Comprehensive evaluation of spinal cord function accompanying Lokomat rehabilitation in patients with incomplete spinal cord injury.

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Introduction & Aims

Body Weight Supported Treadmill Training (BWSTT) has been identified as a valuable locomotor training tool [1] and it is recognized as being of functional benefit in the rehabilitation of Incomplete Spinal Cord Injured (ISCI) patients.[2] The improved locomotor function often observed with BWSTT therefore offers an appropriate platform on which tests of spinal cord anatomy and physiology can be developed and studied in relation to the adaptations induced by rehabilitation or recovery. In this study Lokomat® (Hocoma AG, Switzerland), a robotic driven gait orthosis that incorporates BWSTT, has been used for locomotor training in patients with ISCI. The objective has been to measure the functional improvements in locomotion associated with Lokomat training and in parallel examine the utility of a comprehensive battery of tests that have the potential to measure changes in spinal cord physiology. The functional gains seen with Lokomat training are highlighted in this poster together with aspects of the on-going pooled analysis of our testing programme.

Methodology

Fourteen Subjects have successfully completed the study (12 Males and 2 Females). The subjects were either classified as Chronic (> 6 months from injury, n=5) or Acute (< 6 months from injury, n=9). The study design adopted is shown in Figure 1. Patients were assessed longitudinally, prior to the onset of Lokomat training, at the mid-point of training and following the cessation of training. The subjects' spatio-temporal gait parameters were recorded using bilateral instrumented insoles. The neuro-physiological tests included Somatosensory Evoked Potentials (SEP), Motor Evoked Potentials (MEP) and Quantitative Sensory Tests (QST). A summary of the comprehensive battery of tests that are performed during the assessment phase of the study are presented in Figure 2.

Week	1	2	3	4	5	6	7	8
Assessment								
Lokomat Training								

Figure 1: A prospective single-subject study design.
- Assessments included both neuro-physiological and Functional tests.
- Lokomat Training was for an hour everyday five days a week.

Clinical neurological assessment

ASIA classification
- Light Touch Score
- Pin Prick Score
- Upper Limb Motor Score
- Lower Limb Motor Score

Functional Independence Measure (FIM)

Sensory assessment

Quantitative sensory testing (QST)
- Vibratory Perceptual Threshold (VPT)
- Electrical Perceptual Threshold (EPT)
- Warmth Sensation (WS)
- Cold Sensation (CS)
- Light Touch – Monofilaments

Locomotor assessment

Evaluation of over ground walking
- Video analysis of Gait using Ranchos Scale
- Foot contact pattern, using FSR based footswitch system
- Functional assessment of locomotion capability (WISCI II)
- Temporal characteristics of Gait

Electrophysiological Sensory Assessment

Somatosensory Evoked Potentials (SEP)
- SEPs responses were recorded through stimulation of bilateral Median and Ulnar nerves in the upper limb and Posterior Tibial nerve in the lower limb.
- Time Domain Analysis - Latency and Amplitude
- Frequency domain analysis (ERD/ERS)

Electrophysiological Motor Assessment

Motor Evoked Potentials (MEP) using TMS
- MEP's were recorded in the upper and lower limb bilaterally in the key ASIA muscles
- MEP's were recorded in bilateral erector spinae muscles at the level of the lesion, one level above and two levels below.
- Time Domain analysis - Latency and Amplitude

Locomotor assessment on the Lokomat

Evaluation of Lokomat assisted walking
- Video analysis of Gait
- Evaluation of Lower limb stiffness using assessment tools on the Lokomat
- Evaluation of Lower Limb Strength using assessment tools on the Lokomat
- EMG activity of key lower limb muscles during lokomat assisted walking (coherence analysis)

Figure 2 : A summary of the comprehensive battery of tests performed during the assessment phase of the project.

Results

All subjects (Average age : 49.3 years) who participated in the study so far went on to complete the study. Compliance to the training regime (30 sessions) for the 14 subjects who have completed the study was high and averaged 94% with the majority of subjects missing fewer than 3 sessions over the 6 week training period. The reasons for missing a session were all unrelated to the use of the Lokomat.

The results from the preliminary analysis of the pooled data in some of the outcome measures used in the this study are individually presented. Analysis is ongoing and a data mining exercise will be conducted on all data sets to establish statistical relationships once our target recruitment level has been reached.

Clinical / Functional Assessment

The main clinical measure used in this study was the Standard Neurological Classification of Spinal Cord Injury (ASIA), which helped classify the type and level of injury. The Patients capacity to ambulate was assessed using the Walking Index in Spinal Cord Injury (WISCI II). Five acute patients were non-ambulant at the start of the study, and three of these five patients subsequently went on to become ambulant by the end of the study (Figure 3). As shown in Figure 3 acute patients seem to have made more gains in their WISCI II scores compared to the chronic patients. A moderate to strong correlation was found between the change in the WISCII score and the patients ability to tolerate reduced body weight support during the treadmill training (Spearman's Rho R= 0.746 p=0.002).

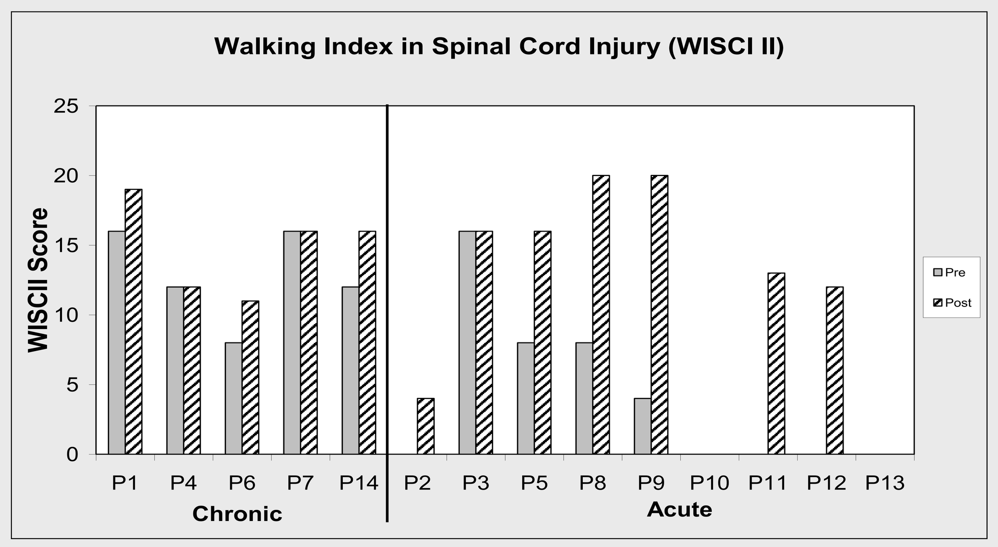

Figure 3: The WISCI-II Scores recorded in all subjects Pre and Post Intervention. A score of zero indicates that the subject is non-ambulant and a maximum score of 20 indicates that the subject is able to ambulate independently

Gait Analysis

The spatio-temporal parameters of gait recorded in four chronic subjects and five acute subjects were analyzed separately in each of these groups. Four acute subjects and one chronic subject were not included the analysis because they were either unable to walk 6 meters (n=3) or they required an orthosis to ambulate (n=2). The analysis of the pooled data showed that the acute patients made significant gains (p<0.05) in walking speed, stride length and cadence during the first three weeks of lokomat training (Pre-mid assessment) (Table 1b), with the exception of walking speed which also improved significantly during the last three weeks of training (Mid-Post assessment). There was a significant increase (P<0.05) between the Pre and Post measures in walking speed, stride length and cadence and a significant decrease (p=0.006) in double support which indicates a better balance (Table 1a).

The chronic patients showed moderate gains in all the spatio-temporal parameters, and perhaps interestingly their walking speed and cadence decreased during the first three weeks of training (Pre-Mid Assessment). There was a trend towards a better symmetry of gait in all patients (Tables 1A and 1B).

	Chronic (n=4)											
	Pre - Mid				Mid-Post				Pre-Post			
	Mean Change	CI-lower	CI-upper	p - value	Mean Change	CI-lower	CI-upper	p - value	Mean Change	CI-lower	CI-upper	p - value
Walking Speed	-1.41	-12.32	9.49	0.708	4.73	-3.69	13.16	0.171	3.32	-6.30	12.93	0.352
Double Support	0.15	-0.64	0.94	0.588	-0.03	-0.19	0.13	0.580	0.12	-0.62	0.86	0.642
Stride Length	0.02	-0.20	0.24	0.820	0.06	-0.14	0.25	0.402	0.08	-0.10	0.26	0.268
Cadence	-1.06	-11.35	9.24	0.765	3.03	-5.14	11.20	0.323	1.97	-6.64	10.58	0.519
Asymmetry Index	9.42	-59.32	78.16	0.692	-13.22	-39.11	12.68	0.203	-3.80	-64.78	57.19	0.856

	Acute (n=5)											
	Pre - Mid				Mid-Post				Pre-Post			
	Mean Change	CI-lower	CI-upper	p - value	Mean Change	CI-lower	CI-upper	p - value	Mean Change	CI-lower	CI-upper	p - value
Walking Speed	23.99	3.93	44.06	**0.029**	4.14	0.73	7.55	**0.028**	28.13	8.48	47.79	**0.016**
Double Support	-0.16	-0.41	0.09	0.114	-0.09	-0.18	0.00	0.054	-0.22	-0.29	-0.14	**0.006**
Stride Length	0.61	0.05	1.18	**0.039**	0.06	-0.04	0.15	0.171	0.67	0.13	1.22	**0.027**
Cadence	16.44	0.82	32.07	**0.043**	2.20	-0.86	5.27	0.117	18.64	3.40	33.88	**0.027**
Asymmetry Index	3.57	-10.35	17.49	0.385	6.74	-33.02	46.50	0.662	29.77	-39.41	98.95	0.205

Table 1 : A: Gait Outcomes in Chronic subjects. CI = 95% confidence Intervals

Table 1 : B: Gait Outcomes in Acute subjects. Significant differences have been highlighted in grey. CI = 95% confidence Intervals

Somatosensory Evoked Potentials

The SEP responses presented here were obtained from (below the level of lesions) through stimulation of the posterior tibial nerve at the ankles. Results from other stimulation sites above the level of lesion are not reported here. Traditional averaging techniques have been used to study the short latency components of the SEP using Brain Electrical Source Analysis (BESA) software whilst a time-frequency representation of the SEP was computed using EEGLAB to investigate late and non-phase locked event realted potentials. Short latency components of the SEP in normal subjects are generally stable with good repeatability. For the patient group the latency of the early SEP components were delayed in comparison to normal. Effects on latency associated over the time course of training were more commonly observed in the acute patient group. The example shown in Figure 4A being the most striking seen so far and contrasts with a chronic patient illustrated in Figure 4B which shows no change. Interestingly, for the acute patients a pooled analysis suggests that the major changes in SEP appear over the first 3 week of training, thereafter amplitude changes may dominate. The averages also suggest marked changes in the late components of the SEPs and this is largely confirmed by time-frequency analysis which shows changes in patterns of Event Related Synchronisation (ERS) and Event Related Desynchronisation (ERD) over the course of Lokomat training. In the example shown in Figure 5 no clear evidence of short latency changes in the SEP were evident.

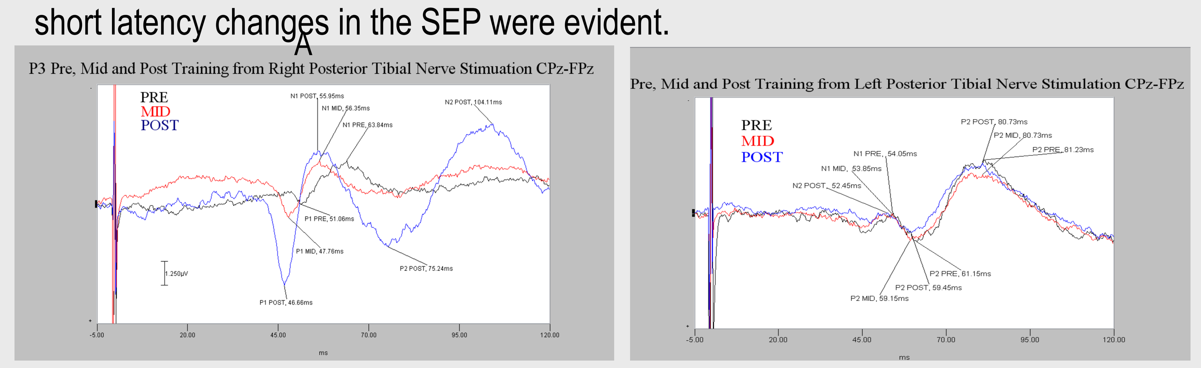

Figure 4:SEP recorded in two subjects, **A**) An acute subject showing changes in the short latencies. **B**) A chronic subject showing no clear change in the short latencies. The pre mid and post lokomat sep traces are shown in black red and blue respectively.

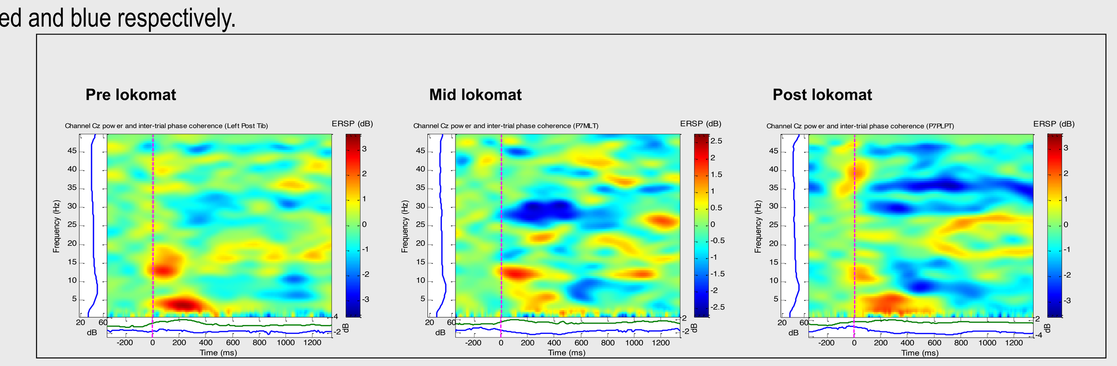

Figure 5: An ERS/ERD analysis of Subject 7 SEP recording during various study phases are presented. The vertical red dotted line indicates the time when the stimulus was delivered (Event). Areas shown in red indicate synchronisation and areas shown in dark blue indicate desynchronisation

Motor Evoked Potentials

The MEP responses were recorded in bilateral erector spinae muscles in all subjects. MEPs were recorded at the level of the lesion, one level above and two levels below. The variability of the MEP responses were quite large as seen in the analyses of the pooled data of both chronic and acute subjects (n=10) (Figure 6).

The area of the MEP responses slightly increased below the level of lesion following the 6 week Lokomat training. However no significant differences were found between the pre and post measures both in chronic and acute subjects.

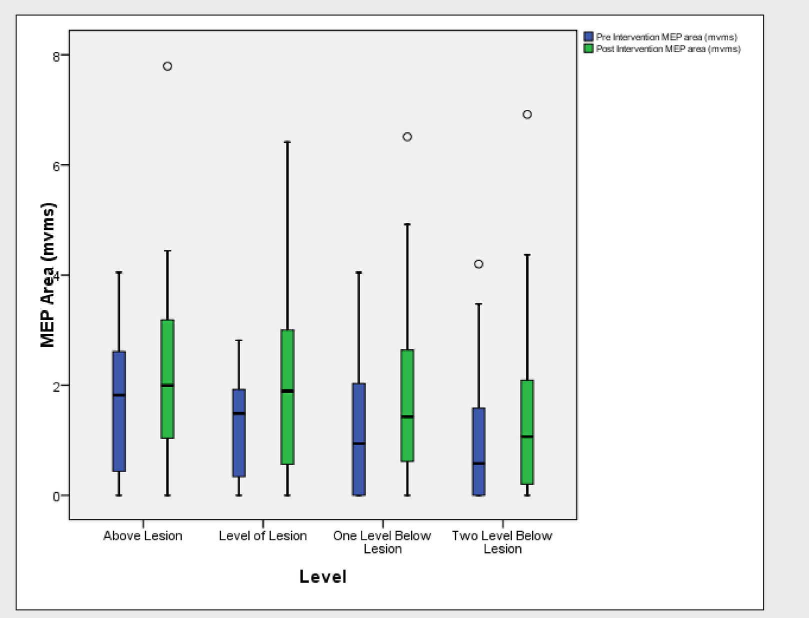

Figure 6: MEP responses in the erector spinae muscle have been presented as MEP area (mvms). The MEP responses Pre-Intervention are displayed in blue and the responses Post-Intervention are displayed in green.

Quantitative Sensory Tests

The Electrical Perceptual Thershold (EPT) and Vibration Perceptual Threshold (VPT), were recorded as part of a battery of QSTs that were performed on all subjects. As these QST measures are believed to reflect the integrity of the dorsal columns their relationship with the short latency posterior tibial nerve SEP has been examined. Using the Standard Deviation (SD) observed in the SEP recording of healthy subjects, the various components in the SEP response in the patients were classified as Normal (within 3 SD of the mean), Impaired (outwith 3 SD of the mean) and absent (could not be detected). The mean EPT (Figure 7A) and VPT (Figure 7B) scores recorded on the L5 dermatome in acute and chronic patients are presented grouped according to the pre-Lokomat P1 SEP latency classification.

The control data of EPT and VPT values were recorded at the L5 dermatome in healthy subjects. The pooled analyses show a similar behaviour in the relationship between EPT and VPT and P1 SEP classification in acute cases. The EPT and VPT values are highest where abnormal SEPs exist and reduce with reductions in the abnormality ascribed to the SEP. However, in chronic subjects this relation can be observed for VPT but is less evident for EPT. This difference in SEP relations to perceptual thresholds requires further investigation but may reflect features of long term adaptive changes to mechanisms associated with sensory perception.

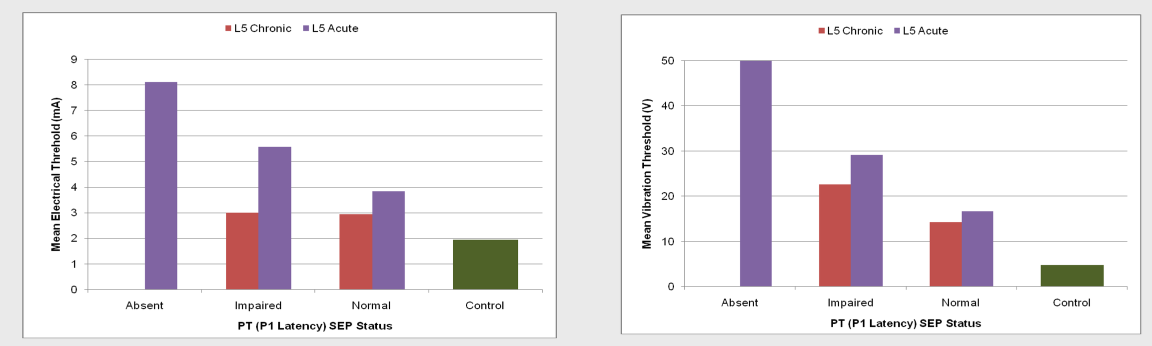

Figure 7: Mean EPT (A) and VPT (B) prior to Lokomat training at L5 dermatome and the LT mean percentage score below the level of lesion in chronic and Acute (B) patients compared to pre Lokomat training P1 Latency.

Discussion & Conclusion

The project so far has been successful in achieving the goals that were set, and can be summarized as follows

- A total of sixteen patients have been recruited so far out of a target of 20 patients. Fourteen patients have completed the study and two are currently undergoing training, and no patients have dropped out of the study.
- Functional gains were made by most patients who participated in the study which is evident from the gait and WISCI – II results. Its clear that acute patients benefit the most in the first three weeks of training compared to chronic patients. This finding can be useful in planning future research projects and also in clinical decision making with regards to Lokomat training.
- The neurophysiological tests such as the SEP have shown differences in some subjects. The ERS/ERD tests have been shown to be useful in assessing the function of ascending pathways in the spinal cord even when the SEPs are absent, or no marked differences in the short latency measurements.
- . The results of this study also suggest close relationships between the EPT and VPT values and SEP responses in acute subjects and there longitudinal study may reveal aspects of adaptive processes that occur post injury.

The future plan is to recruit the remaining patients. The data obtained from various other outcome measures are also currently being analyzed. Further detailed analysis of the data is also planned.

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