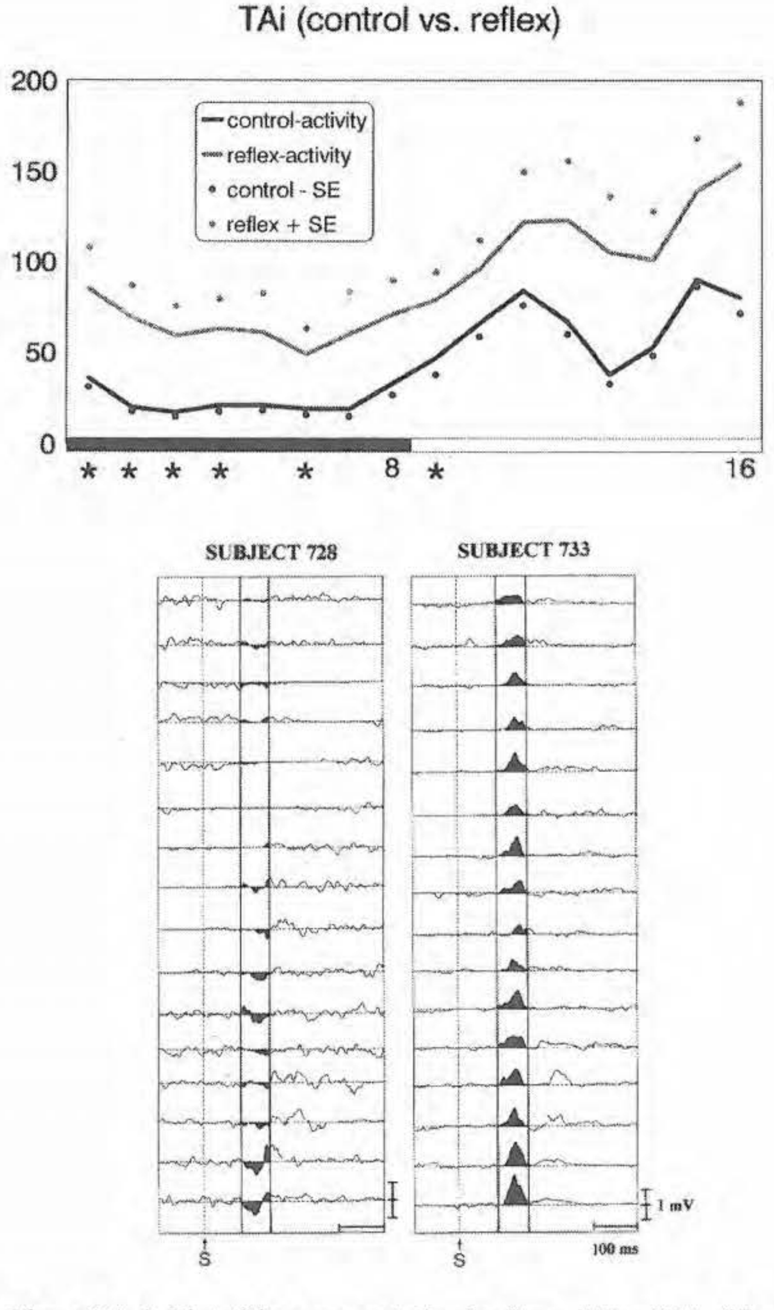
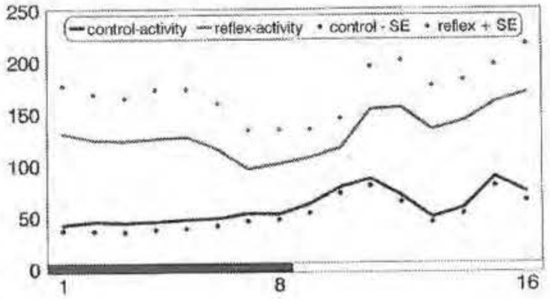
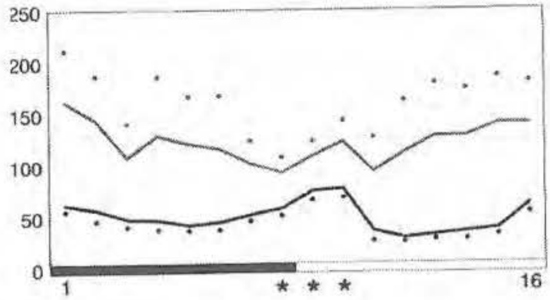


Figure 2.4. A. Plot of the mean control and reflex activity of TA of the whole population (n=9) during the walking movement. B. The same plot of TA of the facilitation group (n=6). C. The same plot of TA of the suppression group. For the legends see figure 2.2.

EHLi (control vs. reflex)



EHBi (control vs. reflex)



FHBi (control vs. reflex)

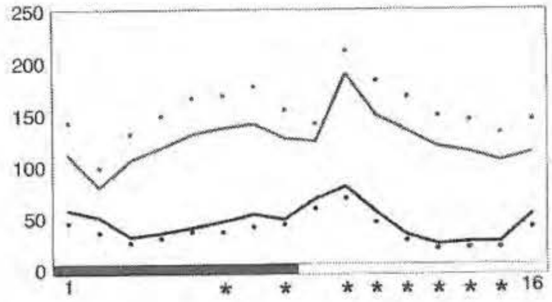


Figure 2.5. Plot of the mean control and reflex activity of EHL (A), EHB (B) and FHB (C) of the whole population during the walking movement. For legends see figure 2.2.

2.4.4. Musculature of the first toe

Although the mean reflex activity of EHL (fig. 2.5., top) is about two times the control activity no significant difference (Student's paired *t* test) between control activity and reflex activity is present. For EHB (fig. 2.5., middle) the facilitation is significant at the stance swing transition (phases 8-10). The lack of significance elsewhere is caused by great intersubject variability in the reflex responses of both extensors of the great toe.

FHB (fig. 2.5., bottom) shows the most significant facilitations of the tested muscles of the first toe. Significant facilitations are seen during the second part of the stance phase (phase 6 and 8) and during the whole swing phase (phases 9-15).

2.5. Discussion

The present study shows a phase-dependent modulation of the mid-latency reflex activity of the lower limb and intrinsic foot muscles after ring stimulation of the digital nerves of the second and fourth toe during the walking movement. Except for both heads of the gastrocnemius muscle which exhibit suppressive responses during the stance phase, all muscles studied show facilitatory responses at swing stance transition. For TA, two types of responders can be distinguished after stimulation, one showing suppressive the other showing facilitatory responses.

Stimulation with ring electrodes to study CMR has mostly been used in studies concerning the upper limb (Caccia et al. 1973; Buller et al. 1980; Garnett & Stephens 1980; Issler & Stephens 1983; Evans et al. 1989, 1990). Studies with ring electrode stimulation of the lower limb have been focussed on the extensor digitorum brevis muscle (EDB) (Jenner & Stephens 1982) and TA (Rowlandson & Stephens 1985a, 1985b). However, Gibbs and co-workers (1995) made a broad study of the reflexes of lower limb muscles after ring stimulation of the digital nerves of the second toe. They studied CMR of EDB, TA, soleus (Sol), quadriceps (Quad) and erector spinae (ES) during two different tasks, voluntary contraction in a lying down position and postural activity during erect position. They found a decrease in the CMR during the second task and they observed that the mid-latency reflexes (E2) had the greatest proximo-distal distribution in the lower limb.

In the present work the mid-latency reflexes after ring stimulation are studied during a natural walking task. It is found that similar to earlier CMR studies of our group (Duysens et al. 1990-1995; Tax et al. 1995) there is a phase-dependent modulation of the reflex activity during walking with a facilitation of the muscular activity around the stance swing transition in most of muscles studied. This facilitation seems to be locomotion related and was also seen after sural stimulation in walking, running, limping and hopping tasks (Hauglustaine 1998b). Similar to sural nerve stimulation (see Hauglustaine et al. 1998a) this end-stance facilitation is not present in the two heads of the gastrocnemius muscle after the present digital nerve stimulation. The origin of the phase-dependent modulation of CMR still remains a question that has to be solved. Recent studies about cutaneous reflexes during limping (Hauglustaine et al. 1998b) and passive cycle movements (Brooke et al. 1999) show that the modulation of mid-latency reflexes during locomotion was not significantly effected by changes in peripheral afferent input. Their findings suggest that modulation of cutaneous reflexes during locomotion is not the result of inhibition arising from motion-related sensory receptor discharge in contrast to H-reflexes, where sensory receptor discharge plays an important role for reflex modulation (Brooke 1993). The phase-dependent modulation of cutaneous reflexes might have a cortical origin. It was Babinski (1898) who showed that the motor cortex can influence transmission in cutaneous reflex pathways in man. In humans, some studies have argued that reflexes such as described in the present paper could well be transcortical (Nielsen et al. 1997; Jenner & Stephens 1982).

The idea of this transcortical pathway is supported by the findings that when sural nerve and cortical magnetic stimulation responses are combined at end swing the responses are larger than for sural nerve stimulation in isolation (Pijnappels et al. 1998; Christensen et al. 1999).

Stimulation of the digital nerves of the second and fourth toe is a mixed nerve stimulation of terminal branches of the tibial (plantar) and the superficial peroneal nerve (dorsal). Most of the studies of CMR have used stimulation of the sural nerve but CMR after stimulation of the tibial nerve (Duysens et al. 1990; Yang & Stein 1990; Van Wezel et al. 1997) and the peroneal nerve (Van Wezel et al. 1997; Zehr et al. 1998b) have also been studied. The results of this study are in line with their results. For BF the phase-dependent reflex modulation after digital nerve stimulation is most similar to the modulation of the reflex responses after stimulation of the superficial peroneal nerve (Van Wezel et al. 1997; Zehr et al. 1998b). For RF and TA, however, the phase-dependent modulation is more similar to the modulation after tibial nerve stimulation (Duysens et al. 1990; Van Wezel et al. 1997). Only the end swing suppression seen for TA after tibial nerve stimulation is absent in the recent study. In the studies of Duysens et al. (1990) and Van Wezel et al. (1997) the stimulation electrode for the tibial nerve was positioned between Achilles tendon and medial malleolus, while in the present study the stimulation occurred more localised at the second and fourth toe. The stimulation of the tibial nerve at the ankle activates both toe afferents and the afferents from the foot sole. Since toe afferent stimulation does not produce the reversal from TA facilitatory to TA suppressive responses at end swing, it follows that the latter suppression is mostly or totally due to activation of sole afferents.

Similar as for sural stimulation (Tax et al. 1995; Yang & Stein 1990) there is a great intersubject variability in the reflex response of TA during the swing phase after stimulation of the digital nerves of the second and fourth toe. For TA the population can be divided in a facilitation and a suppression group concerning the reflex response during the swing phase. Additional, it is remarkable that for the extensor muscles of the great toe there is also a greater intersubject variability than for the FHB. Further research on the phase dependency of the cutaneous reflexes of EDB and EDL have to be done to study whether the intersubject variability is greater in all the dorsiflexors of the ankle and all the extensors of the toes.

The CMR evoked in the two heads of the gastrocnemius muscle are of very great interest concerning the location specific responses after cutaneous stimulation. In the present study is seen that GM and GL both are suppressed during the stance phase after tibial nerve stimulation, thereby decreasing the plantar flexion to avoid the stimulation. Tax et al. (1995) suggested that tactile cutaneous feedback may be used to move the perturbed leg away from the stimulus, with the general constraint of preserving both the cadence and the balance at all times during the step cycle. The presently observed responses of GM and GL are completely in line with this suggestion.

In a previous study (Hauglustaine et al. 1998a) was shown that MG and LG react differently after sural nerve stimulation. The activity of MG is facilitated while the activity of LG is suppressed after non-nociceptive sural stimulation. This difference is maintained during different locomotion tasks as walking, running and hopping. Lawrence et al. (1993) showed that MG causes more toe-out torque than LG after stimulation of the muscle nerve. This toe-out torque during sural stimulation possibly moves also the perturbed leg away from the stimulation site. Contralateral to the sural stimulation both heads show similar phase-dependent reflex responses (Hauglustaine et al. 1998a) increasing the stability of the body.

The neural pathway for the control of location-specific information in cutaneous reflexes is not known yet but Van Wezel et al.(1997) suggested that the observed location specificity must arise at the premotoneuronal level. It is thought that the various cutaneous nerves project to the same motoneurones, but the pathway to the motoneurones can differ in the overall strength of excitatory and inhibitory connections.

Further experiments on CMR of MG and LG after saphenal nerve stimulation (medial site of the foot) are needed to further test these ideas about location specific cutaneous reflexes. One would expect a toe-in torque with suppression of MG and facilitation of LG and the peroneus muscles.

Whatever the outcome of these experiments is, the current data already show that in humans, as in cat (Moschovakis et al. 1991), there is a very precise reflex regulation from various skin regions of the foot.

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3. PHASE-DEPENDENT MODULATION OF CUTANEOUS REFLEXES FROM THE FOOT DURING WALKING, RUNNING AND LIMPING.

3.1. Abstract

Although it is well established that the amplitude of cutaneously-evoked responses from the sural nerve depends on the phase of the step cycle ("phase-dependent reflex modulation") it is largely unknown which features of this modulation are locomotor specific and whether the strength of the responses depends on the locomotor task. Nor is it known what the importance is of the movement-related feedback for this type of modulation. To examine these questions the modulation of responses in TA (tibialis anterior) and BF (biceps femoris) were examined in different locomotor tasks. For alternating types of gait, walking and running at the same speed were compared. For gait with a restriction in the movement component, a study was made of limping (reduced form of gait with one leg held stiff).

For TA it was found that there is a large significant facilitation of responses at the onset of swing in all three types of alternating locomotion (walking, running, limping). However, at end swing the reflex gain in TA is dependent on the executed tasks. This could be expected because foot placement during this phase of the step cycle differs strongly for the 3 tasks. During walking a significant suppression of TA activity was seen while during running there was no reflex activity detected at end swing. During limping a significant facilitation of the reflex activity was seen at heel strike.

For BF it was seen that the net reflex response during the swing phase of the step cycle of all three movements do not differ significantly. During the first part of the stance phase of the excecuted movements this difference is more significant.

It is suggested that for sural nerve induced reflexes a common locomotor-related

mechanism is responsible for the facilitation of responses of TA at end stance or at onset swing. However, in contrast to early swing facilitations, the reduction and/or reversal of the responses at end swing is much more specific and may depend on the type of heel strike and the related ankle movement.

3.2. Introduction

During human gait it is well-known that there is a phase-dependent modulation of cutaneous reflexes from the foot. The task dependency of this modulation has not received much attention for cutaneous reflexes as compared to proprioceptive reflexes (Edamura et al. 1991). The cutaneous reflexes during walking and running have not been compared systematically although data are available for walking (Yang and Stein 1990; Duysens et al. 1990, 1996; Van Wezel et al. 1997; Zehr et al.1998) and running separately (Duysens et al. 1993; Tax et al. 1995). However, in the studies mentioned, the speeds used for walking and running were different (usually about twice as high for running than for walking) and therefore it is impossible to judge whether changes in reflex amplitudes are due to task changes (walking versus running) or to speed differences. For Soleus H-reflexes, Edamura et al. (1991) found that the slope of the relationship between H-reflex and background EMG differed between these two tasks even when velocity was the same for both conditions. For sural nerve reflexes a similar comparison has not been made so far. This question can be solved by having the subjects either run or walk at the same speed (6 km/h).

During both walking and running, one of the most consistent features of the modulation pattern for flexor muscles such as TA (tibialis anterior) is that the facilitatory responses are largest near the onset of the swing phase while suppressive responses prevail near the transition from swing to stance (Yang and Stein 1990; Duysens et al. 1990; Van Wezel et al. 1997; Zehr et al. 1998). This phase-dependent reversal of reflexes is not related to the recruitment of different populations of motoneurons since it can be observed in single motor units from TA during gait (De Serres et al. 1995). To examine how much of this modulation pattern is due to the locomotor movement itself (i.e. presynaptic interactions between movement-related -feedback, see Stein et al. 1995) we previously introduced a paradigm of "reduced gait" (Van de Crommert et al. 1996; Faist et al. 1999). This consists of limping with one leg on a moving split belt while the other leg is held as stiff as possible on a stationary belt to reduce sensory feedback. In these previous studies, it was shown that the basic features of the phase-dependent modulation during normal gait were preserved for biceps femoris tendon reflexes in the limping leg.

One might predict on the basis of experiments with H-reflexes (Brooke et al. 1997) that interactions between sensory inputs play a role in the modulation of the cutaneous reflexes. If this is the case one would expect changes in the modulation pattern during reduced gait (reduced sensory input). Very recently Brooke and co-workers (1999) found that cutaneous reflexes did not change significantly after passively induced change in afferent input and they suggested that there are different pathways for the modulation of H-reflexes and cutaneous reflexes after experiments during passive leg movement. A study with a comparison of cutaneous reflexes during walking, running and limping could throw light on this issue.

Alternatively the gating could have a central origin. In the cat there is some evidence that the spinal CPG for locomotion can underlie the phase-dependent modulation of some cutaneous reflexes (Burke et al. 1991; Schomburg and Behrends 1978a,b). In humans a similar intervention of a CPG-like center has been proposed to play a role as well (based on indirect arguments related to the reflex modulation during backward as compared to forward walking see Duysens et al. 1996, for review see Duysens and Van de Crommert 1998).

To investigate how the modulation of the cutaneously-evoked responses depend on the locomotor specificity of tasks, a series of experiments was done in which we investigated the changes in amplitude of these reflexes in various locomotor tasks (walking and running at the same speed) and in "reduced" gait (in which the sensory feedback on the side of stimulation is reduced because the leg is held as stiff as possible). A preliminary account of the results has been published (Hauglustaine et al. 1998b).

3.3. Methods

3.3.1. Experimental stimulus and protocol

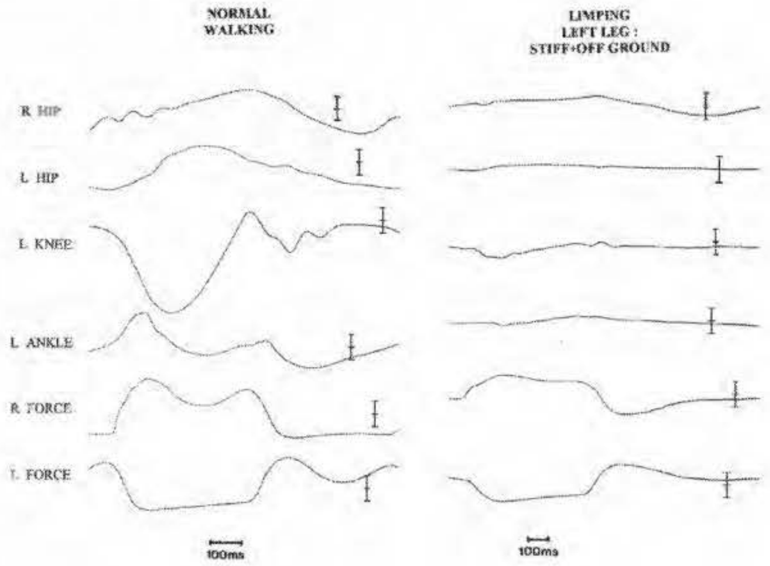
A detailed description of some of our methods can be found in previous publications (Duysens et al. 1990, 1996). In brief, stimulating electrodes were positioned at the ankle over the left sural nerve (near the middle of the distance between the external malleolus and the Achilles tendon). The stimulation consisted of a train of 5 rectangular pulses of 1 ms, given over a period of 21 ms. These shocks were first applied while the subjects were standing on the treadmill. The perception threshold was determined by gradually increasing and decreasing the stimulus intensity in at least three series. The whole procedure was repeated between all experimental runs to ascertain that stimulus conditions were stable. Runs in which a large (>15 %) change in threshold was seen in the test following an experimental run were discarded. When the change was smaller, the averaged threshold over the pre-and post-trial session was determined and used as reference for that session. During the first 30 to 60 minutes of the experiments, there usually was a slow decrease in perception threshold but later measurements were generally stable.

During the experimental runs, stimulus trains at 2 times perception threshold (2PT) were given in some of the cycles at a predetermined delay after footfall. The different delay conditions were randomly mixed. Moreover, to avoid habituation of the reflexes a period of one or more cycles without stimulation always preceded the stimuli. To avoid that the subjects would be able to predict the stimulus trains, the interval between trains was randomly varied with periods ranging between 2 and 5 seconds. For all conditions, the stimuli were delivered at one of a series of 16 intervals, spread evenly over the cycle period. At least 10 responses for each type of stimulus conditions (with a given fixed intensity and delay after trigger) were sampled. The control trials (0xT) were matched for timing of stimulation and they were randomly mixed with the stimulus trials within the same experimental run. The controls were simply obtained by giving a series of "dummy" stimuli (the output to the stimulator being blocked). A major concern was the stability of the stimulation during the course of the experiments. The same precautions were taken as in our previous studies (Duysens et al. 1990-1995; Hauglustaine et al. 1998a; Tax et al. 1995).

3.3.2. Three conditions: walking, running and limping

Basically the experiments consisted of 3 conditions. The “walking” and “running” conditions occurred with a belt speed of 6 km/h. For the “limping” condition (same as “reduced gait” of Van de Crommert et al. 1996 and Faist et al. 1999) the subjects walked normally on the side contralateral to the stimulation (at 4 km/h) while the ipsilateral side was periodically lifted from the immobile part of the belt (split belt with 0 km/h on the ipsilateral side). The subjects were instructed to keep the ipsilateral leg as stiff as possible. This resulted in a dramatic reduction in the moments of all joints of the leg at the ipsilateral side (as shown in fig. 3.1.). The resulting movement was strictly alternating and resembled 'limping’. Typical for limping is that the loading period is much shorter on one side versus the other. This was clearly present here as well, with the stiff leg used for the brief periods of support (force traces in Fig. 3.1.; stiff leg is left).

Figure 3.1. Goniometric and force data of one step cycle of respectively normal walking and limping. For the goniometric data of hip and knee the baseline is 180 degrees (°) while for the ankle it is 90°. The indicated Y-scale for the goniometric data is 15°. The baseline of the force data is 0 Newton meter (Nm) and the indicated Y-scale is 500 Nm.



Five subjects (four male and one female between 24 and 45 years old) participated in all three tasks (walking, running and limping). For one of the conditions (limping) the results were supplemented with recordings in an additional group of four subjects (four male between 27 and 40 years old). To avoid sequence effects the order of the conditions was varied as much as possible.

The experiments were performed in conformity with the principles described in the declaration of Helsinki for experiments on humans. All subjects gave their informed consent and they could stop the experiment at any given point.

3.3.3. Data sampling and analysis

Surface electromyography (EMG) electrodes were used to record the activity of various leg muscles (including tibialis anterior, TA, and biceps femoris, BF) on both sides (8 channels in total). Changes in the angles of hip, knee and ankle were measured with goniometers. Two force plates, one under each part of the belt, were used to detect foot contact. These events were used as a reference for stimulus triggering. The EMG analysis started with a procedure for the detection of reflex responses. First, the 10 different trials of each stimulus condition were averaged. This resulted for each stimulus phase in an averaged 'reflex' trial. An equal number of averaged 'control' trials without stimulation were taken at the equivalent phases. To obtain the 'pure' reflex responses the averaged control trials were subtracted from the corresponding reflex trials.

The windows were set around the earliest reflex responses by visual inspection, taking in account criteria described earlier (Hauglustaine 1998a; Duysens 1991, 1993; Yang and Stein 1990). The window setting for BF and TA during the three different tasks are shown in table 3.1.

	WALKING		RUNNING		LIMPING	
Subject	BF (ms)	TA (ms)	BF (ms)	TA (ms)	BF (ms)	TA (ms)
1	80-114	80-116	80-120	80-116	80-120	82-116
2	78-124	80-114	78-124	80-116	78-126	78-116
3	78-124	80-116	78-124	80-112	78-124	80-116
4	78-124	80-114	78-126	80-116	78-124	80-116
5	78-124	80-110	78-124	78-114	78-122	82-114
6	/	/	/	/	76-120	78-114
7	/	/	/	/	78-122	80-116
8	/	/	/	/	80-126	80-116
9	/	/	/	/	80-124	82-114
Mean	78.4-122	80-114	78.4-123.6	78.8-114.8	78.4-123.1	80.2-115.3

Table 3.1.: Window settings for P2 responses following onset of stimulation for TA and BF during walking, running and limping.

For the averaged reflex, control and the corresponding subtracted trials the mean EMG-values within the window were calculated. The resulting data underwent both an amplitude and a time normalization procedure in order to enable a proper intersubject comparison. For the amplitude normalization the EMG data were scaled for each muscle to the maximum control value in the step cycle (i.e., the maximum spontaneous activity during forward walking). For the normalization of the time axis the step cycle was subdivided into 16 equal time intervals. The responses were plotted according to their appearance in one out of the 16 intervals. The statistical significance of the responses was tested by comparing the averaged reflex peaks with the control activity in each condition using either a student's t-test for paired samples or a Wilcoxon matched-pairs signed-rank test for the experiments with 9 and 5 subjects respectively (significance at $p<= 0.05$). Additional an ANOVA-test was carried out between the three locomotor tasks to test the significance of the task-dependent differences between the obtained net responses.

3.4. Results

To study the phase- dependent modulation of cutaneous reflexes from the foot during locomotor tasks, three tasks were selected: walking, running and limping as a form of reduced gait (see methods). The activity of two leg muscles was analyzed; the ipsilateral tibialis anterior muscle (TAi) in the lower leg and the ipsilateral biceps femoris muscle (BFi) in the upper leg.

3.4.1. Tibialis anterior ipsilaterally

The modulation of the amplitude of the responses was investigated by stimulating the sural nerve at 2 times perception threshold (2xT) at 16 phases of the step cycle. The averaged subtracted ipsilateral TA responses are seen in fig. 3.2. for one subject tested during walking, running and limping. After window setting the mean amplitude of the middle latency (P2) reflexes is measured. The plot of the measured data is shown as fig. 3.3. During both walking and running, the facilitatory responses occurred mostly at the onset of the activity period (begin of the swing phase; phase 9 to 14 in figs. 3.2. and 3.3.) while they were absent or even suppressive at the end of the activity period (near touchdown; phases 15 and 16 in figs. 3.2. and 3.3.), despite the presence of a large amount of background activation. During running the facilitatory responses were already present during end stance phase. Part of the modulation pattern was basically preserved during limping since the responses occurred at the onset of the swing phase. This feature was not seen in all of the subjects (such as the one shown in Figs. 3.2. and 3.3.) but it was clearly seen in the population average (Fig. 3.4.).

In contrast, the response modulation at end swing was clearly different in limping as compared to walking and running. During walking and running the responses could be suppressive, in confirmation of previous work ("phase-dependent reflex reversal", Yang and Stein, 1990; Duysens et al. 1990). In limping, both in the single subject (Figs. 3.2., 3.3.) and in the population (Fig. 3.4.), such suppressive responses were absent and instead a strong facilitatory response is seen at the end of the swing phase (near touchdown; phase 15 and 16).

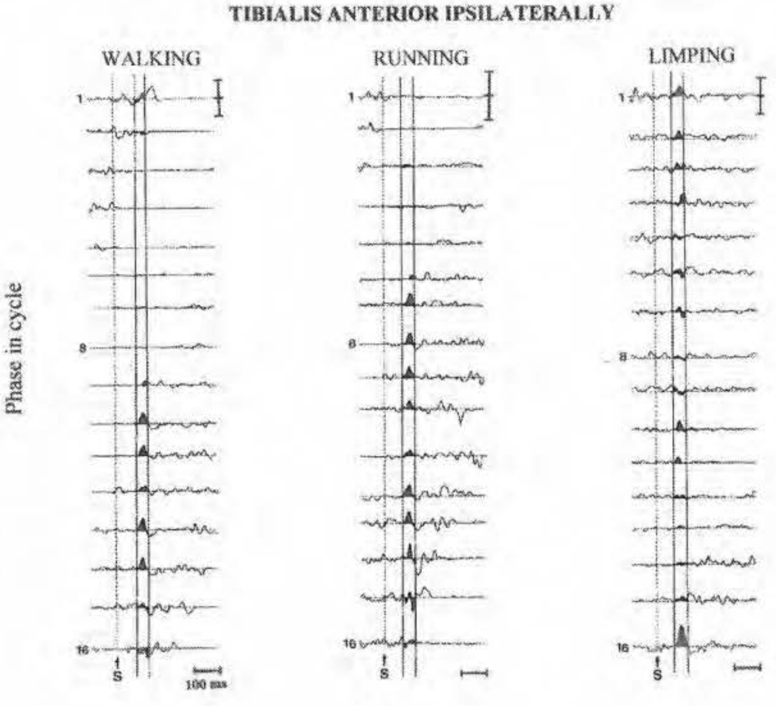


Figure 3.2. Phase-dependent changes in the subtracted and averaged (n=10) responses of the ipsilateral tibialis anterior muscle. Window settings (full vertical lines) show the periods taken for measurement of the reflex activity, starting at about 80 ms after cutaneous stimulation (s; vertical dashed line) in one subject during 16 different phases of respectively a walking, a running, and a limping cycle. The indicated Y-scale is 1 mV.

TIBIALIS ANTERIOR IPSILATERALLY

(one subject)

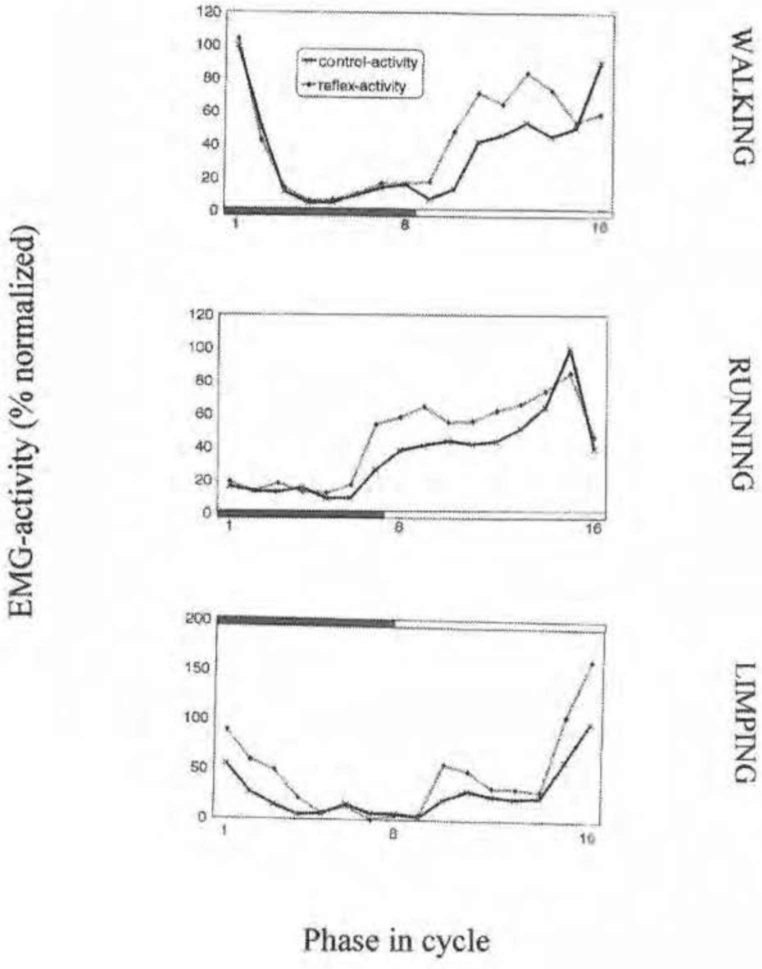


Figure 3.3. Difference between mean control and mean reflex activity (n=10) of the ipsilateral tibial anterior muscle in one subject during walking, running and limping. The highest control activity is normalized at 100 % for each condition to improve interindividual comparison. For all three movements black indicates the stance phase and white indicates the swing phase (horizontal bar).

TIBIALIS ANTERIOR IPSILATERALLY

(population)

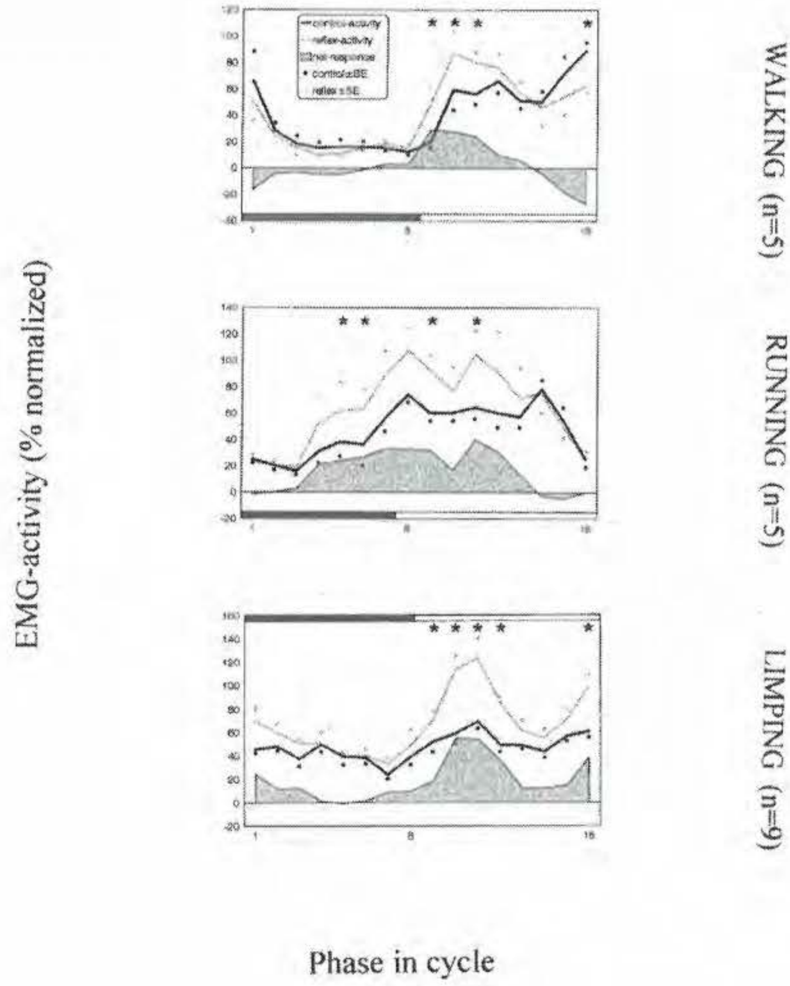


Figure 3.4. Same data as in figure 3.3. but for the whole population (walking: n=5; running: n=5; and limping: n=9). The significance of the difference between control and reflex activity is indicated with an arrow (p ≤ 0.05). As in figure 3.3. black indicates stance phase and white indicates swing phase. The data were normalized for each subject and each condition. This explains why the mean of background activity does not always reach the 100 % in the same phase of the step cycle.

3.4.2. Biceps femoris ipsilaterally

In biceps femoris it is common to see large responses following sural nerve stimulation. The phase-dependent modulation pattern of the pure averaged "subtracted" reflex responses is illustrated for one subject during walking, running and limping in Fig. 3.5., while the plots of the measured amplitudes of these data are shown in Fig. 3.6.

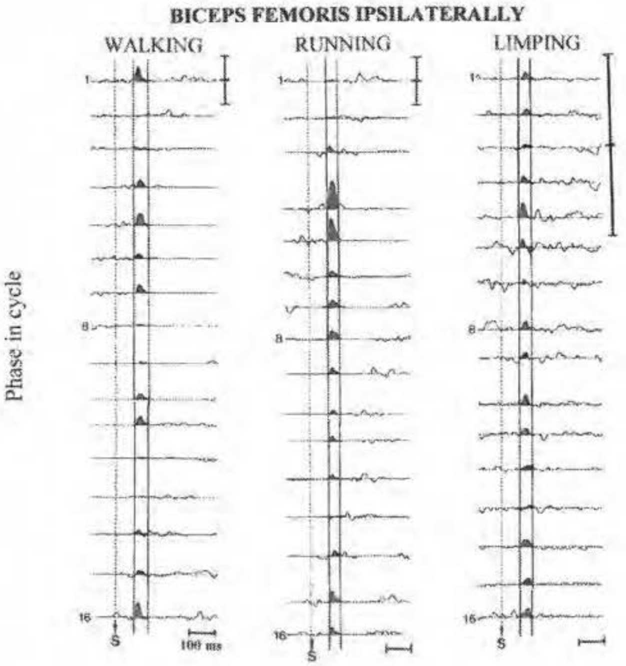


Figure 3.5. Phase-dependent changes in the subtracted and averaged (n=10) responses of the ipsilateral biceps femoris muscle during walking, running and limping. For further legends see figure 3.2.

BICEPS FEMORIS IPSILATERALLY

(one subject)

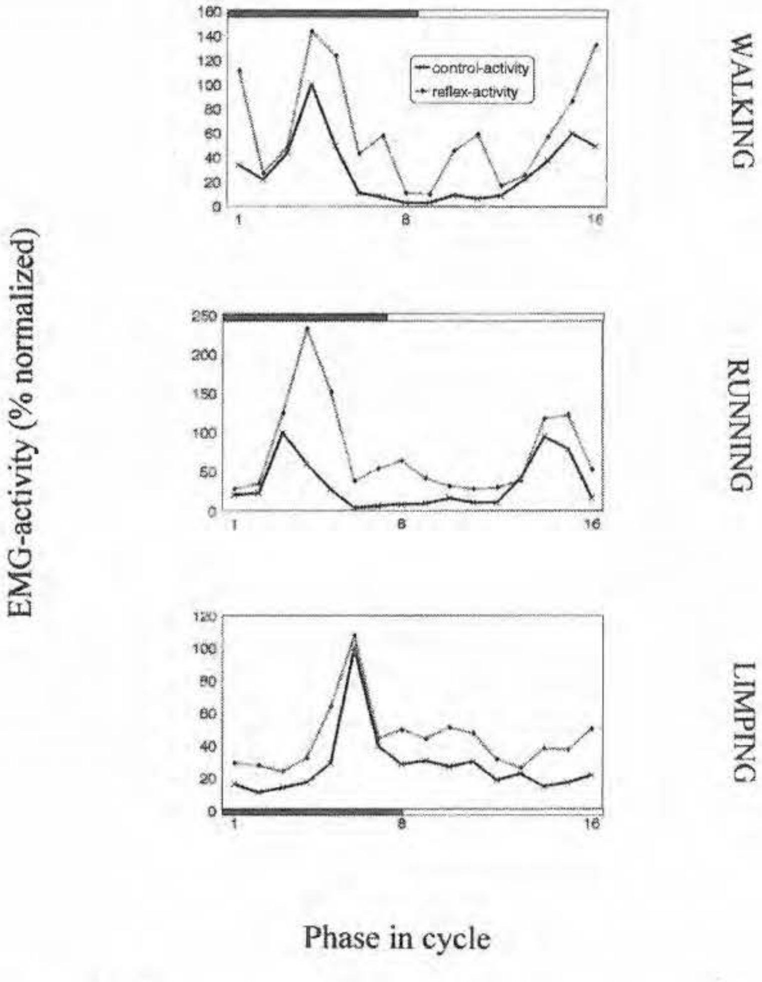


Figure 3.6. Electromyographic data of the ipsilateral biceps femoris muscle. Difference between mean control and reflex activity (n=10) in one subject during walking, running and limping. For further legends see figure 3.3.

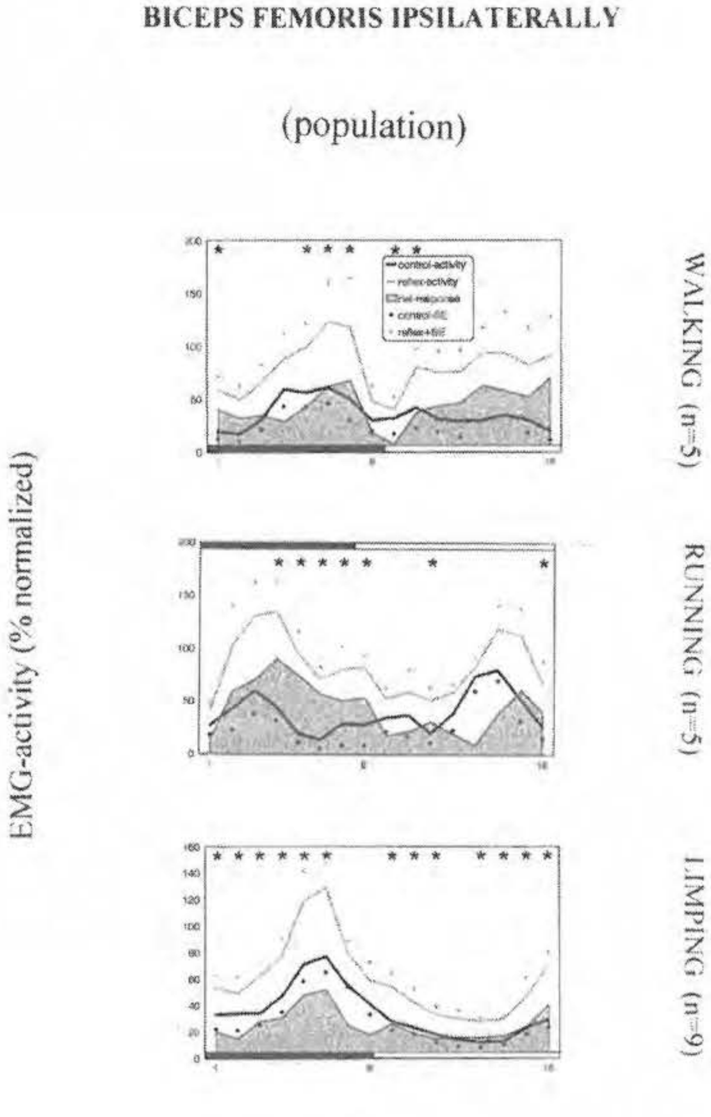


Figure 3.7. Same data as in figure 3.6. but for the whole population (walking: n=5; running: n=5 and limping: n=9). For further legends see figure 3.4.

From Fig. 3.5. it is clear that responses appeared more widespread in the cycle than was the case for the TA responses. The plot of the reflex responses (Fig. 3.6.) shows that the amplitude of the responses mostly followed the underlying background activity during the walking, running and limping movement. For all conditions the responses were relatively small around middle and end of swing (phase 13). For the whole population (Fig. 3.7.) the same tendencies were present.

Large responses were present throughout most of the step cycle, while minimum responses occurred in the stance-swing transition (phases 8-9) during walking and midswing (phases 12-13) during running. In all cases the largest responses occurred in mid and late stance. The main difference between the limping and walking/running was the absence of a clear minimum in the reflex response for limping. In the limping condition the reflex activity follows more strictly the envelope of the background activity with an increase of the reflex activity during end stance (phases 5-6) where the background activity is also increased.

3.4.3. Statistical difference of the task-dependency of the net responses

An ANOVA-test was carried out on the net responses of TA and BF after sural nerve stimulation during walking, running and limping as shown in table 3.2.

For BF is shown that there is less significant difference between the net responses during the swing phase of the step cycle of the different locomotor tasks. For TA in the beginning of the swing phase (phase 9) of the step cycle the net response seems to be similar in the three different tasks despite significant difference of the control activity. Knowing that the facilitation in this phase is significant for all three movements, this facilitation seems to be locomotion related and not task-dependent.

	Tai			Bfi		
Phase	Control-activity	reflex-activity	Net-response	control-activity	reflex-activity	net-response
1	5,09	**11,52**	**11,68**	**8,88**	2,58	4,02
2	**24,89**	**97,37**	**41,06**	**58,97**	**24,06**	**15,71**
3	**18,43**	**105,62**	**6,58**	**23,45**	**21,25**	**7,07**
4	**94,71**	**2051,00**	**99,89**	1,26	**8,68**	**37,51**
5	**44,27**	**1185,83**	**88,67**	**25,79**	1,64	**10,45**
6	**65,05**	**427,60**	**655,55**	**28,09**	4,39	0,20
7	**563,37**	**1281,42**	**900,58**	3,23	1,18	2,64
8	**1075,75**	**884,67**	**137,00**	3,36	**6,35**	5,41
9	**72,83**	**8,23**	1,68	0,40	1,77	**292,95**
10	0,02	**8,00**	**28,38**	1,99	3,88	1,57
11	5,02	**73,64**	**53,68**	2,48	3,64	1,44
12	5,42	2,91	**20,26**	**6,34**	4,73	2,18
13	2,89	3,86	2,22	**28,11**	**12,32**	**6,78**
14	**25,00**	**7,73**	5,68	**18,47**	7,32	1,11
15	3,05	3,84	**20,89**	**7,97**	4,91	1,28
16	**250,51**	**22,99**	**21,77**	2,79	0,67	1,06
If d*f*E=16 and d*f*W=2 then critical F < 6.23 (p<0.01)						

Table 3.2.: The resulting F-values of the ANOVA-test for control activity, reflex activity and net response between the three different locomotor tasks, walking, running and limping. The bold printing indicates the significant (p<0.01) phases of the step cycle.

3.5. Discussion

The main findings of the present study are that the phase-dependent modulation of the sural nerve induced P2 reflexes (net responses) in BF are quite similar for the three kinds of locomotion, while for TA this similarity is only seen in the beginning of the swing phase and at mid swing. For TA the modulation of the reflexes at end swing are locomotor task specific.

For BF a widespread facilitation that follows the envelope of the background activity with a maximum of reflex activity during the stance phase is seen during walking, running and limping. This maximum facilitation during walking and limping is seen in the second half of the stance phase, while during running an increase in facilitation during stance is more widespread with a maximum around mid stance. During walking and running a minimum of this facilitation occurs respectively at begin swing and at mid-swing, while during limping this dip in reflex activity is absent. BF is an important stabilizing muscle of the lower limb (Suzuki et al. 1982) that gets facilitated during disturbed locomotion to improve this stability and the equilibrium, irrespective of the phase in the step cycle.

TA has two types of responses to sural stimulation. During all three movements a facilitation at the beginning of the swing period is seen. But near the end of the swing period a more specific pattern of reflex activity is shown. During walking and running a decrement of the reflex activity is seen during this period even leading to a reflex reversal during walking where the muscle activity gets suppressed at end swing (consistent with previous publications: Yang and Stein 1990; Duysens et al. 1990; Tax et al. 1995). A new finding of this study is that during limping this reduction of reflex activity of TA at end swing is absent and, on the contrary, TA gets strongly facilitated in this period.

3.5.1. Maximum facilitations at end stance and onset swing

From experiments on H-reflexes (Stein and Capaday 1988; Simonsen and Dyhre-Poulsen 1999; Edamura et al. 1991) it is known that there are differences in reflex activity during walking and running. To make it possible to relate the difference in reflex modulation to the change in speed or to the change in task, Edamura et al. (1991) had the same subjects either walk or run at overlapping speed. They concluded that locomotor tasks affected reflex strength.

Other studies, however, found little evidence for task dependency. For SOL H-reflexes for example, Crenna and Frigo (1987) found basically the same phase-dependent modulation during normal walking as during stepping on the spot. Similarly, in the study of Lavoie et al. (1997) the strong inhibition of SOL H-reflexes during swing was found to be present both during normal walking and during various forms of "one leg stepping". Similarly Garret et al. (1999) found that the midswing inhibition of maximum SOL H/M ratios was unaffected by changing from normal to fixed-knee walking (knee motion restricted by a cast).

In the present study the question of task-dependency and origin of the phase-dependent modulation is extended to cutaneous reflexes. In this case a comparison of slopes between reflex amplitude and background level is not very meaningful since the responses show a pronounced phase-dependency, leading even to reflex reversal. Nevertheless the strength of the sural nerve reflexes can be compared in the different tasks by considering the maximum responses in a given period of the step cycle.

Both for BF and TA it was found that the maximum facilitations (respectively at end stance and at onset swing) were quite similar in all alternating types of locomotion (walking, running, limping).

Those results indicate that ankle movement itself is not very essential for the generation of those facilitations at end stance and at onset swing. The finding that the facilitations were just as strong in limping as in normal gait indicates that the joint movements and the concomitant presynaptic interactions between afferents do not play an important role in the generation of facilitations of BF and TA in those phases of the step cycle.

These results are in line with a very recent study of Brooke and co-workers (1999). They studied the sural nerve reflexes in TA during passive cyclic movement and saw that the modulation of mid-latency reflexes during locomotion were not significantly affected by changes in peripheral afferent input. Their findings also suggest that modulation of cutaneous reflexes during locomotion is not the result of inhibition arising from motion-related sensory receptor discharge. This is in contrast to H-reflexes, where sensory receptor discharge plays an important role for reflex modulation (Brooke 1993). Very recently, however, Schneider et al. (2000) suggested a central modulation of H-reflexes and could not corroborate the movement-induced inhibition hypothesis of Brooke (1993).

A central origin of the TA facilitations at the beginning of the swing period is therefore more likely. One possible source for this facilitation is the spinal or supraspinal circuitry involved in the generation of locomotor output (Central Pattern Generator, see Duysens and Van de Crommert 1998 for review). Evidence for such a mechanism was provided by experiments in which sural nerve reflex modulation was compared during forward and backward locomotion (Duysens et al. 1996). The results were compatible with the modulation being produced by a central program working in reverse.

It is proposed that the enhancement of P2 responses prior to the onset of the swing phase reflects an opening of pathways which could assist or exaggerate flexion in the ensuing swing phase (see also Duysens and Loeb 1980; Duysens et al. 1992). In humans such facilitation of P2 responses was described in several studies both during running (Duysens et al. 1992, 1993; Tax et al. 1995) and walking (De Serres et al. 1995; Duysens et al. 1990-1992). The present data further extend these observations to walking with an extended leg ("limping"), thereby supporting the notion of a central modulation mechanism which is common for a wide variety of locomotory tasks.

The enhancement of cutaneous reflexes at end stance might have a cortical origin. It has long been known that the motor cortex can influence transmission in cutaneous reflex pathways in man (Babinski 1898). In humans, Nielsen et al. (1997) have argued that reflexes such as described in the present paper could well be transcortical. One possibility is that during locomotion the end stance facilitations are related to the opening of spinal pathways through locomotor circuits (such as from a CPG) and that the cortex has the ability to potentiate this facilitation through disinhibiting projections onto this circuitry. Pijnappels et al. (1998) were able to show that the sural nerve induced facilitations at end stance can be further facilitated by cortical magnetic stimulation (TMS), indicating a convergence in the pathways involved. Later, Christensen et al. (1999) confirmed this finding and demonstrated that, in contrast to TMS, cortical electrical stimulation is ineffective, thereby strongly supporting a role for a transcortical reflex pathway in the end stance facilitations.

The question remains however, how specific this facilitation is for different types of afferents. Because all cutaneous afferents from the foot supposedly belong to the "FRA" system (Lundberg et al. 1987) one might expect the facilitation to occur for a wide variety of afferents. However, this was not found by Van Wezel et al. (1997) or Zehr et al. (1998). For example, stimulation of the superficial peroneal nerve (innervating the foot dorsum) did not yield end stance facilitation of P2 responses in TA. Tibial nerve stimulation yielded TA facilitations but they were relatively weak.

3.5.2 Locomotor task specificity of reflex responses of TA at end swing

In normal walking the TA responses are usually either small or even suppressive near the end of the swing phase, thereby possibly leading to a phase-dependent reflex reversal (see introduction). The suppression in that part of the step cycle can be seen for stimulation of a wide variety of nerves innervating the skin of the foot (Van Wezel et al. 1997). The new finding of the present study is that for TA the reduction in reflex amplitude was not present in limping. A possible explanation for this difference in the cutaneous reflex gain in TA in the different locomotor tasks at end swing can be the differences in foot placement and concommitant loading receptors activation in this phase of the step cycle.

For normal walking at end swing the background activity of TA increases to bring the ankle and foot in the right position (maximal dorsiflexion) for touchdown at the heel. A facilitation of TA during this phase of the step cycle at end swing can be harmfull for the ankle joint. The locomotor task related suppression of TA at end swing during walking can have a protective function.

During limping the ankle is artificially held as stiff as possible in a neutral position of ninety degrees (see figure 1) so the TA background activity remains almost constant during the swing period. The facilitation of TA is not harmfull at end swing during limping.

For running there is no difference between TA reflex activity and background activity at end swing. They both decrease to a minimum prior to touchdown. In contrast to walking the foot touches the surface with the midfoot and the heads of the metatarsal bones, which explains the low background activity. The lack of facilitatory TA reflexes in running can be explained by the need for building up potential energy to increase the propulsion force during the onset of the consecutive stance phase. This building up of potential energy will be decreased by increased TA activity and consecutive disturbed foot placement. In a way this is similar to what occurs for SOL H-reflexes during high speed locomotion (running). In that case the stretches of the ankle muscles are large but there may be less need to suppress SOL H-reflexes since the latency is such that these reflexes can contribute to the propulsive phase (Dietz et al. 1978, 1979). A similar reduction in reflex gain at end swing is also seen during the hopping movement (Hauglustaine et al. 1998b). A change in the activity of TA at end swing during the hopping movement may have a disturbing effect on the spring unit created by the extensor muscles of the ankle at end swing (Melvill-Jones and Watt 1971).

An explanation for this task dependency of the cutaneous reflexes is proposed by Hultborn and Illert (1991) in their FRA-hypothesis. They suggested that a group of interneurons in one of the several pathways is activated and will be supported by the locomotion pattern itself. In this way it is not unrealistic to think that dependent of the kind of locomotion some of the axonal projections of the cutaneous afferents on the spinal interneurons will be presynaptical inhibited while other projections will be postsynaptical facilitated by spinal or even supraspinal pathways. From the work of De Serres et al. (1995), it is known that sural nerve afferents can either excite or suppress individual TA motoneurons over parallel facilitatory and suppressive pathways. Faist et al. (1995) showed a phase-dependent variation in the strength of presynaptic inhibition during human gait.

In principle the reduction in facilitatory responses, or the presence of suppressive responses, at end swing could be either due to an active post-synaptic inhibition of the TA motoneurons or they could be due to the blocking of excitatory pathways to these motoneurons in this period of the step cycle. So far the evidence is in favor of the second alternative. When sural nerve and cortical magnetic stimulation responses are combined at end swing then the responses are larger than for sural nerve stimulation in isolation (Pijnappels et al. 1998; Christensen et al. 1999). If TA motoneurons were suppressed postsynaptically then one would expect instead that cortical stimulation would not be able to add excitation and thus the responses should have the same amplitude as for sural stimulation alone.

Further experiments in which cutaneous reflex responses of lower limb muscles are compared between locomotion and other voluntary and involuntary induced movements of the legs are needed to further clarify which modulation features are locomotor specific.

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4. PHASE-DEPENDENT MODULATION OF CUTANEOUS EVOKED REFLEXES OF TIBIALIS ANTERIOR MUSCLE DURING HOPPING

4.1. Abstract

During human gait, the amplitude of cutaneous reflexes in the leg is modulated as a function of the phase of the step cycle. In tibialis anterior (TA) the responses to sural nerve stimulation are facilitatory at end stance while they are suppressive at end swing. To investigate in how far this modulation is specifically related to alternating locomotion the modulation of such reflexes was studied during a symmetric rhythmic movement, namely hopping (as equivalent of galopping). The end stance facilitation was present during hopping while the end swing suppression was absent. It is concluded that the end stance facilitation is not specific for alternating gait. The absence of the end swing suppressive reflexes may be related to the absence of heel strike in hopping.

4.2. Introduction

During human gait it is well-known that there is a phase-dependent modulation of cutaneous reflexes from the foot (Yang et al. 1990; Duysens et al. 1990). The source of this modulation is unknown. In the cat there is some evidence that the spinal CPG (Central Pattern Generator) for locomotion can underlie the phase-dependent modulation of some cutaneous reflexes (Schomburg and Behrends 1978). In humans a similar intervention of a CPG-like center has been proposed to play a role as well (see Duysens et al. 1996). During both walking and running, one of the most consistent features of the modulation pattern for flexor muscles such as TA (tibialis anterior) is that the facilitatory responses are largest near the onset of the swing phase while suppressive responses prevail near the transition from swing to stance (Yang et al. 1990; Duysens et al. 1990).

Do these modulation features depend on alternating gait? To answer this question the present study was undertaken to examine the phase-dependent modulation of sural nerve reflexes during in-phase hopping on two legs. Hopping can be considered the human equivalent of galopping but for technical reasons the experiments were restricted to in-place hopping. The joint movements resembled those seen during walking and running except for the heel strike wich is absent in hopping.

4.3. Methods

A group of 5 normal subjects (1 female and 4 males) aged between 20 and 46 participated in the hopping experiment. The experiments were carried out in conformity with the declaration of Helsinki for experiments on humans. All subjects had given informed consent and had no known history of neurological or motor disorder.

The hopping experiment typically started with several short periods of hopping on the treadmill to adjust to the experimental situation. In this period the subject was trained to hop at a comfortable, constant rhythm dictated by a metronome at 2Hz, which gave a mean cycle time for the whole population of 540.24 ms (S.D. 31.97 ms) during the real experiment. Foot contact with the split-belt treadmill was detected with two built-in force plates. Bipolar EMG activity was recorded in the ipsilateral leg by means of surface electrodes over the tibialis anterior muscle. Between these training periods, during quiet standing, the perception threshold (PT) was determined psychophysically by gradually increasing and decreasing the stimulus amplitude in at least three series.

The stimulation electrodes were positioned near the middle of the distance between the external malleolus and the Achilles tendon, where the sural nerve is very close to the skin surface. During the experiment the electrical stimulus intensity was set at 2xPT. The electrical stimulus consisted of 5 rectangular pulses of 1ms given over a period of 21 ms. A custom-made constant voltage stimulator provided the desired stimulus amplitude.

The stimuli were varied with respect to the timing of presentation in the movement cycle. Detection of ground contact could trigger the computer to release a stimulus after a certain delay which is a multiplication of a sixteenth of the movement cycle time. So there were 16 stimulus conditions (timing) and every stimulus was presented 10 times. Beside the stimulation the computer did measure also 10 control activities for each time delay. Hence 320 ad random activities were measured.

The EMG analysis started with a procedure for the detection of reflex responses. The 10 trials of each stimulus condition were averaged. For each stimulus phase this resulted in one average 'reflex' trial and one 'average' control trial. The average control trials were subtracted from the corresponding average reflex trials to obtain the 'pure' reflex responses (Belanger et al. 1987; Yang et al. 1990; Duysens et al. 1990). The subtraction technique allowed both facilitatory and suppressive responses to be measured. The mean EMG values within a by visual inspection set time window (for methodology of window setting see Belanger et al. 1987; Yang et al. 1990; Duysens et al. 1990) were calculated for the average reflex, control and the corresponding subtracted trials. The resulting data underwent both an amplitude and a time normalization procedure so that a proper intersubject comparison could be made. For the amplitude normalization, the EMG data were scaled for each muscle to the maximum control value in the step cycle. For the normalization of the time axis, the step cycle was subdivided into 16 equal intervals (phases). Phase 1 in the hopping experiment is for all subjects the beginning of the stance phase of the ipsilateral leg. The significance of the difference between the control and reflex activity was tested with a student *t*- test for paired samples.

4.4. Results

During the hopping movement bipolar EMG signals of the tibialis anterior muscle were obtained. Goniometric devices at ipsilateral ankle, knee and hip joint detected joint displacements. Two built-in force plates detected foot placement of the ipsilateral and the contralateral foot. Figure 4.1. shows the experimental data during a period of 1600 ms of the hopping movement of a single individual.

The averaged control activity was subtracted from the reflex activity resulting in the 'pure' reflex activity. A time window was set by visual inspection around the mid-latency reflexes (P2) and the mean amplitude of this time window was measured. In figure 4.2. the pure reflex activity of one subject of the ipsilateral tibialis anterior muscle is shown. The corresponding mean amplitudes of the control activity and the reflex activity of both muscles were measured for each individual and underwent an amplitude normalization with the maximum control activity equal to 100 %.

The amplitude normalization makes it possible to look upon the mean control and reflex activity of the whole population (n=5). During the hopping movement the responses in the ipsilateral tibialis anterior muscle were most strongly facilitated near stance swing transition (phases 7 till 9). During the other phases of the hop cycle there is no important significant difference between control activity and reflex activity after sural stimulation (see fig.4.3.).

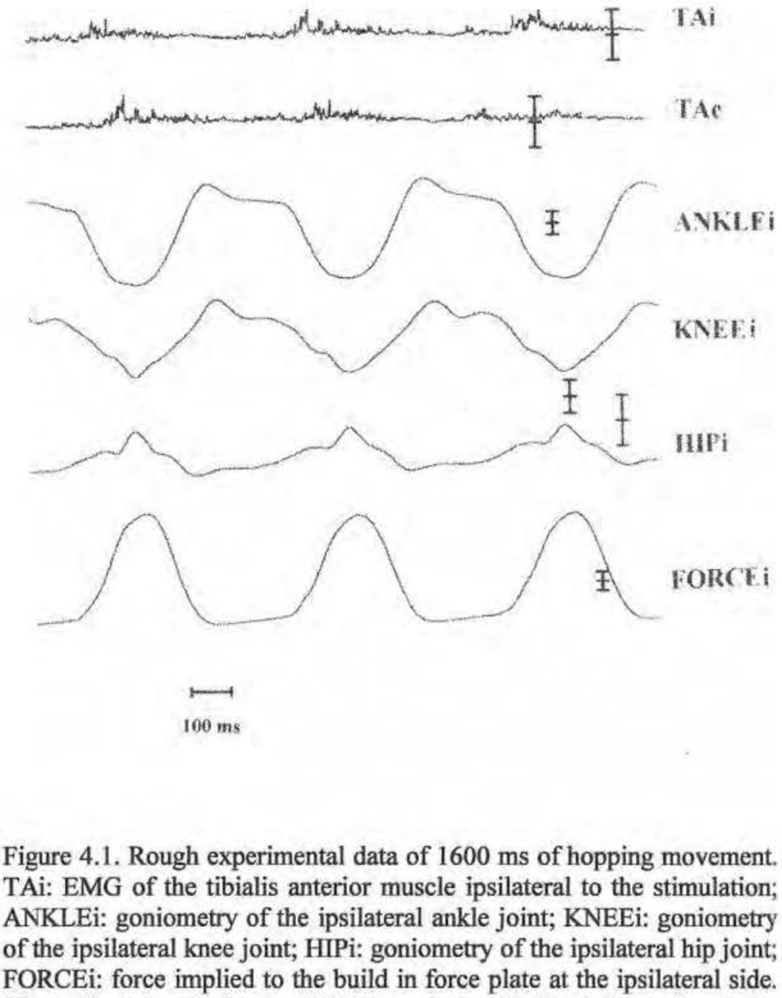

Figure 4.1. Rough experimental data of 1600 ms of hopping movement. TAi: EMG of the tibialis anterior muscle ipsilateral to the stimulation; ANKLEi: goniometry of the ipsilateral ankle joint; KNEEi: goniometry of the ipsilateral knee joint; HIPi: goniometry of the ipsilateral hip joint; FORCEi: force implied to the build in force plate at the ipsilateral side. The indicated scale for the EMG trace is 1 mV. The indicated scale for the goniometry traces is 15 degrees with for knee and ankle joint as reference point 90 degrees and for the hip joint 180 degrees. The indicated scale for the force trace is 50 Nm.

HOPPING

One subject

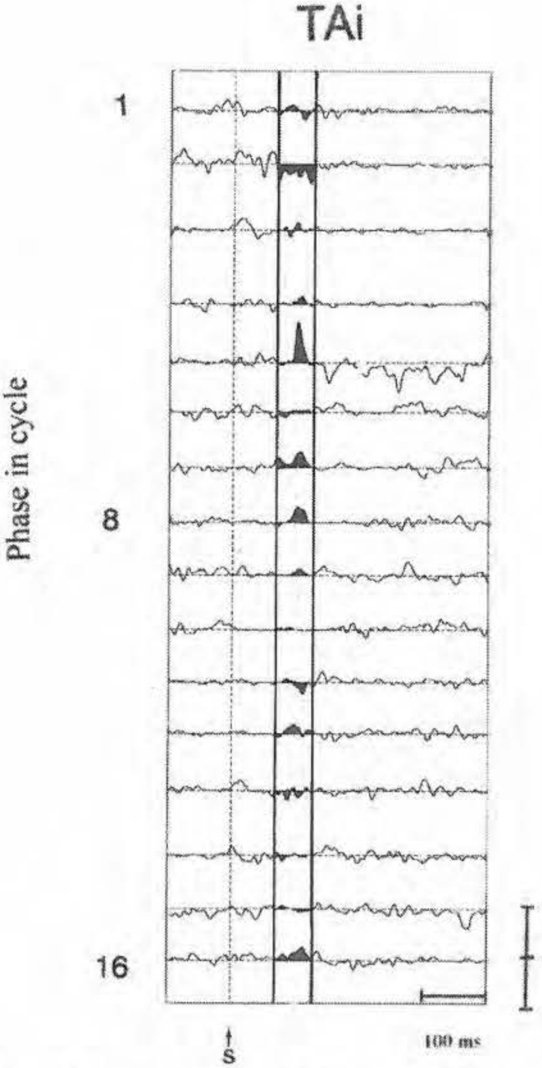

Figure 4.2. The hopping data of the ipsilateral tibialis anterior (TAi) muscles of one subject. Phase-dependent changes in the subtracted and averaged (n=10) responses of TAi. Window settings (full vertical bars) show the periods taken for measurement of the reflex activity, starting at about 80 ms after cutaneous stimulation (S; vertical dashed line) during 16 different phases of a hopping cycle.

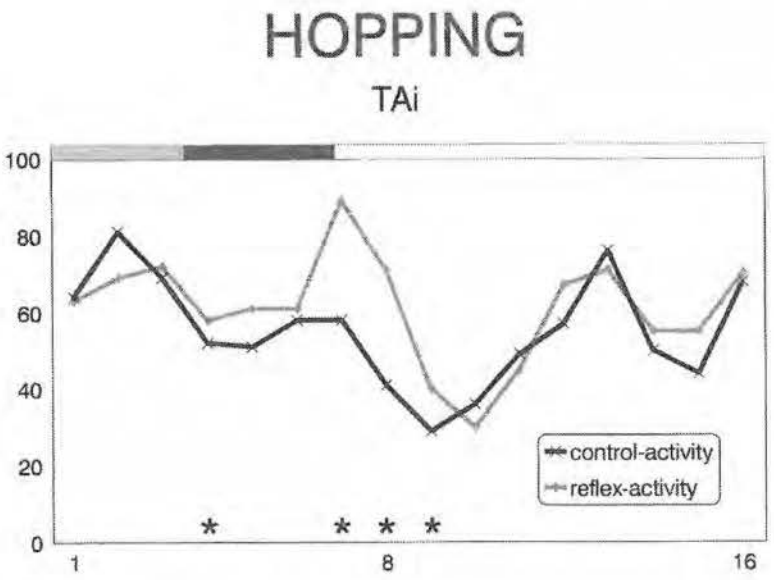

Figure 4.3. Plot of the mean control and reflex activity of the whole population (n=5) of the ipsilateral tibialis anterior muscle during the hopping movement. The phases with a significant difference between control and reflex activity are indicated with an asterisk ($p \leq 0.05$ after a Student *t*-test for paired samples). Horizontal bars: eccentric phase (gray), concentric phase (black) and swing phase (white). The data were normalized for each subject to improve intersubject comparison. This explains why the mean of the background activity does not always reach 100 %.

4.5. Discussion

The present work shows that, for some aspects, the phase-dependent modulation of sural nerve induced responses in TA during hopping is similar to the modulation seen during locomotion. It was seen for TA that ipsilaterally the reflexes are enhanced at the stance swing transition (phase 7 till 9) which was also seen during running (Tax et al. 1995) and walking (Duysens et al. 1990, 1992; Van Wezel et al. 1997; Yang and Stein 1990; Zehr et al. 1998).

In accordance with previous work it is proposed that this enhancement of P2 responses prior to the onset of the swing phase reflects an opening of pathways which could assist or exaggerate flexion in the ensuing swing phase (Duysens and Loeb 1980; Duysens et al. 1992; Duysens et al. 2000). Supporting this idea it was found that the TA activations were correlated with induced extra ankle dorsiflexion (Duysens et al. 1992; Van Wezel et al. 1997; Zehr et al. 1998).

How is this pre-swing facilitation organized? Does it originate from the output of a locomotor CPG circuitry? Or is the cortex involved, perhaps through activation of a CPG-like circuitry? Cortical involvement in the pre-contraction TA facilitations of reflexes seems to be important since several studies have shown that TA is easily recruited by magnetic stimulation of the motor cortex in periods preceding TA activation either in locomotor tasks (Schubert et al. 1999; Pijnappels et al. 1998) or at the onset of voluntary contractions (Capaday et al. 1999). Is this due to a direct activation of TA motoneurons or to an indirect activation through excitatory pathways projecting to these motoneurons? The latter is an attractive alternative since Pijnappels et al. (1998) and later Christensen et al. (1999) have shown that sural nerve evoked facilitatory responses in TA are potentiated by TMS (transcranial magnetic stimulation) at the transition from stance to swing.

Some differences between hopping and alternating gates were observed as well. The suppressive response at end swing seen during walking (Duysens et al. 1990) is absent during the hopping movement. Preliminary results (Hauglustaine et al. 1998) on cutaneous reflexes during different locomotion tasks (walking, running and walking with one stiff leg) show that the endstance facilitations are locomotion related but that the end swing reflexes differ between the different locomotor tasks. The end swing suppression of TA during walking is absent during running where more propulsion force is needed. This is also seen in the results of this hopping study where no significant reflex activity of TA at end swing is seen. It is suggested that this is due to the difference in landing (no heel strike in hopping). A preprogrammed cocontraction of the triceps surae and TA is seen during the end swing phase of the hopping movement (Mellvill-Jones and Watt 1971; Moritani et al. 1991). Both muscles create together a spring unit that enhances the elastic properties of the lower leg during the hopping movement. Suppression or facilitation of the muscle activity would disturb the foot placement in this period of the movement cycle causing lowering of the kinetical energy build up in this spring unit. Hence it is proposed that the absence of TA reflexes in this phase of the hopping cycle is important to avoid disturbance of the normal hopping movement. It can be concluded that in general the phase-dependent modulation during hopping resembles the one seen during alternating gait except when movements are different (e.g. heel strike).

4.6. References

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5. SELECTIVE ACTIVATION OF MG IN SURAL NERVE REFLEXES DURING HOPPING, RUNNING AND WALKING.

5.1. Abstract

Stimulation of the sural nerve activates MG (medial gastrocnemius) more strongly than LG (lateral gastrocnemius) in acute cat experiments. In contrast, in sitting man previous studies have failed to establish such differential effects. Since some cutaneous reflexes are suppressed under passive conditions, the issue was reexamined using electrical stimulation of the sural nerve at the ankle during various kinds of rhythmic activities such as hopping, walking and running. Stimuli at 2 times perception threshold were applied at each of 16 phases of the cycle in 5 human volunteers.

For all three movements the responses in MG were mostly facilitatory on the ipsilateral side while for LG the responses were almost always suppressive. The MG facilitatory responses were more prominent during running and hopping as compared to walking. During running the MG responses were most prominent when elicited in the second half of the stance phase. During hopping the largest responses were present in the period prior to contact, when background activity was low. Presumably this latter activation could contribute to "anticipated stiffness" prior to touchdown. In contrast, only small responses were present in the second half of the contact period. Finally, the MG responses were small or even absent in the early contact phase.

In general , contralateral to the stimulus the reflex responses of medial and lateral head of the gastrocnemius muscle were quite similar, except for running where facilitatory responses were more activated in LG than in MG. It is speculated that the difference between MG and LG in the ipsilateral leg is "hard-wired" and expressed even in movements such as

hopping..

5.2. Introduction

Activation of ankle extensors prior to landing during running or hopping can be seen as an example of preprogrammed stiffness (Moritani et al. 1991). In the prelanding phase there is evidence that stretch reflex pathways to these muscles are opened as well, so that reflexly generated EMG activity is generated shortly after touchdown (for running see Dietz et al. 1979 and for hopping see Dyhre-Poulsen et al. 1991). In the case of hopping it was shown that H-reflex amplitude increments preceded landing by some 45-67 ms for MG (Medial Gastrocnemius) and some 39-54 ms for SOL (Soleus).

The same muscles can also be activated through exteroceptive reflexes from the skin of the foot but such reflexes have not received much attention until recently. During walking, Duysens et al. showed that reflexes of middle latency (P2) can be recruited in MG in the period just prior to touchdown (Duysens et al. 1991). The latter results indicate that MG facilitatory reflex pathways can be opened in anticipation of foot contact. However, it is not known whether a similar facilitation of P2 responses occurs in anticipation of landing during hopping.

In the present study the P2 responses in MG will be compared with those obtained in LG (Lateral Gastrocnemius). Previous work has suggested some intrusive differences between these muscles in this type of reflex during gait (Duysens et al. 1994a, 1993, 1994b, 1996). During various locomotor tasks Duysens et al. found that MG generally showed P2 facilitations while LG exhibited mainly suppressive P2 responses (Duysens 1996), much in analogy with findings in the cat (LaBella et al.1989). However it is still controversial whether these differences are a general finding in humans. Some studies have failed to find clear MG-LG differences in non-moving humans (who were either standing or sitting). For example, using sural nerve stimulation-induced responses in MG and LG, Kukulka found that the only significant difference was the presence of larger suppressive responses in LG as compared to MG (Kukulka 1994). The failure to detect differences in facilitory responses in MG and LG in this and other studies may be due to relative absence of facilitory responses under static conditions (Aniss et al. 1992) as compared to locomotion (Duysens et al. 1994a). Therefore, in the present study such responses were reinvestigated under different dynamic conditions, not only including gait but also hopping. In the latter activity the force required from ankle extensors is substantial. It has been suggested that MG and LG differ with respect to force production (Duysens et al. 1994b) and it may therefore be of interest to include forceful tasks such as hopping to highlight potential differences between these two muscles.

The study of MG-LG contribution in P2 responses both during locomotion tasks such as walking and running, and during non-locomotion tasks such as hopping in the same subjects, allows the testing of the hypothesis that the MG-LG difference is specifically related to the locomotor task. Duysens et al. proposed that one of the explanations for the MG-LG difference may be related to rotatory movements of the leg during the step cycle (Duysens et al. 1996). If so then one might expect this difference to be less during hopping when such rotations are absent.

In addition, by comparing the P2 responses during walking, running and hopping, one might be able to estimate task-related changes in reflex gain. For the SOL H-reflex, Capaday and Stein showed that the amplitude decreased when tested during running as compared to walking and that it increased during standing as compared to walking (Capaday and Stein 1987). In contrast, for MG the H-reflexes were larger during hopping and running than during walking (Moritani et al. 1991). For P2 cutaneous reflexes Duysens (1993) et al. found that TA (tibialis anterior) reflexes were larger in running than during standing. For P2 responses in MG the task-dependency is unknown.

5.3. Methods

A detailed description of the methods has been given elsewhere (Duysens et al. 1993). In 5 adult subjects, the EMG activity was recorded by means of surface electrodes over MG and LG. The EMG was amplified (FM-microvolt amplifier, band width 1-1000 Hz), full-wave rectified and transferred on-line over an AD-converter (sampled at 500 Hz). Force plates were used to determine footfall and lift-off of each leg.

Stimulating electrodes were positioned at the ankle over the sural nerve (near the middle of the distance between the external malleolus and the Achilles tendon). The stimulation consisted of a train of 5 rectangular pulses of 1 ms , given over a period of 21 ms. These shocks were first applied while the subjects were standing on a treadmill. The perception threshold was determined by gradually increasing and decreasing the stimulus intensity in at least three series. The whole procedure was repeated between all experimental runs to ascertain that stimulus conditions were stable. To obtain these stable conditions, the stimulating electrodes were firmly held pressed over the nerve with an elastic strap. A custom-made constant current stimulator, controlled by a personal computer, provided the desired current levels. Both the output current and the voltage across the electrodes were monitored.

During the experimental runs, stimuli at 2 times perception threshold were given. Stimulus trains were delivered in various parts of the step cycles at a predetermined delay after footfall. The step cycle was divided in 16 phases of equal length of time. Stimuli were given at one of the 16 intervals spread evenly over the step cycle. At least 10 responses for each type of stimulus condition were sampled. To be able to distinguish between reflex responses and cyclic background activity, control trials were taken at exactly the same intervals in the step cycle as used for the stimulus trials. During these control trials no stimulus was given. All trials (stimulus and control) were randomly mixed to prevent subjective anticipation. Moreover, stimulus trials were separated by a random interval of 3-5 seconds. Under these conditions the effects of habituation were not significant. Each subject was tested in three experiments (walking, running and hopping) to examine the stability of the observed responses under a variety of dynamic conditions. Subjects walked or ran at the same speed (6 km/h). For the hopping experiments, the rhythm was dictated by a metronome at 2 Hz, which gave a mean cycle time for the whole population of 540.24 ms (SD.31.97 ms).

The experiments were performed in conformity with the principles described in the declaration of Helsinki for experiments on humans. All subjects gave their informed consent and they could stop the experiment at any given point.

5.3.1. Stability of stimulation

The stability of the stimulation conditions within a given experiment was a primary concern for the present study as it was for our former studies (Duysens et al. 1990, 1991, 1992a, 1993, 1995; Tax et al. 1995). In principle instability could arise from the movements during gait. Such movements could have caused variations in the transfer impedance of the stimulus electrode configuration and as a consequence result in deviations of the applied currents (as constant voltage stimulation was used). Therefore, the current variations were determined in each experiment. The current was measured in a window between the onset of stimulation and the following 50 ms as described in our earlier studies (see above). In the experiments to be reported here, the mean values at any given phase did never deviate significantly from the mean across all phases. Hence the applied current was basically constant throughout the step cycle and no correction was needed for systematic variations at any given phase (Duysens et al. 1995).

It may also be argued that even for constant currents one cannot be sure that the current to the nerve stays constant. Some authors have controlled for the constancy of stimulation by using mixed nerve stimulation and monitoring of the M-waves (Yang and Stein 1990). So far all our previous results on reflex modulation, using mixed nerve stimulation (tibial nerve in Duysens et al. 1990, 1991, 1992a, 1993), have been completely compatible with the results obtained by other authors using the M-wave control method. The latter method cannot be applied to pure cutaneous nerves such as used here.

Although stimulus conditions were sufficiently constant within each experiment, there were slow changes over time in some of the subjects. These were monitored by measuring the perception threshold (PT) before and after each experiment.

5.3.2. Data analysis

Off-line, the full wave rectified EMG signals were averaged (n=10) for all stimuli belonging to the same phase. Sometimes the responses were suppressive. In that case the reflex activity was below the background EMG level normally present at that particular time of the step cycle. To be able to show such responses it was essential to subtract the controls from the corresponding reflex data to obtain the 'pure' reflex responses, independent from the background EMG activations.

To quantify the magnitude of the reflex responses, a fixed time window was set around the averaged responses and the mean amplitude was calculated within the window. The window was chosen such that all the responses from a given experiment fell within the window limits. The representative onset latency of a series of such responses was determined as the onset of this time window (hence this latency is always close to the shortest latency observed in a given serie). The time window for the reflexes was set by visual inspection (time resolution of 2 ms) taking the following criteria into account:

i. The windows were set around those reflex responses which appeared most consistently over the muscles and the subject. These were the so-called 'middle' latency reflexes (Yang and Stein 1990), or P2-responses (Duysens et al. 1990) which occurred roughly 70 to 80 ms after stimulation and typically lasted for about 30 ms.

ii. One single optimal window was set for all 16 stimulus phases [17].

iii. When a muscle showed little or no responses no adequate window could be set, yet an equivalent response measure was required to calculate population averages. In that case an extrapolated window was used, calculated from the time windows determined for (in order of priority) the same muscle at another gait experiment, other nearby muscles in the same leg, or the same muscles in other subjects (Tax et al. 1995).

For the averaged reflex, control and corresponding subtracted trials, the mean EMG-values within the window were calculated. The resulting data underwent both an amplitude and a time normalization procedure in order to enable a proper inter-subject comparison. For the amplitude normalization the EMG data were scaled for each muscle to the maximum control value in the step cycle (i.e., the maximum spontaneous activity). For the normalization of the time axis the step cycle was subdivided into 16 equal intervals. The responses will be presented according to their appearance in one out the 16 intervals. The statistical significance of the responses was tested with a Wilcoxon matched-pair signed-rank test (significance at $p <= 0.05$).

5.4. Results

The medial head of the gastrocnemius is most strongly activated during the hopping movement (fig. 5.1.). Comparing the EMG-activity of this muscle during the stance phase (beginning at phase 1) of the running and walking movement, a larger activity is observed during running. The mean cycle time of hopping was 540.24 ms (SD. 31.97 ms), with a mean stance phase of 207.85 ms (which is 38.47 % of the cycle; SD. 2.21 %). For walking the mean cycle time is 938.90 ms (SD. 13.16 ms) with the stance phase covering 53.19 % (SD. 1.03 %). The mean cycle time for running is 764.50 ms (SD. 27.74 ms). The part of the stance phase during this movement is 32.60 % (SD. 3.25 %).

In fig. 5.1. is also seen that during hopping MG is already about 120 ms activated before ground contact (corresponding to phases 12 till 16). Hence muscle stiffness is induced by a preprogrammed motor neuron activity (see above).

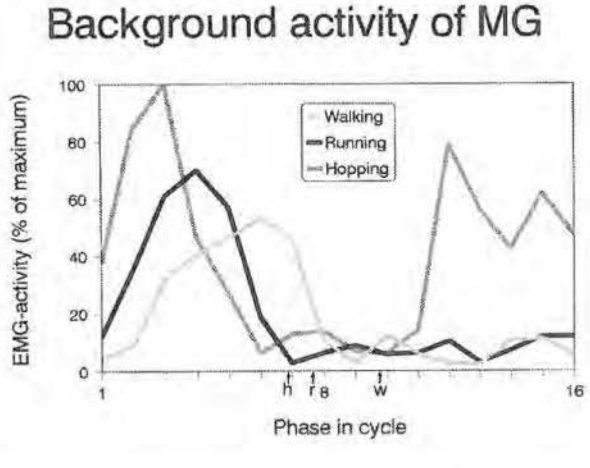

Figure 5.1. Comparison of EMG-activity of the medial head of the gastrocnemius (MG) during three rhythmic activities. Phase 1 is the beginning of the stance phase. The beginning of the swing phase is indicated with the first letter of the corresponding activity (w: walking; r: running; h: hopping).

5.4.1. Ipsilateral responses

Stimulation of the sural nerve at 2 times the perception threshold (2xT) during hopping mainly elicited P2 facilitatory responses in ipsilateral MG. These responses will be compared to those found in LG. An example of P2 responses in MG and LG of the ipsilateral leg is shown in fig. 5.2.A and 5.2.B respectively for stimulation in 16 different phases of the hopping cycle.

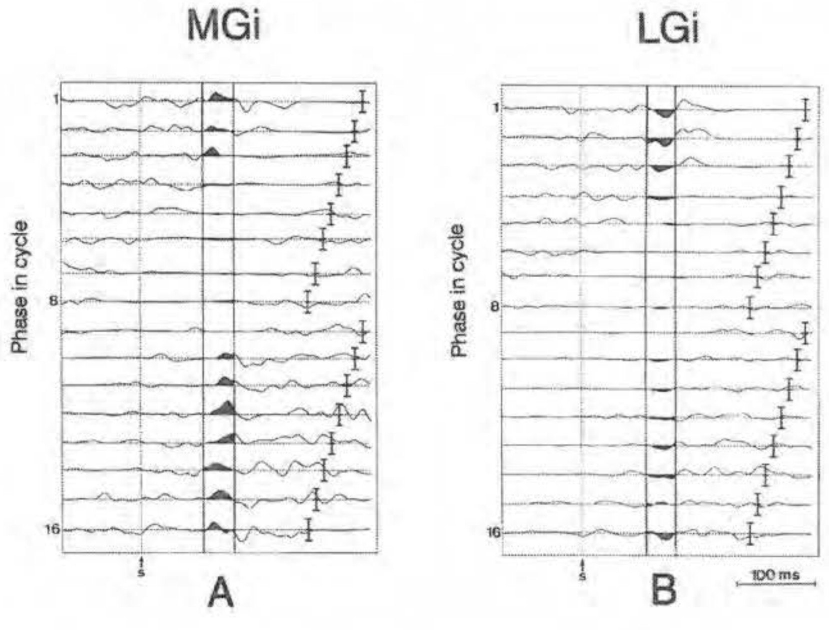

Figure 5.2. Window setting (vertical bars) for measuring the reflex activity at about 80 ms after cutaneous stimulation (S) of one subject during sixteen different phases of a hopping cycle. A. Ipsilateral medial head of the gastrocnemius (MGi). B. Ipsilateral lateral head of the gastrocnemius (LGi).

To obtain these responses for each phase the average of 10 control trials was subtracted from 10 trials with stimulation (see methods). In such subtracted records the facilitatory and suppressive responses show up as positive or negative deviations from the baseline.

For MG (Fig. 5.2.A) can be seen that a facilitatory response occurs at a latency of 80 ms in most of the traces. These responses, known as P2 responses (Duysens et al. 1993), occurred with a latency between 78 and 80 ms in the various subjects. The time window settings used to measure the response peaks (integrated area) in MG and LG are given in Table 5.1.

subject	MG (ms)	LG (ms)	BF (ms)
1	80-116	80-116	80-114
2	80-118	80-118	78-124
3	80-116	78-124	78-124
4	80-118	80-118	78-124
5	80-116	78-120	78-124
mean	80-116.8	79.2-119.2	78.4-122

Table 5.1. Window settings for P2 responses following onset of stimulation.

For comparison the window setting for the larger simultaneously generated BF responses are shown as well. Note that the latency of these responses (78 ms) was similar to the latency of the MG responses.

In contrast to MG a facilitory P2 response was rarely present in LG, although LG is mostly a synergist of MG. In fact, the responses within the identical P2 window, used to highlight the P2 responses in MG, were suppressive in the simultaneously recorded LG (Fig. 5.2.B).

This basic difference in P2 responses between MG and LG was present in all subjects and for the three types of movements studied. A summary is given in figure 5.3.

To obtain these plots, a window was set around the responses and the mean integrated EMG was measured on the data on walking, running and hopping (see methods). For all three movements the responses in MG were mostly facilitatory while for LG the responses were almost always suppressive. The MG facilitatory responses were more prominent during running and hopping as compared to walking. During running the MG responses were largest when elicited in the second half of the stance phase. In contrast, during hopping the largest responses were present in the second half of the swing phase. Both during running and hopping, little or no responses were present when the control EMG activity reached its peak. In LG, the same stimulation induced suppressive P2 responses which were especially prominent when the background activity was large in either one of the three movements studied.

5.4.2. Contralateral responses

In the leg contralateral to the stimulus (Fig. 5.4.) the responses were smaller and little difference between control and reflex activity is seen. For all three rhythmic activities the reflex activity of MG and LG was mostly comparable. During the swing phase of running however the facilitatory response was more expressed in LG than in MG.

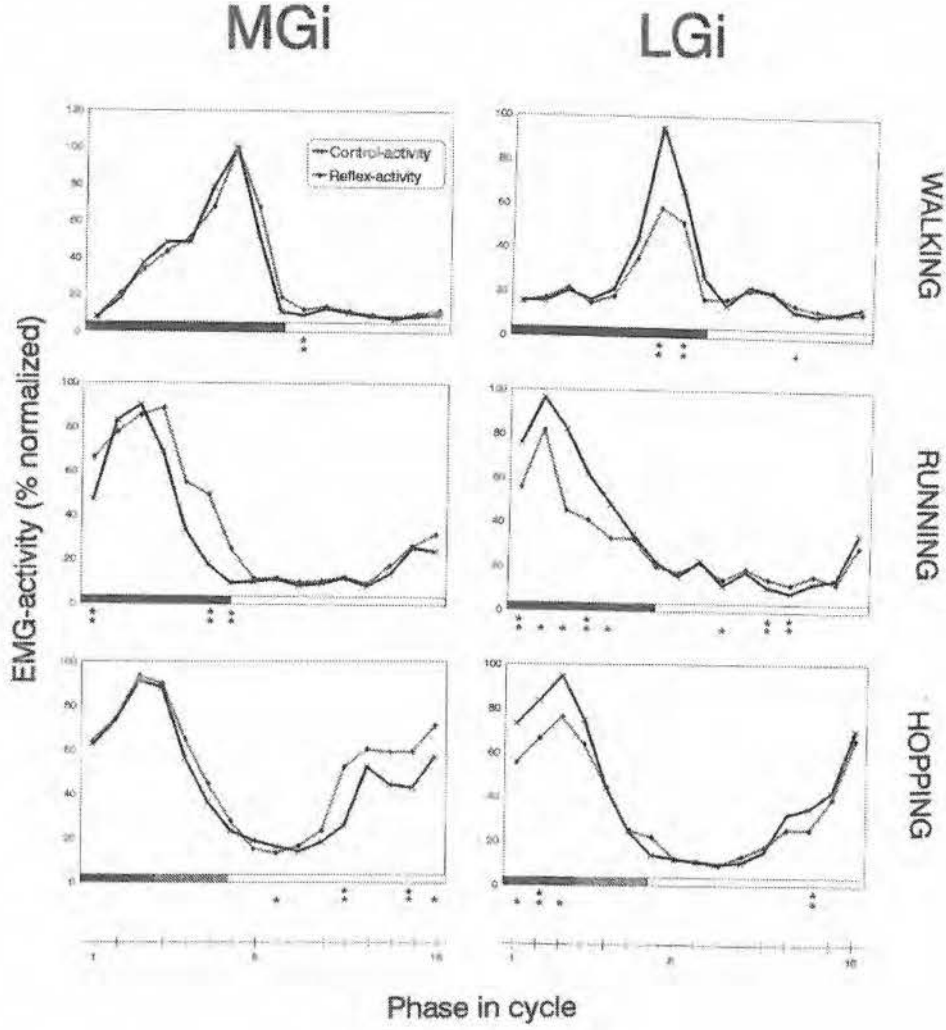

Figure 5.3. Difference between mean (n=5) control and reflex activity of medial and lateral gastrocnemius of the ipsilateral leg after cutaneous stimulation during walking, running and hopping. To avoid cluttering the standard deviations are not shown, but instead the significance is given at the bottom of each plot ((**) $p<0.05$ and (*) $p<0.08$). For running and walking: dark gray = stance phase; white = swing phase. For hopping: dark gray = eccentric phase; light gray = concentric phase; white= swing phase. The data were normalized for each person and each condition. This explains why the mean of background activity does not always reach the 100 % in the same phase of the step cycle.

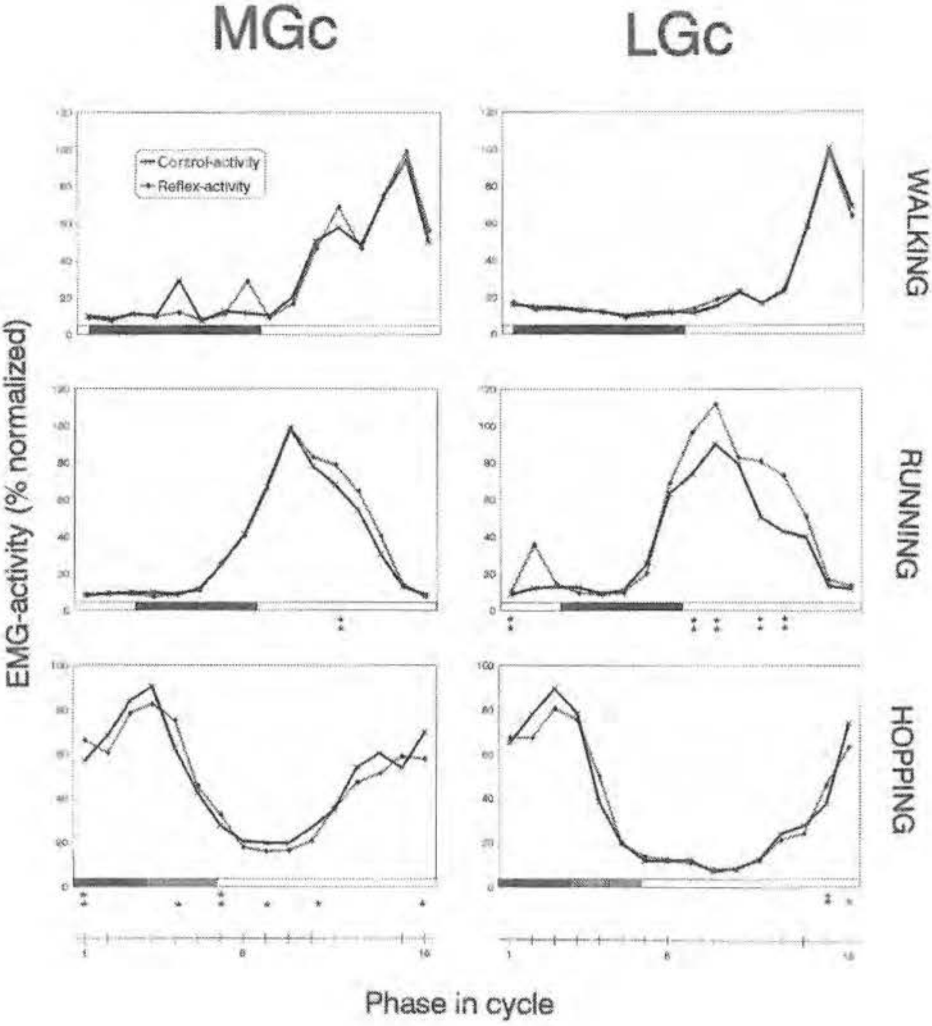

Figure 5.4. Difference between mean control and reflex activity of medial and lateral gastrocnemius of the contralateral leg after cutaneous stimulation (legends see fig. 3).

5.4.3.Reflex/background ratio

From previous figures it is clear that the responses were not large but they were quite consistent in some parts of the step cycle, and they did not reverse from facilitatory to suppressive responses as a function of the phase. For the latter reason it was felt that a method could be used which summarizes the strength of the responses in any given experiment throughout the step cycle, irrespective of the phases in which the responses appear (Duysens et al. 1993). A reflex/background ratio was calculated by adding all the measurements of the raw P2 reflex responses at the 16 phases and dividing this sum by the sum of all the 16 corresponding controls. Hence, a ratio of 1 means that, on average during a single experiment, the EMG level in the reflex window was equal to the EMG level, measured in the controls. A value above 1 indicates the predominant presence of facilitatory reflexes while a ratio below 1 is consistent with a majority of suppressive reflexes. This method neglects the phase-dependency of the responses but it has the advantage that it summarizes effectively large sets of data. The reflex/control ratios for all data are listed in Table 5.2.

Ipsilaterally, the mean ratio for MG was 1.14 (SD. 0.20), while it was 0.87 (SD. 0.14) for LG. A significant difference ($p = 0.001$) between the two muscle heads was seen with a Student's t-test for paired samples. Especially in the hopping movement the reflex/control ratios of MG and LG were very indicative for facilitation respectively suppression. For the running movement the difference is smallest.

Contralaterally, the mean control/reflex ratio for MG and LG were 0.99 (SD. 0.09) and 1.08 (SD. 0.16) respectively.

Subject	Experiment	MGi	LGi	MGc	LGc
1	1	1.05	0.90	0.99	0.89
	2	0.98	1.01	0.78	0.93
	3	1.09	1.05	0.91	1.13
2	1	1.07	0.97	0.99	1.04
	2	0.84	0.87	1.09	1.06
	3	0.97	0.87	1.08	1.36
3	1	1.26	0.82	0.90	0.94
	2	1.31	0.86	1.07	0.97
	3	1.50	0.94	1.16	1.37
4	1	1.24	0.63	0.97	1.01
	2	1.31	0.95	0.95	0.93
	3	1.48	0.68	0.97	1.34
5	1	1.08	1.09	0.97	0.98
	2	0.86	0.76	0.94	1.03
	3	1.09	0.64	1.05	1.18
Mean		1.14	0.87	0.99	1.08
SD.		0.20	0.14	0.09	0.16

Table 5.2. Reflex/background ratios for each subject and each experiment of MG and LG (hopping (1), running (2) and walking (3)).

5.5. Discussion

The present results show that sural nerve stimulation can elicit middle latency (P2) responses of different amplitude and sign in MG and LG during various locomotor and hopping tasks. Facilitatory responses dominated in MG while suppressive responses prevailed in LG. This basic result is in line with some of the data derived from animal studies, but it is in apparent conflict with some reports in humans. Stimulation of low threshold cutaneous afferents in the sural nerve of the cat can give rise to excitatory responses in motoneurons of the triceps surae (Creed et al. 1932; Hagbarth 1952; Wilson 1963; Engberg 1964; Burke et al. 1970). However, the different parts of this muscle group are not equally involved in these reflexes. MG motoneurons innervating fast twitch muscle units, show more sural nerve evoked EPSPs than slow soleus (Sol) units (Burke 1970, 1973). LaBella et al. (1989) found that sural nerve stimulation yielded EPSPs in almost all MG units but only in a small percentage (15%) of the units in LG. In decerebrated cats, Nichols et al. (1994) showed that sural nerve stimulation produced both plantar flexion and abduction at the ankle and that most of the torque was due to activation of the MG.

Several authors have studied the responses to electrical stimulation of the sural nerve in cats during walking on a treadmill (Abraham et al. 1985; Duysens 1977; Pratt et al. 1991). In the intact cat , short latency responses (P1 at 10 ms) were not consistently seen but responses with a P2 latency (about 25 ms) were generally present. The latter responses were usually suppressive in Sol while being facilitatory in MG (Duysens and Loeb 1980. Moreover, Abraham et al. (1985) showed that the facilitatory responses were larger in MG than in LG during treadmill locomotion.

In humans studied with postural perturbations, Nardone et al. (1990) found that medium latency facilitatory responses (comparable to the present P2 responses) were larger in MG than LG. In general, a comparison with the sural nerve studies on humans at rest is difficult because the medium latency responses are less prominent in sitting or standing than during gait (Duysens et al. 1993). The available data concern mostly the short latency responses and furthermore they were obtained with a different technique, namely single unit EMG recording. Kukulka (1994) found that short latency suppressive responses to sural nerve stimulation were significantly larger in LG than in MG. For the short latency facilitatory responses, Aniss et al. (1992) described early facilitations with a latency of 52-53 ms, while Kukulka (1994) found short latency enhancements (E1) with a latency of 31-32 ms in a small percentage of cases. No clear difference was found between MG and LG responses (for the Aniss study it is difficult to judge wether MG and LG responses were different since the P1 amplitudes were expressed relatively to peaks occurring at longer latencies). With respect to the facilitatory P2 responses, Aniss et al. (1992) described facilitatory responses in MG with a latency of 94 ms (their Fig. 8) while Kukulka (1994) found similar responses with a latency of 72 ms (+/- 15). The present P2 responses with a latency between 80 and 93 ms can be seen as equivalent to those responses when the differences in definitions of latency are taken into account (e.g. Kukulka's latencies are shorter since he basically defines the termination of suppressive responses as the onset of a facilitatory peak while in the present study the latency is defined by the onset of a positive 'subtraction' peak).

The apparent difference with the present results may have several causes. First, several studies have shown that cutaneously evoked reflex responses are task-dependent (Evans et al. 1989; Burke et al. 1991) and may be selectively facilitated during gait (Duysens et al. 1993). Second, under the present conditions with long and variable interstimulus intervals, habituation of facilitatory responses is small (Tax et al. 1995). In contrast however, in the single unit studies mentioned, the stimuli were given at a fixed rate of either 1 or 3 Hz and it is possible that habituation was an important element in these studies (Aniss et al. 1992; Kukuka et al. 1994). Third, as mentioned by Kukulka (1994), the technique used for single unit recordings requires long spike trains and therefore is limited to recordings from low threshold units. Since the larger units in MG may be expected to be recruited selectively by the sural nerve input (Burke et al. 1970, 1973), it is likely that the facilitatory responses of these units are missed by the single unit technique, but not by the presently used surface EMG method. Fourth, it may be argued that the difference in amplitude of the MG and LG responses was related to differences in the background activity profiles of MG and LG during the step cycle. In fact, minor differences were observed (higher EMG activity in MG than in LG during early stance, resulting in a more biphasic profile in LG as compared to MG)(Wilson 1963). However, these differences in profiles cannot explain the presently observed dominance of MG facilitatory and LG suppressive responses since the sign of the responses (facilitatory versus suppressive) was largely independent of the level of background activity.

5.5.1. Hopping, running and walking tasks

Selective facilitatory MG responses are present during hopping as well as during walking and running. Hence the contribution of these responses is not strictly locomotor dependent [24]. Furthermore the responses were smaller during walking as compared to running and hopping. This is opposite to what is seen with SOL H-reflexes. The amplitude of the latter responses is largest while standing and decreases when elicited during walking (Capaday and Stein 1986; Morin et al. 1982) and even further during running (Capaday and Stein 1987). This difference between SOL and MG may be related to the function of these muscles as SOL is primarily a slow postural muscle while MG is much faster than SOL. In agreement with this Moritani et al. (1990) found that MG H-reflexes are larger during running than during walking. In general, most of the evidence in favor of a role of stretch reflexes in MG was obtained in running or jumping but not in slower movements such as walking (for review see Dietz 1992).

What could be the role of these reflexes during hopping, bearing in mind that the electrical activation of the sural nerve provides a rather artificial stimulus? Hopping is a good example of a partial preprogrammed movement. The plantar flexors of the ankle, especially the gastrocnemius muscle, are already active some 84 ms before ground contact by a preferred hopping frequency of 2,06 Hz (SD. 0.02 Hz) (Mrllvill-Jones and Watt 1971). In the present study this preactivation started some 120 ms prior to touchdown and it was accompanied by an opening of sural reflex pathways to MG. Touchdown should lead to synchronous activation of sural nerve afferents and it is therefore reasonable to assume that the opening of these pathways is related to the anticipation of touchdown. In agreement with this idea is the finding that the H-reflex of medial gastrocnemius during hopping started to increase in late precontact phase to reach a peak amplitude at or just after contact phase(Dyhre-Poulsen et al. 1991; Moritani et al. 1991). Furthermore, in a previous study it was shown that sensory perception and cortical evoked potentials following sural nerve stimuli are enhanced in the period just prior to foot contact (Duysens et al. 1995).

It is still unclear why the sural nerve induced facilitatory responses were selectively enhanced in MG and not in LG during the various tasks. A rotatory moment may be important. In the cat, MG causes more toe-out torque than LG after stimulation of the muscle nerve [34] or the sural nerve (Bonasera et al. 1992; Nichols et al. 1993). If the same applies to humans, the present data indicate that sural nerve afferent activity induces an exorotatory torque during the stance phase of normal walking (Hugon 1973). During the support phase, when the foot is on the ground, the toe-out moment caused by sural nerve activity can be translated into an inward rotation of the leg, thereby resisting the passive outward rotation of the leg due to the rotation of the body (caused by the controlateral inward swinging leg). Further evidence for an interpretation in terms of exorotation comes from an earlier finding that sural nerve stimulation during running induces clearly more facilitatory responses in biceps femoris muscle (BF) than in semitendinosus (ST), which would also favour exorotation (Tax et al. 1995; Duysens et al. 1992b).

It is difficult to see, however, that exorotation is important in hopping where the MG responses are present as well. Therefore other explanations should be considered. Buchanan et al. (1993) have argued that MG and LG play an important role in the production of varus and valgus torques, respectively. During the stance phase of gait, the body makes a lateral movement with respect to the supporting foot and this movement may be counteracted by the preferential activation of MG. Alternatively, it has been stated that MG is possibly able to produce a higher peak force than LG (Tjoe et al. 1991; Perell et al. 1991)[46, 42]. Gregor (1994) suggested that a preferential recruitment of MG over LG may be equivalent to using the most powerful source first and holding the weaker source in reserve. This is reminiscent of the difference in activation of MG versus Sol. Sural nerve stimulation in decerebrated cats evokes predominantly EMG facilitation in MG while producing simultaneous suppression in Sol Kanda et al. 1977 (see also Cope and Clark 1993 for critique). For the elaboration of this hypothesis it is essential to determine in future experiments whether, as in the cat, the human MG is more powerful than the LG. Furthermore, even in the cat there is no consensus whether MG is more powerful (Sacks and Roy 1982).

Whatever their precise role, it is clear that cutaneomuscular reflexes in MG and LG can be elicited by sural nerve stimulation of low intensity, making it likely that such reflexes play a role especially in the normal regulation of fast rhythmic movements such as running and hopping. In the case of hopping the predominant facilitation of MG responses prior to touchdown is consistent with the idea that reinforcing reflex pathways are opened to strong and fast plantar flexors in order to provide extra stiffness in the period after touchdown.

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6. ANATOMICAL FINDINGS SUPPORTING THE FUNCTION OF THE GASTROCNEMIUS MUSCLE IN NON-SAGITTAL PLANES

6.1. Introduction

The gastrocnemius muscle is the most superficial muscle of the posterior crural muscle group. Together with the soleus muscle it forms the triceps surae that has a common insertion by means of the Achilles tendon (tendo calcaneus) on the calcaneal bone.

After cutaneous stimulation of the sural nerve the reflex activity of the medial head differs from the reflex activity of the lateral head of the gastrocnemius muscle. The medial head gets reflexly facilitated while the lateral head gets inhibited during the stance phase of walking, running and hopping (see chapter 3 and Hauglustaine et al. 1998a). After cutaneous stimulation of the digital nerves of the second and fourth toe both heads get inhibited (chapter 4). A possible explanation for this phenomenon is a function of the gastrocnemius in the sagittal plane (flexion of ankle and knee) as well as in non-sagittal planes during disturbed gait.

Because there is a difference in the two heads of the gastrocnemius muscle, seen during neurophysiological experiments, we wanted to study the origins and the insertions of the two heads anatomically. In this part of the study a review of anatomical data on the gastrocnemius muscle with its Achilles tendon is given together with some new data from dissection work and magnetic resonance imaging (MRI).

6.2. The origins of the gastrocnemius muscle at the knee joint and the medial and lateral muscle belly.

6.2.1. Anatomical findings in the adult

To study the origins of the heads of the gastrocnemius muscle a dissection of ten lower limbs of human adults was performed. The cadavers were fixated with a formaline solution of 2% with glycerin added. We looked to the origins of the two muscular heads on the femur and tried to find some anatomical data that could explain a function of the gastrocnemius muscle out of the sagittal plane.

In the anatomical textbooks such as Gray's Anatomy (Williams et al. 1995) the origins of medial head and lateral head are widely described. The two heads of the gastrocnemius muscle arise at the condyles of the femoral bone. The medial head arises from a depression at the upper and posterior part of the medial condyle behind the adductor tubercle and from an area on the popliteal surface of the femur just above the medial condyle. The lateral head arises from the lateral surface of the lateral condyle and from the lower part of the lateral supracondylar line. Both heads also arise from the attached part of the capsule of the knee joint. Rarely presenting anatomical variations are the absence of the lateral head or the presence of a third head arising at the popliteal fossa (Williams et al. 1995).

The main findings of our dissection work confirmed the anatomical data given in the textbooks. In our findings however, two not in extenso described origins were constant. First, in all our ten specimens a part of the origin of the medial head of the gastrocnemius surrounds the medial condyle inferior to the adductor tubercle of the femur. A bundle of fibers from the 'hamstring' part of the adductor magnus muscle converge into this surrounding origin (see figure 6.1.).

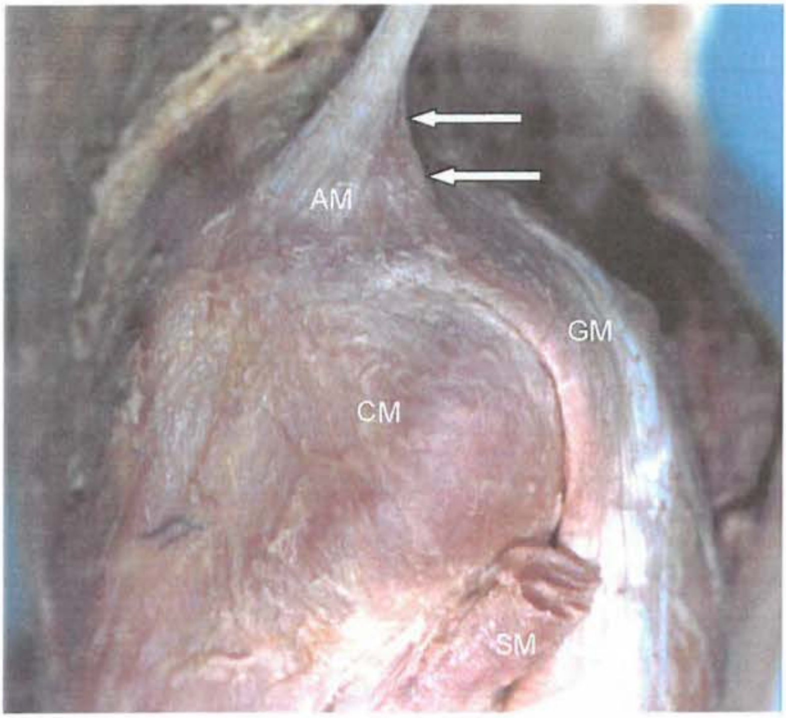


Figure 6.1. The medial head of the gastrocnemius muscle (GM) arises with some fibers (see arrows) from the hamstring part of the adductor magnus (AM). The rest of the medial head of the gastrocnemius arises from a depression at the upper and posterior part of the medial condyle behind the adductor tubercle and from an area on the popliteal surface of the femur just above the medial condyle. CM: medial condyle. SM: tendon stump of semimembranosus muscle.

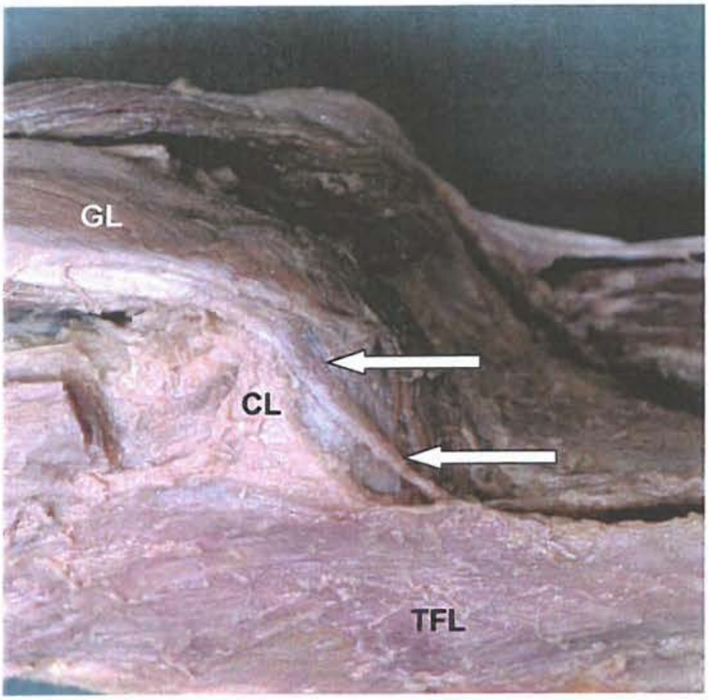


Figure 6.2. The lateral head of the gastrocnemius muscle (GL) has a thin origin (see arrows) coming from the tractus iliotibialis (TFL). CL: lateral condyle. Orientation: distal (left); proximal (right).

In table 1 the width of this constant surrounding origin relative to the width of the total origin is plotted for all ten subjects.

	Width	
Specimen	Total origin MG (cm)	Surrounding origin (cm)
1	2,9	0,8
2	3,5	0,6
3	3,2	0,9
4	3	0,8
5	3,1	0,7
6	2,8	0,7
7	3,4	0,9
8	3,4	1,1
9	2,3	0,4
10	2,8	0,6
Mean	3,04 (±0,36)	0,75 (±0,19)

Table 6.1. Width of the total origin of the medial head of the gastrocnemius muscle compared with the width of its surrounding part.

The importance of this origin of the medial head of the gastrocnemius muscle can be demonstrated by the following maneuver: When force is exerted manually according to the direction of the medial head of the gastrocnemius muscle, this force is partially transferred to the 'hamstring' part of the adductor magnus. Reversibly, force following the length of the 'hamstring' part of the adductor magnus is also partially transposed to the medial head of the gastrocnemius muscle. When one of the two muscles contracts it will have an effect on the afferent structures of the other muscle that will react on it properly. To test such an hypothesis it would be interesting to look electromyographically to the activity in the medial head of the gastrocnemius during active and passive ab- and adduction of the hip respectively.

Our second finding concerns the lateral head of the gastrocnemius muscle, which has an almost constant very dense and thin origin coming from the tractus iliotibialis (see figure 6.2.). This anatomical structure was found in seven of our ten specimens. The function of this structure is not entirely clear as it seems relatively small to transfer heavy forces.

6.2.1. Anatomical findings in the fetus

The gastrocnemius muscle of a nineteen-week-old human fetus shows the medial and lateral head of the muscle to be practically separated (see figs. 6.3.-6.5.). Medial head and lateral head can be separated bluntly. The medial head has its own tendon, while the muscle belly of the lateral head is attached directly on the tendon plate of the soleus muscle (fig. 6.5.).

In a thirty-week-old stillborn child this distinction between medial and lateral head is less clear but still exists as shown in figures 6.6. till 6.9. The separation between the medial head (fig. 6.8.) and the soleus muscle is more clear and extends farther than the separation between lateral head (fig. 6.9.) and soleus muscle. The tendon leaf of the medial head is still more pronounced than the insertion of the lateral head on the Achilles tendon. This is quite different from the anatomical situation in the adult human where both heads have their own tendon blending together with the soleus tendon into the Achilles tendon.

As a consequence, one may also ask if it is justifiable to look upon the lateral head of the gastrocnemius muscle together with the soleus muscle as two parts of one muscle. The medial head of the gastrocnemius would then be a separate muscle.

Figure 6.3. Under knee amputation of the lower limb of a nineteen-week old fetus.

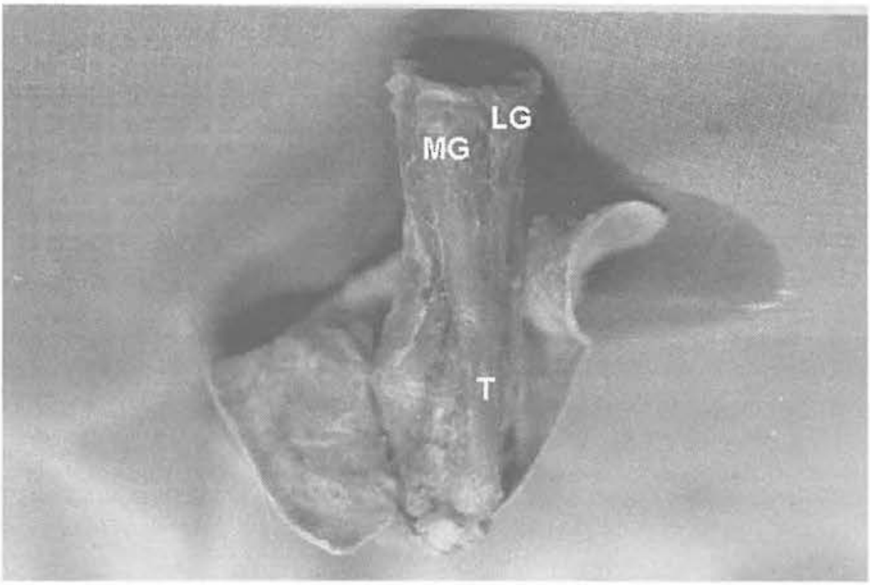


Figure 6.4. Same specimen with the skin removed showing the medial head (MG) and the lateral head (LG) of the gastrocnemius muscle blending together in the Achilles tendon (T).

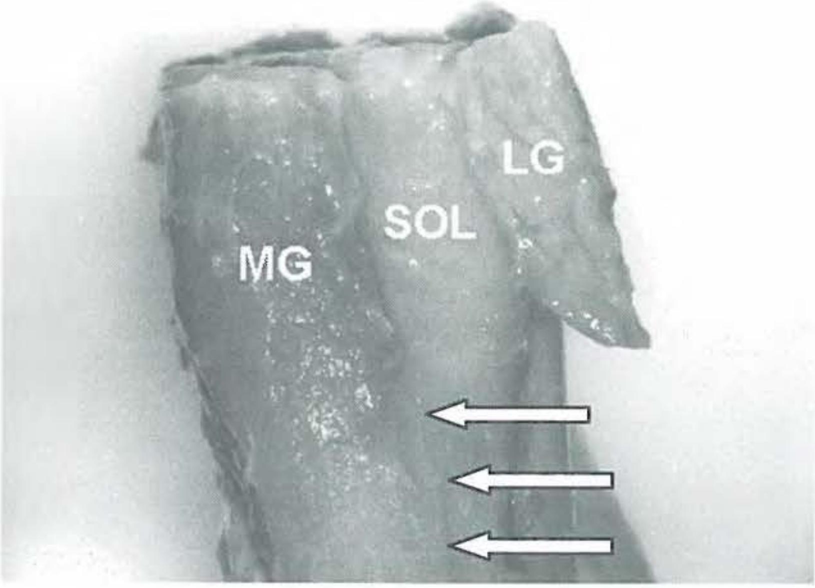


Figure 6.5. Medial head (MG) and lateral head (LG) of the gastrocnemius can be separated bluntly. The medial head has its own tendon (see arrows), while the lateral head is attached directly on the tendon plate of the soleus muscle (SOL).

Figure 6.6. Above knee amputation of the lower limb of a thirty-week old stillborn infant.

Figure 6.7. Skin removed from the dissected specimen showing the medial (MG) and lateral (LG) head of the gastrocnemius muscle and the Achilles tendon (T).

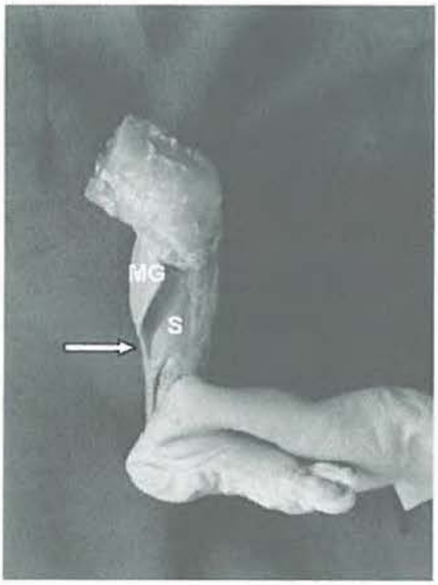


Figure 6.8. Medial view of the same specimen of figure 6.7. showing the medial head (MG) of the gastrocnemius muscle blending into the Achilles tendon with a pronounced tendon leaf (see arrow). S: soleus muscle.

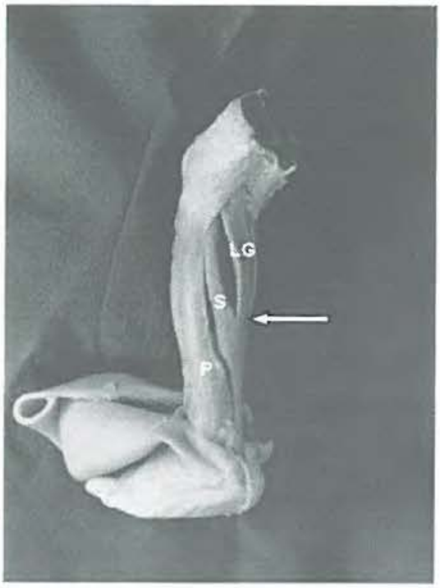


Figure 6.9. Lateral view of the specimen showing the lateral head (LG) of the gastrocnemius muscle with its muscular insertion (see arrow) on the soleus muscle (S). P: compartment of the peroneus muscles.

Bergman and co-workers (2000) state in their Illustrated Encyclopedia of Human Anatomic Variation: "The soleus first appears in lower mammals and may be a derivative of the lateral head of the gastrocnemius. It has been suggested that the medial head of gastrocnemius is a medial extension from the fibular head."
Following this phenomenon it is favorable to speak rather about the triceps surae muscle than about gastrocnemius muscle and soleus muscle.

To describe the architecture of the muscle bellies of the human gastrocnemius, Huijing (1985) performed measurements on eight human cadavers. He concluded that the architecture of the muscle bellies is well suited for exertion of a high force over a relatively small range. This feature, he concludes, suits it very well for the transport of power from the knee to the ankle joint, during which it does not necessarily have to shorten a great deal. Huijing however did not investigate the anatomical situation of the insertion of the muscular heads at the Achilles tendon.
Traditionally, control of motor units within any striated limb muscle through activation of motoneurons within the central nervous system has been thought to be directed by a single muscle nerve that innervates a single, whole muscle. Recent studies on cadaver dissections (Segal et al. 1991; Segal 1992; English et al. 1993) and electromyographic analyses (Wolf et al. 1993) have shown that the traditional concept of whole muscle activation by innervation of motor units is more complex than originally perceived. English et al. (1993) state in their 'partitioning hypothesis' that most mammalian skeletal muscles are composed of smaller elements called neuromuscular compartments, which are the portions of a muscle innervated by a primary muscle nerve branch. Those neuromuscular compartments can be partitioned according to their architecture, to their innervation patterns and to their histochemical profiles for functional or task-specific roles. This hypothesis is derived from

earlier animal studies using glycogen depletion methods to characterize the different compartments (Burke et al. 1973; Letbetter 1974; English 1980).

In humans, EMG recordings of LG muscles revealed that different areas of the LG showed varying levels of muscle activity depending on the kind of motor task. Electrodes placed in the distal lateral sites of the LG showed the greatest activity during step-up exercises and the proximal lateral site showed the least activity in most lower extremity tasks (Wolf et al. 1993). By this method, three distinct compartments of LG were defined (Segal et al. 1991; Wolf et al. 1997a).

The morphology and nerve innervation pattern of the medial gastrocnemius muscle was studied by Wolf and Kim (1997b). They saw that width and muscle nerve entry point vary across specimens while total muscle length, individual muscle fiber length and maximal muscle depth were relatively constant. They concluded that at present it is not possible to distinguish human MG compartments based upon architecture. Unlike the LG which has three distinct compartments (Segal et al. 1991; Wolf et al. 1997a), the MG is an architecturally homogenous muscle. This finding may suggest that the MG has less specific functions compared to the LG.

Soleus and gastrocnemius are seen as postural muscles. In normal stance in humans a vertical from the center of gravity (a point about one centimeter posterior to the promontorium) of the whole body lays anterior to the ankle joint. Electromyography during normal stance shows continuous activity at the soleus muscle, but intermittent activity in the two heads of the gastrocnemius muscle (Smith 1954; Levy 1963, Basmajian & De Luca 1985).

Only near full knee extension the gastrocnemius muscle as a whole is important in generating a flexion moment in the knee (Hoy et al. 1990). Concerning the ankle joint, the relative contribution of the gastrocnemius muscle to the ankle moment depends on the knee angle. Hoy and co-workers saw that with the knee in anatomical position the gastrocnemius muscle contributed 38% to the total ankle moment, but with the knee flexed at 90° this contribution of the gastrocnemius muscle dropped to 7%.

The origin of the two muscular heads at the facies poplitea of the femur suggests also rotation functions of the gastrocnemius muscle with respect to the lower leg around its vertical axis. However, a thorough description of this rotation activity is hard to find in literature. Interesting to know is the envelope of passive knee joint motion studied by Blankevoort et al. (1988). They used four fresh knee joints and mounted them in a specially developed motion and loading apparatus. The knee-joint specimens were moved through flexion under several combinations of external loads. They concluded that the envelope of internal and external rotation of the knee increased with increasing flexion of the knee joint.

6.3. The Achilles tendon as an insertion of the triceps surae muscle at the calcaneal bone

6.3.1. The Achilles tendon

The Achilles tendon is the thickest and strongest human tendon. Macroscopically the tendon fibers spiral through 90° in descending, so that the medial fibers become the most posterior (White 1943). White, an orthopedic surgeon, was interested in this spiraling to improve the technique of subcutaneous tenotomy.

6.3.1.1. Kinematic model

The gastrocnemius muscle is described as a typical flexor of ankle and knee. The gastrocnemius is a biarticular muscle of which the efficiency as flexor at the ankle depends on the simultaneous flexor activity at the knee (see Hoy et al. 1990). The highest flexion forces at the ankle joint are developed with the knee in extension. Biesalski and Mayer (1916) showed in their experiments by means of anatomical specimens adduction of 13 degrees and supination of 12 degrees of the ankle joint during extreme flexion of this joint. In the following study it is shown, by means of a very simplified model, in which way the spiraling of the Achilles tendon can contribute to this supination movement. This model does not represent the in vivo situation because the biomechanical characteristics of the knee and ankle joints with their ligaments are not taken into account. Neither movement restrictions by surrounding tissues are taken into account.

The kinematic model of the phenomenon of intercrossing tendon fibers within the Achilles tendon is based on models that were originally introduced by Huson (1974, 1983), and elaborated to a certain extent by Oonk (1988). In his concept of the kinematic chain, Huson (1974, 1983) presented the planar simple closed four-bar chain, consisting of four rigid bodies connected to each other by four hinges. He demonstrated that such a chain has only one degree of freedom and displays only one pattern of movement. Further he stated that ligaments could also function as the rigid bars of a four-bar chain, provided that these ligaments are kept under tension.

Our simplified model was explicitly based on from the anatomical situation of the Achilles tendon in the opossum, as schematically represented by Stein (1981), and depicted in Fig. 6.12. as well. The opossum may be observed as a predecessor of the primates. We assumed that muscles and tendons too, like ligaments, can be observed as rigid bars in a four-bar chain, provided that they are kept under tension. To test the feasibility of this assumption, such a model was applied on the jaw muscles, namely the superficial part, and the deep part of the masseter muscle, in order to analyze the movements of the lower jaw. In this test model, the two other bars represented the bony zygomatic arch, and the bony tuberositas masseterica at the angle of the lower jaw.

The result of this test and the outcome of the analysis, proved to be representative for the resulting jaw movements (Hauglustaine and Van Zwieten 1998).

6.3.1.1.1. Collateral four-bar system model, input and results.

As was mentioned by Oonk (1998), the four-bar chain with two vertical bars which run more or less parallel to each other, is said to be a collateral four-bar system.

For a clear demonstration, we shall start with this non-realistic situation (figure 6.10.), representing the lateral gastrocnemius muscle plus tendon (AC), more or less parallel to the medial gastrocnemius muscle plus tendon (BD). The lengths of these bars are comparable to the real lengths of these muscles plus their tendons in man. The two horizontal bars represent a line between the condyles of the femur at the base of the facies poplitea (CD) where the two muscles arise, and the tuber calcanei (AB) where they are thought to insert, respectively. As was indicated by Huson (1983) as well as by Oonk (1988), one of the four bars can be observed to be motionless, in order to obtain a clear and recognizable pattern of movement of the rest, i.e. the model. In this model, the upper horizontal bar (representing the origin of LG and MG on the femur) is kept motionless, while the other bars can be moved.

A tilt of 12° is now imposed to the lower (movable) horizontal bar (representing the calcaneus or, in a wider sense, the sole of the foot), thus mimicking the maximum of inversion of the human foot during activity of the gastrocnemius muscle (Biesalski and Mayer 1916). To obtain such an inversion or supination, the vertical (more or less parallel) bars are seen to sway laterally in the model, in a wide displacement that is likewise non-realistic and, even more unreal, directed to the opposite side (figure 6.10.). The use of a collateral four-bar system model , to analyze the pattern of movement of LG and MG, can therefore be rejected.

6.3.1.1.2. Crossed four-bar system model, input and results.

To cite Huson (1983), the four-bar system described above is "profoundly changed by the arrangement of two crossed bars". These bars are supposed to glide freely over each other. This is depicted in figure 6.11.

The same lengths as in the previous model are used – the only difference being the crossing of two of its bars, which represents the crossing of the medial gastrocnemius muscle plus its tendon over the lateral gastrocnemius muscle plus its tendon. The crossing itself, including its level, nicely conforms the characteristic narrowest part of the Achilles tendon in man, some lower one fourth of the calf. Imposing the tilt of 12° to the lower horizontal bar representing the sole of the foot in this model (figure 6.11.), now reveals the following three features :

1. There is only a modest displacement of the model itself
2. This displacement stays within the boundaries of the lower leg
3. The resulting displacement as well as the imposed tilt show the same direction, in other words the displacement can be interpreted as some degree of adduction of the foot, that normally accompanies inversion of the foot during activity of the gastrocnemius muscle (Biesalski and Mayer 1916).

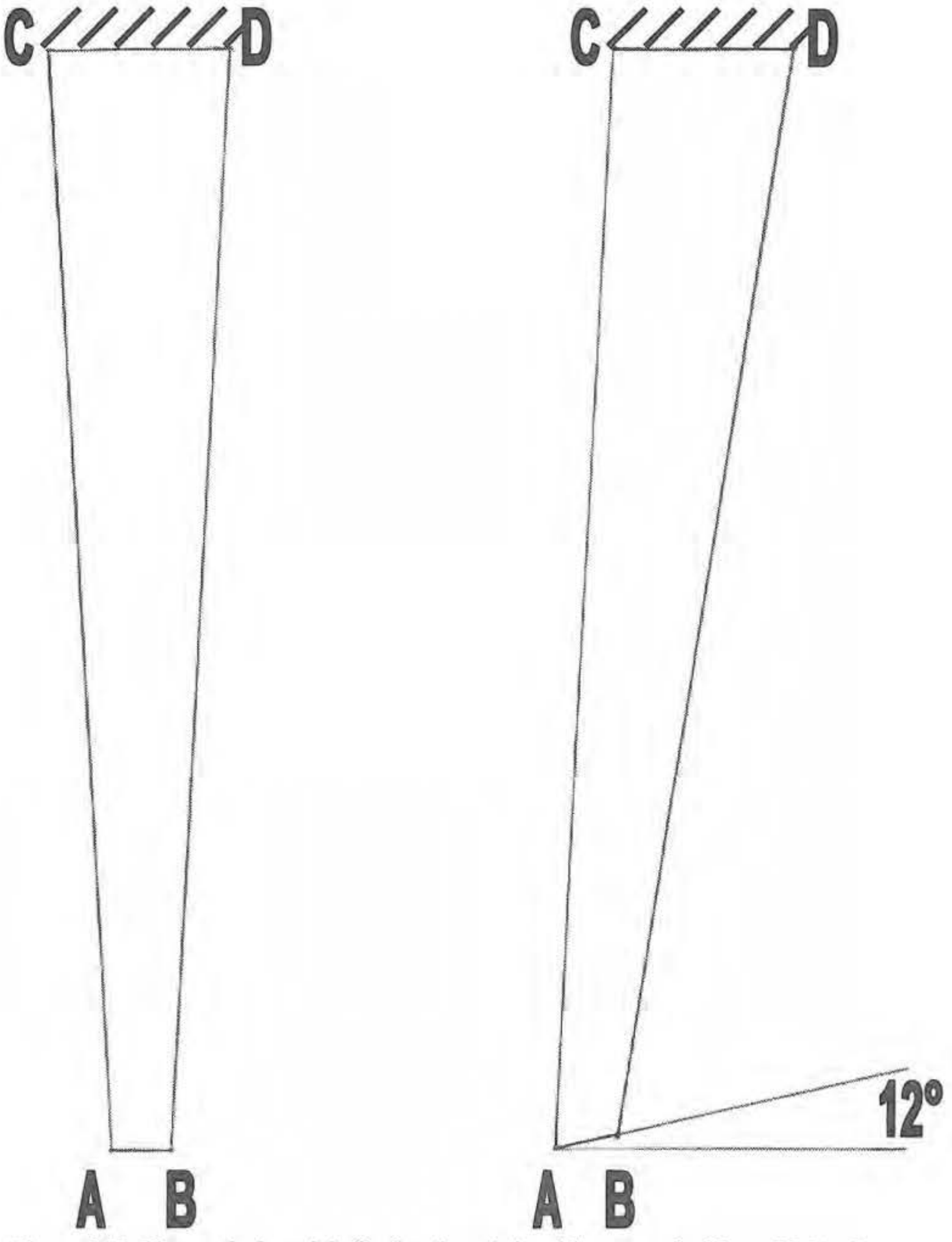


Figure 6.10. Kinematical model of a four-bar chain with two vertical bars. 33 % of real size, man, posterior view left lower leg. Vertical bars AC and BD represent LG and MG respectively. Lower horizontal bar AB represents position of left foot. Upper horizontal bar CD (fixed) represents facies poplitea of left femur. Measurements were done in the adult anatomical human specimen. Actual sizes: AC and BD 45 cm; AB 2,5 cm; CD 7,5 cm. In the left part of the figure is shown that to obtain a supination of 12 degrees the bars have to sway laterally, presenting an non-realistic situation.

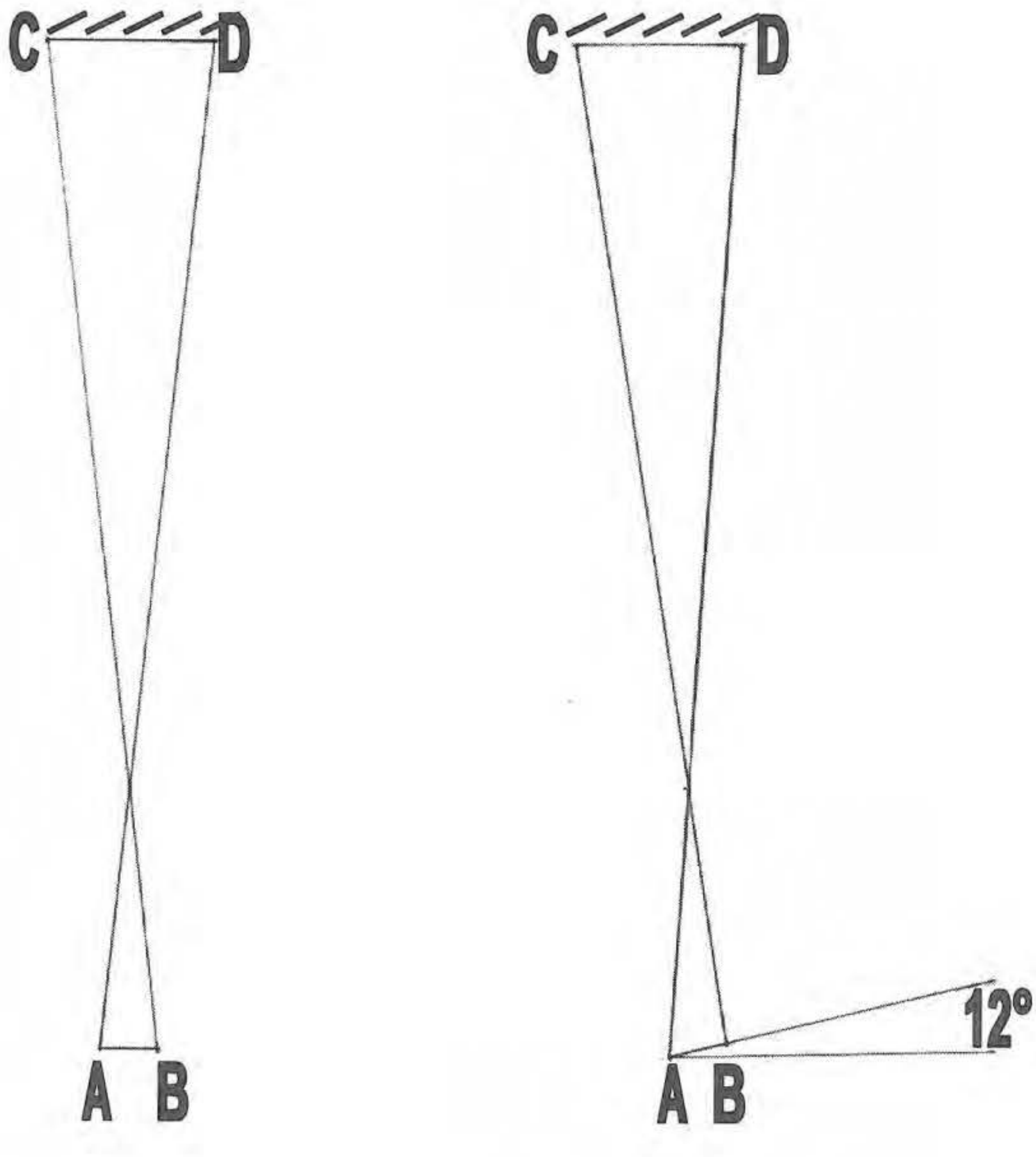


Figure 6.11. Kinematic model of a four-bar chain with two crossed bars. To obtain a supination of 12 degrees the two crossed bars stay in place. This is a more realistic situation than the situation presented in figure 6.10. For legends to the figure see figure 6.10.

The planar closed four-bar model with two crossed bars, of the tendons from medial and lateral gastrocnemius, clearly shows kinematic advantages over the so-called collateral four-bar system model, with respect to supination of the foot. An important prerequisite for this model, however, is the separate movement of two parts of the Achilles tendon formed by the two heads of the gastrocnemius muscle.

6..3.1.1.3. Spiraling of tendon fibers

Another biomechanical 'advantage' of the spiraling of the tendon fibers is the concept of a 'spring' system. As seen in chapter 3 (see figure 3.1.) the background activity of the muscle heads of the triceps surae increases during the end of the swing phase of the hopping movement, building up potential energy for the propulsion phase during the stance phase. It was thought that during contraction, the Achilles tendon stored this potential energy in the same matter as a spring unit. Alexander and Vernon (1975) described this phenomenon in kangaroos during the hopping movement.

6.3.1.2. Comparative anatomy

6.3.1.2.1. Superficial flexors of the hindlimb

In comparative anatomy it is interesting to study the opossum, as an example of a lower mammal with a fully developed hindlimb, existing since a geologically old period. The opossum may be observed as a predecessor of the primates.

An extensive and up-to-date survey of the muscular system in the opossum was given by Barbara Stein (1981). Not especially from her description, but actually from her schematic drawings it becomes clear, that in a posterior view of the opossum lower leg, the individual tendon of medial gastrocnemius muscle crosses over the tendon of the lateral gastrocnemius muscle, which together with m. soleus forms one muscle. The tendon of m. plantaris is overcrossed by medial gastrocnemius tendon too. All these tendons together form the Achilles tendon of the opossum.

We compared this phenomenon with the anatomical situation in the lower leg of baboon (Swindler and Wood 1973), chimpanzee and man respectively (figure 6.12). In these primates, the crossing of medial gastrocnemius tendon fibers over the other tendon-elements in the Achilles tendon was a constant finding. Moreover, the same direction of crossing appears in the well-known chiasma cruris and chiasma pedis, namely : medial crosses over lateral in a posterior view of the lower leg.

This crossing or spiraling within the Achilles tendon in man was related by Williams et al. (1989) to storing of energy during locomotion by means of elastic recoil. We were able to recognize the result of such "unloading", namely supination, by indicating supination positions of the foot in higher primates during bipedal walking (Van Zwieten et al. 1997).

6.3.1.2.2. Supination.

The position of the foot during the step-cycle has been well-documented in man (Williams et al. 1995; Rose and Gamble 1994), in higher primates like baboon and chimpanzee (Schmitt and Larson 1995), and in the opossum (Jenkins 1971). In most of these genera, including man, supination appears to increase during the stance-phase, from mid-stance on, especially during the interval between heel off and toe off.

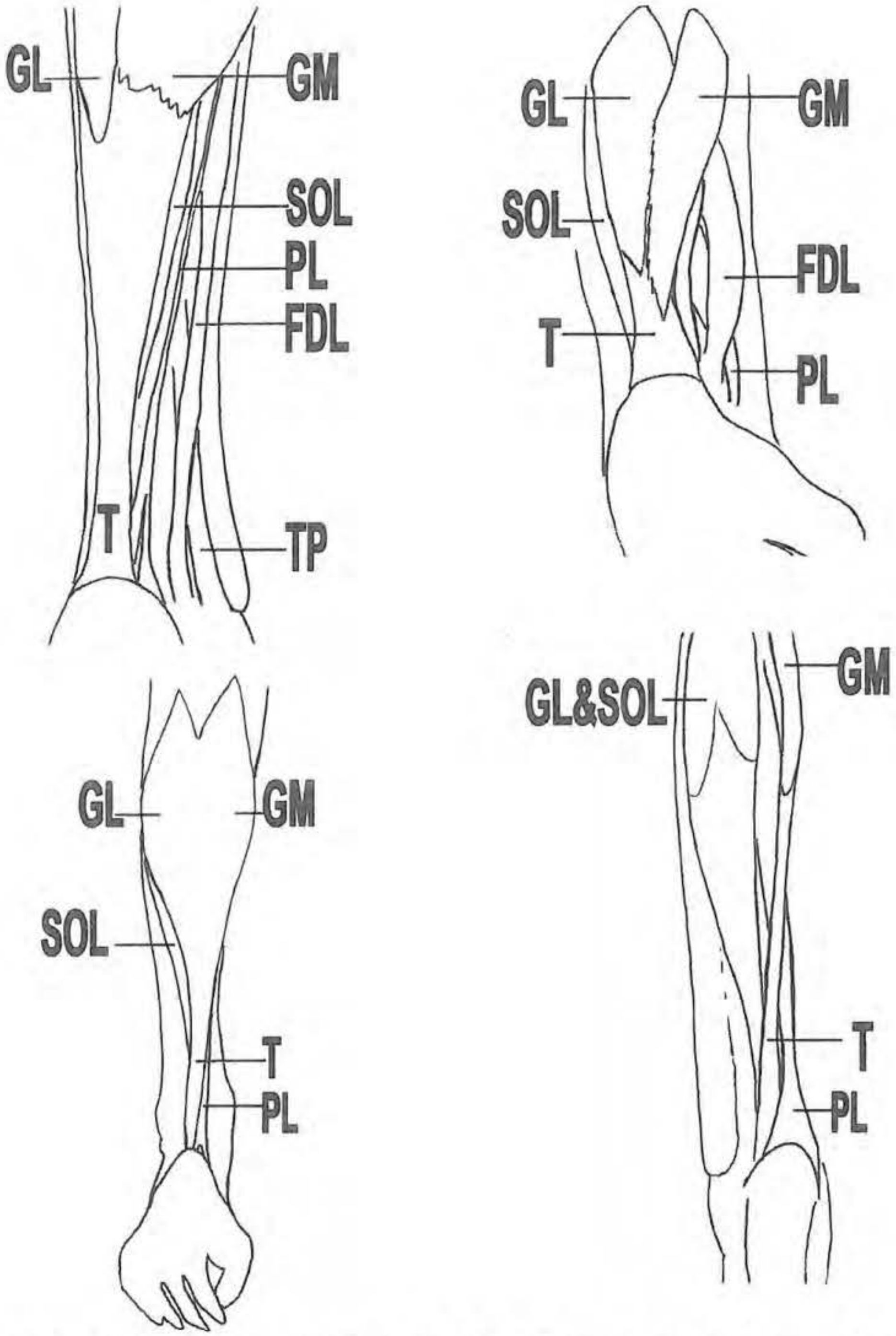


Figure 6.12. Posterior views on the outlines of the left lower legs of the human (left, up), the chimpanzee (right, up), the baboon (left, under) and the opossum (right, under). GM: medial head of the gastrocnemius muscle; GL: lateral head of the gastrocnemius muscle; SOL: soleus muscle; PL: plantaris muscle; FDL: long flexor of the toes; TP: posterior tibial muscle; T: achilles tendon.

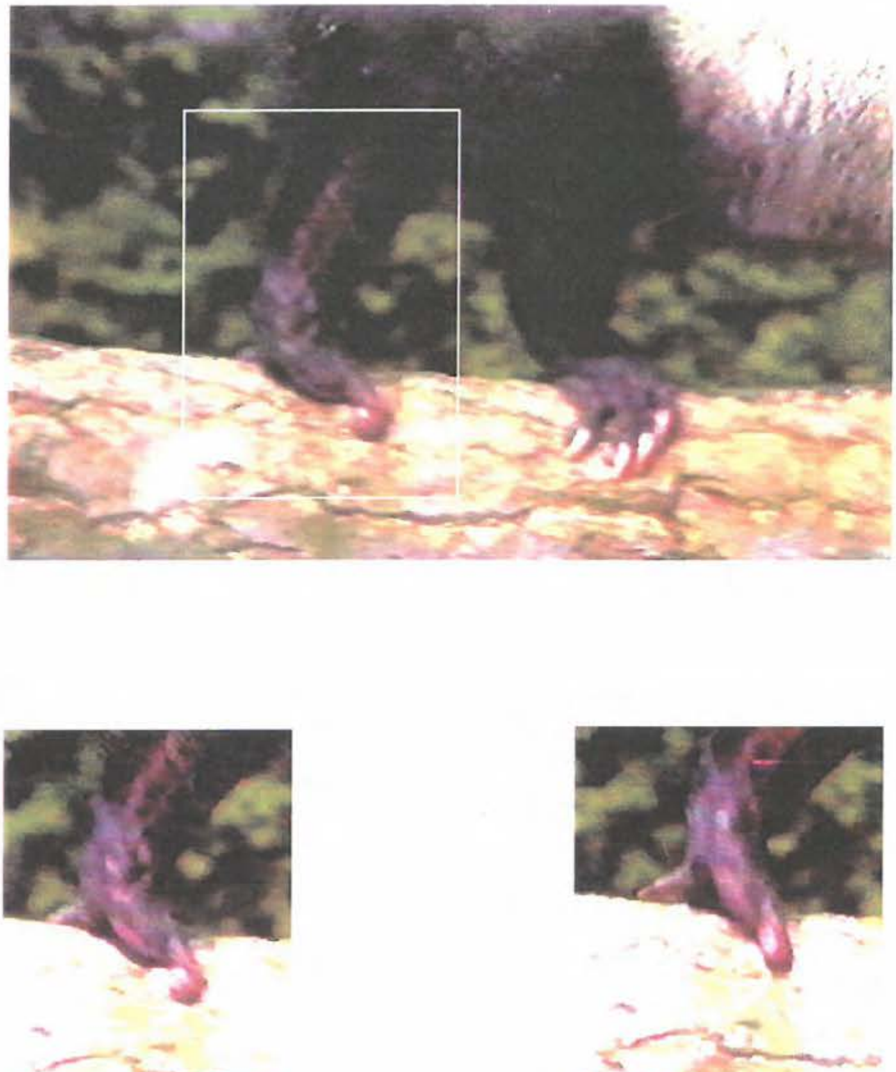


Figure 6.13. Detailed figure of the end of phase III (Narain 1998) showing supination of the foot of the opossum. In this figure phase III is subdivided to clarify the supination movement of the hindlimb. Evolution in the step cycle is in this figure given from up to down and from left to right, starting up and ending right under.

This increase of supination in walking opossums (Van Zwieten et al. 1983) was studied in our department, by means of planar videotapes. Jenkins (1971) divided the opossum step-cycle into four Phases, I – IV. Narain (1992, 1998) described the end of Phase III in the opossum as follows: "elevation of the sole of the foot until tiptoe; the sole of the foot points more and more towards medially". This medial position of the sole of the foot in the opossum is equal to supination. A detailed display of the end of Phase III in the opossum is given in figure 6.13.

A kinematical analysis of the tarsal joints in man was done by Van Langelaan (1983). He determined the absolute helical movements for the tibia, calcaneus, talus, navicular bone and cuboid and the relative helical movements for the relation between those bones. He saw that during laterorotation of the tibia in relation to the fixed foot the rotation between the tibia and talus was significantly less than the rotation between the talus and the calcaneus. The typical form of the talo-calcaneal joint surfaces contributes to the existence of supination (Biesalski & Mayer 1916), a combined movement of adduction, flexion and inversion.

6.3.1.3. MRI of the Achilles tendon

To study the morphology of the Achilles tendon a microscopic MRI of a human Achilles tendon was done. The aim of the study was to describe the orientation of the tendon fibers within the tendon.

Normal tendons produce little or no signal on conventional MRI sequences (Peh and Chan 1998). This is because the tendon consists of type I collagen fibers orientated in a parallel manner into highly ordered bundles. Tendons, therefore, display structural anisotropy, creating a static local magnetic field which further contributes to spin-spin interaction, causing normal tendons to have ultra-short T2 relaxation times in the order of 250 µs. The resultant rate of T2 decay is so rapid that a very low signal is obtained irrespective of TE value. In other words, the visualization of tendons in conventional magnetic resonance imaging is very difficult and the resulting images do not give much information about the tendons themselves.

High resolution MRI, however, gives more information about fibrous structures than conventional MRI (Lippens et al. 1997). In our study, a microscopic magnetic resonance study of the Achilles tendon was carried out in order to describe the anatomical architecture of the tendon. The lower third of the triceps surae muscle with the attached part of the calcaneal bone was isolated from a human cadaver conserved at 4°C one day post mortem. The specimen itself was fixed on a piece of wood and immediately preserved in a 35% formaline solution to prevent drying and shrinking.

After full fixation, the distalmost 8 cm of the Achilles tendon with the attached part of the calcaneal bone was isolated and placed in a micro MRI tube filled with fresh clear 35% formaline solution. This tube was placed in the micro MRI. The scanned area was limited to approximately 4 cm. After the first imaging session a second imaging series followed in the opposite direction so that the whole tendon was scanned.

The MRI took slices every 2 mm in the coronal, sagittal and transversal planes. The obtained data were analyzed by a Sun software system. The windows of contrast and brightness were set to obtain as much relevant anatomical information as possible. To transfer the obtained data to a format of image that is readable by a normal personal computer the data underwent a Fourrier analysis. In the detailed figure 6.14. the orientation of the presented slices is shown. It appeared that the most relevant information could be obtained from the sagittal and the transversal slices.

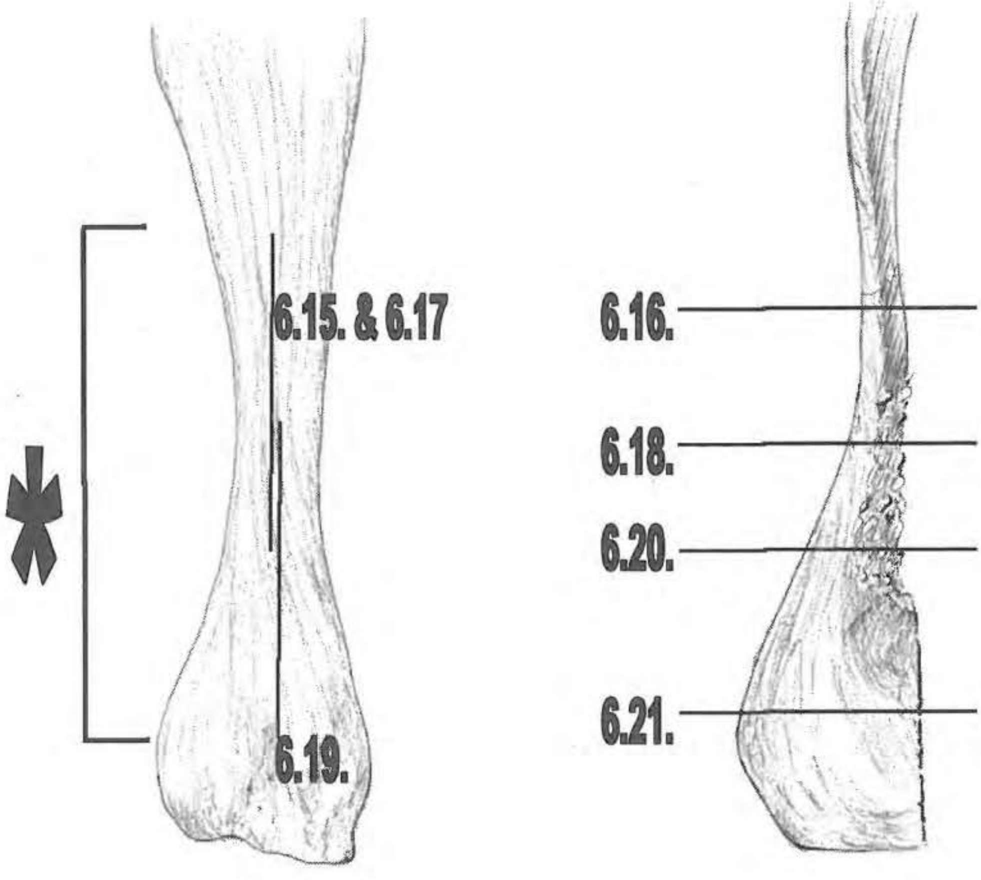


Figure 6.14. Posterior and medial view on the specimen of the right Achilles tendon of an adult human. Scanned area is indicated with a large asterisk. Sagittal and transversal slices are indicated with the corresponding figure numbers. Figure 6.17. is a detail of figure 6.15.

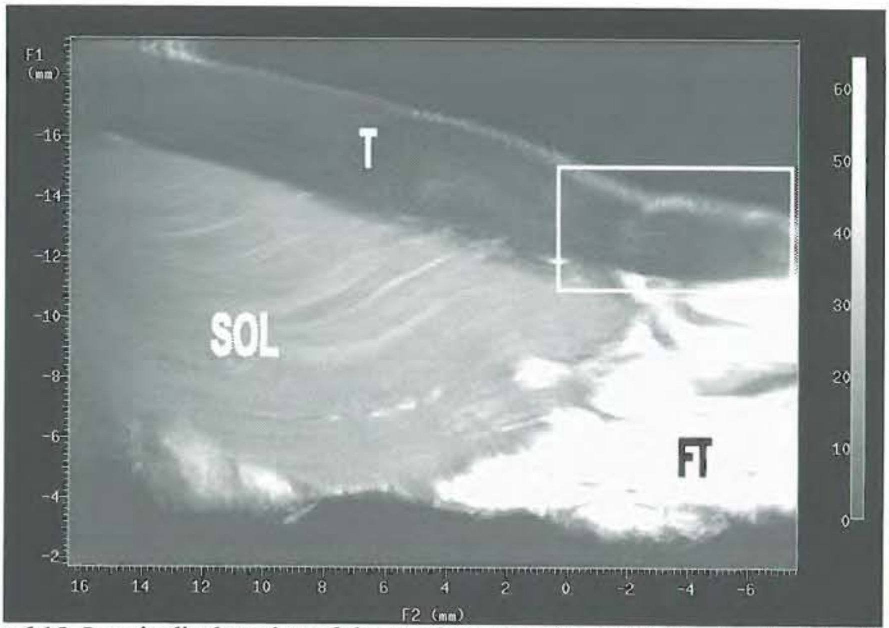


Figure 6.15. Longitudinal section of the specimen (see fig. 6.14.) showing the blending of the muscle belly of the soleus muscle (SOL) with the Achilles tendon (T). The hyper-reflective mass anterior of the Achilles tendon is the fat tissue (FT) that fills up the space between tendon and ankle joint. The indicated (white square) is the area scanned in figure 6.17. Orientation: under (anterior); above (posterior); left (proximal); right (distal).

Figure 6.16. Transversal slice in the same area as fig. 6.15. (see specimen in fig. 6.14.) showing the relative volumes of the Achilles tendon (T) and the muscle belly of the soleus muscle (SOL). Orientation: left corner, down (posterior); left corner, up (medial); right corner, up (anterior); right corner, down (lateral).

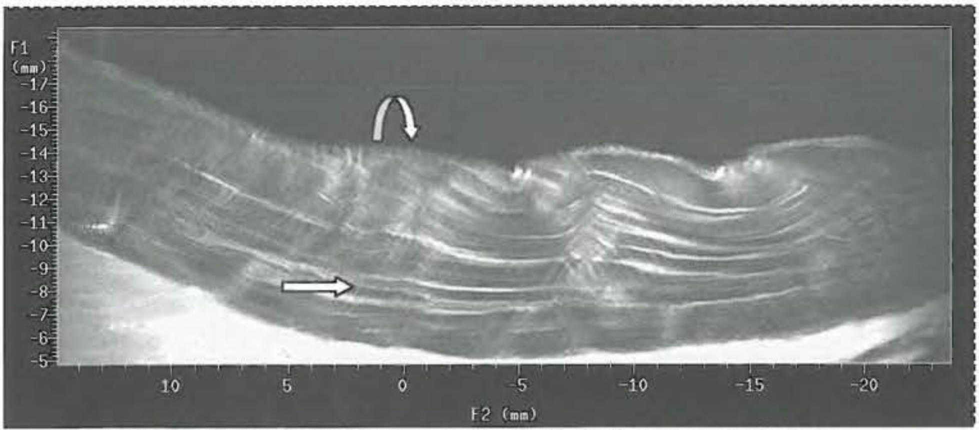


Figure 6.17. Detail of the Achilles tendon that is indicated on figure 6.15. Superficial tendon fibers have a coiling component (see curved arrow), while the deeper fibers are straight (see straight arrow).

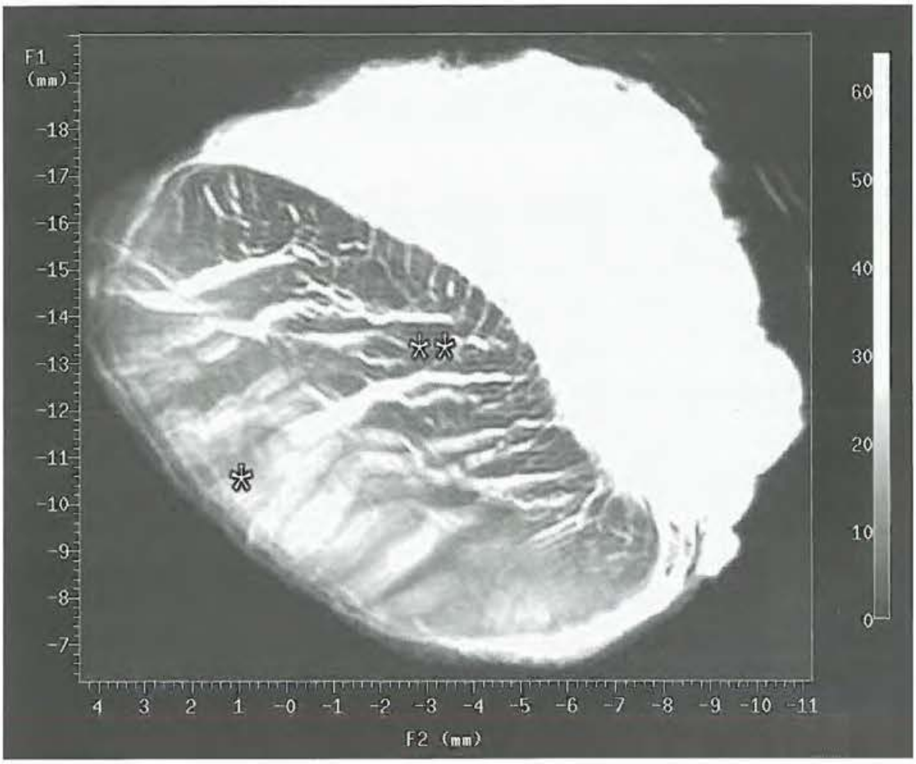


Figure 6.18. Transversal slice in the same area as in fig. 6.17. (see specimen fig. 6.14.). The superficial fibers (see single asterisk) have a fuzzy aspect, partially caused by the coiling of the fibers and partially caused by an artifact (the superficial border of the tendon is much sharper than the outline of the superficial fibers). The deeper fibers (see double asterisks) are perpendicular to the transversal plane and show a more clear outline. Orientation: see figure 6.16.

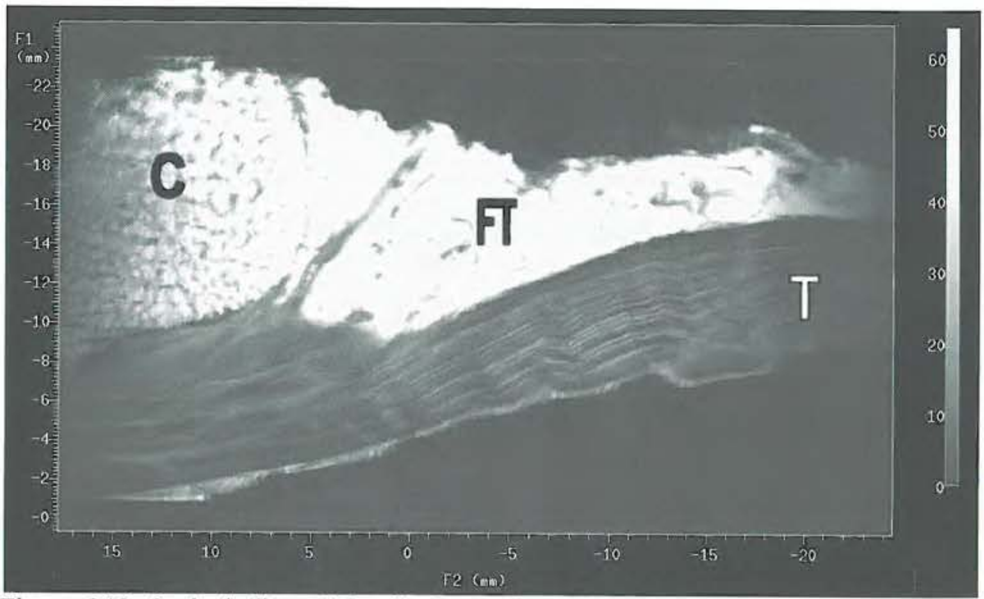


Figure 6.19. Sagittal slice of the distal part (see fig. 6.14.) of the Achilles tendon (T) showing straight tendon fibers. The coiling of the superficial fibers is absent. Calcaneal bone (C) and fat tissue (FT) are hyper-reflective. Orientation: posterior (down); anterior (up); distal (left); proximal (right).

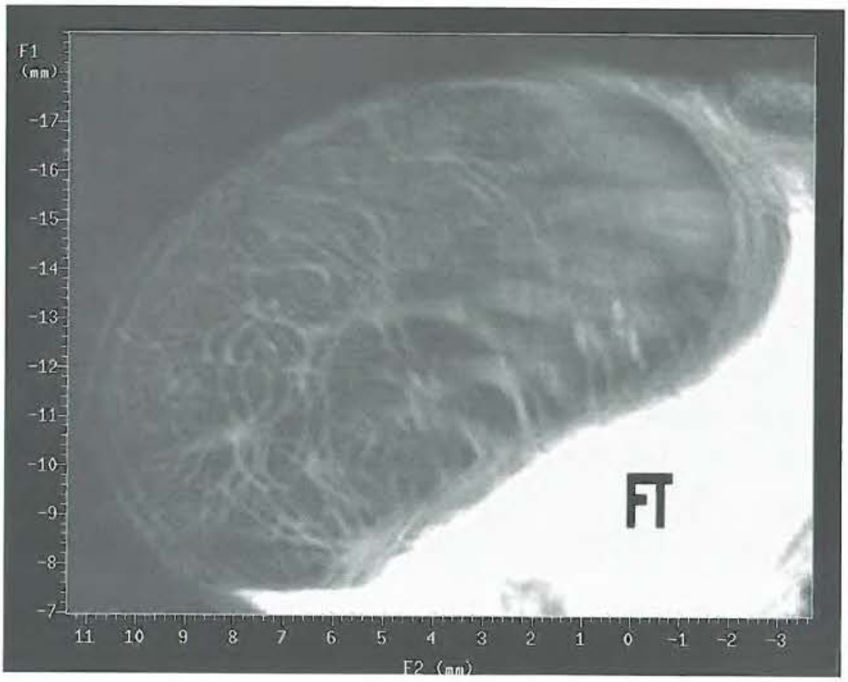


Figure 6.20. Transversal slice in the same distal area of fig. 6.19. (see specimen in fig. 6.14.). There is a more clear outline of the Achilles tendon because the straight tendon fibers become relatively more important. FT: fat tissue.

The direction of the fibers of the soleus muscle at their insertion at the Achilles tendon is seen in fig. 6.15. The tendon fibers are not in line with the muscular fibers, but they are attached to them under an angle. The mass of the tendon does not increase in a distal direction during the insertion of the soleus muscle. A transversal slice (fig. 6.16.) in the same area shows the volumes of the soleus attachment and of the gastrocnemical part of the Achilles tendon relative to each other.

Because the tendomysium and the surrounding fat tissue have a high signal intensity, the direction of the tendon fiber bundles can be followed. On a sagittal slice from a proximal area (fig. 6.17.) it is seen that the superficial tendon fiber bundles have a coiling component, while the deeper fibers are straight. Total spiraling of the total tendon can not be indicated.

On the transversal slice (fig. 6.18.) from this proximal area it is seen that the superficial fibers are coiling (fuzzy aspect) while the deeper fibers (clear outline) are perpendicular to the transversal plane.

In the distal area of the Achilles tendon the amount of coiling fibers decreases as seen on the sagittal image (fig. 6.19.) and on the transversal image (fig. 6.20.). The straight fibers become relatively more obvious.

It seems that in the proximal part of the Achilles tendon the superficial tendon fibers cover in a spiraling way the deeper straight tendon fibers. This is conform with descriptions in 19th century anatomical textbooks cited by Parsons (1894) that state that the fibers of the medial head of the gastrocnemius pass obliquely downwards and outwards over the rest of the tendon, to be inserted on its outer (i.e. lateral) side.

6.3.2. The attachment of the Achilles tendon: the Achilleo-Calcaneal-Plantar (ACP) Complex

The attachment of the Achilles tendon on the tuber of the calcaneal bone is very dense. The insertion forms macroscopically the surrounding of the calcaneal tuber but in the MRI image of this region (fig. 6.21.) a different signal intensity between bone mass and tendon is seen. Between the clearly defined areas of the Achilles tendon, and that of the bone mass, a very dense line of about 1 mm is seen.

Chao et al. (1997) studied the Achilles tendon insertion anatomically in order to outline this insertion on the calcaneal bone. They did a dissection of the Achilles tendon and its insertion in seventeen adult fresh-frozen below knee amputation cadaver specimens. The insertion site was immediately outlined with waterproof paint. To determine the length of insertion on lateral radiographs, lead beads were placed on the most superior and most inferior aspects of the insertion. All specimens showed that the tendon terminated at the medial and lateral bone borders of the calcaneus without significant extension around its medial or lateral wall. All specimens revealed a greater distance of insertion on the medial side of the calcaneus than on its lateral side. The averaged proximo-distal length of Achilles tendon insertion on the calcaneal tuber in their study was approximately 2 cm.

This is in contrast with the idea of the achilleo-calcaneal-plantar (ACP) system. French and Spanish research groups defined this system from embryological, anatomic, phylogenetic, kinematic and histological viewpoints (Bonnel and Claustre 1985; DePalma et al. 1985; Domingo-Pech et al. 1985; Husson et al. 1985; Viladot 1985; Sanz-Hospital et al. 1997). The ACP system is defined as a anatomical entity that is composed of the gastrocnemius, plantaris and soleus muscles plus the Achilles tendon; the posteroinferior surface of the calcaneus; and the middle strand of the plantar aponeurosis and some of the short muscles of the foot (adductor hallucis, flexor hallucis brevis and flexor digitorum brevis).

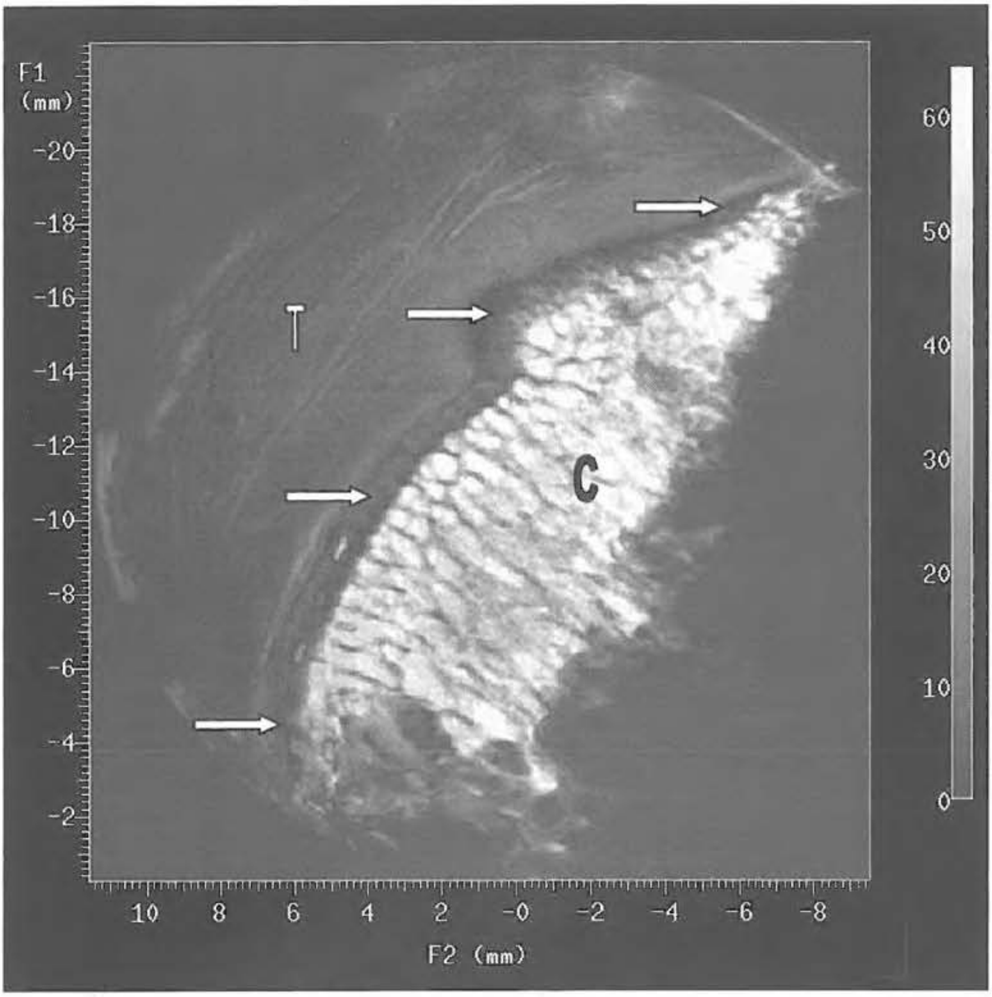


Figure 6.21. Transversal slice through the specimen (see fig. 6.14.) at the level of the attachment of the Achilles tendon (T) at the calcaneal bone (C). A different signal intensity between bone mass and tendon is seen. A very dense line (see arrows) of about 1 mm is seen between tendon and bone mass.

When an individual is walking, the muscles that constitute this system contract simultaneously; this synchronized action has been confirmed electromyographically (Viladot 1985). This also speaks in favor of the ACP system as a functional unit.

Sarrafian (1983), Waller & Maddalo (1986) and Snow et al. (1995) described in their works the continuity between the Achilles tendon fibers and the plantar aponeurosis. Snow and co-workers (1995) agree that the fibers of the Achilles tendon are continuous with the plantar aponeurosis in fetal and neonatal feet but refer to a decrease in this continuity with age.

In the fourteen-week-old fetus, histological studies of sections at the level of the calcaneus demonstrate the continuity of the Achilles tendon with the short muscles of the foot (DePalma et al. 1985; Viladot 1985). In fetal material, Parsons (1894) could distinctly trace the soleus tendon from the rest of the Achilles tendon and saw that the tendon continued in the flexor digitorum brevis in the sole.

In our study of a nineteen-week-old fetus the continuity between Achilles tendon and plantar aponeurosis is shown (figs. 6.22.-6.24.). This continuity is more clear at the medial side of the calcaneus than at the lateral side of the calcaneus where Achilles tendon and calcaneal bone are macroscopically harder to distinguish (see fig. 6.24.). In this nineteen-week-old fetus it was not possible to trace the soleus tendon from the rest of the Achilles tendon as was done by Parsons (1872).

In the child, the Achilles tendon passes behind and inferior to the tuber of the calcaneus and is continuous with the plantar aponeurosis and the intrinsic muscles of the foot. The posterior-inferior trabecular system is not yet present but will be formed with the fusion of the ossification center to the rest of the calcaneus at the age of 17 years. It is evident that this ossification center acts as a sesamoid bone between the Achilles tendon, aponeurosis and the short muscles of the ACP-system (Snow et al. 1995; Waller & Maddalo 1986).

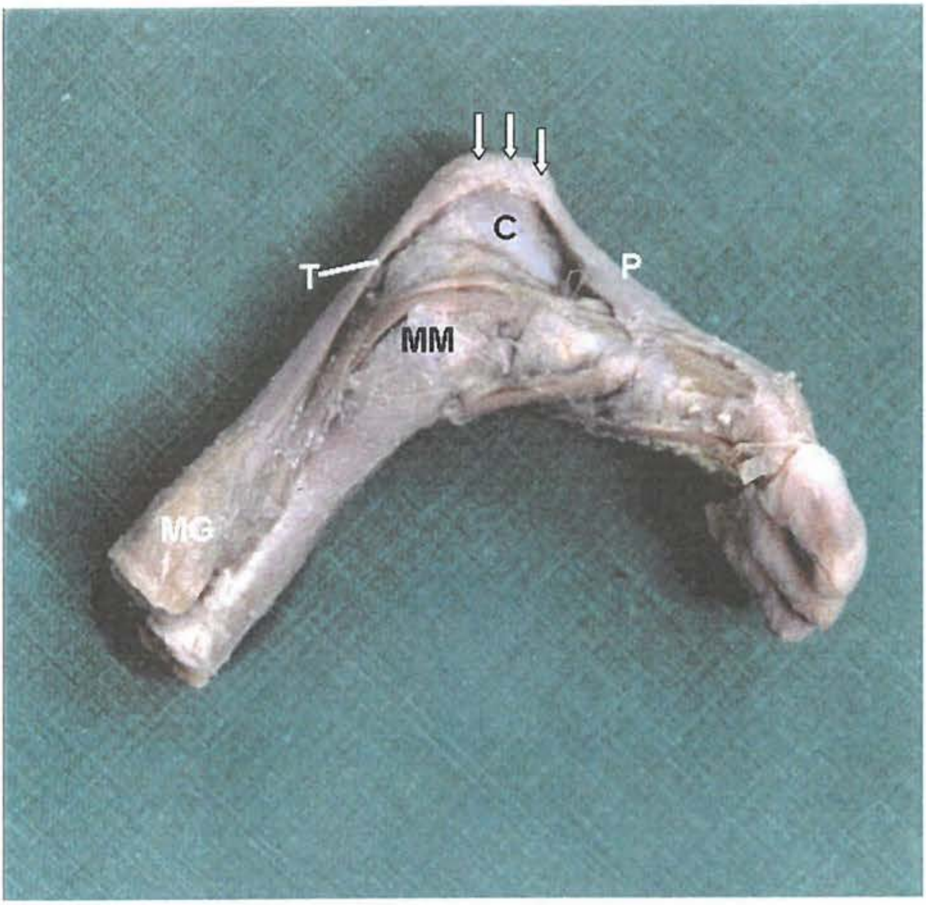
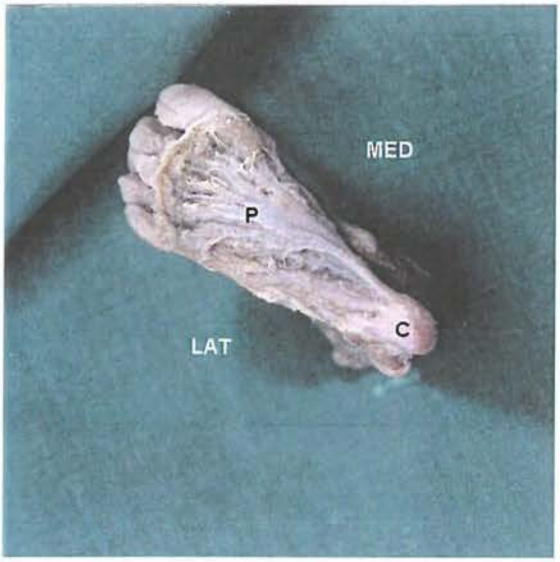


Figure 6.22. Under knee amputation of a nineteen-weeks old fetus (see fig. 6.3. for real size) showing the continuity (see arrows) of the Achilles tendon (T) and the plantar fascia (P) in the sole of the foot. Posterior tibial neurovascular bundle has been removed. C: calcaneus; MM: medial malleolus; MG: medial head of the gastrocnemius muscle.



Figures 6.23. and 6.24. Two different views on the specimen of fig. 6.22. to show the continuity of Achilles tendon (T) and plantar fascia (P). This continuity is more clear at the medial side (MED) than at the lateral side (LAT) of the calcaneus (C).

The dense line of 1 mm seen in figure 6.21. is possibly the anatomical structure caused by the attachment of the Achilles tendon to the calcaneal tuber bone mass which starts during fetal development and completes during childhood. The MRI findings of the present study strongly support the concept of the ACP system.

6.4. Conclusions

- The described extensions of the origins of the gastrocnemius muscle give the muscle the opportunity to transpose forces to nearby muscles. The biomechanical and neurophysiological importance of those origins has to be studied.
- Total spiraling of the Achilles tendon could not be indicated with MRI. Biomechanical advantages of the spiraling as shown in the presented kinematic model could not be supported by our anatomical findings.
- The spiraling of the bundles of tendon fibers could only be shown in the proximal superficial part of the Achilles tendon. The resolution of the images is not strong enough to detect the tendon fibers within the bundles. Spiraling of the fibers themselves however, and the consecutive biomechanical advantage of storing potential energy in the Achilles tendon could be confirmed to a certain extent on the ground of our MRI study.

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SUMMARY

Cutaneomuscular reflexes are reflexes seen in muscles after pure cutaneous stimulation. In this thesis some neurophysiological and anatomical aspects of those cutaneomuscular reflexes in some human lower leg muscles are studied.

A reflex arc can be divided into an afferent (input) part, a central modulation part and an efferent (output) part.

The influence of altering the afferent information was studied during the limping experiment and the experiment with ring stimulation of the second and fourth toe.

During the limping experiment, the range of motion and also the afferent information of the studied leg was diminished. The results of this experiment support the idea that sensory receptor discharge does not play an important role for the modulation of cutaneomuscular reflexes.

In the experiment with ring stimulation of the second and fourth toe this technique was executed during a continuous movement. The same experiments during different steady state tasks had been done earlier, but ring stimulation during a continuous movement was a new challenge. The phase-dependent modulation of the cutaneomuscular reflexes was also seen after this technique.

During this experiment the importance of the stimulation site was also studied. The resulting cutaneomuscular reflexes were discussed and compared with cutaneomuscular reflexes after surface electrode stimulation at comparable stimulation sites and at different stimulation sites.

It is concluded that the site of stimulation is very important for the modulation of the cutaneomuscular reflexes. It is suggested that reflexes seen after stimulation of cutaneous

nerves at the ankle show a mixed pattern of reflexes seen after stimulation of toe and sole afferents.

The central modulation of the reflexes was studied in all experiments. The well-known phase-dependent modulation was seen in all experiments. The cause of this reflex modulation was studied, and the idea that this modulation was not sensori-afferent related could be supported with the limping experiment.

The task-dependent modulation was studied very precisely. It was seen that the stance-swing facilitation of the tibialis anterior muscle was locomotion related but not task related. The end swing modulation at touch down, however, was strongly task related. A significant difference between cutaneomuscular reflexes during walking (suppression), running and hopping (no reflex), and limping (facilitation) was seen. The idea of a swing assisting facilitation was supported by this study of the cutaneomuscular reflexes of the tibialis anterior muscle during walking, running, limping and hopping.

The efferent part of the reflex arc of the cutaneomuscular reflexes was studied in the two heads of the gastrocnemius muscle. The gastrocnemius muscle is a flexor of ankle and knee. After sural stimulation (cutaneous innervation of the lateral side of the sole) the reflex in the two muscular heads differ at the ipsilateral side while contralaterally both heads get facilitated. Ipsilaterally the medial head gets facilitated while the lateral head gets suppressed.

After ring stimulation of the second and fourth toe, however, both heads get suppressed at the ipsilateral side.

This difference in reflex modulation supports the idea that the resulting muscle activity avoids destabilizing stumbling and suggests an activity of the gastrocnemius muscle in non-sagittal planes.

In the last chapter the anatomy of the gastrocnemius muscle was studied. The aim of this study was to detect anatomical data that could support the idea of the functioning of the gastrocnemius muscle in non-sagittal planes. Beside a macroscopic study of adult and fetal specimens a microscopic MRI study of the Achilles tendon of an adult was done. A simplified model based on the Achilles tendon in the opossum, a predecessor of the primates, was made to show how crossing of fibers can influence movement in the frontal plane.

In this study some new aspects of cutaneomuscular reflexes are described, but there is still a lot of fundamental work to do to understand this kind of reflexes and there neurophysiological function. A good understanding of these reflexes in the future can maybe provide us some clinical benefits for the revalidation of spinal cord injuries and for the prevention of falling of elderly people.

SAMENVATTING

Huid-spier-reflexen (HSR) zijn spierreflexen welke ontstaan na huidstimulatie. In deze thesis werden enkele neurofysiologische and anatomische aspekten van deze reflexen bestudeerd in enkele spieren van het onderste lidmaat. Een reflexboog kan opgedeeld worden in drie delen: een afferent deel (input), een centraal modulatie deel, en een efferent deel (output).

De invloed van wijziging van de afferente informatie werd bestudeerd tijdens twee experimenten, namelijk het 'limping'experiment waar de proefpersonen wandelden met een stijf been, en het eperiment waar de afferent stimulatie plaatsvond met ringelectrodes rond de tweede en vierde teen.

Het doel van het 'limping' experiment was de invloed van reductie van beweging en afferente input op de HSR te bestuderen. Het resultaat van dit experiment ondersteunt het idee dat de prikkeling van afferente receptoren geen belangrijke rol speelt in het patroon van de modulatie van de HSR.

In het experiment waar ringstimulatie van de tweede en vierde teen werd uitgevoerd, werd deze techniek op een continue beweging toegepast. Dit was een nieuwe uitdaging daar gelijkaardige experimenten enkel werden uitgevoerd tijdens verschillend stilstaande taken. De fase-afhankelijkheid van HSR werd ook hier vastgesteld.

Gedurende hetzelfde experiment werd ook de invloed van de plaats van stimulatie op de resulterende reflex aktiviteit bestudeerd. Deze reflexen werden bestudeerd en vergeleken met gelijkaardige reflexen na huidstimulatie met oppervlakte-electroden op vergelijkbare en andere stimulatieplaatsen.

Er werd besloten dat de plaats van stimulatie zeer belangrijk is voor de reflexmodulatie. Er werd tevens vooropgesteld dat HSR na stimulatie van de huidafferenten ter hoogte van de enkel een gemengd patroon vertonen van reflexen verkregen na stimulatie van huidafferenten afkomstig van respectievelijk tenen en voetzool.

De centrale modulatie van de HSR werd in alle experimenten bestudeerd. De reeds uitvoerig bestudeerde fase-afhankelijkheid werd in alle experimenten gezien. De oorzaak van deze reflex werd bestudeerd en het idee dat deze modulatie niet afferent bepaald is, kon worden ondersteund tijdens het 'limping' experiment.

De taak-afhankelijkheid van de HSR werd uitvoerig bestudeerd. Er werd geconstateerd dat de facilitatie van de HSR aan het begin van de swingfase locomotie-gebonden was, doch niet taak-afhankelijk. De HSR op het eind van de swingfase daarentegen was sterk taak-afhankelijk. In deze fase van de stapcyclus werd een significant verschil tussen stappen (suppressie), lopen en huppelen (geen toegevoegde reflexaktiviteit), en 'limping' (facilitatie) gezien. De hypothese van de 'swing assisterende facilitatie' werd ondersteund door deze studie van HSR in de m. tibialis anterior gedurende stappen, lopen, huppelen en 'limping'.

Het motorische gedeelte van de reflexboog van HSR werd bestudeerd in de twee spierkoppen van de gastrocnemiusspier. De gastrocnemius is een flexor van de enkel. Na stimulatie van de nervus suralis (huidinnervatie van de laterale zijde van de voetzool) verschillen de HSR in beide spierkoppen aan de ipsilaterale zijde, terwijl ze gelijkaardig zijn aan de contralaterale zijde (facilitatie). Aan de ipsilaterale zijde word de mediale spierkop gefaciliteerd, terwijl de spieraktiviteit in de laterale kop onderdrukt wordt. Daarentegen, na ringstimulatie van de tweede en vierde teen wordt de aktiviteit van beide spierkoppen aan de ipsilaterale zijde onderdrukt.

Dit verschil in reflexmodulatie in beide koppen ondersteund het idee dat HSR destabilizerende stoornissen in het gangpatroon trachten op te vangen. Aktiviteit van de gastrocnemiusspier buiten het sagittale vlak lijkt dus zeer waarschijnlijk.

In het laatste hoofdstuk werd de anatomie van de gastrocnemiusspier bestudeerd. Het doel van deze studie was anatomische gegevens over deze spier te verzamelen die een aktiviteit buiten het sagittale vlak kunnen verklaren. Naast een macroscopische studie van volwassen en foetale anatomische preparaten, werd een microscopische NMR-studie van een volwassen Achillespees uitgevoerd. Een zeer simpel model gebaseerd op de anatomie van de Achillespees van de opossum als voorloper van de primaten werd beschreven om aan te tonen hoe kruisen van vezels of pezen bewegingen in het frontale vlak kunnen beïnvloeden.

In deze studie werden enkele nieuwe aspekten van HSR beschreven, maar er is nog zeer veel studiewerk te verrichten om de betekenis en de aard van deze reflexen te begrijpen. Een goed begrip van deze reflexen kan ons misschien in de toekomst veel klinische voordelen opleveren in de behandeling van patiënten met ruggenmergletsels en in de preventie van vallen van bejaarden.

De eerstvolgende stap in dit onderzoek zal het verder uitdiepen zijn van het verband tussen topografie van stimulatie en de verkregen HSR in de gastrocnemiusspier.

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Stephan.

CURRICULUM VITAE AND BIBLIOGRAPHY

Stephan Hauglustaine werd geboren op 22 december 1968 te Hasselt. In 1986 behaalde hij het diploma middelbaar onderwijs Wetenschappelijke A aan het St.-Jozefsinstituut te Bokrijk. In 1986 startte hij de opleiding Geneeskunde aan het LUC, om met deze basis in 1993 zijn doctoraatsjaren aan het UIA te beëindigen. Aansluitend startte hij in november 1993 een academisch assistentschap aan het LUC op de afdeling Medische Basiswetenschappen, vakgroep Morfologie/Anatomie.

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