Phase Modulation of the Short-Latency Crossed Spinal Response in the Human Soleus Muscle

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Stubbs PW, Nielsen JF, Sinkjær T, Mrachacz-Kersting N. Phase modulation of the short-latency crossed spinal response in the human soleus muscle. J Neurophysiol 105: 503–511, 2011. First published November 24, 2010; doi:10.1152/jn.00786.2010. Short-latency spinal mediated interlimb reflex pathways were recently reported between the left and right soleus muscles in the human lower-limb during sitting. The aim of the current study was to establish if these pathways were observed during a functional motor task such as human gait and modulated by the gait cycle phase and/or electrical stimulation intensity. The second aim was to elucidate on the afferents involved. Two interventions were investigated. First was ipsilateral tibial nerve (iTN) stimulation at motor threshold (MT), 35% of the maximal peak-to-peak M-wave (M-Max) and 85% M-Max (85M-Max) with stimuli applied at 60, 70, 80, 90, and 100% of the gait cycle of the ipsilateral leg. Second was ipsilateral sural nerve (SuN) and medial plantar nerve (MpN) stimulation at 1, 2, and 3 perceptual threshold at 90% of the gait cycle. The root mean squared (RMS) of the contralateral soleus (cSOL) responses were analyzed in a time window, 40–55 ms (or 45–60 ms for subjects >50 y/o) following iTN stimulation. The most consistent responses occurred at 90 and 100% of the gait cycle at higher stimulation intensities of the iTN. Significantly inhibitory responses (P = 0.006) were reported at 60 versus 80% (P = 0.03), 90% (P = 0.006), and 100% (P = 0.002) and 70 versus 90% (P = 0.02) and 100% (P = 0.009) of the gait cycle at 85M-Max. The responses became more inhibitory with increasing stimulation intensities at 80% (P = 0.01), 90% (P = 0.001), and 100% (P = 0.004) of the gait cycle. Stimulation of the MpN and SuN at all stimulation intensities demonstrated no short-latency responses. Therefore, it is unlikely that afferents within these nerves contribute to the response. This is the first study to show short-latency spinal mediated responses in the cSOL following iTN stimulation, during walking. It provides evidence for a new spinal pathway contributing to motor control and demonstrates that the response likely has functional relevance.

INTRODUCTION

In the human lower limb, evidence for spinally mediated interlimb reflex pathways have been reported in a number of studies from cutaneous (Burke et al. 1991; Delwaide et al. 1981; Duyssens et al. 1991) and possibly muscular (Bachmann et al. 2008; Berger et al. 1984; Dietz et al. 1986, 1989) afferents. Although the onset latencies proposed from ipsilateral muscle afferents to the contralateral muscles ranged from 65 to 112 ms, it is possible that these responses were mediated by cutaneous afferents or through mechanical interactions due to the displacement of the contralateral leg. As ipsilateral muscular responses reported in the lower limb of >79 ms maybe partially mediated by supraspinal pathways (Petersen et al. 1998), it is possible that the aforementioned studies have either contralateral muscle responses that are supraspinally mediated or contralateral responses that are not generated by the ipsilateral muscle afferents. A recent study (Stubbs and Mrachacz-Kersting 2009) reported contralateral soleus (cSOL) responses, 37–41 ms following ipsilateral tibial nerve (iTN) stimulation. In Stubbs and Mrachacz-Kersting (2009), it was shown that cutaneous afferents were an unlikely source of the observed responses and demonstrated, through the application of ischemia to the ipsilateral thigh, that the crossed response was in part mediated by group I muscle afferents of the ipsilateral leg. These findings suggest that crossed spinal muscular connections are present in the human.

In the cat, crossed spinal connections have been observed from group I (Baxendale and Rosenberg 1976, 1977; Holmquist 1961; Jankowska and Noga 1990; Jankowska 2005; Perl 1958), group II (Arya et al. 1991; Edgley et al. 2003; Jankowska et al. 1990, 2005) and cutaneous afferents of the sural, saphenous and superficial peroneal nerves (Edgley and Angelopoulos 2006). These have also been observed from most muscle groups of one leg to most muscle groups of the contralateral leg. The crossed spinal interneurons, linking the two sides of the body, have been identified in the dorsal horn of lamina IV, V (Matsushita 1970), and VIII (Edgley et al. 2003; Jankowska and Noga 1990; Matsushita 1970) within the spinal cord of the anesthetized cat. These connections are also active during walking (Frigon and Rossignol 2008). Frigon and Rossignol (2008) observed an inhibition followed by facilitation in the contralateral triceps surae complex following ipsilateral inferior tibial nerve stimulation and the authors propose that these connections enable electromyography (EMG) synchronization between the muscles of the legs. Further, Arya et al. (1991) observed a short-latency inhibition in the nonlocomotor cat and suggest that these short-latency inhibitory mechanisms may signal extension in the contralateral limb while the ipsilateral limb is switching from extension to flexion. In addition, these short-latency pathways may provide interlimb communication when contralateral limb extension would be inappropriate (Arya et al. 1991).

Although studies in the cat have reported crossed connections from the ipsilateral leg to the contralateral leg during walking, the short-latency response observed by Stubbs and Mrachacz-Kersting (2009) has not been investigated during more functional tasks in the human. The first aim of this study...
was to observe if these short-latency inhibitory responses were observed during gait. The second aim was to observe if these responses were modified by the phase of the gait cycle and/or electrical stimulation intensity. The third aim was to investigate if cutaneous afferents of the sural nerve (SuN) or medial plantar nerve (MpN) contribute to the response.

**Methods**

**Subjects**

A total of 26 subjects [11 males; mean age: 34.5 ± 2.8 (SE) yr], participated in this study. Twenty-eight experimental sessions were conducted. At the time of the study, all subjects were free of any known physical or neurological disorders and provided written informed consent to participate in the study. Approval was obtained from the Scientific Ethics Committee of Mid-Jutland and conformed to the standards of the Declaration of Helsinki.

**Apparatus and instrumentation**

Surface electrodes (20 mm Blue Sensor Ag/AgCl, AMBU A/S, Denmark) were used to record the EMG activity of the left and right soleus muscles (iSOL and cSOL) for all aspects of the experiments. The electrodes were placed in accordance with the recommendations of Cram et al. (1998). Electrical stimulation was administered by an “isolated stimulator (Noxitest IES 230).” Surface stimulating electrodes PALs Platinum round electrode, Model No. 879100, 3.2 cm diam, Axelgaard Man (cathode for experiment 1 and both stimulation electrodes for experiment 2) and PALs Platinum rectangular electrode, Model No. 895340, 5 × 9 cm, Axelgaard Man (anode for experiment 1) were used for electrical stimulation. A force sensor was attached to the left heel of the subjects to indicate heel strike. All data were sampled at a frequency of 4 kHz. The EMG signals were amplified and band-pass filtered at 10 Hz to 1 kHz.

**General experimental setup**

For both experiments, the subjects walked at 3.5 km h⁻¹. Prior to testing, the subjects walked for five minutes to become accustomed to the walking speed. Following this, 30 steps were recorded to establish the nonstimulated walking profile of the subject. From the walking profile, 60, 70, 80, 90, and 100% (experiment 1) and 90% of the gait cycle (experiment 2) of the ipsilateral leg were calculated. The gait cycle percentage was defined as one ipsilateral leg heel contact (corresponding to 0% of the gait cycle) to the next ipsilateral leg heel contact (corresponding to 100% of the gait cycle). These percentages of the gait cycle were chosen to explore the interactions during the swing phase and swing to stance transition of the stimulated leg. In addition, as the cSOL is active, a facilitation or inhibition may be observed in the cSOL. For both experiments, predefined stimuli were administered randomly every three to five steps. The subjects were allowed to rest between each gait cycle phase (experiment 1) and between experiments (experiment 2) and were able to pause the experiment at any stage if they reported fatigue. If the subjects began to sway from their initial stride time (±50 ms), they were asked to increase or decrease their stride time. For both experiments, data were analyzed off-line.

**Experiment 1**

**STIMULATION OF THE IPSILATERAL TIBIAL NERVE**

Twenty-one subjects (mean age: 36.4 ± 3.3 yr) partook in this experiment. Subjects were stimulated at MT, 35M-Max, and 85M-Max (including a “no stimulation” condition) at 60% (sometimes up to 65% if subjects demonstrated no cSOL EMG activity at 60% of the gait cycle; n = 13), 70% (n = 14), 80% (n = 16), 90% (n = 16), and 100% (n = 13) of the gait cycle. Stubbs and Mrachacz-Kersting (2009) demonstrated that during sitting, the inhibitory responses became more prominent with increasing stimulation intensities. Therefore, to observe the modulation of the response with stimulation intensity, the three incremental stimulation intensities were chosen.

**Protocol.** Prior to testing, the stimulating electrodes were attached while the subject was standing. The electrodes were attached to stimulate to the tibial nerve of the left leg (iTN). The cathode was affixed to the popliteal fossa, and the anode was affixed to the anterior aspect of the knee at the level of the patella. The cathode was pressed into the skin with a rod affixed to the distal thigh to optimize the observed M-wave in the iSOL EMG trace. If this was not observed, the cathode and rod were removed and reattached to a different site in the popliteal fossa. This continued until an optimal position had been located. For each gait cycle percentage, the stimulation intensity evoking MT, 35M-Max, and 85M-Max was established while the subjects walked at the testing velocity. Single rectangular stimuli, 1 ms duration, were delivered every three to five steps. The stimulus intensity was increased in 5 mA increments until an M-wave was observed. When the M-wave was observed for three trials, at the same stimulation intensity, the stimulation intensity was reduced by 1 mA. Again three trials were observed. This process continued until no M-wave was observed. The stimulation intensity preceding this intensity was deemed the MT. Following this, the M-Max was established. The stimulation intensity was increased in 5 mA increments. At each set of three trials, the preceding M-wave peak-to-peak amplitude was compared with the new M-wave peak-to-peak amplitude. Once the preceding M-wave peak-to-peak amplitude and new M-wave had plateaued for three trials, the electrical stimulus was decreased to the previous stimulation intensity and labeled the M-Max. From the peak-to-peak M-wave at M-Max, 35M-Max and 85M-Max were calculated. The electrical stimulation intensities used to elicit MT, 35M-Max, and 85M-Max (including a no stimulation condition) were entered into and controlled by a computer program. The output of this delivered random stimuli at each of the four stimulation intensities every three to five steps. A total of 30–40 recordings for each stimulation intensity were collected. In addition, the iSOL peak-to-peak M-wave was monitored on-line to ensure consistency throughout testing for each phase of the gait cycle. The process described in the preceding text was repeated for each percentage of the gait cycle tested in the testing session.

Seven subjects were stimulated at 10 even incremental stimulation intensities ranging from no stimulation to M-max at 90% of the gait cycle. The purpose of this was to construct an input/output curve and demonstrate the modulation of the cSOL response as a function of the iSOL peak-to-peak M-wave.

**Experiment 2**

**STIMULATION OF THE SUN AND MPN AT 90% OF THE GAIT CYCLE.** Seven subjects (mean age: 31.6 ± 4.8 yr) partook in this experiment. All subjects participated in both protocols in which the ipsilateral SuN and MpN were stimulated at 90% of the gait cycle. The SuN and MpN adjoin to the tibial nerve distal to the stimulation site at the popliteal fossa and were stimulated to exclude these afferents as a source of the cSOL short-latency response.

**Protocol.** The stimulating electrodes were attached while the subject was standing. For MpN stimulation, stimulating electrodes were attached posterior and inferior to the medial malleolus and for SuN stimulation were attached posterior and inferior to the lateral malleolus in the notch between the lateral malleolus and calcaneal tendon. Three consecutive stimuli, 1 ms duration, at an interval of 3 ms (used in Nielsen et al. 1997), were applied at an intensity of 5 mA. Subjects were asked to describe the sensation, and if the desired sensation was not reported, the electrodes were moved until this was felt. The desired sensation for MpN stimulation was a triply spreading sensation toward the first and second metatarsal on the...
plantar side of the foot and for SuN stimulation was a sensation on the lateral side of the foot toward the fifth metatarsal. For testing, subjects were stimulated at an intensity of 1×, 2×, and 3× PT. The electrical stimulation intensities (including a no stimulation condition) were presented randomly every three to five steps for a total of 45–60 recordings per stimulation intensity.

**Measurements recorded**

For experiment 1, the magnitude of the response was calculated as a root mean squared value (RMS) of the cSOL, 40–55 ms following iTN stimulation for subjects <50 yr and 45–60 ms for subjects >50 yr. This was compared with the control step RMS over the same time interval. This time frame has been chosen based on the results in sitting. Through various pilot experiments when the iTN was stimulated at 75–85% M-Max and the cSOL precontracted to 10% of the maximum voluntary contraction, 37/40 subjects demonstrated a time of minimum within these time windows. In the current study, as not all subjects displayed a response for all stimulation intensities and all phases of the gait cycle, an RMS measurement was more appropriate than the minimum value.

For experiment 2, the RMS of the cSOL over the time windows of 48–63 ms (for subjects <50 yr) and 53–68 ms (for subjects >50 yr) following ipsilateral SuN and MpN stimulation was calculated. This was compared with the control step RMS over the same time intervals. A delay of 8 ms was added to the iTN response window onset as the MpN and SuN were stimulated at the ankle and the iTN was stimulated at the popliteal fossa. Assuming the speed of the low threshold (Aβ) cutaneous afferents range from 45 to 62 ms⁻¹ (Willer et al. 1978) with a tibial leg length of ~0.4 m, a delay of ~8 ms would be expected when compared with electrical stimulation applied at the popliteal fossa.

**Statistical analysis**

For experiment 1, one-way ANOVA were performed for each electrical stimulation intensity with the response variable; magnitude of response, and factor variables; 60, 70, 80, 90, and 100% of the gait cycle. Repeated-measures ANOVA were performed for each phase of the gait cycle investigated with the response variable; magnitude of response, and within factor variables; MT, 35M-Max, and 85M-Max. The onset and duration of facilitatory/inhibitory responses were assessed using visual inspection. These were defined as an increase/ decrease in the cSOL EMG activity of >10 ms in duration, when compared with the control step EMG, between a time frame of 30–60 ms (subjects <50 yr) and 35–65 ms (subjects >50 yr) following iTN stimulation. One-way ANOVA compared the response variable: onset/duration of response and factor variables; phase (60, 70, 80, 90, and 100% of the gait cycle) and stimulation intensity (MT, 35M-Max, and 85M-Max).

For experiment 2, one-way ANOVA were performed with the response variable; magnitude of the response and within factor variables; SuN and MpN stimulated at 1×, 2×, and 3× PT and iTN stimulation at either 85M-Max, 35M-Max, or MT.

For both experiments 1 and 2, when significant differences were identified, the Fishers LSD multiple comparisons test was performed (post hoc) to establish the location of the differences.

**RESULTS**

**cSOL response following iTN stimulation**

**PHASE OF THE GAIT CYCLE.** Figure 1 (A–F) displays cSOL EMG traces with an average of 30 recordings for one subject following stimulation of the iTN at 85M-Max of the iSOL. Figure 1A displays a normal cSOL EMG trace over the entire gait. The arrows below Fig. 1A indicate heel contact. Figure 1, B–F, displays (with truncated axis) a 100 ms window of the cSOL following iTN stimulation for 63% (Fig. 1B), 70% (C), 80% (D), 90% (E), and 100% (Fig. 1F) of the gait cycle. The vertical long dashed lines indicate electrical stimulation of the iTN (Fig. 1, A–F) and the vertical short dashed lines represent the analysis window (RMS between 40 and 55 ms as this subject was 27 yr). The black line represents the cSOL EMG with no electrical stimulus, and the gray line represents the cSOL EMG following iTN stimulation at 85M-Max. A short-latency facilitation was observed at 63% (Fig. 1B), no response was observed at 70% (Fig. 1C), and a short-latency inhibition was observed at 80% (D), 90% (E), and 100% (F) of the gait cycle. The onset of the short latency responses ranged from 37 to 43.6 ms, and the duration ranged from 20 to 30 ms. For all subjects, the average onset of the response was 39.5 ± 0.4 ms and the average duration was 24.7 ± 1.1 ms. There were no significant differences for the onset and duration of the response as any phase or stimulation intensity (P > 0.05).

The magnitude of the response was significantly different across phases of the gait cycle at iTN stimulation intensities of 85M-Max and 35M-Max (P = 0.006 and P = 0.01, respectively). Table 1 and Fig. 2 (A–C) display the means ± SE magnitude of the response as a percentage of the control step for MT (Fig. 2A), 35M-Max (B), and 85M-Max (C) for 60, 70, 80, 90, and 100% of the gait cycle. Figure 2 (A–C) indicates the location of the significant differences. At stimulation intensities of 85M-Max and 35M-Max, the inhibition becomes more prominent toward the swing to stance transition (100% of the gait cycle) of the ipsilateral leg.

**Electrical stimulation intensity**

Figure 3, A and B displays the effect of stimulation intensity on the cSOL response. Figure 3A shows (with truncated axis) the cSOL EMG trace with an average of 40 recordings for one subject for the control step (thin black line) and iTN stimulation at MT (thick black line), 35M-Max (thick light gray line), and 85M-Max (thick dark gray line) at 90% of the gait cycle. The vertical long dashed line indicates electrical stimulation of the iTN, and the vertical short dashed lines represents the analysis window 45–60 ms post iTN stimulation (as this subject was 60 yr). A short-latency inhibition was observed at 35M-Max (onset: 43 ms, duration: 41 ms) and 85M-Max (onset: 42 ms, duration: 53 ms), but no response was observed at MT. Figure 3B demonstrates the means ± SE for magnitude of the short-latency response as a percentage of the control step RMS at 90% of the gait cycle for MT (97.5 ± 1.8%), 35M-Max (93 ± 2.3%), and 85M-Max (88.8 ± 2.6%) for all subjects. Also shown are the significant differences and the level of significance.

The magnitude of the response was significantly affected by the stimulation intensity at 80% (P = 0.01), 90% (P = 0.001), and 100% (P = 0.004) of the gait cycle. Post hoc analysis demonstrated significant differences between MT and 85M-Max for 80% (P = 0.002), 90% (P = 0.003), and 100% (P = 0.01) of the gait cycle, between MT and 35M-Max for 90% (P = 0.008) and 100% (P = 0.006) of the gait cycle, and between 35M-Max and 85M-Max for 80% (P = 0.02) of the gait cycle.

Figure 4(A) displays the iSOL peak-to-peak M-wave (mV) and the cSOL RMS (in the time window of 40–55 ms as this
subject was 25 yr; μV) as a function of stimulation intensity (mA) for one subject. Figure 4B displays the mean response size ± SE of the cSOL as a percentage of the control cSOL RMS in relation to the average stimulation intensity for all subjects tested (n = 7). Figure 4, A and B, suggests that as the stimulation intensity increases the reduction in the cSOL RMS becomes more prominent when compared with the control step.

**SuN and MpN stimulation at 90% of the gait cycle**

Figure 5 (A–D) displays cSOL EMG traces with an average of 50 recordings for one subject following stimulation of the MpN (Fig. 5, A and B) and SuN (C and D) at a stimulation intensity of 3 × PT at 90% of the gait cycle. Figure 5, A and C, represents the entire gait cycle, whereas B and D represent (with truncated axis) a 190 ms time window when ipsilateral nerve stimulation occurred. The black line represents the control step and the gray line represents the stimulated step. The long dashed vertical line (Fig. 5, A–D) represents the time of ipsilateral nerve stimulation, the short dashed vertical lines (Fig. 5, B and D) represent the analysis window 48–63 ms post-stimulation.

**TABLE 1. Magnitude of the response RMS**

<table>
<thead>
<tr>
<th>Gait cycle percentage</th>
<th>Stimulation Intensity</th>
<th>MT</th>
<th>35% M-Max</th>
<th>85% M-Max</th>
</tr>
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<tbody>
<tr>
<td>60%</td>
<td></td>
<td>107.1 ± 5.1</td>
<td>106.5 ± 6.7</td>
<td>100.9 ± 4.1</td>
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<tr>
<td>70%</td>
<td></td>
<td>100.7 ± 3.2</td>
<td>96.6 ± 2.8</td>
<td>98.5 ± 2.9</td>
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<tr>
<td>80%</td>
<td></td>
<td>97.6 ± 1.9</td>
<td>96.4 ± 3.2</td>
<td>91.1 ± 2.4</td>
</tr>
<tr>
<td>90%</td>
<td></td>
<td>97.5 ± 1.8</td>
<td>93 ± 2.3</td>
<td>88.7 ± 2.6</td>
</tr>
<tr>
<td>100%</td>
<td></td>
<td>99.4 ± 5.2</td>
<td>85.6 ± 3.4</td>
<td>86.5 ± 3.6</td>
</tr>
</tbody>
</table>

Means ± SE of the magnitude of the response root mean square (RMS; in the defined time windows) as a percentage of the control RMS for 60, 70, 80, 90, and 100% of the gait cycle with the ipsilateral tibial nerve stimulated at MT, 35M-Max, and 85M-Max.
ipsilateral nerve stimulation (as this subject was 29 yr) and the arrows (below A and C) represent heel contact. No short-latency responses were observed in the cSOL following ipsilateral MpN (Fig. 5B) or SuN (Fig. 5D) stimulation at 90% of the gait cycle.

The cSOL RMS as a percentage of the control step is shown in Fig. 5E, for the time windows of 48–63 ms (for subjects <50 yr) and 53–68 ms (for subjects >50 yr) following ipsilateral nerve stimulation of the SuN and MpN at 1×, 2×, and 3× PT. As a comparison the RMS, as a percentage of the control step for the age appropriate time windows following iTN stimulation, at 85M-Max, is provided. Also indicated are the significant differences and level of significance. No short-latency responses were observed following stimulation of the SuN or MpN at any stimulation intensity.

The one-way ANOVA revealed a significant difference for the MpN, SuN, and 85M-Max (P = 0.009), and post hoc analysis revealed significant differences between 85M-Max and all MpN (P < 0.01) and SuN stimulation intensities [1× PT, 2× PT (P < 0.01) and 3× PT (P < 0.05); Fig. 5E]. No significant differences were found for the SuN, MpN versus 35M-Max or MT (P > 0.05).

The repeated-measures ANOVA revealed no significant differences comparing 1×, 2×, and 3× PT, for the MpN or SuN (P > 0.05).

**DISCUSSION**

This is the first study to demonstrate short-latency crossed spinal responses in the cSOL following iTN stimulation, during human walking. The onset latency of the cSOL responses were on average 39.5 ± 0.4 ms and are therefore too short to be mediated by supraspinal pathways (see Petersen et al. 1998). The responses differed depending on the electrical stimulation intensity and the phase of the gait cycle in which iTN stimulation was applied. Crossed inhibitory responses were predominantly observed at 80, 90, and 100% of the gait cycle when the stimulation intensity was 85M-Max and 90 and 100% of the gait cycle for 35M-Max. The response became significantly inhibitory with higher stimulation intensities at 80, 90, and 100% of the gait cycle. Stimulation of the MpN and SuN at 1×, 2×, and 3× PT (at 90% of the gait cycle) revealed no short-latency response and was significantly different to iTN stimulation at 85M-Max. Therefore it is unlikely that afferents from the MpN or SuN contribute to the short-latency response.

**Phase modulation**

The short-latency crossed response was inhibitory at 90 and 100% of the gait cycle (for 85M-Max and 35M-Max) compared with 60 and 70% of the gait cycle. Previous studies on ipsilateral (and contralateral) reflex pathways have demonstrated phase modulation (for example, Andersen and Sinkjaer 1999; Baken et al. 2005; Capaday and Stein 1987; Dietz et al. 1986; Duyssens et al. 1990–1992; Faist et al. 1999; Sinkjaer et al. 1996; Yang and Stein 1990; Zehr et al. 1998). Some of these studies have noted that responses were most prominent during gait phase transitions from stance to swing [for example, Andersen and Sinkjaer 1999 (for H-reflex but not stretch reflex modulation); Capaday and Stein 1987 or swing to stance phase (for example, Baken et al. 2005; Dietz et al. 1986; Duyssens et al. 1991; Faist et al. 1999) in various lower limb muscles. The responses in the current study were most prominent before and during the swing to stance transition of the ipsilateral limb. This indicates that the phase transition of the ipsilateral leg maybe important for the modulation of the response (although stance to swing of the ipsilateral leg was not investigated as there was no cSOL EMG activity to show an inhibitory
tion of the cSOL EMG activity). However, with this reasoning, it is difficult to ascertain if it is the transition phase of the ipsilateral leg, the push off phase of the contralateral leg, or a combination of both that contributes to the increased response through the gait cycle. Direct projections to the stance leg (cSOL) could account for the increases in the inhibitory response. Previous studies have demonstrated an increase in the magnitude of responses (H-reflex modulation) through stance peaking at the end of the stance phase (Andersen and Sinkjaer 1999; Capaday and Stein 1987) and it is possible that the increase in the inhibition of the cSOL responses in late stance is due to pathways projecting to the contralateral side. However, as these studies were assessing ipsilateral H-reflex modulation, the responses in the current study may not be comparable.

Another possible explanation of the results in the current study could be the increase in the background EMG activity of the cSOL at 90% of the gait cycle when compared with 60 and 70%. This explanation is unlikely as 100% of the gait cycle also revealed an inhibition and had similar background activation levels to 70% of the gait cycle (see response windows; Fig. 1, C and F). In addition, during sitting, the magnitude of the response remained unchanged despite an increase in the cSOL precontraction level from 5 to 15% of the maximum voluntary contraction (MVC) to 15–30% of the MVC (Stubbs and Mrachacz-Kersting 2009).

Functional significance of the response

A sudden plantarflexion of the swinging foot while the foot is supposed to be dorsiflexing indicates a threat to the stability of the body. The threat to balance is greatest if this occurs at the gait transition phase. The stimulation intensity evoking the most prominent crossed responses in this study were at 85M-Max. It is hypothesized that the large synchronous afferent volley to the spinal cord possibly signals a mechanical disturbance in the ipsilateral soleus muscle. Therefore such an

FIG. 3. The affect of stimulus intensity on the modulation of the response. A: (with truncated axis) the average raw cSOL EMG activity for a 150 ms period following iTN stimulation at MT, 35M-Max, and 85M-Max for 90% of the gait cycle of the ipsilateral leg (n = 1). The thin black line represents the control step, the thick black line represents stimulation at MT, the thick light gray line represents stimulation at 35M-Max and the thick dark gray line represents stimulation at 85-Max. The vertical long dashed line indicates iTN stimulation, the vertical short dashed lines indicate the analyzed (RMS) response window 45 and 60 ms following iTN stimulation (as this subject was 60 yr). Each trace is the average of 40 trials. B: mean ± SE of the magnitude of RMS the cSOL EMG as a percentage of the control (for the age appropriate analysis windows) at 90% of the gait cycle following iTN stimulation at MT, 35M-Max, and 85M-Max (n = 16). **, significant differences to P < 0.01.

FIG. 4. Comparison of the ipsilateral soleus peak-to-peak M-wave, magnitude of depression, and stimulation intensity. A: graph displaying the ipsilateral soleus peak-to-peak M-wave (mV) following iTN stimulation (○) and the cSOL RMS (µV) 40–55 ms following iTN stimulation (as this subject was 25 yr) as a function of the iTN stimulus intensity (mAmps; n = 1). Each data point represents a different stimulation intensity and is the average of 30 trials. B: mean ± SE of the cSOL RMS activity as a percentage of background RMS (analyzed in the age appropriate time windows) as a function of stimulation intensity for all subjects tested in this protocol (n = 7).
inhibitory response in the cSOL EMG activity could be a method to halt the forward progression of the contralateral leg (in push off) toward the source of the disturbance. Furthermore, Zehr and Duysens (2004) stated that as the feet are the first to make contact to a new environment, rapid pathways signaling corrections and protective responses would be desirable. Although the authors of that review were referring to connections from the lower to upper limb, it is plausible that a similar concept applies to the connections observed from the iTN to cSOL in the current study. The inhibition may also be a method to reduce the EMG activity until supraspinal pathways have time to act voluntarily and appropriately modify the EMG activity (as suggested by Frigon and Rossignol 2008).

In the cat, studies have suggested that these short-latency inhibitory pathways may provide interlimb communication when contralateral limb extension would be inappropriate and that the response may be a spinally mediated way of synchronizing the EMG of the two legs (Arya et al. 1991; Frigon and Rossignol 2008). Despite these explanations, because the re-
sulting force was not recorded in the cSOL, the functional significance of the response can only be speculative.

It should be noted that not all subjects displayed inhibitory responses, and some subjects displayed very small inhibitory responses at 80, 90, and 100% of the gait cycle (although the overall effect was a significant inhibition). In addition, the percentage of the gait cycle in which the inhibition commenced varied between subjects. This could be explained by subjects employing different walking strategies causing an alteration to the reliance on feedback from the ankle extensors, and subsequent projections to the cSOL. This could direct descending projections from supraspinal centers to presynaptically inhibit (or facilitate) interneurons mediating the response. This may result in a reduced (or increased) expression of the crossed response at different phases of the gait cycle. The magnitude of the reflex could be altered based on the requirement of the subject for the reflex. A reduced need for the short-latency crossed response may cause an up/downregulation of the response in some subjects.

Stimulus intensity modulation of the response

The inhibitory response became more prominent as the stimulus intensity increased; this agrees with the results in sitting (Stubbs and Mrachacz-Kersting 2009). This inhibitory trend was observed at 80, 90, and 100% of the gait cycle. In general, the responses were most prominent at 85M-Max, less prominent at 35M-Max and mixed at MT (resulting in minimal modulation). Sensory afferents recruited are loosely based on the electrical stimulation intensity, and therefore the different responses with electrical stimulation intensity could be due to the additional recruitment of a greater number of afferents. If approximate afferent recruitment thresholds are observed, MT would recruit mainly group Ia and Ib afferents (see Hultborn et al. 1987; Pierrot-Deseilligny et al. 1981a,b). Stimulation at 35M-Max would recruit a greater number of group II afferents as stimulation intensities between 1.3 and 2 × MT probably recruit group II afferents (Pierrot-Deseilligny and Burke 2005). Stimulation at 85M-Max would recruit group II afferents and other smaller afferents (but consequently slower). Despite these nerve thresholds, Gracies et al. (1994) reported that group II afferents can be recruited at ≤4–5 × MT. Due to the latency of the crossed response, it is likely that group Ia, Ib, or group II afferents from the ipsilateral leg contribute to the crossed response.

MpN and SuN stimulation

Stimulation of the ipsilateral SuN and MpN at 90% of the gait cycle displayed no short-latency responses (Fig. 5, A–E). As these afferents adjoin the iTN distal to the stimulation site, it is unlikely that the cSOL response originates from these afferents. In addition, lower limb cutaneous stimulation latencies have never revealed contralateral reflexes at the latencies observed in this study (for examples see Burke et al. 1991; Delwaide et al. 1981; Duyssens et al. 1991; Stubbs and Mrachacz-Kersting 2009) although ipsilateral latencies have been reported at similar (Nielsen et al. 1997; Shoji et al. 2005) or shorter latencies (Delwaide et al. 1981). The results of the current study suggest that the inhibitory response in the cSOL arises from muscle afferents of the ipsilateral soleus/gastrocnemius and not the SuN and MpN.

Conclusion

From the current study, it can be concluded that there are phase dependent short-latency crossed spinal responses following iTN stimulation to the cSOL during gait. At 85M-Max, inhibitory responses were observed in the cSOL EMG at 80, 90, and 100% of the gait cycle and lowering the stimulus intensity decreased the prominence of the inhibitory response. The MpN (muscular and cutaneous afferents) and SuN (cutaneous afferents), adjoining the tibial nerve distal to the stimulation site, were not the source of the short-latency responses, indicating that the response originates from the muscle afferents of the ipsilateral leg within the iTN. The results of the current study suggest that this short-latency crossed spinal response has a role in locomotion and due to its phase dependence likely has functional relevance. Despite this, more research is required to establish its significance to function.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

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