We have completed the Aim-1 study’s data collection and analysis. The study manuscript is just about to be submitted for peer-reviewed journal publication.

**Aim 1:** To test the hypothesis that the soleus stretch reflexes are abnormally modulated during walking in people with spasticity due to chronic incomplete spinal cord injury (SCI).

**Status — In Progress.** The data collection and analysis have been completed. We have collected the stretch reflex data from 9 subjects with chronic incomplete SCI and 9 age-matched subjects with no known neurological conditions. Key findings and significance of this study are summarized here.

**Significance:** Exaggerated stretch reflexes have been long presumed to be potential contributors to spastic gait, since muscle spasm and involuntary rhythmic contraction of muscles (clonus) are frequently observed in people with chronic incomplete SCI. This study investigated, for the first time, the soleus stretch reflexes during walking in spastic people with SCI, and showed that the excitability of soleus spinal stretch reflex pathways was abnormally high from the stance-swing transition through the late swing phase of walking. Heightened spinal stretch reflexes in the late swing often triggered clonus in the following stance and affected the gait, suggesting a link between the abnormal stretch reflex activity and features of spastic gait in people with chronic incomplete SCI.

**Summary:** Despite a long accepted presumption that the abnormal stretch reflex activity impairs gait, locomotor stretch reflexes across all phases of walking have never been investigated in people with spasticity due to chronic incomplete SCI. Here, we examined the locomotor soleus stretch reflexes in 9 neurologically normal subjects and 9 subjects with spasticity due to chronic incomplete SCI (AIS D, 2.5-11 years post injury). Soleus stretch reflexes were elicited in natural standing (with stable background EMG) by 6° of ankle dorsiflexion perturbation at 250 °/s. Following that, locomotor stretch reflexes were measured while the subject walked on the treadmill at his/her comfortable speed with a portable joint perturbation device on. Rapid dorsiflexion (6° at 250 °/s) was introduced in 8 equal bins of the step cycle (Fig. 1). Before or after locomotor stretch reflex measurement, locomotor H-reflex was also measured; soleus H-reflexes were elicited by tibial nerve stimulation at just above M-wave threshold in 8 bins of the step cycle, comparable to the stretch reflex measurement.

In standing, the soleus H-reflex and stretch reflex excitabilities appeared to be higher in subjects with SCI than in normal subjects, although the differences were small and often statistically insignificant. Such insignificant differences were unexpected, as higher $H_{max}/M_{max}$ ratios and exaggerated stretch reflexes have been reported in people with SCI and other CNS disorders previously. It might be that in relatively high-functioning subjects with SCI (i.e., ambulatory, AIS D), these reflexes may be less abnormal during standing. It is also possible that anti-spastic medication that was being taken regularly by these subjects affected the reflex amplitudes and modulation measured in this study, as baclofen is known to increase the stretch reflex threshold in spastic multiple sclerosis patients. Of the present 9 subjects with chronic incomplete SCI, seven had been taking a stable dose of baclofen, with or without other anti-spastic medication (e.g., tizanidine and diazepam), for at least 6 months prior to the study. Despite this fact, malmodulation of the M1 and M2 stretch reflexes and H-reflex was quite clear during walking.
and after a therapeutic intervention, status modulation is linked to the improvement of spastic gait, facilitating stumble and exacerbating foot drop during the mid-slow gait late stance phase, which likely results in ineffective propulsive force generation breaking force motion reflexes in the mid stance phase from subjects with SCI?

Would increased and unsuppressed spinal stretch reflexes during walking in subjects with chronic incomplete SCI be able to help to develop effective therapy strategies for improving spastic gait in people after SCI.

In normal subjects, the soleus EMG activity is phase-dependently modulated during walking throughout the step cycle; its high in the mid stance phase and very low (little to none) in the swing phase. Modulation of the soleus H-reflex and all three components of stretch reflexes matches the EMG modulation. In the present study, spinal short-latency “M1” (mainly Ia afferent origin), spinal medium-latency “M2” (presumably mainly II afferent mediated), and long-latency “M3” (presumably supraspinal) were clearly modulated throughout the step cycle; the responses were largest in the mid stance phase and almost completely suppressed during the stance-swing transition and swing phases (Fig. 2).

In subjects with SCI, modulation of the soleus EMG was found less, reflecting the reduced burst amplitude in the mid stance and the reduced EMG suppression in the swing phase (Fig. 2). Spinal stretch reflexes (i.e., M1 and M2) were modulated, but differentially and to lesser extent than those in normal subjects. In subjects with SCI, M1 and M2 were not only unsuppressed, but rather facilitated in the mid-late swing phase; unlike normal subjects, these subjects often showed larger responses in the mid-late swing phase than in the mid stance phase. These enhanced and unsuppressed spinal stretch reflexes could contribute to the reduced soleus suppression in the swing phase, and the unsuppressed muscle could further enhance the increased excitability of these spinal pathways.

Would increased and unsuppressed spinal stretch reflexes in the mid-late swing phase impair walking in subjects with SCI? As shown in Fig. 3, stretch reflex (or H-reflex) elicitation in the mid-late swing phase produces phasic excitation (i.e., clonus) that continues into the stance phase, which then, interferes with smooth forward motion. Large bursts of clonic activity in the early and early-mid stance phase enhance generation of posterior breaking force, negatively impacting forward propulsion. Furthermore, clonic bursts in early and early-mid stance are often followed by more clonic burst(s) and/or diffused and less prominent push-off burst in the mid-late stance phase, which likely results in ineffective propulsive force generation, more severe asymmetry, and slower gait. Unsuppressed spinal stretch reflexes in the soleus could also inhibit the antagonist TA activity, facilitating stumble and exacerbating foot drop during the mid-late swing to swing-stance transition phase. The findings of this study suggest a link between the abnormal stretch reflex activity and features of spastic gait, which may help to develop effective therapy strategies for improving spastic gait in people after SCI.

Aim 2: To obtain the pilot data towards testing the hypothesis that the improvement in the stretch reflex modulation is linked to the improvement of spastic gait in people with chronic incomplete SCI.

Status – In Progress. In this study, we plan to measure the modulation of stretch reflexes during walking, before and after a therapeutic intervention (e.g., such as operant conditioning of the H-reflex) that improves...
locomotion. In the past reporting period, we have not enrolled Aim-2 study eligible subjects with SCI, who were able to complete the stretch reflex testing protocol (i.e., able to walk on a treadmill) AND have been enrolled in other therapeutic intervention studies. (In the past several months, we have studied control subjects with SCI for the therapeutic intervention study. Unfortunately, those subjects were not suitable for this study.) We continue to plan on enrolling subjects for the Aim-2 study at any appropriate opportunities we have, for the rest of the grant period.

References