Since the beginning of this project, we have been steadily making progress in both Aim-1 and 2 studies. We are currently preparing a study manuscript for Aim-1 study.

**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).

**6-month report**
All the necessary equipment has been acquired. Installation of the treadmill with safety-harness and handrails has been completed. The IRB protocol has been approved. Operation test of the software-hardware system for eliciting and recording the soleus stretch reflexes has been completed. The actual data collection will start next week. We have scheduled several subjects for the Aim 1 experiment for the week of September 7, 2015.

As of September 1, 2015, data collection has not occurred, and thus, there is no description of data analysis or result charts/tables provided in this report.

**12-month report**
Currently, the data collection and analysis are in progress. We have collected the stretch reflex data from 8 subjects with chronic incomplete SCI and 7 subjects with no known neurological conditions. Our findings to date are summarized here. Figure 1 (*of 12-mo report) shows an example of stretch reflexes measured in a normal subject. It consists of M1 (predominantly muscle spindle Ia afferent origin), M2 (spindle II (and some Ia) origin), and M3 (presumably transcortical) responses. All three components are highly modulated during walking in normal subjects (Figure 1B, from Clin Neurophysiol 1999;110: 951-959). Figure 3 (*of 12-mo report) summarizes the results of ongoing study in people with SCI. Similar to the previous findings in people after stroke and people with multiple sclerosis, M1 and M2 components of stretch reflexes are unsuppressed during the swing phase of walking, likely contributing to their spastic gait disorders. In this coming year, we will finalize the analysis of this Aim-1 study, and prepare a manuscript for peer-reviewed journal publication. This is the very first study of soleus stretch reflexes during walking in people with incomplete SCI, and thus, the impact of the study is expected to be very high.

**18-month (current) report**

*Status – In Progress.*

The data collection and analysis have almost 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. Our findings are summarized here. Figure 1 shows the experimental setup view and a typical example of stretch reflexes in a normal subject. In normal subjects, all three components of M1, M2, and M3 stretch reflexes are highly modulated during walking, similar to the known phase-dependent modulation in the H-reflex (Figure 2, black lines). In contrast, in people with chronic incomplete SCI, modulation of M1 and M2

![Figure 1. Top: Setup for stretch reflex testing. Bottom: An example of normal soleus stretch reflexes. M1, M2, and M3 reflexes to a rapid 6° ankle dorsiflexion (250°/s) during standing.](image)
components of stretch reflexes are less pronounced and the M1 and M2 amplitudes are high in the mid-to-late swing phase (Figure 2, blue lines), where little to no reflexes are present in normal subjects. Interestingly, modulation of M3 component in people with SCI was similar to that in normal subjects. Relatively normal M3 modulation in our subjects with SCI may reflect the fact that there are some supraspinal connections remaining (i.e., classified with AIS D, incomplete SCI), and suggest that the pathways responsible for generation of transcortical M3 response are available and functional, at least partly. M3 response has been reported to be small or absent in people with multiple sclerosis or after stroke (Nielsen et al., 1998; Sinkjaer et al., 1999). Hence, the current finding in M3 response is significant in two aspects: it delineates the neurophysiology of soleus stretch reflexes and differentiates neurological damage across different populations of spastic individuals with CNS disorders.

Figure 3 shows two typical examples of locomotor EMG and joint motion in subjects with chronic incomplete SCI and soleus stretch reflexes measured in the mid-to-late stance phase (bin 3) and the mid-to-late swing phase (bin 7). In the subject of column A, locomotor EMG activity is clearly impaired in both the soleus and tibialis anterior (TA); in the swing phase, there is an abnormal soleus burst while little TA activity is present. Both of these likely lead to foot drop that this subject suffers from. Large M1 and M2 stretch reflex responses in bin 7 could be the cause of the swing phase burst in the soleus. In the subject of column B, his spastic clonus is obvious in the locomotor soleus activity (see bins 1-3). Despite a clear TA activity in the late stance to mid swing phase (bins 4-6), the ankle joint motion indicates that this subject suffers from foot drop. Large M1 and extremely large M2 responses are observed in bin 7. Our study shows, for the first time, the presence of strikingly large M1 and M2 stretch reflexes in the mid-to-late swing phase.

Figure 2. Soleus stretch reflexes and the H-reflex during walking in normal subjects (N=9, black) and subjects with chronic incomplete SCI (N=9, blue). Step cycle (from the beginning of the stance phase to the end of the swing phase) is divided into 8 equal bins; bins 1-4 are for the stance phase, bin 5 for the stance-swing transition, and bins 6-8 for the swing phase. Peak-to-peak (p-p.) amplitudes of M1, M2, and M3 responses elicited by 6° ankle dorsiflexion at 250°/s and the H-reflex at just above M-wave threshold are normalized to the maximum M-wave (M_max) amplitude in each subject’s each step bin, and then, group mean±SE values are calculated for each bin. M1 and M2 are larger in subjects with SCI than in normal subjects in bins 7 and 8. The H-reflex amplitude is larger in subjects with SCI than in normal subject across the step cycle, with the clearest difference in bins 7 and 8.

Figure 3. Locomotor EMG, ankle joint motion, and soleus stretch reflexes measured in the mid-to-late stance phase (bin 3) and the mid-to-late swing phase (bin 7) in subjects with chronic incomplete SCI. Middle panels: Locomotor EMG for the soleus (black) and tibialis anterior (red). >100 unperturbed steps are averaged together for each sweep. Bottom panels: Average ankle joint motion from unperturbed steps that correspond to the EMG sweeps. Top panels: Ankle joint motion of unperturbed (black) and perturbed (dotted blue) steps and corresponding soleus EMG in bins 3 and 7. In EMG panels, unperturbed steps’ EMG activity is subtracted from the perturbed steps’ EMG; thus, positive bursts indicate excitatory reflex responses.
phase of walking in people with chronic incomplete SCI. Because these stretch reflexes are normally suppressed during the swing phase of walking in a functionally appropriate manner (Zehr and Stein, 1999), it is highly probable that unsuppressed stretch reflexes during the swing phase contribute to spastic gait disorders in these subjects with incomplete SCI. We are currently finalizing the analysis of this Aim-1 study, and preparing a manuscript for publication in respected high impact journal.

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.

6-month report
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. We anticipate that some of the people with chronic incomplete SCI who participate in the Aim 1 (acute) study will also participate in a chronic therapeutic intervention study. Therefore, we expect that the data collection of the Aim 2 study will start this year.

12-month report
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. We have measured the pre-intervention stretch reflexes in two subjects with SCI who were able to complete the stretch reflex testing protocol. We will make the post-intervention measurements with these subjects. In this coming year, we plan to enroll more subjects in therapeutic intervention studies, and with all of those who are able to walk on a treadmill (necessary for the stretch reflex testing during walking) we will measure stretch reflexes before and after the completion of intervention.

18-month report
Status – In Progress.
We have measured the pre-intervention stretch reflexes in several subjects with SCI who were able to complete the stretch reflex testing protocol. We have little luck with post-intervention measurements due to scheduling challenges; that is, as other intervention studies include several of their own post-intervention testing sessions, scheduling post-intervention stretch reflex measurements in a timely (i.e., within a week from the last intervention session) manner has been difficult. Thus, we will extend the post-intervention testing period from 1 week to 2 weeks, so that we can increase the chance of performing post-intervention stretch reflex measurements. We plan to enroll more new subjects in therapeutic intervention studies, and with all of those who are able to walk on a treadmill, we aim to measure stretch reflexes before and after the completion of intervention.

References