The Development of Limb Accelerations as a Measure of Neuromuscular Impairment and Predictor of Ambulatory Ability Following Spinal Cord Injury

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After a spinal cord injury (SCI), clinicians must quickly decide if they want to focus therapy towards gait training or wheeled mobility interventions to maximize an individual's functional mobility by discharge. Clinical prediction rules (CPRs) such as those that use age, strength, and sensation, can assist clinicians in making those difficult decisions, but for individuals with an incomplete SCI, these CPRs are often inaccurate. Additionally, these models only predict whether an individual can walk a short distance without physical assistance, which is not a sufficient description of functional ambulation. Limb accelerations (LA), captured unobtrusively and at a low cost from wearable accelerometers, may provide a responsive and informative movement biomarker of neuromuscular impairment that can be used to determine more accurate predictions of ambulatory ability among those who would benefit from them the most.

Our long-term goal is to build a new CPR using LA that predicts functional ambulation after SCI, thus enabling appropriately targeted mobility training. As a first step towards this goal, we utilized a cross-sectional study to build a foundational knowledge of LA and its relationship to measures of neuromuscular impairment (Aim 1) and ambulatory ability (Aim 2) using machine learning techniques and a sample with chronic, motor incomplete SCI and known, diverse functional abilities. Using a longitudinal study consisting of individuals with acute, incomplete SCI, we established that LA is reliable when measured acutely at admission to inpatient rehabilitation (Aim 3a). We also investigated the changes in LA over time (Aim 3b) and in relation to clinical measures (Aim 4a) and explored the potential utility of LA measured at admission to

inpatient rehabilitation to predict long-term ambulatory ability (Aim 4b) for those with acute, incomplete SCI. These results demonstrated that LA is a reliable and clinically-relevant metric that is likely to improve the prediction of ambulatory ability, thus improving long-term, functional outcomes for individuals with SCI.

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Preface

I would like to recognize all of the amazing people who have supported me and helped me grow as a research, clinician, and a person throughout my time in the DPT-PhD program at the University of Pittsburgh. First, I would like to thank my advisor, Michael Boninger, for being willing to accept me as his student when the DPT-PhD program was still forming and for all of the guidance and support he has provided for my research, clinical, and career development since then. Mike's depth of knowledge, endless work ethic, and push to always stay curious and continue to improve have kept me motivated and furthered my passion in this field. I also want to especially thank Lynn Worobey who is on my committee, but has gone above and beyond the duties of a normal committee member. Lynn has had an enormous role in my mentoring and has been incredibly supportive, whether it be with weekly meetings, answering my day-to-day questions, traveling with me to data collection events or conferences, or being the first to edit a draft for a paper. I would not be where I am today without the joint mentoring of Lynn and Mike and I could not have asked for a better mentoring team.

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willing to listen to me vent, helping me through an analysis question, and for all of the great times outside of research. Lastly, I want to thank my family who have always been supportive of all that I do.

1.0 Overview and Aims

Ambulation is often a goal of individuals after spinal cord injury (SCI), and therefore, gait training is a common intervention during inpatient rehabilitation (IPR).[1, 2] In the context of decreasing length of stays in IPR,[3] clinicians must quickly make critical decisions regarding the focus of therapy: towards ambulatory or wheelchair-related interventions. Unfortunately, time spent on gait training may be detrimental if the individual does not become a functional ambulator, as demonstrated by decreased participation outcomes a year after injury.[1] While there are clinical prediction rules (CPRs) that estimate the probability of becoming an independent ambulator, these rules struggle to delineate ambulators among the population that needs these rules the most, those with incomplete SCI.[4-7] To predict walking, these rules generally use clinical tests of strength and sensation which have been shown to have limited responsiveness and inconsistent reliability.[8, 9] Additionally, because these models only predict the ability to walk versus not walk, they do not provide insight into gait quality or efficiency, which are important components of functional mobility.[6]

Recent analyses of the shortcomings and inaccuracies of current CPRs for ambulation after SCI encouraged the use of alternative predictors and machine learning to provide improved predictions.[6, 7] Recording limb movements using wearable accelerometers is likely to provide more insight into an individual's strength, sensation, and spasticity than traditional physical examination measures. Limb accelerations (LA), defined as accelerations from any movement of the limbs during sleep at night, may be more responsive to identify differences in neuromuscular impairment and ambulatory ability compared to common clinical assessments. Also missing from current CPRs is any consideration of personal, psychosocial and environmental factors (PPEF) that

influence an individual's ability to adjust to his or her SCI and thus impact rehabilitation outcomes. Successful adjustment to SCI relies on aspects such as an individual's coping style, social support, socioeconomic status, and home and community accessibility, which should all be considered when predicting long-term functional outcomes such as ambulatory ability.[10-12]

Our overall goal is to improve the prediction of ambulatory ability after SCI through establishing LA as a movement biomarker that will provide a more descriptive measure of neuromuscular impairment than traditional clinical tests and that can be measured reliably in the inpatient setting. This dissertation consists of the findings from 2 studies: one cross-sectional among those with chronic (≥ 1 year), primarily motor incomplete SCI (Aims 1 and 2) and one longitudinal over the first year post-injury among those with acute, incomplete SCI (Aims 3 and 4). More specifically, Aim 1 will provide the foundational knowledge of LA by determining which LA features explain the greatest amount of variability in measures of neuromuscular impairment (lower extremity strength, sensation, and spasticity) among individuals with chronic SCI. In Aim 2, we will target a sample with chronic, motor incomplete SCI and known, diverse functional abilities to evaluate the usefulness of novel predictors (LA and PPEF) and machine learning techniques to classify functional categories of ambulatory ability as defined by measures of gait speed and endurance. We will also evaluate LA measured longitudinally in a population with acute, incomplete SCI to determine which features of LA can be reliably measured from admission to IPR through the first 6-months post-discharge (Aim 3a) and which features remain stable over that time (Aim 3b). Lastly, utilizing that same sample with acute SCI, we will examine how LA changes in relation to measures of ambulatory ability over time (Aim 4a) and explore the utility of reliable LA features measured at admission to IPR to predict ambulatory ability at 6-months post-discharge (Aim 4b).

Collectively, these findings will demonstrate the validity and reliability of LA as a clinical measure in both chronic and acute populations with SCI, establish the relationship between LA and measures of impairment and ambulatory ability, and provide evidence to support the future development of a CPR using acutely measured LA to predict long-term measures of functional ambulation.

1.1 **Specific Aim 1**

Determine the association between limb accelerations (LA) and clinical measures of neuromuscular impairment among individuals with chronic SCI.

Hypothesis 1: Features of LA such as those related to amplitude and duration of movements will be related to clinical assessments of strength, sensation, and spasticity among individuals with chronic (≥ 1 year) SCI.

1.2 **Specific Aim 2**

Develop machine learning models to classify ambulatory ability using LA and PPEF among a population with chronic, motor incomplete SCI.

Hypothesis 2: Random forest models including quantitative measures of LA and PPEF will produce higher classification accuracies for categories of functional ambulation (speed, endurance) than models including only clinical and demographic measures.

1.3 **Specific Aim 3**

Determine a) which features of LA are reliable between nights when measured at admission to IPR and b) which remain stable over the first 6-months post-discharge among participants with acute, incomplete SCI.

Hypothesis 3: A set of LA features can be identified that a) produce at least moderate reliability when examining intra-subject variance at admission to IPR and b) produce at least moderate stability between time points through 6-months post-discharge.

1.4 **Specific Aim 4**

a) Explore the how LA features which are not stable across the first 6- months following discharge (variable LA) change in relation to measures of ambulatory ability and impairment over time among participants with acute SCI.

Hypothesis 4a: The change in variable LA features will be significantly correlated with the change in measures of ambulatory ability (need for assistance, speed, endurance) and impairment (strength, sensation) from admission through 6-months post-discharge from IPR.

b) Explore the relationship between reliable LA features measured acutely at admission to IPR and ambulatory ability at 6-months post-discharge.

Hypothesis 4b: Features of LA measured at admission to IPR will be significantly correlated or show clear visual separation of categories of ambulatory ability measured at 6-months post-discharge.

1.5 **Overall Impact**

Information gained from these aims will provide insight to guide a future, multisite longitudinal study that will assess a new, more effective CPR for ambulatory ability in a larger population with acute, incomplete SCI. This new CPR will better aid clinical decision-making for individuals with SCI, allowing for optimally targeted therapies to be employed throughout the rehabilitation continuum. Additionally, this dissertation will provide a necessary understanding of the psychometric properties of LA in both chronic and acute populations with SCI, opening the door for many future uses of this metric.

2.0 Background

2.1 **Recovery and Rehabilitation after SCI**

Nearly 18,000 people in the United States sustain a spinal cord injury (SCI)[a] every year and almost 300,000 people in the United States are currently living with a SCI.[3] An SCI is a life-changing injury that often leaves an individual with strength and sensory deficits below their level of injury, in addition to many other changes such as bowel and bladder function. Once medically stable after a new SCI, patients often leave the acute care medical units to go to inpatient rehabilitation (IPR) for intensive physical, occupational, and speech therapy as needed, for 3 hours every day. It is in IPR that patients work to increase strength, balance, and motor control to restore function as much as possible. During this time, they also are learning new compensatory techniques and how to use assistive devices to maximize functional mobility and independence.

Early after an SCI, one of the first questions an individual may ask is "Will I ever walk again?" The decision to pursue ambulation or wheelchair focused mobility is not a trivial one. Decreasing length of stays from a median of 98 days in the 1970's to 30 days in 2021, force clinicians to quickly make critical decisions regarding the focus of therapy towards walking or wheelchair-based interventions.[3, 13] Gait training following SCI can be both time and effort intensive and for those who regularly walk for mobility, this exertion is worthwhile. However, some individuals with the potential to walk may not be receiving gait training during this time while the potential for neurorecovery is the highest. Conversely, for someone who will primarily

[a] All abbreviations are also defined in Appendix A and used consistently through the dissertation.

use a wheelchair following discharge, focusing on gait training can result in decreased time practicing transfers and wheelchair skills and lead to long-term negative consequences.[1, 14-17] The challenge in deciding who should complete gait training is exacerbated by the fact that patients with new injuries often push for gait training regardless of the extent of injury.[2]

Studies have shown that quality of life is more related to effective mobility and functional independence than the mode of locomotion.[17, 18] Thus, it is important to consider not just if a person can walk, but how well and whether walking is likely to be functional. Achieving functional ambulation indicates that the individual can walk with minimal assistance and sufficient quality, speed, and endurance to be able to safely and efficiently complete their activities of daily living. Since the most rapid rate of neurological recovery occurs in the first 3 months and significantly declines by 12-18 months post-injury,[19] it is critical that time in therapy is optimally utilized early after injury to maximize long-term functional mobility.

2.2 **Importance of Understanding Long-term Mobility Prognosis after SCI**

2.2.1 **Positive Impacts of Ambulation**

If able to achieve long-term, functional ambulation after SCI, there are many benefits to returning to walking. Among individuals with SCI, non-ambulators were found to have increased cartilage atrophy and degradation compared to ambulators, which can lead to pain and functional limitations.[20] Walking has also been associated with improved retention of bone mineral content, as up to half of the mineral content below the level of lesion can be lost in the first year after injury which significantly increases the risk of osteoporosis and fractures.[21] Also, sitting in a wheelchair

for extended periods of time can lead to increased risk of joint contractures and decubitus ulcers, especially when decreased sensation is present. Standing and walking allows for greater variability in positioning, which may decrease the risk of deformities and pressure injuries, as well as decrease spasticity.[22] Cardiovascular and respiratory benefits have also been noted when ambulating for exercise.[23] Although gait training is often considered a frustrating experience filled with "ups and downs", individuals with SCI who are ambulatory have also discussed relearning to walk as "powerful" and associated with "feeling extremely grateful."[24] Decreased depression and higher satisfaction with life scores have been shown among ambulatory individuals compared to those who use a wheelchair.[17]

2.2.2 **Negative Impacts of Ambulation**

While ambulation is achievable for some individuals during initial rehabilitation, only 25 to 34% of all individuals with SCI become functional ambulators.[17, 25] Factors such as spasticity, muscle weakness, pain severity, cognitive impairments, balance, proprioception deficits, and the need for assistance may limit the ability to ambulate.[17, 19] A focus on gait training while in IPR may be related to negative outcomes for individuals who will primary be wheelchair users. Our analysis of the SCIRehab database, a multicenter study that documented interventions received by patients with SCI throughout IPR and at a one-year follow-up, showed that one-third of patients who were primarily using a wheelchair at one year after discharge received gait training in IPR.[1] As a percentage of their time in physical therapy, these individuals received significantly less transfer and wheeled mobility training, compared to those who used a wheelchair and did not receive gait training. In addition, the group of wheelchair users who received gait training reported significantly worse measures of Craig Handicap Assessment and Reporting Technique

participation at one year, in the domains of physical independence, mobility, and occupation than the group of wheelchair users who did not have gait training while in inpatient rehabilitation.[1]

Unfortunately, even household or limited ambulators may be at risk for additional consequences. Marginal ambulation after SCI is associated with risks of musculoskeletal injury, pain, and physiological costs. Compared to wheelchair users, individuals with SCI who ambulate were more likely to report a fall, recurrent falls, and a fall-related injury, especially if they required assistance to ambulate.[26-28] Individuals with SCI who require an assistive device to ambulate also reported increased shoulder pain and fatigue compared to both power and manual wheelchair users.[15] This is likely resulting from the increased demands on a musculoskeletal system that already compensates for strength and sensory deficits, as forces of up 170% of an individual's body weight have been measured at the shoulder when walking with crutches after SCI.[29, 30]

When individuals with SCI are able to achieve functional ambulation, it is demonstrated to be far less efficient and more physiologically demanding than for able-bodied individuals. When compared to able-bodied controls, individuals with incomplete SCI were 200% less efficient while walking at their preferred velocity, demonstrated by increased oxygen use, heart rate, and lactate concentration. Additionally, even when ambulating at their maximal velocity, individuals with SCI were still walking 30% slower than able-bodied individuals walking at their preferred pace.[31] Self-selected gait speed in individuals with SCI is generally reported from 0.21 to 0.69 m/s, which is far below the able-bodied speed of 1.22 m/s and the average velocity to safely cross a street of 1.06 m/s.[31] Previous research demonstrated that people who walk at low speeds or high energy expenditure were limited in functional community ambulation and had poorer physical functioning.[32] Thus, many of these individuals for whom walking is painful or inefficient may be more functional and active in their communities by using a wheelchair for mobility.

If an individual is primarily ambulating at discharge from IPR, but cannot sustain ambulation and transitions to wheelchair use by 1-year, they may also be prone to more negative outcomes. Riggins et al. evaluated 4 groups based upon the primary mode of mobility at discharge from IPR and one year later: transition from wheelchair to ambulation, transition from ambulation to wheelchair, ambulating at both time points or using a wheelchair at both time points.[17] The group transitioning from ambulation to wheelchair use had significantly worse participation in the domains of mobility, occupation, and social integration, self-perceived health status, satisfaction with life, depressive symptoms, and pain severity scores of any mobility group, including the group who maintained wheelchair use at both time points.[17] These negative effects may persist for up to 10 years after injury.[16] This emphasizes the importance of selecting the most effective mode of mobility during IPR in order to prevent the need to transition from ambulation to wheelchair use.

2.3 **Current Methods for Prediction of Ambulation after SCI**

The American Spinal Injury Association Impairment Scale (AIS) determined as part of the examination standardized by the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) was often used to guide the prognosis of ambulation. The AIS is a measure of impairment of a traumatic SCI from A (complete SCI) to E (normal), determined by light touch (LT) and pinprick sensation to all spinal levels from C2 to S4-5 and manual muscle test (MMT) motor scores from the upper (C5-T1) and lower (L2-S1) limbs. MMT consists of "the use of observation, palpation, and force application by an examiner to determine the strength of a muscle action", while LT testing consists of the clinician touching a specific dermatome location while the individual's eyes are closed and determining if they can feel the touch (Table 2.1).[8, 9, 33]

Table 2.1: Scoring of clinical tests

Clinical Test	Scoring
Manual Muscle Test (MMT) to Assess Strength[33]	0= Total paralysis 1= Palpable or visible contraction 2= Active movement, full range of motion with gravity eliminated 3= Active movement, full range of motion against gravity 4= Active movement, full range of motion against gravity and moderate resistance in a muscle specific position 5= (Normal) active movement, full range of motion against gravity and full resistance in a functional muscle position expected from an otherwise unimpaired person
Light Touch (LT) Test to Assess Sensation[33]	0= Absent 1= Altered, either decreased/impaired sensation or hypersensitivity 2= Normal
Modified Ashworth Scale (MAS) to Assess Spasticity[34]	0= No increase in muscle tone 1= Slight increase in muscle tone, manifested by either a catch and release or minimal resistance at the end of the range of motion when the affected part is moved in flexion or extension 1+= Slight increase in muscle tone, manifested by a catch followed by minimal resistance throughout the remainder (less than half) of range of motion 2= More marked increase in muscle tone but through most of the range of motion the affected part easily moved 3= Considerable increase in muscle tone, passive movement difficult 4= Affected part rigid in flexion or extension

Individuals with complete SCI (AIS A) generally have a low likelihood of ambulating, as less than 8.5% typically regain functional ambulation.[3, 19, 35, 36] Although individuals with diagnoses of AIS B SCI (sensory incomplete, motor complete) may not be ambulating initially at admission to IPR, approximately 18-33% will recovery the ability to functionally ambulate and this recovery maybe be related to better sensory preservation after injury.[35, 36] Overall, about 52-75% of individuals with AIS C SCI (motor incomplete with more than half of the motor levels below the level of injury unable to lift against gravity [MMT score < 3/5]) will regain ambulation, but this seems to vary dramatically by age as individuals less than 50 years of age have higher rates of recovering functional ambulation (71-91% of < 50 years vs 25-42% > 50 years).[35, 36] While the vast majority of individuals with AIS D SCI (motor incomplete with at least half of the motor levels below the level of injury able to lift against gravity [MMT score ≥3/5]) are able to walk household distances (≥ 92%), approximately 20% cannot achieve community ambulation.[3, 35, 37, 38]

Factors that affect whether an individual recovers ambulation and the rate at which they do so include the level and severity of injury, lower extremity motor function, spasticity, trunk control, age, sensation, proprioception, balance, and cognitive impairments.[19]

Clinicians primarily use clinical judgement to determine the ambulatory prognosis of a patient with a new SCI and plan their therapeutic interventions accordingly. One study showed that while clinicians were fairly accurate in predicting ambulatory ability of patients 3-months post-discharge, their mobility predictions were less accurate when only including participants with motor incomplete (AIS C and D) injuries.[39] Another study evaluated the accuracy of both patient's ambulatory prediction and the predictions of therapists and found that neither group was successful in predicting if the patient would walk 1-year after injury. About 66% of patients predicted that they would be able to walk household distances and 45% of therapists believed they could do so, but only 38% were actually able to ambulate a year later. Physicians of various specialties and years of experience were not able to accurately predict whether individuals would be able to walk household distances one year after injury. Specifically for individuals with AIS C injuries, physicians ranged from 42-84% accuracy with 4 of the 6 physicians (67%) incorrectly predicting more than 30% of patients.[37]

CPRs are developed to help guide clinicians in critical decision-making regarding patient treatment and intervention selection. These tools can also be useful in providing education to patients about expected outcomes.[40-42] Decision-making tools to improve the quality of care and efficiency of IPR for individuals with SCI have been evaluated with positive outcomes in clinical practice.[42-44]

2.3.1 **van Middendorp CPR**

Although a number of CPRs exist regarding ambulation in the SCI population,[5, 36, 45-48] the most cited rule in research and clinical settings for predicting ambulation in people with an acute, traumatic SCI is a logistic regression model created by van Middendorp et al. ("van Middendorp CPR").[4] This CPR uses LT sensation and MMT motor scores at L3 and S1, collected in the first 15 days after injury and age (< 65 years, ≥ 65 years) to generate a score from -10 to 40 that is associated with the probability of walking independently at one year. The ability to walk independently was defined by the Spinal Cord Independence Measure item 12 as the ability to walk indoors, on an even surface less than 10 meters without physical assistance or supervision. In the derivation and validation models, the areas under the receiver operating characteristics curves (AUC) were .956 and .967, respectively, representing excellent discriminative ability in predicting individuals with SCI as walking or not walking (AUC= 1 is perfect discrimination, .5 is unable to detect any difference between the 2 groups).[4] Additionally, the van Middendorp CPR was demonstrated high accuracies when externally validated in other samples with traumatic SCI (AUC range= 0.889- 0.939)[5, 49, 50] and among a group with non-traumatic SCI (AUC= 0.94, OCA= 82%).[51]

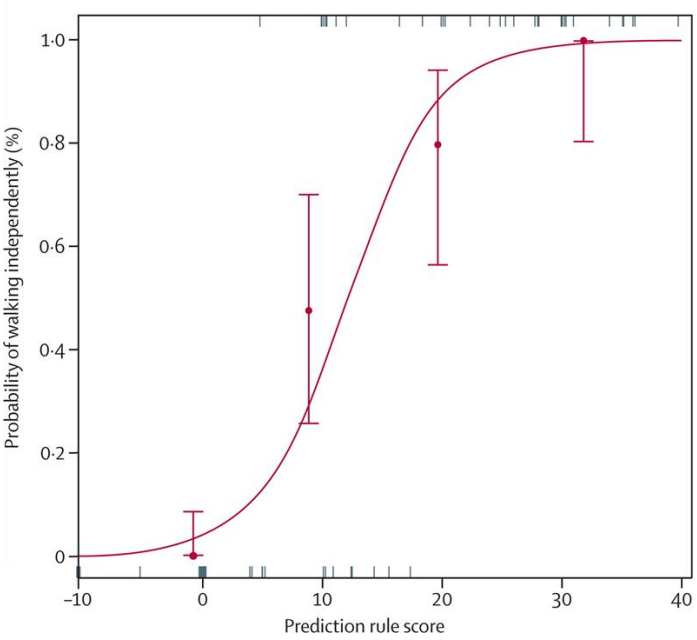

Figure 2.1: Validation group plot from the van Middendorp CPR[4] displaying 95% confidence interval as vertical bars. Vertical stripes at the horizontal borders represent those who could (top) and could not (bottom) walk independently.[b]

2.3.2 **Clinical Utility of the van Middendorp CPR**

Recently, researchers have begun to assess how the van Middendorp CPR compares to ambulatory predictions by clinicians based on clinical judgement and the overall clinical utility of this CPR in affecting clinical decision-making and outcomes. The van Middendorp CPR slightly

[b] Reprinted from The Lancet, 377, van Middendorp JJ, Hosman AJ, Donders AR, Pouw MH, Ditunno JF Jr., Curt A, Geurts AC, Van de Meent H, EM-SCI Study Group, *A clinical prediction rule for ambulation outcomes after traumatic spinal cord injury: a longitudinal cohort study*, 1004-1010, Copyright (2011), with permission from Elsevier.

outperformed physician predictions by 81% vs. 79% accuracy, but the difference was not significant. Particularly when predicting ambulation for individuals with AIS C injuries, the differences between the van Middendorp CPR and predictions from physician ranged from 32% higher predictions using the van Middendorp CPR to 10% lower.[37]

In our medical center, the van Middendorp CPR was also assessed to determine the clinical utility of this CPR. This was done by sharing the van Middendorp CPR score with the primary therapist after the initial evaluation in IPR for individuals with SCI whose ambulation prognosis was judged by the therapist to be difficult to determine (n=52).[42] The majority of the sample included in the study had AIS C and D injuries, further highlighting the challenges of predicting walking outcomes in this population. Therapists reported knowing the probability of walking was useful for 88% of cases for patients with non-traumatic SCI for establishing prognosis or setting goals. However, for individuals with moderate impairments whose CPR scores ranged from 10-17 (predicted probability of independent ambulation from 35-78%), 50% of therapists did not find the CPR prediction useful. Since the individuals in this range are often the most difficult group to determine a mobility prognosis based upon clinical judgement, this finding emphasizes the weakness of the van Middendorp CPR for predictions with this population. Compared to therapists with greater than 10 years of experience, newer therapists were more likely to find the CPR results useful (68% vs 18%, p= 0.001) and more likely to share the CPR results with the patient (50% vs 14%, p= 0.011).[42] Thus, an improved CPR may be particularly useful to new therapists and for patients with motor incomplete SCI.

This analysis also found that ambulation goals as described by the Functional Independence Measure (FIM), were not related to CPR probability of independent ambulation. Even among participants with very high probabilities of ambulating (98-99%), there was a wide

range of FIM goals from ambulating with total assistance to modified independent.[42] This suggests that factors beyond just clinical impairment and age are incorporated into clinical judgement regarding a patient's mobility prognosis. The FIM score is based on an individual's level of assistance to walk 150 feet (45.7 meters), while the van Middendorp CPR is only predicting an individual's ability to walk 32.8 ft (10 meters). Thus, the lack of relation between van Middendorp CPR predictions and FIM goal setting or goal achievement may emphasize that the van Middendorp CPR's outcome is not a sufficient measure of functional ambulation and that other factors that are not accounted for in the van Middendorp CPR may influence functional, community ambulation more than household ambulation. Therefore, CPRs for long-term ambulation after SCI are useful in clinical settings especially for less experienced therapists, but would likely be improved by more descriptive predictors than only clinical measures of impairment, more accurate CPR predictions for individuals with incomplete injuries, and a CPR outcome that better captures functional ambulation.

2.3.3 **Additional CPRs for Ambulation**

Additional CPRs for ambulation that are simpler[52] or use a sample with only motor incomplete SCI,[53] a variety of predictors,[53] more functional descriptions of impairment,[36] or improved model building and analysis techniques[36, 53] are described in Appendix B. However, each of these CPRs also present with methodological or clinical application flaws that are further discussed in the appendix.

2.4 **Areas for Improvement in Current CPRs for Ambulation**

As touched upon in the previous sections, many models have been developed for the prediction of ambulation after SCI, but they suffer from a variety of methodological issues that could be addressed in future CPRs to improve the accuracy and clinical utility. Multiple recent publications have highlighted 4 major areas of improvement for CPRs: uninformative predictors, biased sample populations, non-functional ambulatory outcomes, and suboptimal model evaluation and validation.[6, 37, 42, 51, 54] The following sections describe the issues that have led to the identification of each area of improvement and propose solutions to resolve them in future CPRs.

2.4.1 **Uninformative and Unresponsive Predictors**

2.4.1.1 Characteristics of a Useful Predictor

For a predictor to be useful in a CPR, it must be demonstrated to be valid, meaning that it is measuring what it is supposed to be measuring.[55-57] Face validity is the intuitive "feeling" that a measurement seems to be valid at its "face value". Face validity is difficult to quantify, but is demonstrated based upon the understanding of how the predictor is measured.[57] Construct validity is the demonstrated relationship that a measurement is comparable to a different measure assessing a similar concept and not similar to unlike measures. Likewise, concurrent validity quantifies the relationship between the novel measure and the "gold standard" or another previously validated measure of the construct that is intended to be measured. For example, if a predictor is intended to measure strength, then it would demonstrate concurrent validity if it is related to other measures of strength, such as MMT scores, but not to measures such as sex and age that may affect an

individual's strength, but are not direct measures of it. To demonstrate concurrent validity, the predictor should be related to Biodex dynamometry which is generally considered the gold standard measure of strength.[57] Predictive validity is a form of criterion validity and determines if the measure has the ability to accurately predict a future outcome. In the case if CPRs, the CPR itself would provide evidence of predictive validity, but preliminary analyses such as correlations can also demonstrate this domain.[57]

A predictor must also be reliably measured such that the same measurements result in the same predictions consistently even if measured under slightly different circumstances or at different times. While there are many domains of reliability, the primary areas that are important for use in a CPR are consistent measurements within each researcher or clinician (intra-rater reliability) and between different raters while measuring the same participant (inter-rater reliability), and consistency of repeated measurements (test-retest reliability).[55-57] When a researcher or clinician is performing a clinical test manually (e.g., MMT and LT assessments), there is a level of subjectivity in scoring as well as differences in how the individual performs the test (e.g., due to the tester's strength or experience). These may result in different scores when an individual is measured by the same tester (low intra-subject reliability), when different testers score the same subject (low inter-rater reliability), or when multiple measurements are performed without any other changes (low test-retest reliability). Using objective measures that are calculated algorithmically and without any bias from the tester ensure that whoever is performing the measurement is not influencing the outcome.[55-57]

Intra-subject reliability (or variability) is also important for a predictor to ensure that changes within the participant do not unduly influence the CPR results (Figure 2.2).[55-57] A predictor should have high intra-subject reliability, meaning that each time you measure the

predictor in a relatively short time frame and given the same conditions, the measurement should produce the same results. In this instance, having high intra-subject reliability would be effectively the same as high test-retest reliability. If a predictor had low intra-subject reliability, then the CPR may produce vastly different results each time it is calculated even within the same participant when no other characteristics have changed that should influence the CPR findings.[55-57]

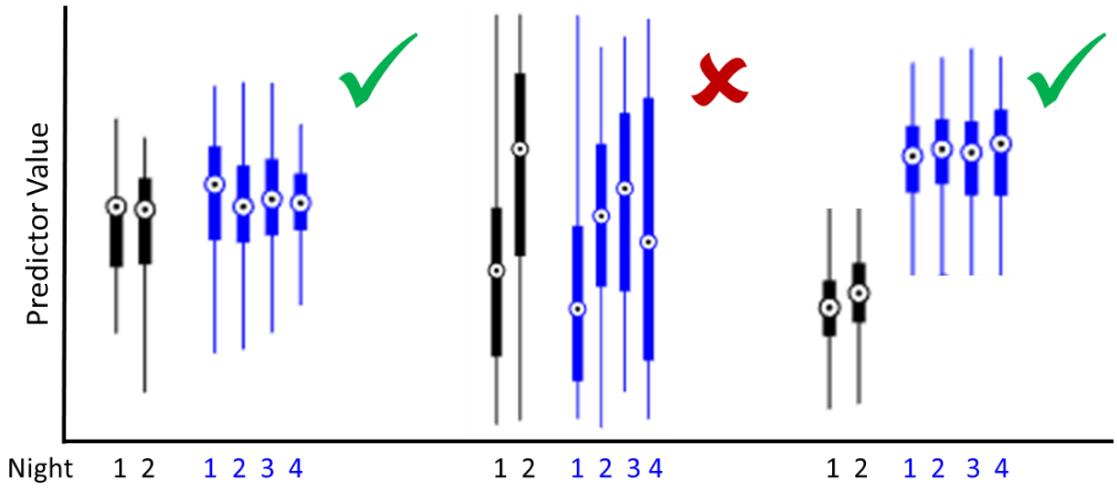

Figure 2.2: Examples of a predictor with high (left, good) and low (middle, bad) intra-subject reliability and high inter-subject variability (right, good) between 2 participants (black and blue) and multiple collection times (nights).

In contrast to intra-subject reliability, a predictor should have high inter-subject variability which indicates that the value of the predictor changes considerably between different participants with different presentations. If the predictor had low inter-subject variability, then every participant would have approximately the same values and the predictor would not be very informative of different abilities in the CPR.[55-57] Inter-subject variability is a measure of responsiveness which is defined as "the ability of the instrument, device, tool, test, or scale to accurately detect meaningful changes".[57] In the case of a CPR for ambulation, predictors must be

able to differentiate between different ambulatory abilities when measured early after injury, such as soon after admission to IPR. Measures such as sensitivity and specificity (or precision and recall in multiclass cases) are often used to calculate responsiveness in classification situations.

Understanding how a predictor is responsive to changes over time is also useful, though not critical, to understand when building a CPR. A measure that is stable, or does not considerably change over time, provides the ability to use it as a predictor at any time after injury and would produce the same results. These predictors represent stable characteristics that are not likely to be influenced by changes in neurorecovery, therapy, or other external factors. Most common predictors used in previous CPRs are clinical measures that are expected to change over time in someone who experiences neurorecovery and may be more likely to ambulate, such as strength and sensation.[4, 5, 53, 58-63] Since someone's strength soon after an SCI may be predictive of future motor recovery,[47, 59, 64, 65] measures of strength may be useful as a predictor and as a clinical outcome measure of neurorecovery. Although these factors are not time invariant like the stable predictors, they change in a predictable fashion over time and may be more responsive to changes than other clinical measures.

2.4.1.2 Common Clinical Measures May Not Be the Best Predictors

The most common predictors used in CPRs are clinical measures such as MMT and LT scores to assess strength and sensation at specific spinal levels. These measures have the benefit of being able to be performed quickly and without any additional equipment and are routinely available in electronic health records for retrospective analyses since they are included in the ISNCSCI exam. However, these clinical measures of strength and sensation lack sufficient reliability, validity, and responsiveness to be optimal predictors of ambulatory ability.

Since MMT has a significant reliance on the tester's experience, applied resistance, and strength, it can be an inaccurate representation of the actual strength of the muscle group.[8] This has also led to substantial variability in the test-retest and inter-rater reliability, especially among muscle groups that are capable of providing larger forces, like the knee extensors and plantarflexors.[8] This is particularly problematic since the knee extensors (L3) and plantarflexors (S1) are frequently included in CPRs.[4, 52]

Additionally, MMT has demonstrated limited responsiveness and is prone to ceiling effects, which can mask small differences in strength that may be clinically relevant to detect, and are especially important in the application of prediction models.[8, 66] For example, studies have shown that clinicians commonly scored an MMT as 5 ("normal") when other measurements have shown muscle strength to only be 50% of the maximal contraction. Similarly, a muscle groups scored as of 4 ("good") using MMT have been shown to be generating as little as 10% of their maximal output during the MMT.[8, 67, 68] While there are other options to record an individual's strength such as hand-held and Biodex dynamometry, MMT is often preferred due to its quick ease of use with no additional equipment, space, or expenses required.[8, 69]

Due to only having a 3 point scoring scale and only assessing one domain of sensation, LT sensation tests have shown limited responsiveness and validity when examining neurological changes.[9] Similar to the strength assessments, it has been shown that the tester's experience can have a large influence on the test-retest reliability and that there is a positive correlation between the amount of tester training and the reliability.[9] As LT scores are included in the most used CPRs,[4, 52] the inability to reliably assign a responsive sensory score is likely a limiting factor in the predictive ability of the current models.

Lastly, spasticity is often not included in the most common CPRs for ambulation, yet it has been reported as a common barrier to achieving ambulation.[19, 42] In multiple populations, the amount of spasticity has had a significant relationship with the ability to walk[70] and spasticity has been reported as one of the top three therapist-reported factors that interfere with therapy post-SCI.[71-74] The Modified Ashworth Scale (MAS) assigns a score based upon the resistance to passive movement of a joint by a clinician. The validity of this measure to quantify spasticity among individuals with SCI as well as limited inter-rater reliability, significant changes in reliability depending on the muscle being assessed and amount of tester training have brought the usefulness of this measure into question.[75-77] Thus, the need for a more accurate measure is needed to assess spasticity and provide additional information for a predictive model for ambulation.

2.4.1.2.1 Novel Predictors: LA and PPEF

If a more responsive measure of neuromuscular impairment could be utilized early after a new SCI, it may give insight into the potential neurological and functional recovery that has not been well predicted previously.[59] In multiple animal models, slight movement of a hind-limb joint after SCI has been found to be an early indicator of neuroplasticity that may lead to significant improvement in function, including the recovery of ambulation.[64, 65] In humans, Waters et al. found that slight motor recovery soon after injury was predictive of functional motor recovery later on.[59]

Inexpensive accelerometers allow for the collection of vast amounts of objective movement data with minimal administrative burden and have previously been used with individuals with SCI to quantify ambulation,[78] wheelchair propulsion,[79] physical activity,[80, 81] sleep characteristics,[82] and activities of daily living.[83] We define LA as accelerations from any limb movements occurring while asleep at night and may include periodic limb movements, spasms, positional shifts, rolling, and turning. We will focus our initial analysis on LA while asleep at night as there may be many

factors that influence the amount of daytime LA such as an individual's occupation and leisure time activities. While asleep, an individual most likely moves mostly subconsciously for comfort, pressure relief, or in response to other sensations.[84, 85] These movements encompass aspects of sensation to cue the individual to move and strength to perform the movement. Additionally, it has been shown that supine positioning may increase spasticity, thus, spasticity may be more prevalent while laying down to sleep at night.[86, 87] Therefore, we believe that measuring LA at night will provide the least biased measure of LA that is most likely to be related to impairment and ambulatory ability. It is important to note that when sleep studies were compared between the hospital and home settings, characteristics of sleep were improved at home, but the periodic limb movements were similar in both settings.[88] This indicates that while sleep may improve once an individual is discharged home, the movements may not significantly change. Additionally, since an individual's sleep quality may affect the intra-subject variability of LA and factors such as alcohol and caffeine consumption and exercise can affect sleep quality, it is important to include these factors in analyses including LA.

In a population of children with Duchenne muscular dystrophy an activity monitor was used to calculate the frequency and amplitude of movements over the course of a week at baseline and one year and compared to measures of functional capacity. A moderate to good relationship was found between the intensity of movements and both knee extension strength and the 6-minute walk test (6MWT, measure of walking endurance), demonstrating the strong potential for LA to be related to neuromuscular impairment and functional mobility.[89]

Also missing from current models that predict ambulation after SCI is any consideration for PPEF that may impact training, challenge, and/or enhance the sustainability of walking for functional mobility. Many factors may influence whether an individual may walk such as

resilience, self-efficacy, coping strategies, social support, home and community accessibility/barriers, socioeconomic status, comorbidities, pain, and sleep quality, and none of these factors are included in current CPRs.[10-12, 90, 91] While studies have evaluated the influence of PPEF in the SCI population,[92-97] how PPEF affect mobility outcomes has not been examined.

Aim 1 evaluated the association between LA and neuromuscular impairment (strength, sensation, and spasticity) in a sample with chronic SCI to establish that LA is a clinically meaningful measure. Aim 2 evaluated the use of LA and PPEF to classify categories of functional ambulation among a sample with chronic, motor incomplete SCI. Aims 3 and 4 established the reliability and stability of LA when measured acutely (Aim 3) and explore the utility of LA collected at admission to IPR as related to ambulatory ability at 6-months post-discharge (Aim 4). Although it was not assessed in a longitudinal sample in this dissertation, PPEF was also collected and is planned to be included in a future CPR using both PPEF and LA measured at admission to IPR to predict long-term functional ambulation.

2.4.2 **Biased Sample Populations**

As previously mentioned, predictions using clinical judgment are most inaccurate for individuals with motor incomplete SCI and the van Middendorp CPR does not substantially improve predictions or clinical utility for this population.[37, 42, 48] An analysis of the van Middendorp CPR by Phan et al. found that the disproportionately high number of individuals with low (AIS A, 49% of derivation population) or high (AIS D, 22% of derivation population) probabilities of walking included in those CPRs led to the misleadingly high predictive accuracies when all AIS classes were presented as a single cohort.[6] However, when a new cohort of 675 patients were predicted using the van Middendorp CPR the AUC were .730, .691, .850, and .516 for AIS classes

A, B, C, and D, respectively. The drastic decrease in AUC values compared to those reported by van Middendorp et al., demonstrates the bias of previous CPRs. This has caused a misperception that these models will produce accurate results for individuals with any AIS grade injury, when it appears its accuracy largely depends on the AIS class and is often not accurate for those with incomplete SCI.

2.4.2.1 Targeted Sample Population

Individuals with incomplete injuries present with varying degrees of strength and sensation initially and are most likely to experience neurologic recovery, thus making prediction of ambulation difficult.[19, 37, 39, 98] Therefore, individuals with incomplete SCI would most benefit from a better understanding of ambulatory prognosis.[19, 98] We carefully targeted individuals for all aims with a variety of impairment levels and functional abilities such that our analyses are not biased towards only those with AIS A or D injuries. Additionally, while most CPRs only include individuals with traumatic SCI, the clinical utility of the van Middendorp CPR was highest when used among a sample with non-traumatic SCI.[42] Therefore, participants with both traumatic and non-traumatic non-progressive SCI will be included in the studies. Those with progressive SCI (e.g., spinal tumor) were not included because their level of impairment can change over time which results in CPRs not being clinically useful in this population.

For Aims 1 and 2, a sample with chronic SCI was utilized because these participants can be recruited in larger numbers, tested cross-sectionally, and ensure a diverse range of functional abilities are collected. For Aim 1, participants were enrolled regardless of level of injury to ensure that we captured the full range of impairment. To ensure the distribution of impairment scores in Aim 1 was not overly skewed by the low scores from the motor complete SCI population, we enrolled those participants in lower proportions than the motor incomplete SCI sample. For Aim

2, the sample consisted of motor incomplete SCI as those with motor complete injuries were not likely to be walking and a future CPR would only focus on those with incomplete SCI.[99, 100]

For the longitudinal study (Aims 3 and 4), only participants with incomplete SCI (AIS B, C, or D) or for whom a walking prognosis was not clear were included. Additionally, the current analysis of the longitudinal study is a pilot analysis as part of a larger study. Data collection of this population is still ongoing to enroll enough participants to build a CPR that is only targeting the those with incomplete SCI who would benefit from improved mobility prediction the most.

2.4.3 **Non-functional Ambulatory Outcome**

Another area for improvement in current models is that they only provide a binary assessment of the ability to ambulate short distances independently and do not predict important characteristics of gait such as need for assistance, speed, or endurance.[4, 5, 36, 45-47, 53] The van Middendorp CPR and others that attempt to predict household ambulation (short distances of 32-150 feet indoors) are inherently flawed, as community mobility is generally of greater importance to individuals with SCI and clinicians.[37] This could lead to negative psychological consequences for individuals if they are not able to achieve community ambulation.[19, 101] Previous CPRs may be misleading and may guide the focus of therapy towards gait training and away from more functional wheelchair-based interventions. If an individual is only able to ambulate a short distance with a slow gait speed or requires significant bracing or assistive devices to walk, then walking may not be the most efficient mode of mobility, despite the potential to ambulate independently (i.e., without physical assistance or supervision from another person). Phan et al. noted that using a binary instead of a continuous outcome may not be truly indicative of an individual's recovery and reduces the subtleties in differences between the two functional abilities.[6] Therefore, CPR

outcomes should give a more thorough, non-binary description of an individual's ability to achieve functional ambulation in terms of the need for assistance, gait speed, and walking endurance.

2.4.3.1 Functional Ambulatory Outcomes

Three measures of ambulatory ability were used to provide a comprehensive understanding of the likelihood of gaining functional ambulation, including the need for assistance (devices, bracing, or hands-on assistance from a caregiver), speed, and endurance. We used a triad of measures to capture these constructs, as the Walking Index for SCI II (WISCI-II), 10 meter Walk Test (10mWT), and 6MWT which have collectively been reported as the most comprehensive ambulatory assessments for individuals with SCI.[102-104] Although keeping the measures as continuous outcomes is ideal for providing the most thorough prediction possible, continuous outcomes are likely too variable to be able to predict accurately without an extremely large sample population that was not feasible for the current studies. Therefore, we were mindful when categorizing the ambulatory outcomes to ensure that the categories still increased resolution over current binary CPR outcomes and provided a comprehensive description of functional ambulation.[2, 105, 106]

2.4.4 **Suboptimal Model Evaluation and Validation**

Most current CPRs could benefit from more advanced analytical methods to build and evaluate the prediction model. Logistic regression is commonly used to produce a mathematical equation that can predict the probability of walking (binary outcome).[4, 5] This standard statistical technique is generally the only algorithm assessed, has difficulty handling large or high dimensional datasets without additional regularization, and requires statistical assumptions to be

met.[107] Phan et al. noted that using logistic regression models and small numbers of clinical variables as predictors may not be sufficient to produce an effective CPR and that new variables and machine learning models may be useful.[6]

Additionally, most CPRs use only AUC and/or OCA as the primary metrics to evaluate the predictions. It has been suggested that AUC may be a misrepresentation of the model performance and that it should only be presented in combination with other measures such as sensitivity and specificity for binary outcomes or precision and recall for multiclass outcomes.[6, 108] Both AUC and OCA can also be significantly affected by imbalanced data. For example, as explained in Section 2.4.2, the van Middendorp CPR appeared to perform accurately for all participants when viewing the AUC for the entire sample. When each AIS class was examined individually, it was found that the portion of the sample that had AIS A injuries skewed the overall results due to that portion of the sample being much larger and better predicted than the other AIS grades.[109] Reporting a variety of metrics that evaluate different aspects of the results including group-level classifications will provide a more accurate and comprehensive understanding of performance.

While the van Middendorp CPR was validated with a separate test set, many of the other CPRs were not. If a model is intended for use in the prediction of unseen data, then you cannot fully understand how it is expected to perform until it is assessed using a held-out test set that was not included in building the model. Methods such as cross-validation can estimate this performance, but all model building steps must be performed inside each cross-validation fold (nested cross-validation) or the model will be biased. Issues such as model overfitting may result in overly-favorable training set performances. Without sufficient validation from a held-out test set of data, biased or overfit models may lead to reporting overly-optimistic results when the model is unlikely to perform as well in practice with new samples.[4, 53, 109]

2.4.4.1 Machine Learning and Model Evaluation

Machine learning is a field of computer science in which patterns and predictions occur by learning from data. This "learning" occurs by unveiling possible hidden structure or regularity patterns in an automated manner. Machine learning is useful for large data sets or when the data set has a wide number of attributes that cannot be efficiently analyzed using traditional statistical techniques.[107] Machine learning techniques are often used in the analysis of accelerometer data to detect and classify activities with high degrees of accuracy (often >90%).[110-114] Accelerometer data has been analyzed using machine learning techniques in the SCI population specifically.[83, 115, 116] Generalization is often pursued empirically through training and testing datasets, making the prediction robust on unseen data. Since we are using small datasets or many more potential features than samples, we can use machine learning methods that reduce dimensionally and assess our results on unseen data in an unbiased fashion. Additionally, we will report outcomes per-class as appropriate using multiple metrics to provide a comprehensive view of model performance and accuracy.

2.5 **Impact of Improved CPRs for Ambulation on Clinical Practice**

The ultimate innovation of this proposal comes from applying the aforementioned techniques to a clinical problem that is directly impacting patient care and outcomes for individuals with SCI. This dissertation aims to provide essential knowledge about LA to support the future development of a CPR to assist clinicians in planning care and helping to ensure individuals with SCI are provided with evidence-based and patient-centered interventions. These measures of ambulatory ability can help clinicians to set real-world expectations for patients by comparison

with easily understood constructs like the time it takes to cross the street, average able-bodied walking speed, and the need for bracing and equipment. This added information can serve to bolster patient motivation when walking is achievable and set realistic expectations when other mobility interventions like wheelchair skills are more appropriate.

3.0 General Experimental Methods

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Although the analyses and subject populations differ between the cross-sectional (Aims 1 and 2) and longitudinal (Aims 3 and 4) studies, the data collection was largely the same. At each time point, participants completed questionnaires, clinical measures, ambulatory assessments as able, and wore accelerometers continuously for up to 1 week. The cross-sectional study participants completed this process once, while for the longitudinal study data was collected upon admission to IPR, just prior to discharge, and 3-, 6- and 12-months post-discharge. For the longitudinal study, the admission and discharge collections were targeted to occur in the first and last weeks of the IPR stay, respectively, with the questionnaires, clinical, and ambulatory assessments occurring as close to beginning or end of the week as possible. Follow-up collections for the longitudinal study began within 3 weeks before or after the target date. The cross-sectional study utilized participants with chronic SCI (any severity for Aim 1, motor incomplete for Aim 2), while the longitudinal study (Aim 3 and 4) was among individuals with acute, incomplete SCI.

3.1 **Questionnaires**

Participants self-reported demographic characteristics and PPEF using questionnaires. Table 3.1 describes the questionnaires used in the cross-sectional study and which variables were extracted from each questionnaire. Similar questionnaires were collected at each time point in the longitudinal study. Since these questionnaires were not used in the current analyses, they are not described specifically.

PPEF assessed included personal and health characteristics,[33, 54, 97] socioeconomic status,[117-119] pain,[120, 121] environmental facilitators/barriers,[122] physical and mental health,[123] social support,[124] self-efficacy,[125] and resilience.[126] These factors represent physical and psychological domains that may influence walking outcomes. For the pain questionnaire, Craig Hospital Inventory of Environmental Factors- Short Form, and Pittsburgh Sleep Quality Index (PSQI), having a higher score is associated with a less favorable outcome, while for the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), Medical Outcome Study Social Support Survey, Moorong Self-efficacy Scale, and Spinal Cord Injury- Quality of Life Resilience Short Form a higher score is associated with a more favorable outcome. These factors were selected as they are stable and unlikely to change substantially after an acute SCI, making them more likely to be useful in a longitudinal CPR.[117, 122, 126-131]

To evaluate other factors that may contribute to nighttime movements, participants were asked to complete a questionnaire each night that asks about medication use,[132] alcohol and caffeine consumption,[133-135] amount of daily activity, participation in sports,[134] and fatigue level.[136] Participants could also record times that the accelerometers were removed during the day to improve compliance monitoring and analysis. For each morning of accelerometer data collection, participants completed a sleep log that records the time they went to sleep and woke up, the self-

reported quality of sleep that night, and if they considered that night to be "typical" of how they normally sleep.[137] Participants were called, emailed, or checked on in-person most days during their data collection to assist in completing the daily questionnaire and sleep log as needed. In combination, these measures will allow us accurately determine times asleep and capture external factors that may influence movements during sleep.

Table 3.1: Self-reported demographic and PPEF questionnaire variables used in the analyses. Variables that are commonly found in an elctronic health record are shown in grey and questionnaire-specific PPEF variables are shown in white.

Measure	Description	Components Included in Analyses

Demographics[33, 54, 97, 117-119]	Personal, health, and SCI characteristics, measures of socioeconomic status	• Age
		• Annual household income
		• Body mass index (BMI)
		• Comorbidities (if present):
		  ○ Any
		  ○ Cardiopulmonary
		  ○ Depression or Anxiety
		• Highest education completed
		• Household size
		• Marital status
		• Medical insurance type
		• Metropolitan classification
		• Race/ethnicity
		• SCI level of injury (tetraplegia/ paraplegia)
		• Sex
		• Veteran status
		• Years since injury

Pain Questionnaire[120, 121]	Pain intensity over the last week using components from the International SCI Pain Basic Dataset and Brief Pain Index	• If pain present • Average pain intensity • Number of pain locations

Pain Questionnaire[120, 121]	Pain interference over the last week using components from the International SCI Pain Basic Dataset and Brief Pain Index	• Pain interference with respect to:
		  ○ General activity
		  ○ Mood
		  ○ Pain
		  ○ Sleep
		  ○ Social activity

Craig Hospital Inventory of Environmental Factors- Short Form[122]	Barriers and facilitators to participation (accessibility, accommodation, resource availability, social support)	• Frequency score • Magnitude score • Frequency-magnitude score

Table 3.1 Continued

Measure	Description	Components Included in Analyses
Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36)[123]	Assessment of physical and mental health	• Domain scores: o Emotional role limitations o Energy/fatigue o General health perceptions o Mental health o Pain o Physical functioning o Physical role limitations o Social functioning
Medical Outcome Study Social Support Survey[124]	Assessment of various dimensions of social support	• Overall support index • Subscales: o Affectionate o Emotional/informational o Positive social interaction o Tangible
Moorong Self-efficacy Scale[125]	Belief in an individual's ability to achieve desired outcomes	Converted to percent of maximum score: • Total score • Subscales: o General o Personal function o Social function
Pittsburgh Sleep Quality Index (PSQI)[138]	Subjective sleep characteristics over the past month	• Global score (sum of 7 components) • Overall sleep quality (global score >5 [poor sleep quality] or ≤5) • Components: o Daytime dysfunction o Disturbances o Duration o Efficiency o Latency o Sleep quality
Sleep/Activity Log[132-134, 136, 137]	Log of factors that are known to affect sleep that is completed each day of the data collection	• Dichotomized to if it occurred over the collection period (yes/no): o Alcohol use (in 6 hours prior to sleep) o Caffeine use (in 6 hours prior to sleep) o Exercise o Sleep medication use • Averaged over nights collected (score 0-10) o Fatigue rating o Sleep rating
Spinal Cord Injury-Quality of Life Resilience Short Form[126]	An individual's ability to psychologically adapt to their SCI	• Total t score

3.2 **Clinical and Ambulatory Assessments**

3.2.1 **Clinical Assessments**

Clinical measures included MMT, LT, and MAS scores, to assess strength, sensation, and spasticity, respectively (Table 3.2).[33, 34] Scoring for each clinical assessment is described in Table 2.1. The strength and sensation assessments were completed as described by the ISNCSCI for Aims 3 and 4; for the cross-sectional study due to setup constraints, they were completed with the participant in a seated position.

Table 3.2: Clinical variables used in the analyses

Assessment	Description	Components Included in Analyses
MMT Motor and LT Sensation scores[33]	Clinical measures of strength and sensory impairment	• Key muscles/sensory points from each level from L2-S1 • Knee flexion (MMT only) • Lower extremity score (sum of scores from L2-S1) • Upper extremity score (sum of scores from C5-T1) • SCI severity (AIS A, B, C or D calculated from clinical exam)
MAS[34]	Clinical measure of spasticity (score of 1+ treated as 1.5)	• Ankle plantarflexors • Knee flexors

3.2.2 **Ambulatory Assessments**

Participants who self-reported the ability to walk completed WISCI-II, 10mWT, and 6MWT, to assess their need for assistance (physical assistance, bracing, or AD), speed, and endurance, respectively.[102, 104] Participants were able to use their normal bracing and equipment. The WISCI-II is a hierarchical scale with the minimal score of 0 indicating "unable to stand and/or participate in assisted walking" and a maximal score of 20 indicating "ambulates with no devices, no braces and no physical assistance, 10m."[102, 104] For the 10MWT, participants were instructed to

walk 10 meters at their preferred pace while their speed was timed. For the 6MWT, participants were instructed to ambulate as far as possible on a level, straight surface for 6 minutes (inclusive of standing rest breaks) and the total distance walked was recorded.[102, 104] Participants received a score of 0 on all 3 tests if they were non-ambulatory. Participants were allotted as many breaks as needed between tests to ensure the clinical and ambulatory assessments were minimally affected by fatigue. All 3 ambulatory ability assessments have demonstrated excellent inter- and intra-rater reliability and good responsiveness to detect changes in locomotion.[102-104] Additionally, the 10mWT and 6MWT have often demonstrated strong correlations to each other, however they have been found to capture different aspects of ambulatory ability and are both important to include.[103]

When possible, the measures of ambulatory ability were kept as continuous outcomes. (Aim 4). However, at times to maximize the clinical utility of the models and to avoid overfitting while still providing increased resolution over current binary CPR outcomes, we categorized the WISCI-II, 10mWT, and 6MWT into 3 clinically relevant divisions based on current literature (Table 3.3, Aims 2 and 4b).[2, 103, 105, 106]

Table 3.3: Categorical measures of ambulatory ability

Measure	Category Description
Walking Index for SCI II (WISCI-II)	Requires physical assistance (or non-ambulatory) Requires an AD, but no physical assistance Requires no AD or physical assistance
10 meter Walk Test (10mWT)[103, 105]	Non-ambulatory (0 m/s) Household ambulator (0.01 - 0.44 m/s) Community ambulator (> 0.44 m/s)
6 Minute Walk Test (6MWT)[2, 106]	Non-ambulatory (0 m) Household ambulator (1 - 204 m) Community ambulator (> 204 m)

3.2.3 **Assessors for Clinical and Ambulatory Measures**

For the cross-sectional study, nearly all clinical and ambulatory assessments were completed by one of two physical therapists on the research team. For the longitudinal study, the inpatient clinical and ambulatory assessments were extracted from the electronic health record when available to decrease participant burden and because these same measures utilized in the study are routinely collected in our IPR unit. Research staff were able to monitor some of these assessments to ensure they were being completed and recorded correctly.

Due to the COVID-19 pandemic and restrictions placed on in-person research, the follow-up data collections for the longitudinal study were collected remotely for many participants. If participants were attending physical therapy (home health or outpatient) and provided permission, then we coordinated the collection of the clinical and ambulatory assessments with the participant's physical therapist. If the participant was not attending physical therapy, then they were given the option to self-assess the ambulatory tests. Participants were provided with a pre-measured string with markers to ensure that the distance and portions measured were correct. They were also provided ample verbal and written instructions including pictures and examples. Due to the excellent reliability of the ambulatory measures, differences in raters were not likely to substantially impact the consistency of the assessments.[102-104] When completing a remote data collection, if the participant was not attending physical therapy or had a recent medical visit where these measures were recorded, then we were not able to obtain the strength, sensation, and spasticity measurements as they cannot be self-assessed.

3.3 **Measuring LA**

3.3.1 **Wearable Sensors**

ActiGraph GT9X Link tri-axial accelerometers were worn on the non-dominant wrist and both ankles continuously for 1-7 days (Figure 3.1 and Figure 3.2).[139, 140] Bilateral ankle monitors were used to account for asymmetric impairments, while upper limb accelerations were measured to account for whole-body movements such as rolling. The non-dominant wrist was used to minimize the noise from non-purposeful movements that may affect the measurement of activities such as counting steps during the daytime.

For the cross-sectional study, the ankle accelerometers are worn on the lateral sides of the ankles and secured by a padded, adjustable velcro strap. Although not utilized in the present analysis, a Modus StepWatch activity monitor was also used in the longitudinal study to measure steps and other walking-related metrics. The StepWatch must be worn on the lateral side of the ankle of the stronger (or dominant if equal strength) lower limb the for best accuracy. For the longitudinal study, the ActiGraphs were worn on the medial side of both ankles and adjustments were made to the axis orientation in the analysis to account for the different positioning.

The accelerometers were only to be removed for periods of water exposure and participants were not to modify any of their normal activities. Participants were instructed in safe use and donning/doffing of the devices and were provided with printed instructions to ensure skin integrity and proper placement. Additionally, for the longitudinal study, clinical staff working on the IPR unit where inpatient data collection occurred were trained on proper use and placement of all study devices to assist participants as needed. All study materials were returned at the end of the data collection period in-person or via a pre-paid USPS envelope.

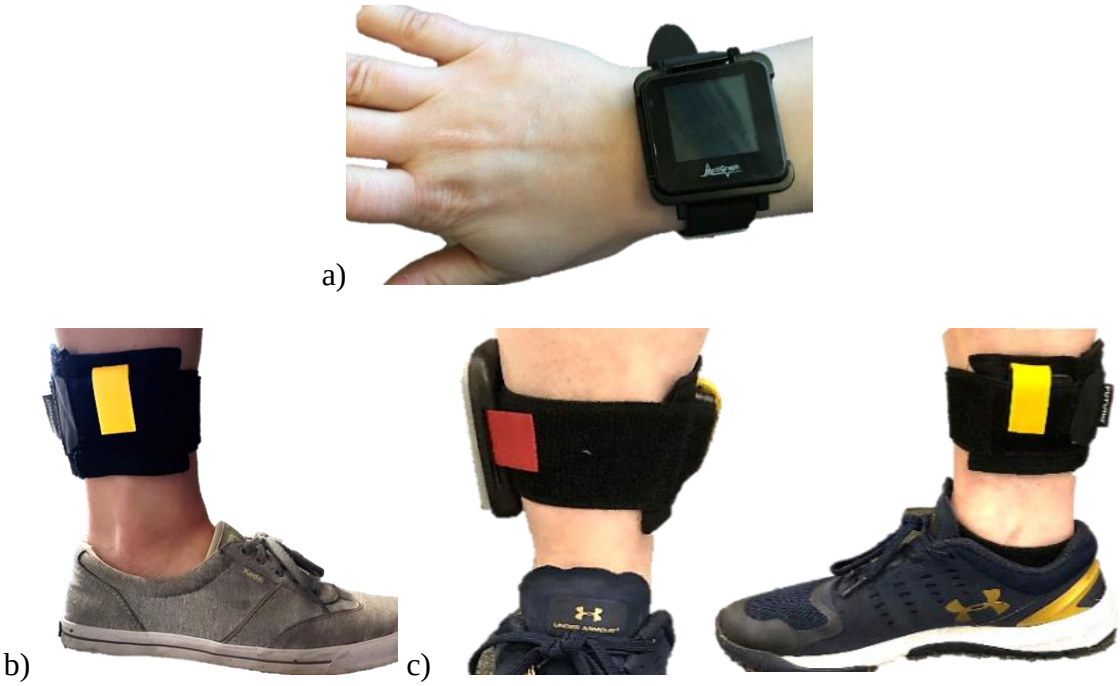


Figure 3.1: Examples of proper accelerometer placement on a) the non-dominant wrist for both studies, b) the lateral ankles for the cross-sectional study (Aims 1 and 2), and c) the medial ankle for the longitudinal study (Aims 3 and 4, lateral ankle shows StepWatch activity monitor that was not used in the current analysis). The ankle accelerometers are marked by yellow velcro for easier identification of proper placement.

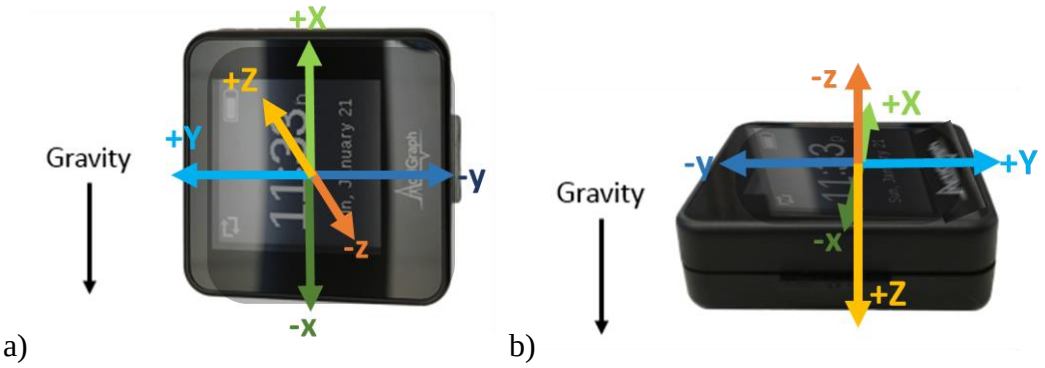


Figure 3.2: Examples of the gravitational vector orientation for the ActiGraph GT9X Link accelerometer for the right ankle of a participant when laying a) supine and b) sidelying on the left side with his or her head on the left side of the page and feet on the right side. The accelerometers are worn and computationally adjusted as needed such that, the x axis runs anterior-posterior, the y axis runs superior-inferior, and the z axis runs medial-lateral.

In the SCI population, ActiGraph sensors have been safely used to assess physical activity and energy expenditure among wheelchair users[81, 141] and sleep assessment among individuals with tetraplegia.[142] ActiGraph accelerometers were also shown to have excellent agreement with manually counted steps during physical therapy sessions in IPR among individuals with incomplete SCI.[143] Additionally, the ActiGraph sensors have been shown to be accurate in predicting in-lab versus at-home activity in ambulatory participants with incomplete SCI.[115]

For these analyses, only the period while the participant was asleep at night was analyzed to minimize biases that might be present in daytime data based on the individual's therapy, interests, or occupation and not their actual abilities. Due to the nature of SCI and the spasticity that often is associated, participants presented with extreme variation in the number of movements per night with some participants having several hundred and some having very few.[140] This variation often caused substantial under or over-estimates of sleep times when automatically detected by algorithms. Therefore, the sleep logs were utilized as the primary method to determine when the participants were asleep, while sleep detection algorithms and visual analyses were used to manually adjust times if needed.[140] To account for any changes to sleep patterns from participants not being in their home environment or otherwise having unusual sleep, only nights identified as "typical" on the sleep log were included in the analysis.

3.3.2 **Pre-processing and Feature Extraction**

Drawing from previous analyses,[89, 111, 112, 144-163] we identified LA as accelerations from any limb movements occurring while asleep, which could include rolling, turning, periodic limb movements, spasms, and positional shifts. LA pre-processing and feature extraction steps are described in (Figure 3.3). Using Matlab 2020a, raw accelerations (sampled at 30 Hz, Figure 3.4)

from all limb accelerometers were band-pass filtered (0.25-10 Hz) to analyze only accelerations that are likely due to human movements (i.e. removing gravitational accelerations and high frequency noise) and the vector magnitude was calculated from each monitor over the collection period.[111, 162, 163] The start and end of each movement was identified as when the standard deviation (SD) of the magnitude in a moving window was greater or less than pre-defined thresholds (Figure 3.5). Thresholds were determined by visually identifying the values that corresponded to the initial increase in acceleration magnitude (SD > 0.03 m/s^2) and return to baseline (SD < 0.02 m/s^2). To ensure the movement was not artifact, the SD had to be above the thresholds for at least 0.5 seconds.[144] The movement was discarded if the root mean square (RMS) of the movement magnitude was not at least equivalent to the local RMS of the noise plus two SD as accelerations that are this small may not represent true movement. Movements were combined if they occurred within 2 seconds of each other.[112, 144]

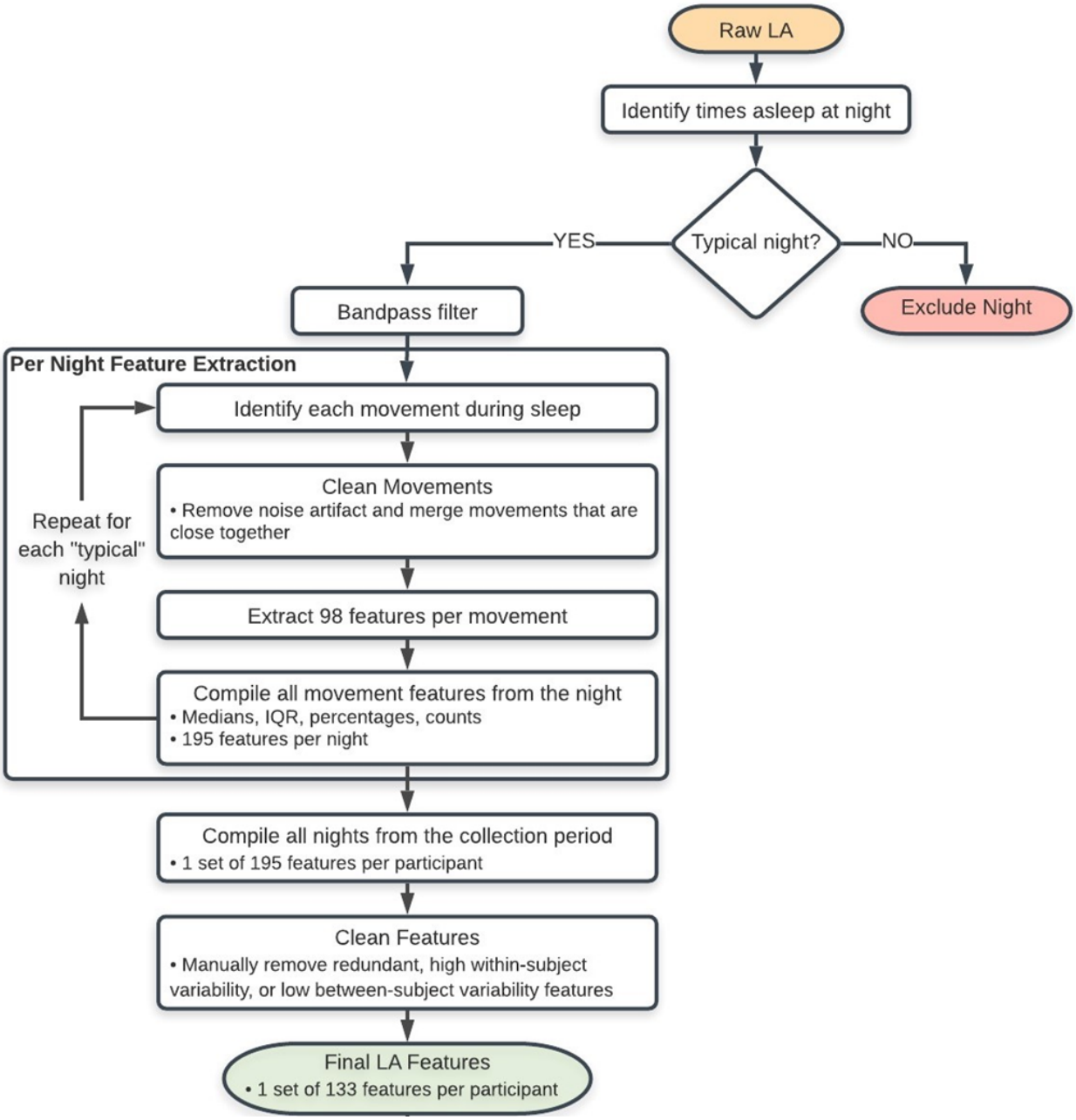


Figure 3.3: Flowchart showing the analysis steps for LA feature extraction from raw accelerations.

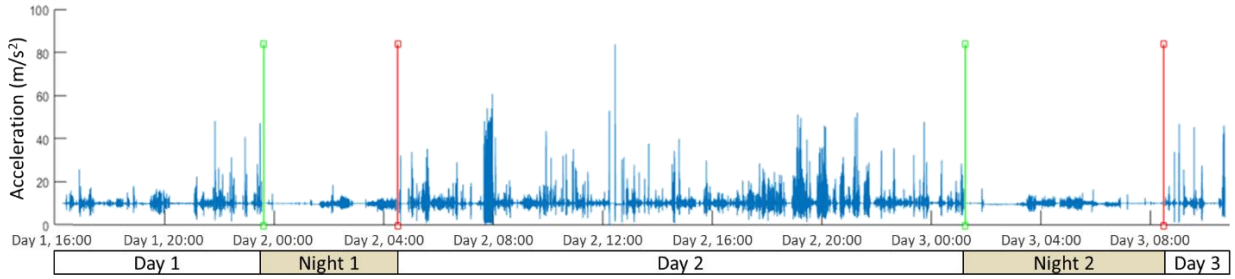


Figure 3.4: Raw accelerations from 1 ankle across portions of 3 days with green and red lines indicating the start and end of each night of sleep, respectively.

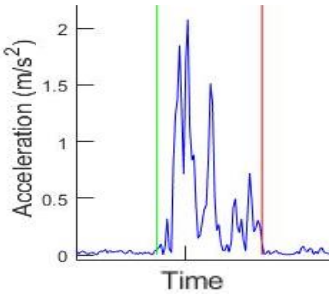


Figure 3.5: An example of acceleration magnitude for 1 movement indicated by the start (green) and end (red) lines.

Features were calculated from each identified movement episode based upon features previous used in PLM, gait, sleep assessment, and other accelerometer analyses.[89, 111, 112, 144-163] This resulted in 98 LA features being extracted from each movement measured from each accelerometer throughout the night for each "typical" night collected. Although some machine learning analyses can utilize many related samples per participant, these models are likely to overfit given our sample size and are not applicable to all of the planned analyses.[164-167]

Based on preliminary analyses, we determined that the best method to result in 1 set of representative, yet stable features per participant was to use the median and interquartile range (IQR) of each feature across all movements from either lower limb per night then across all

"typical" nights per collection to result in 196 features per participant. We assessed the use of only the stronger/weaker or dominant/non-dominant limbs, but found the best preliminary results when combining the limbs such that all movements identified by either lower limb per night had LA features extracted before being condensed into 1 set of representative movement features per night using the median and IQR. Other methods assessed to combine individual movements into 1 feature set per participant were to take the mean and SD across all movements per night and then across all typical nights or to take the median/IQR or mean/SD of all movements across the collection without separating by night. Additionally, we also counted the number of movements that fell into sized bins per category (e.g., short, moderate, and long duration movements), but due to the arbitrary nature of assigning the cutoff values for many features, this was not utilized.

Features that were visually examined to have high within-subject variability (indicating an unreliable feature) or low between-subject variability (uninformative feature) when examined visually using boxplots were excluded. Some of the features provided detailed information regarding the direction and type of movement being performed were likely not reliably measured due small variations in the accelerometer position on the ankle throughout the night or occasional misplacements of the accelerometers noted mostly in the acute setting for the longitudinal analysis. Thus, the positional features that remained in the analysis were ones that related to overall changes in position and were robust to small fluctuations in accelerometer positioning. For example, the features quantifying the pre-movement angles with respect to each axis were initially calculated to provide information regarding a participant's position (e.g., supine, side-lying, etc.). However, if the accelerometer is moved slightly on the limb, then this information was inaccurate or inconsistent. Thus, these features were removed, but features that measured the total change in the angle or gravitational vectors remained since those features were not as sensitive to the exact start

and end positions. Additionally, some features were removed that were found to be repetitive with another feature (highly correlated, but not identical features were still included at this stage). This all resulted in the exclusion of 63 features and a final LA feature set of 133 features being included in further analyses. Those 133 LA features are described in Table 3.4. The “Feature Short Name” is the name used to reference the LA feature throughout the dissertation.

Table 3.4: Descriptions and abbreviation key of LA features extracted and included in the analysis. "Feature Short Name" is the name used to reference the LA feature throughout the dissertation. All features are calculated per ankle accelerometer and per movement and combined by taking the median and IQR across nights unless otherwise noted (* indicates a feature calculated per night, † indicates maximum across nights also calculated).

Feature Category	Feature	Feature Short Name	Feature Description	Larger value indicates…
Change in angle of inclination [155, 157-159]	Net	Angle Net Change	Change from the start and end position angles	Larger net change in body position
	Rate	Angle Rate Change	Total change in position divided by duration of movement	Faster positional changes
	Total	Angle Total Change	Total change in position throughout movement	Larger positional changes
Change in gravitational acceleration [154, 159, 162]	x	Grav Change X	Describes changes in body positions with respect to the gravitational (DC) vector	Larger change in proportion of gravitational vector in each direction
	y	Grav Change Y		
	z	Grav Change Z		
Correlation coefficients between axes [154, 160, 162]	x-y	Corr XY	Describes the relationship between axes during a movement	Movements occurring in more consistent directions
	x-z	Corr XZ		
	y-z	Corr YZ		
Frequency domain [146-154, 161]	Bandwidth	Bandwidth	Range of frequencies that contain 95% of the total power	Movements use a larger range of frequencies
	Centroid frequency	Centroid Freq	Frequency that divides the spectral power distribution into two equal parts	Higher frequency movements
	1st dominant frequency	Dom Freq 1	Frequency at maximum spectral power	
	2nd dominant frequency	Dom Freq 2	Frequency at 2nd highest peak of spectral power	
	Dominant frequency in low frequency range	Dom Low Freq	Isolating just frequencies most likely to contain human movements (0.6-2.5 Hz)	
	Mean/Median frequency	Mean Freq, Med Freq	Estimate of mean/median normalized frequency	
	Ratio power at dominant frequency to total	Power Dom Freq 1/ Total	Proportion of the total power that occurs at the dominant frequency	Higher proportion of the total energy occurred at the dominant frequency
	Power at 1st dominant frequency	Power Dom Freq 1	Maximum power	More powerful movements
	Power at 2nd dominant frequency	Power Dom Freq 2	Max power at 2nd highest peak of power spectrum	
	Power at dominant frequency in low frequency range	Power Dom Low Freq	Power at frequencies most likely to contain human movement (0.6 - 2.5 Hz)	
	Ratio of high frequency power to total	Power High Freq/Total	Proportion of power that may likely be noise and not produced from movement (> 3.5 Hz)	More noisy movement signals
	Total power	Power Total	Area under the power spectral density curve	Higher energy, more powerful movements

Table 3.4 Continued

Feature Category	Feature	Feature Short Name	Feature Description	Larger value indicates…
Limb movement percentages	Bilateral ankle	Bilat Ankle %	Proportion of movements where both ankles are moving simultaneously	Possible increased synergistic movements or lack of motor control to isolate limbs independently
	Unilateral ankle	Unilat Ankle %	Proportion of movements where only the unilateral ankle is moving	Possible increased spasticity or strength on one lower limb
	Wrist and bilateral ankles	Whole Body %	Proportion of whole body movements (i.e., rolling)	More whole body movements
	Wrist and unilateral ankle	Wrist Ankle %	Proportion of movements where both the ankle and wrist are moving simultaneously	Possible increased strength on one side of the body
Median crossings [89, 149, 150]	Number of crossings	Num Med Crossings, Num Med Crossings Norm	Measure of movement smoothness	Less smooth movements
Periodic limb movements (PLM) [112, 152]	* Number of series	Num PLM Norm	Total number of movements meeting approximate criteria to be defined as PLM	More series of short, repetitive movements (likely spastic or PLM)
	* Index	PLM Index	Total number of movements meeting approximate criteria to be defined as PLM divided by the number of hours asleep (>15 events/hour is indicative of possible dysfunction)	
	* Percentage of movements	PLM %	Percent of all movements occurring during the night that could be classified as PLM	Higher proportion of total movements are occurring in short, repetitive series (likely spastic or PLM)
Relationship to recent movements [146, 147, 149, 160, 162]	Dominant frequency in last 90s	Dom Freq Last 90s	Frequency of recent movement series	More movements occurring in series
	Cross-correlation/ covariances in last 90s	Close Cross Cov/Corr Peak, Max Cross Cov/Corr, Mean Cross Cov/Corr Peaks Num Cross Cov/Corr Peaks	Similarity between recent movement (calculates: maximum value, closest and mean peak values, number of peaks)	More similar/repetitive recent movements
	Number of movements in last 90s	Move Last 90s	Quantifies if movement occurred as part of a series	More short, frequent movements are part of a series
	Time since previous movement	Time Since Prev	Seconds since last movement ended	More sparse movements
Signal characteristics [146-148, 160]	Entropy rate	Entropy Rate	Measure of signal regularity	More regular movement accelerations (samples within a movement are more related and less random)
	Lempel-Ziv complexity	Lempel-Ziv Comp	Measure of complexity-probability	Less predictable, more complex accelerations
	Maximum Lyapunov exponent	Lyapunov Exp	Measure of local dynamic stability (sensitivity to perturbations)	More chaos/divergent accelerations, less stable
	Wavelet energy	Wave Approx, Wave Energy 1, Wave Energy 2, Wave Energy 3	Approximation, 1st - 3rd details of the wavelet transform to evaluate the relative energy in each time-frequency band	Higher energy concentration
	Wavelet entropy	Wave Entropy	Measure of signal disorder	More random process/more disorder

Table 3.4 Continued

Feature Category	Feature	Feature Short Name	Feature Description	Larger value indicates…
Statistical [146, 147, 149-153, 162]	Area under the curve	AUC Acc, AUC Acc Norm	Total change in velocity	Larger total change in speed
	Signal magnitude area	SMA Acc		
	Duration †	Duration	How long each movement lasts	Longer movements
	Kurtosis	Kurtosis	Describes weight of the movement's tails relative to the center of the movement	More widely spread accelerations (less distinguishable max value)
	Maximum to RMS	Max-RMS Acc	Measure of movement smoothness	More jerky movements
	Maximum	Max Acc	Measure of acceleration magnitude	Larger changes in speed
	Range	Range Acc	Maximum to minimum acceleration	
	Median	Med Acc	Median of acceleration magnitude	Larger magnitude movements
	Root mean square (RMS)	RMS Acc	RMS of acceleration magnitude	
	SD	SD Acc	Variability of acceleration magnitude	Larger variation within movements
	Skewness	Skewness	Describes the symmetry of the temporal spread of a movement	Positively skewed movements: largest acceleration for movements occur early and then there are longer slow-down periods
Timing [112, 156, 162]	* Number of movements	Move/night, Move/hour	Number of movements (calculates: movements per night, movements per hour)	More movements
	When movements occurred in night	Start Move %, End Move %	Determine if movement are clustered in a certain portion of the night or well distributed	Movements occur later in the night
	* Time asleep	Time Asleep	Hours asleep	Longer time asleep
Velocity and distance [155, 156]	Median velocity	Med Vel	Movement speed	Faster movements
	RMS velocity	RMS Vel		
	Total distance	Total Dist	Total meters traveled	Further distance moved

4.0 Cross-Sectional Study Among Individuals with Chronic SCI

4.1 Study Population

Participants were recruited locally using a research registry as well as at the 2018 and 2019 National Veterans Wheelchair Games and the 2019 National Disabled Veterans Winter Sports Clinic. Participants were enrolled if they were at least 18 years of age, had a chronic (≥ 1 year), non-progressive SCI. Participants were excluded if they had a medical diagnosis of a condition that may affect sleep (e.g., sleep apnea or restless leg syndrome), were unable to wear activity monitor devices on wrist and ankles continuously for up to 1 week (e.g., due to autonomic dysreflexia or sores), or had an injury to the legs that would significantly impair ambulation (e.g., amputation or severe trauma). If the individual had a lower extremity motor score (LEMS) of zero (no voluntary movement) they were classified into the motor complete SCI group, otherwise if some voluntary lower limb movement is present, they were classified into the motor incomplete SCI group. All participants completed informed consent as approved by the VA Pittsburgh Healthcare System Institutional Review Board.

4.2 Sample Size Considerations

Traditional statistical models can be used as a conservative method for estimating power with machine learning approaches. This is especially true when considering that machine learning techniques tend not to require as large of sample sizes to produce accurate results.[168] Since Aims

1 and 2 have overlapping samples, we identified the number of individuals with chronic, motor complete SCI from Aim 1 and the number of individuals with motor incomplete SCI from Aim 2, as this resulted in the largest samples needed to complete all analyses.

For the original analysis for Aim 1, we had planned to compare LA between individuals with able-bodied controls and motor complete and incomplete SCI. We estimated sample size for Aim 1 using a one-way ANOVA with three impairment groups which required a total sample size of 66 participants (n= 22 in each group) to detect a significance level of α= 0.05 with power= 0.8 and an effect size of 0.40. Using a regression model based on the analysis for Aim 2, we would need an estimated 58 subjects to detect a significant R^2 increase (from 0) for each individual predictor with acceptable power ($\geq$ 0.8), assuming small to moderate effect sizes (f^2 = 0.11; alpha= 0.1; G*Power 3.1.9.2). To ensure a final sample size of 22 participants with motor complete SCI and 58 with motor incomplete SCI and accounting for a 15% rate of missing or non-usable data, we had planned to recruitment a goal of 25 and 68 participants with motor complete and incomplete SCI, respectively.

Due to funding delays, restrictions on research from the COVID-19 pandemic, and other recruiting difficulties, we did not achieve these goals. We were able to recruit 36 participants with motor incomplete SCI and 13 with motor complete SCI. Based upon preliminary results, we estimated the actual effect size for the analyses would be much larger (0.39 - 1.13) than was used for the sample size calculations, and thus our power analysis was likely conservative. Thus, we implemented more strict forms of cross-validation and other machine learning methods to account for the smaller sample size and continued the analysis with the 49 total participants with chronic SCI.

4.3 **Aim 1: Association Between LA and Neuromuscular Impairment**

4.3.1 **Introduction**

For decades researchers have been trying to understand which clinical variables are related to or able to predict long-term ambulatory ability after a new SCI. Although many different clinical variables have been assessed as predictors of ambulation, such as AIS/Frankel Grades,[45, 48, 53, 63, 169] demographic information such as age and sex,[4, 5, 45, 58] and somatosensory evoked potentials,[53] the most common predictors are simple clinical measures of strength and sensation.[4, 5, 53, 58-63] Clinical measures such as MMT, LT, and the MAS to assess strength, sensation, and spasticity, respectively, are performed frequently after an SCI. These measures have the advantages of being quick to perform, requiring no additional equipment, and the MMT and LT are included in the ISNCSCI exam.

Despite the many attempts to use strength and sensation as predictors of ambulation, studies have shown that these predictors are not able to consistently produce accurate predictions of ambulatory ability, especially among those with incomplete SCI.[7, 51, 109] While these tests may be sufficient for clinical use, they likely lack the reliability and responsiveness needed to provide adequate predictions for individuals with incomplete SCI. Additionally, spasticity is not generally included in prediction models, despite being one of the top three therapist-reported factors that interfere with therapy post-SCI and its known relationship to pain and function.[71-74] Spasticity can at times be helpful for mobility, but it can also often increase pain, lead to contractures, and destabilize balance which negatively affect ambulatory ability.[170, 171]

We proposed that measuring an individual's actual movement would be a more sensitive and responsive measure of an individual's level of impairment than traditional clinical tests. Since

daytime activity can be biased by an individual's interests, occupation, participation in rehabilitative therapy, and activity level, measuring movement characteristics at night may be less affected by these external factors. For example, a movement at night may be triggered by the tactile sensation of pressure building in an area of the body and then an individual must possess the strength to be able to voluntarily adjust their positioning.[84, 85] Additionally, it has been shown that supine positioning may increase spasticity, thus, spasticity may be more prevalent while laying down to sleep at night.[86, 87] Therefore, LA, defined as accelerations from any movement occurring while asleep at night, may be able to capture more responsive information about an individual's neurological impairment than clinical measures, such as MMT, LT, and the MAS.

To provide foundational knowledge of LA as a meaningful clinical metric, we aim to determine the association between LA and current clinical measures of neuromuscular impairment among individuals with chronic SCI. We hypothesize that features of LA such as those related to amplitude and duration of movements will be most strongly related to clinical assessments of strength, sensation, and spasticity among individuals with chronic SCI. Determining the relationship between clinical measures of impairment and LA will provide evidence of face, construct, and concurrent validity for LA and support the clinical use of LA as a predictor of ambulation (additional information about validity in Section 2.4.1.1).

4.3.2 **Methods**

Individuals with chronic, motor complete and incomplete SCI were included in this analysis as described in Sections 4.1 and 4.2. Since individuals with motor complete SCI will have a LEMS= 0, they were intentionally enrolled in a smaller proportion in comparison to the number of participants with motor incomplete SCI and LEMS > 0. Each participant completed

questionnaires, clinical, and ambulatory assessments as applicable during 1 in-person visit and then wore the ActiGraph GT9X Link accelerometers for 1-5 days as described in Section 3.0.

4.3.2.1 Analysis

4.3.2.1.1 Input Variables: LA and Covariates

The raw accelerations were processed as described in Section 3.3.2 to extract 133 LA features per participant (Table 3.4). Since both LA and each impairment outcome were measured bilaterally, analyses were performed to assess independence between sides (Appendix D.1). Due to the high correlation between LA features and impairment outcomes between the stronger and weaker lower limbs and covariates assessed once per participant, only 1 sample was calculated per participant by combining the LA features from each limb as described in Section 3.3.2.

Three feature sets were produced during the analysis that contain: the LA features alone, LA features and other possible covariates/confounders, and the covariates/confounders alone (just referred to as "covariates" for simplicity). Since the impairment outcomes were measured cross-sectionally, the measurement of both impairment and LA could be affected by factors such as pain, demographics, sleep quality, exercise, sleep medication, or consumption of caffeine or alcohol.[120, 121, 123, 132-134, 136-138] For example, if an individual has slept poorly, they may be less able to exert themselves during the strength measurements, less focused during the sensation assessment which may introduce more error, and have atypical movements during their sleep the following night (e.g., less movements if sleeping more soundly). Therefore, it is important to assess how these covariates may affect the relationship between LA and impairment, and how much additional variance in impairment is explained by adding LA to the covariates. All covariates included in the models are listed in Appendix Table D.1.

All features were normalized so that all LA and covariate features carried equal weight in the machine learning model. Since LA needs to be reproducible for clinical use even if new samples are added, we scaled each feature such that the minimum value was recorded as 0 and the maximum as 1.

4.3.2.1.2 Output Variables: Strength, Sensation, and Spasticity

Measures of strength, sensation, and spasticity were used as the dependent variables in models as an estimate of neuromuscular impairment. Strength was quantified by the LEMS which sums the MMT motor scores from the L2 to S1 myotomes across both lower limbs for a score between 0 (total paralysis) to 50 (normal, Table 2.1, Table 3.2). Lower limb LT sensation was similarly calculated by summing the individual LT sensation scores from each dermatome across the lower limbs (L2-S1) for a total score between 0 (no sensation) and 20 (full sensation).[33] Strength and sensation scores were used as continuous outcomes.

Spasticity was measured by the MAS for the knee flexors and ankle plantarflexors of both lower limbs. Since MAS had a skewed distribution in our sample with many participants having no spasticity, it was categorized into 3 groups: no, mild, and moderate spasticity. Participants were categorized as "no spasticity" if they had a MAS score of zero for all lower limb areas assessed. Participants were categorized as "mild spasticity" if they had some spasticity (MAS > 0) recorded, but all MAS scores were less than 2 for both lower limbs. Participants were categorized as having "moderate spasticity" if any MAS score was 2 or higher. The cutoff score of 2 was used based upon the finding by Baunsgaard et al., that about 80% of MAS scores reported in a sample with SCI had a score of 0, 1, or 1+. Therefore, if a participant had a score of 2 or higher it was above average and could be considered as moderate to severe spasticity.[77]

4.3.2.1.3 Machine Learning Models

A three-step process was used to 1) determine the optimal LA and covariate features using algorithms with built-in feature selection, 2) reestablish the baseline model performance for just the selected features using algorithms without feature selection, and 3) add the selected LA features to the covariates model to determine the additional explained variance in each impairment outcome (Figure 4.1). The least absolute shrinkage and selection operator (LASSO) implemented with least angle regression (LARS) and logistic regression with ℓ_1 regularization algorithms were utilized to select the important features for the continuous outcomes (strength and sensation) and categorical outcome (spasticity), respectively. The full description of the algorithms is provided in Appendix D.1. These models were chosen based upon their efficiency, ability to perform feature selection as part of the model building process, and ability to determine the relative strength of each selected feature to the impairment outcome. The coefficient values and features selected by the models can provide information about the relative importance of each feature as related to the impairment outcome. Approaches using a LASSO or similar machine learning models have been used to assess improvements lower limb rehabilitation using accelerometers after anterior cruciate ligament reconstruction.[172, 173] Specifically among individuals with SCI, similar methods have been used to predict neurological recovery from MRI findings,[174] classifying activities in-lab versus at-home among ambulatory participants,[115] and determining the association between an unsupervised home sleep apnea test and sleep-disordered breathing and nocturnal hypercapnia.[175]

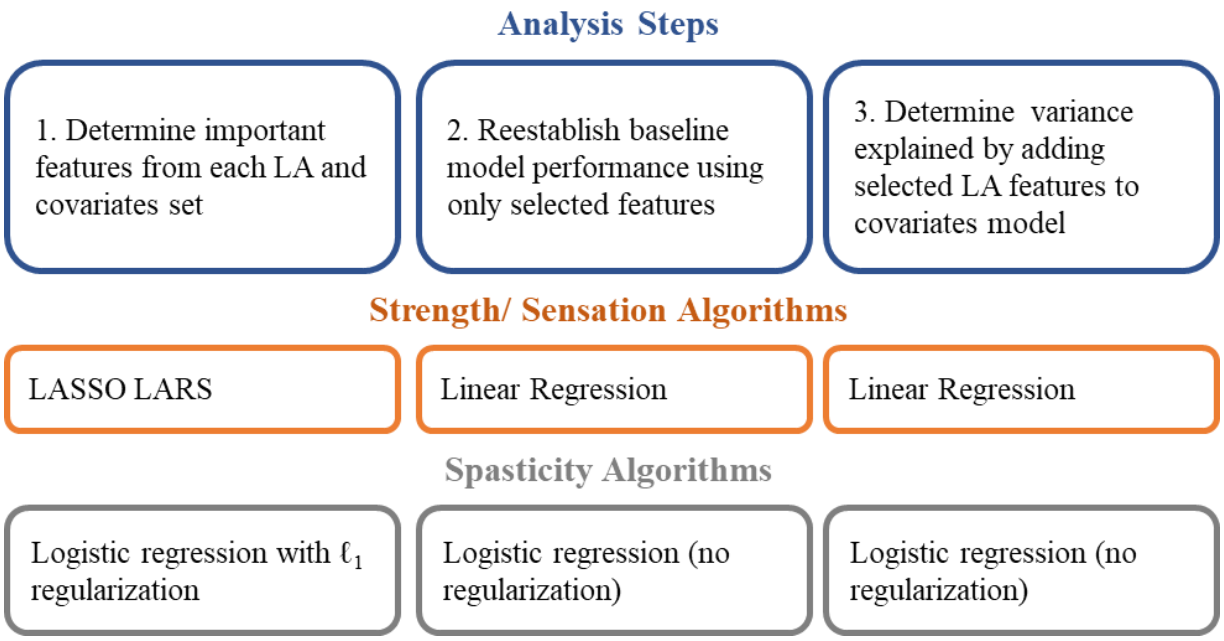


Figure 4.1: Impairment algorithms used for each analysis step in Aim 1

For both the LASSO LARS and logistic regression with ℓ_1 regularization models, 10-fold cross-validation was used to determine the regularization parameters and then the model was trained and evaluated on the full dataset. The features selected by the LASSO LARS and logistic regression models for each impairment outcome when including only LA or covariate features were recorded. To assess the variance explained by the selected covariate features and then by the addition of LA features, linear regression models were used for the strength and sensation outcomes and logistic regression without regularization was used for spasticity. Due to slight differences in the analysis methods, the models built using the algorithms with or without feature selection produce slightly different results when the same final feature sets are used. Therefore, models were assessed using linear regression and logistic regression without regularization and only the selected features from the previous models to ensure that an accurate baseline model performance was recorded. Those baselines would then be compared to the model performance

when selected LA and covariate features were combined to determine the additional amount of variance in each impairment outcome that was explained by adding LA compared to the model with covariates alone.

4.3.2.1.4 Model Evaluation

For the continuous strength and sensation outcomes, the coefficient of determination (R^2) was used to determine the model's ability to explain the variability of the impairment outcome.[176] The adjusted R^2 was also assessed as a correction to the R^2 for the number of features included in the model so that models with different numbers of features can be compared more equitably. Other evaluation metrics included mean and median absolute error which are calculated by taking the absolute value of the difference between each predicted and measured impairment score and then taking the average or median across the sample. Mean squared error (average of the squared difference between the predicted and measured score) was also included as it weighs larger errors more heavily. Lastly, root mean squared error was calculated as this evaluates the standard deviation of the prediction errors by taking the square root of the mean squared error. For each of the measures of error, a lower score is preferable.

The OCA, precision, recall, and F1-score were used to describe the spasticity multinomial model performance (Appendix B). OCA represents the percentage of participants that were correctly classified. Precision represents the accuracy of the true classifications (i.e., positive predictive value) while recall represents the fraction of the correctly identified positive classifications (i.e., true positive rate, equivalent to sensitivity for binary classification). The F1-score is the weighted average of precision and recall.[177, 178] For all classification metrics, a higher score (range=0-1) is indicative of higher accuracy and better model performance. Additionally, the full confusion matrices were examined to look at errors in classification and per-class statistics.

4.3.3 **Results**

4.3.3.1 Participants

Thirty-six participants with motor incomplete SCI and 13 with motor complete SCI completed the data collection. Eight participants (n= 6 motor incomplete and n=2 complete SCI) were excluded because they self-reported that they had no “typical” nights recorded during the collection period. One additional participant with complete SCI was excluded because the accelerometers were likely removed at night and no movements were recorded. Data collection was completed for 2 participants before the spasticity measures were added to the study, so the spasticity analysis has 38 participants included, while the strength and sensation analyses have 40 participants. The demographics for participants that were included in the analysis are shown in Table 4.1. Participants were primarily male, non-Hispanic White, Veterans, with paraplegia who used a manual wheelchair as their primary mode of mobility.

Table 4.1: Participant demographics

Categorical Demographics	**Motor Incomplete** n (% of group)	**Motor Complete** n (% of group)	**Total** N (%)
Sex			
Female	4 (13.3)	2 (20.0)	6 (15.0)
Male	26 (86.7)	8 (80.0)	34 (85.0)
Race/Ethnicity			
Non-Hispanic White	14 (46.7)	6 (60.0)	20 (50.0)
Non-Hispanic Black	10 (33.3)	3 (30.0)	13 (32.5)
Non-Hispanic Other Race	3 (10.0)	0 (0.0)	3 (7.5)
Hispanic (Any Race)	3 (10.0)	1 (10.0)	4 (10.0)
Veteran			
Not Veteran	5 (16.7)	0 (0.0)	5 (12.5)
Veteran	25 (83.3)	10 (100)	35 (87.5)
Annual Household Income			
<$25,000	9 (30.0)	2 (20.0)	11 (27.5)
$25,000-$49,999	3 (10.0)	5 (50.0)	8 (20.0)
$50,000-$74,999	5 (16.7)	2 (20.0)	7 (17.5)
≥$75,000	9 (30.0)	1 (10.0)	5 (12.5)
Decline to Answer or Unknown	4 (13.3)	0 (0.0)	4 (10.0)
Education			
High School Diploma/GED	17 (56.7)	2 (20.0)	19 (47.5)
Associate's Degree	7 (23.3)	4 (40.0)	11 (27.5)
Bachelor's Degree	4 (13.3)	2 (20.0)	6 (15.5)
Graduate Degree	2 (6.7)	2 (20.0)	4 (10.0)
SCI Injury Level			
Paraplegia	19 (63.3)	9 (90.0)	28 (70.0)
Tetraplegia	11 (36.7)	1 (10.0)	12 (30.0)
SCI AIS Classification (Calculated)			
A	0 (0.0)	6 (60.0)	6 (15.0)
B	0 (0.0)	4 (40.0)	4 (10.0)
C	15 (50.0)	0 (0.0)	15 (37.5)
D	15 (50.0)	0 (0.0)	15 (37.5)
Data Collection Location			
Local	8 (22.2)	0 (0.0)	8 (20.0)
Adapted Sporting Event	22 (73.3)	10 (100)	32 (80.0)
Primary Mode of Mobility			
Walk	5 (16.7)	0 (0.0)	5 (12.5)
Manual Wheelchair	20 (73.5)	8 (80.0)	28 (70.0)
Power Wheelchair/Scooter	4 (8.8)	2 (20.0)	6 (15.0)
Equally Walk and Wheel	1 (3.3)	0 (0.0)	1 (2.5)
Continuous Demographics	**Motor Incomplete** Mean ± SD (Range)	**Motor Complete** Mean ± SD (Range)	**Total** Mean ± SD (Range)
Age	54.0 ± 10.5 (25-70)	52.9 ± 14.2 (34-77)	53.7 ± 11.4 (25-77)
Body Mass Index (BMI)	28.2 ± 5.4 (18.5-38.7)	24.4 ± 3.7 (18.7-30.4)	27.2 ± 5.2 (18.5-38.7)
Years Since Injury	18.8 ± 12.5 (3.0-48.7)	16.0 ± 9.5 (5.6-28.9)	18.1 ± 11.8 (3-48.7)

4.3.3.2 Impairment Scores

Impairment scores for all participants are shown in Table 4.2. Participants with motor incomplete SCI had LEMS scores spanning nearly the entire possible range from 2 to 49. Similarly, both motor complete and incomplete SCI groups had participants spanning the entire range of LT sensation scores, though those with motor complete SCI had lower scores on average than those with motor incomplete SCI. Ten (25%), 7 (17.5%) and 15 (39.5%) of participants had strength, sensation, and spasticity scores of 0, respectively. The 60.5% of individuals in this study presenting with spasticity is slightly lower than other studies that have found approximately 65-78% of individuals with SCI having symptoms of spasticity.[74, 77, 179]

Table 4.2: Strength, sensation, and spasticity impairment scores

	Motor Incomplete	**Motor Complete**	**All Participants**
Continuous Impairment Outcomes	Mean ± SD (Range)	Mean ± SD (Range)	Mean ± SD (Range)
Strength (LEMS)	26.9 ± 15.0 (2-49)	0.0 ± 0.0	8.2 ± 8.1 (0-49)
Sensation (Lower Limb Summed LT)	10.9 ± 6.5 (0-20)	3.8 ± 6.6 (0-20)	9.1 ± 7.2 (0-20)
Categorical Impairment Outcomes	n (% of group)	n (% of group)	n (%)
Spasticity (Lower Limb Categorized MAS)			
No Spasticity (MAS=0)	13 (46.4)	2 (20.0)	15 (39.5)
Mild Spasticity (MAS all < 2)	9 (32.1)	5 (20.0)	14 (36.8)
Moderate Spasticity (≥1 location with MAS ≥ 2)	6 (21.4)	3 (30.0)	9 (23.7)

4.3.3.3 Strength (LEMS)

Sixteen LA and 19 covariate features were selected using the LASSO LARS models which independently explained 67.0% and 49.2% of the variance (adjusted R^2) in lower limb strength, respectively (Table 4.3). When LA features were combined with covariates, an additional 35.5% of the variance in strength could be explained (adjusted R^2= 0.847), as compared to the model with only covariates. The features with the greatest association with higher strength scores from the models with LA features were larger variations in energy (Wave Approx- IQR) and local dynamic stability (Lyapunov Exp- IQR, variations in the response to perturbations), fewer variations in the

similarity between recent movements (Max Cross Cov- IQR), smoother movements (Num Med Crossings Norm- Med), and faster rotational movements (Angle Rate Change- Med, Appendix Table D.4 and Appendix Table D.5). When only covariates were included in the model, having more pain (SF-36: Pain), a higher BMI, and fewer pain locations were among the features most related to greater strength. However, when LA and covariate features were combined, the LA features maintained a similar order of association, while the covariate features that were most related to strength in the LA + covariates model were amongst the features that had the lowest associations with strength for the covariate model (more years since injury, more sleep disturbances generally [PSQI: Sleep Disturbance], and better average sleep rating during collection).

Table 4.3: Strength and sensation LASSO LARS and linear regression model results

Strength (LEMS)								
Analysis Step	Feature Set	Number of Features Selected (Initial)	Adj. R^2	R^2	Mean Absolute Error	Median Absolute Error	Mean Squared Error	Root Mean Squared Error
1. LASSO LARS for feature selection	LA	15 (133)	0.469	0.687	8.17	7.87	93.56	9.67
	Covariates	19 (24)	0.394	0.689	8.08	7.67	92.86	9.64
2. Linear regression to reestablish baseline	LA	15	0.670	0.805	6.71	6.61	58.13	7.62
	Covariates	19	0.492	0.740	7.52	7.32	77.75	8.82
3. Linear regression for additional variance explained by LA	LA + Covariates	34	0.847	0.984	1.68	1.18	4.68	2.16
Sensation (Lower Limb LT)								
Analysis Step	Feature Set	Number of Features Selected (Initial)	Adj. R^2	R^2	Mean Absolute Error	Median Absolute Error	Mean Squared Error	Root Mean Squared Error
1. LASSO LARS for feature selection	LA	15 (133)	0.566	0.733	2.91	2.50	13.32	3.65
	Covariates	2 (24)	0.111	0.157	5.70	5.44	42.07	6.49
2. Linear regression to reestablish baseline	LA	15	0.717	0.826	2.21	1.88	8.68	2.95
	Covariates	2	0.222	0.262	5.11	5.25	36.83	6.07
3. Linear regression for variance explained by LA	LA + Covariates	17	0.714	0.839	2.03	1.69	8.05	2.84

4.3.3.4 Sensation (LT)

The sensation model containing only LA features explained more of the variance in lower limb sensation (adjusted R^2= 0.717) than just covariates (adjusted R^2= 0.222, Table 4.3). When combined, LA explained an additional 49.2% of the variance in sensation (adjusted R^2= 0.714) compared to the model with covariates alone. The features selected per model are shown in Appendix Table D.6 and Appendix Table D.7. Only 2 covariates were associated with higher sensation scores: fewer pain locations and better sleep efficiency (PSQI: Sleep efficiency). Additional analyses were performed to minimize the chance that the much lower model performance for the covariates model was due to a data irregularity (Appendix D.3) and no irregularity was identified. Having a less variable time between movements (Time Since Prev- IQR), more consistent movement directions (Corr YZ- Med), lower frequency movements (Dom Freq 1- Med), and less variability in the similarity between recent movements (Num Cross Cov/Corr Peaks- IQR) were most strongly associated with more intact sensation.

4.3.3.5 Spasticity (MAS)

Spasticity categories were more accurately classified using 7-10 selected LA features (F1-Score= 0.765) than 5-6 covariate features (F1-Score= 0.668). When combined, the LA + covariates model achieved nearly 90% accuracy in classifying spasticity categories, including increases in F1-score and OCA of 0.228 and 13.2%, as compared to the model using only covariates. For all models, no participants were falsely predicted as having moderate spasticity (precision= 1). Recall was generally the highest for the mild spasticity category, indicating that those who actually had mild spasticity were more likely to be correctly classified than those with no or moderate spasticity. For the LA + covariates model, the moderate spasticity group had the highest F1-score (0.941), while the mild spasticity group had the lowest F1-score (0.875, no spasticity F1-score= 0.889).

In the model with only LA features, the features most associated with having no spasticity included less power at the second dominant frequency (Power Dom Freq 2- Med), lower percentage of movements that met PLM criteria (PLM %), moving in more variable directions (Corr YZ- Med), more variable energy (Wave Approx- IQR), and more variability in the similarity to recent movements (Num/Close Cross Corr/Cov Peak- IQR, Appendix Table D.8 and Appendix Table D.9). LA features associated with moderate spasticity include less variable movement disorder (Wave Entropy- IQR), lower and less variable energy (Wave Energy 2- Med, Wave Approx- IQR) and, moving in more consistent directions (Corr YZ- Med), less variable symmetry of movements (Skewness- IQR), more frequent movements (Move/hour), and more movements that met PLM criteria (PLM Index). For the covariates, having a longer time since injury, not using sleep medication during the data collection, and having more pain interference with sleep (Pain Interfere: Sleep) were associated with having no spasticity while using sleep medication, having worse nightly sleep ratings (Ave Sleep Rating), sleeping for shorter durations (PSQI: Sleep Duration) and having fewer sleep disturbances (PSQI: Sleep Disturbances) were associated with having moderate spasticity.

Table 4.4: Spasticity logistic regression analysis results*

Analysis Step	Feature Set	Number of Features Selected (Initial)	F1-Score	Precision	Recall	OCA
1. Logistic regression with ℓ1 regularization for feature selection	LA	7-10 (133)	0.814	0.833	0.816	0.816
	Covariates	5-6 (24)	0.764	0.790	0.763	0.763
2. Logistic regression to reestablish baseline for selected covariates model	LA	7-10	0.765	0.820	0.763	0.763
	Covariates	5-6	0.668	0.741	0.684	0.684
3. Logistic regression for additional variance explained by LA	LA + Covariates	12-16	0.896	0.918	0.895	0.895

* Precision, recall, and F1-score represent the weighted average of the per-class scores.

4.3.4 **Discussion**

By demonstrating that machine learning models consisting of only LA features were able to explain approximately 67% of the variance in measures of lower limb strength and 72% of the variance in sensation as well as an F1-score of 0.765 when classifying participants into spasticity categories, we have provided evidence of face and construct validity for LA as a measure of impairment. Further, the adjusted R^2 increased by 72% and 222% for the strength and sensation models, respectively, when LA was added to the covariate features, as compared to using the covariates alone. Similarly, the F1-score for the spasticity classification was 34% higher when including LA, as compared to when only using covariate features. This shows that LA provides additional, unique information that is related to measures of strength, sensation, and spasticity beyond what could be measured using covariate and confounding variables. The models that only included covariates consistently had the poorest performance, thus emphasizing the additional utility and information that LA can provide beyond what is available through demographic information and questionnaires. This further supports that LA features are directly related to measures of impairment, not just a proxy for sleep quality or another related metric.

Although an R^2 of 1 would explain 100% of the variance in the outcome and would be considered a perfect result for a model, we would not expect or want LA to explain that much variance in this case. As explained in Section 2.4.1, the clinical measures used as the outcomes in this analysis have inherent weaknesses and lack the responsiveness required to differentiate between individuals for prediction models, especially among motor incomplete SCI.[8, 9, 34] Since all features of LA are continuous and there are 133 features available, LA is able to provide variability and detailed information about impairment that clinical measures may currently lack.

Thus, the finding of LA having a strong, yet imperfect relationship to each impairment outcome is supporting the aim of the analysis and clinical use of LA as a measure of impairment.

It was hypothesized that LA features such as those measuring amplitude and duration of movements would be most related to the measures of impairment, which is somewhat supported by the findings. Although movement duration was not selected for any of the models, other features such as the percentage of movements that meet the criteria for PLM were selected. By definition, PLM must be short duration movements that occur in series.[112, 152] Therefore, having a higher percentage or larger number of movements that meet the criteria for PLM or PLM indices, being related to better sensation, greater strength, and less spasticity provides support for this hypothesis.

Although more intuitive statistical LA features such as the RMS and maximum movement acceleration were not related to any of the impairment measures, multiple features evaluating the spectral power and energy of movements in the frequency domain were related to each measure of impairment (e.g., Power Dom Freq 2- Med, Power Dom Freq 1/Total- IQR, Wave Approx- IQR, etc.). Additionally, these features often had some of the strongest associations with the measures of impairment. Both the statistical and frequency domain features consist of similar information about the intensity of movements, but the statistical features are with respect to time while features like power and energy are with respect to the movement frequency or both time and frequency. Therefore, it makes intuitive sense that higher energy movements may be associated with greater strength and worse spasticity. Similar features have also been found to be related to improvements in the lower limb after rehabilitation[148] and have been able to differentiate between healthy controls and individuals with Parkinson's Disease and peripheral neuropathy, further indicating the clinical relevance of these measures.[146]

The finding of moderate spasticity being associated with more frequent, less variable, lower energy movements supports visual findings seen during the analysis (Figure 4.2). For some participants, very frequent, low amplitude movements would be observed while they were asleep and these findings were thought to be associated with PLM or spastic movements.[180-184] These findings support that individuals presenting with these movements are more likely to have more severe spasticity. Alternatively, participants with less consistent movements (lower Corr YZ- Med, higher Num Cross Cov Peaks- IQR, Close Cross Cov/Corr Peaks- IQR), higher and more variable energy movements (Wave Energy 2- Med, Wave Approx- IQR) and a smaller proportion of movements meeting the criteria for PLM (PLM %) were more likely to have no spasticity. Since both voluntary and subconscious movements are more likely to occur in variable directions and with variable timing (e.g., when rolling or adjusting positioning periodically throughout the night), it is logical to infer that participants with more frequent, consistent, repetitive movements may have more spasticity while those with more variable, less consistent movements have little to no spasticity.

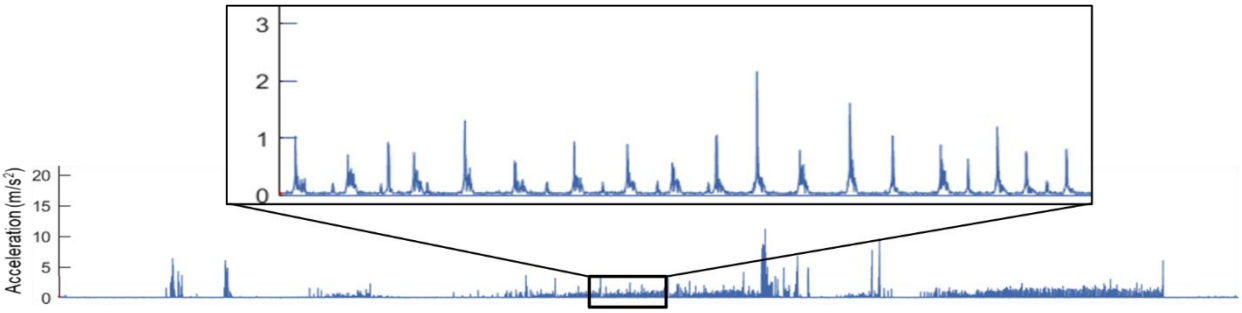


Figure 4.2: Example of potential spastic movements in the acceleration magnitude vs time plot from 1 participant's ankle across the whole night and zoomed in for additional detail. This participant had a T7 AIS C injury and MAS scores of 2 at the knee flexors and 1 at the plantarflexors for each lower limb.

Movement consistency also played a large role in the estimation of strength and sensation scores. Seven of the 16 LA features (43.8%) selected for strength and 6 of 15 (40.0%) of the LA features selected for sensation were associated with movement consistency or related characteristics. Having less consistent movements and wider variability of movements overall, but less variable recent movements were associated with greater strength. Someone with limited strength may also be limited in the types or directions of movements they can perform; thus, they may have a more limited variety of movements as compared to someone with greater strength. For example, if an individual has a low LEMS due to only having motor function of the knee extensors, they may be able to voluntarily straighten their knee during the night, but not be able to move their leg in other directions. This would result in movements consistently occurring in a particular direction and likely presenting with similar characteristics, as opposed to someone with greater strength that could move in a variety of directions.

Additional measures of movement consistency that were related to greater strength include having a wider range of local dynamic stability and chaos (higher Lyapunov Exp- IQR), smoother movements (lower Num Med Crossings Norm- Med), and more negatively skewed movements (lower Skewness- Med). These findings are supported by previous studies that have shown that healthy controls generally had smoother movements and more negative skewness than individuals with Parkinson's disease[146] and Lyapunov exponent being related to improvements in lower limb rehabilitation.[148]

Limb movement percentages and velocity and distance features were not selected in any of the impairment models using LA. Features associated with the change in the angle of inclination or gravitational acceleration were also infrequently selected. This may infer that the distribution of which limbs are moving and the exact amounts and directions may not be as related to

impairment, which further supports that the consistency and variety of movements may be more meaningful than the specifics of the movements being performed. Velocity and distance features are calculated through integration of the acceleration of each movement and are highly correlated with other features that statistically describe the acceleration (Med Acc, AUC Acc, SMA, etc.) and frequency characteristics (Power). Since frequency and time-frequency features were frequently chosen in the models and the LASSO LARS algorithm is intended to minimize collinearity, it may not be that the velocity and distance features are not related to impairment, but just that they were less in informative than other related features.

Although LA features were specifically extracted to be clinically meaningful individually, they provide the most beneficial and comprehensive information when interpreted together.[146] Additionally, since all LA features are extracted using the same data set and the computational time to extract additional features is minimal, there is no additional burden to extract one versus many LA features. Therefore, in addition to providing support for LA as a clinical metric, this analysis demonstrates the potential benefits of having versatile set of detailed features related to impairment available from one data collection with minimal burden the to the participant.

4.3.4.1 Limitations

Especially in small sample sizes, attention must be paid to machine learning models to ensure that overfitting does not occur and that the results are an appropriate estimation for the goal of the analysis. For prediction models, it is critical that the model is assessed using a separate, unseen test set. If this does not occur, the model performance will appear inappropriately favorable as compared to when it is used in practice, since the model was assessed with the same data that was used in building it. A nested, leave-one-out cross-validation model was initially considered to estimate the performance of the LA and covariate features in calculating estimates for each

outcome. This model uses all participants but 1 for an inner-loop cross-validation to calculate model parameters and then tests the model built using those optimal parameters on the 1 held-out sample. It then iterates until each participant is used as an independent test set in the outer-loop. This method is able to estimate the model performance on unseen data while maximizing the size of the training set and without inducing bias.[185-187] However, for the current analysis, we only aimed to determine the association between the measures of impairment and LA in a cross-sectional sample and do not intend to use LA as a predictor of impairment, as this is not clinically useful. Thus, holding out a separate test set of samples or using a computationally intensive analysis such as nested cross-validation to assess the model performance on unseen data was not deemed necessary. Additionally, due to the large variability inherent to continuous outcomes (e.g., the LEMS 0-50 range of outcomes for strength), very large sample sizes are frequently required to obtain an adequate prediction and was logistically not possible for the current analysis.

For the strength model with both LA + covariates, 35 features were included which is a large number given the sample of 40 participants. This large number of features combined with the unadjusted R^2 for that model of 0.984 likely indicate that this model is overfit and would not generalize well to unseen data. As this analysis is only aimed at assessing the relationship between LA, covariates, and impairment and is not intended for prediction, this is not a critical issue. Despite the overfitting, there is still clearly additional variance explained by adding LA to the covariate features with respect to the strength outcome. Overfitting is not apparent in the sensation and spasticity models. Therefore, the results from this analysis are valid for estimating the relationship between LA and measures of impairment in our sample and additional steps were taken (cross-validation for feature selection parameters, targeted participant recruitment, etc.) to minimize the bias in the analysis and maximize the generalizability of the findings.

Although efforts were made to recruit a diverse sample particularly with respect to AIS grade, ambulatory ability, and the impairment outcomes, it is still possible that the sample does not fully capture the demographic characteristics of the whole SCI population.[3] In addition to the model validation, the specific distribution of demographic characteristics among our sample population should be considered when generalizing the findings from this study to the wider population with SCI.

Although only nights "typical" to how the participant normally sleeps were included in the analysis, it is possible that LA was affected by unusual sleep patterns, especially for the portion of the sample that had data collected while participating in adaptive sports events. Covariates that were likely to affect the LA data collection such as exercising, consuming alcohol, and daily and overall sleep quality were included in the models to ensure that these factors were accounted for in the analysis. The minimal change or decreased performance of the models when covariates were included supports that LA was not substantially affected by these factors.

Although preliminary analyses to visually evaluate the intra- and inter-subject variance using boxplots were performed to improve the reliability and usefulness of LA and resulted in the core set of 133 features (described in Section 3.3.2), a formal reliability analysis has not been performed. LA features must be found to be reliable to ensure that the current findings represent the true relationship between LA and impairment and are not the result of chance from inconsistent LA features.

Lastly, although we want LA to capture information that clinical tests lack, using those clinical measures as the outcome of the models limits extent to which the relationship between LA and impairment can be quantified. This limitation is because we cannot be sure how much of the variance in each impairment outcome that was not explained by the LA models is due to variance

induced by other sources not captured in this study or is due to the outcome not providing a sufficient measure of impairment. In the latter case, if an improved measure of impairment was used for each outcome, it is possible that LA would explain more of the variance than was reported in the current analysis. Although using alternative methods for assessing strength and tactile sensation would have been preferred such as using Biodex Dynamometry and monofilaments,[8, 9, 188] due to logistical constraints that was not possible. Using summed measures of strength and sensation over the whole lower limbs and a categorized measure of lower limb spasticity and only two clinicians for all assessments should minimize the effect of the limitations in reliability and responsiveness seen in the individual MMT, LT, and MAS measurements.[56, 189, 190]

While determining the relationship between LA and impairment is important to understand the clinical relevance of this metric, measures of function, participation, and quality of life are more meaningful outcomes for individuals with SCI. The relationship between LA and ambulation with and without the inclusion of personal, psychosocial, and environmental factors (PPEF) was assessed in Aim 2. The finding that LA is moderately to strongly related to measures of impairment provides sufficient evidence of the validity of this measure, despite possible limitations associated with the strength, sensation, and spasticity outcomes.

4.3.5 **Conclusions**

These findings provide evidence of face, construct, and concurrent validity that LA measured from movements during sleep are related to measures of strength, sensation, and impairment among a sample with chronic SCI. This demonstrates that LA is a clinically meaningful metric of neuromuscular impairment that could be useful in many future applications including CPRs for ambulation after an acute SCI.

4.4 **Aim 2: Use of LA and PPEF to Classify Ambulatory Ability**

Reprinted from Archives of Physical Medicine and Rehabilitation, In Press Journal Pre-Proof, Rigot SK, Boninger ML, Ding D, McKernan G, Field-Fote EC, Hoffman J, Hibbs R, Worobey LA, *Towards Improving the Prediction of Functional Ambulation after Spinal Cord Injury Through the Inclusion of Limb Accelerations During Sleep and Personal Factors,* Copyright (2021), with permission from Elsevier.

4.4.1 **Introduction**

Of the nearly 18,000 people in the United States who sustain a SCI each year, about half are likely to regain ambulation with one-third likely to ambulate in the community.[191, 192] Although walking is often a primary goal of patients,[2, 193] there are negative consequences of attempting gait training if the person does not become a long-term functional ambulator.[194-196] Similarly, there may be missed opportunities from not attempting gait training during the period with the highest possibility of neurorecovery if a person will likely ambulate in the future.[197-200] CPRs have the potential to aid clinicians by determining a patient's likelihood of ambulation early in the rehab stay so that therapies and expectations can be adjusted appropriately, which is especially important in the context of decreasing length of stays.[43, 191, 201]

The most cited CPR for ambulation after SCI is by van Middendorp et al. which uses age, strength and sensation to predict the probability of walking 10m independently one year post-injury.[4, 5] This CPR demonstrated high accuracies in the original publication,[4] external validations,[5, 49, 50] and among a group with nontraumatic SCI (area under the curve=0.889-0.967).[51]

When used clinically, the van Middendorp CPR was found to be useful for patient motivation and setting realistic expectations.[42] Variations of this CPR have also been published that include fewer predictors[5] and different age cut offs.[54]

However, recent publications have highlighted shortcomings of existing CPRs.[6, 51, 54] Outcomes are more poorly predicted for those with an incomplete SCI, the cohort for whom a better understanding of ambulatory prognosis would be most useful.[19, 98] Further, most CPRs only predict whether or not an individual is likely to walk a short distance without assistance, but this may not be representative of whether the individual will walk functionally.[4, 5, 58, 202] Rather, measures of speed and endurance can provide a more comprehensive view of functional ambulation and help to guide therapeutic interventions and patient expectations.[102, 104] Additionally, recent studies have highlighted the benefits of leveraging machine learning techniques to include a larger number of predictors and identify complex, non-linear relationships between predictors.[58, 202, 203]

PPEF such as resilience, social support, accessibility, socioeconomic status, and pain can influence one's ability to ambulate but have not been included in previous CPRs.[10-12, 90, 91] Further, measures of actual movement, which can be collected through low-cost wearable accelerometers, may be more reliable, objective, and responsive following SCI than clinical measures.[8, 9, 68, 75-77] In humans and animals, it has been found that slight motor recovery soon after injury was predictive of functional motor recovery.[59, 64, 65] In a pediatric population with muscular dystrophy, a moderate to good relationship was found between the intensity of movements measured with an activity monitor and both knee extension strength and the 6MWT, demonstrating the strong potential for LA to be related to functional mobility.[204] Activity during sleep may encompass aspects of sensation to cue the individual to move and strength to perform the movement, as well

as other extraneous movements such as those triggered by spasticity.[205-209] Since therapy may bias daytime activity early after SCI, LA is defined as movements during sleep at night.

The objective of the current study was to assess the ability of LA and PPEF to classify functional measures of ambulation using random forest machine learning models among individuals with chronic, motor incomplete SCI. Evaluating this relationship in a cross-sectional study is a first step towards the development of a more accurate CPR that can be used early in acute rehabilitation to predict long-term functional ambulation after a new SCI.

4.4.2 **Methods**

4.4.2.1 Study Population

In addition to the study criteria described in Section 4.1, participants were only included if they had voluntary leg movement (LEMS > 0). Those with motor complete injuries were not included, as they were not likely to be ambulating.[99, 100]

4.4.2.2 Questionnaires, Clinical and Ambulatory Assessments

All questionnaires, clinical and ambulatory assessments were collected as described in Section 3.0. Each clinical measure described in Table 3.2 to assess strength, sensation, and spasticity was included in the analysis both as the "best" limb (better of scores from right and left) and "bilateral" limb scores (sum of limb scores). For spasticity scores, the "worst" limb (higher limb spasticity score) was also included.

4.4.2.3 Analysis

4.4.2.3.1 Model Input Variables

LA features were collected and extracted from raw accelerations as described in Section 3.2.3. Four sets of features were used to assess the classification accuracy of ambulatory outcomes: 1) clinical/demographic, 2) LA and clinical/demographic, 3) PPEF and clinical/demographic, and 4) all features (LA, PPEF, clinical/demographics, Figure 4.3). Clinical/demographic features are widely available in clinical settings and include a larger selection than just from the ISNCSCI exam that are generally used in previous CPRs.[4, 5, 33]

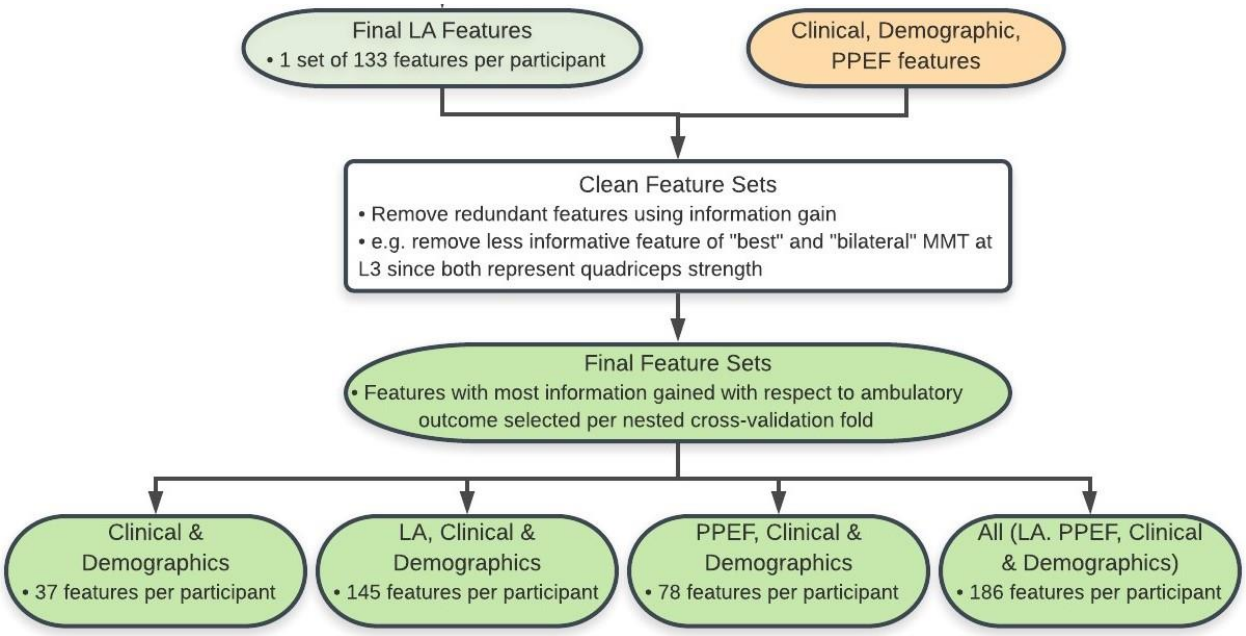


Figure 4.3: Flowchart describing the feature sets for Aim 2

4.4.2.3.2 Model Outcome Variables

To maximize the clinical utility of the model and to avoid overfitting while still providing increased resolution over current binary CPR outcomes, we categorized ambulatory ability into 3 clinically relevant divisions based on literature (Table 3.3).[2, 103, 105, 106] Due to an insufficient distribution of WISCI-II scores, only 10mWT and 6MWT were included in this analysis.

4.4.2.3.3 Model Selection and Tuning

Random forest models were used to classify each of the ambulation outcomes in Python 3.8.[178] Random forest is an ensemble method that uses subsets data to build many decision trees and then determines final predictions from the majority classifications of the individual trees. This results in a robust prediction that is often considered one of the most effective methods for handling high-dimensional data due to the ability to automatically handle interactions, ignore uninformative features, and resist overfitting.[210, 211]

A nested, 4-fold inner-loop and leave-one-out (27-fold) outer-loop cross-validation procedure was used to avoid overfitting (Figure 4.4)**.** Within each outer-loop fold, we simultaneously performed hyperparameter tuning and feature selection using a grid search algorithm with a 4-fold cross-validation using the inner-loop data and then applied the best parameters to a model made from the whole inner-loop dataset. This model is then applied to the individual, held-out, outer-loop test sample which is classified into 1 of the 3 ambulatory ability classes. Due to never pooling the full train and test sets, even with small sample sizes, this method produces a nearly unbiased estimate of the true error expected, instead of the overly-optimistic results expected without this method.[185, 187] While it is possible for the inner-loop to choose suboptimal parameters due to overfitting, this would result in more misclassifications when applied to the test set and poorer overall model performance. Thus, by utilizing this strict cross-validation

method, our small sample would produce a conservative estimate of the possible performance expected in a larger sample, unlike other validation methods which would erroneously increase the test set accuracy.[185-187]

Within in the inner-loop, the random forest models were tuned for the number of features to include by selecting between 3-20 features with the highest information gained with respect to the ambulatory outcome. Information gain is a feature selection algorithm that measures the amount of information gained (reduction in entropy) from the outcome variable by observing a given feature. A feature with more information gained provides a greater reduction in outcome unpredictability and is therefore more useful as a predictor of the given outcome than a feature with less information gained. Only the features that provided the most information about the ambulatory outcomes would be included in the final feature set for each outcome. Additionally, the random forest models were tuned for the number of features to be included per tree (20-75% of number of features selected), number of trees (50-500), and maximum depth of each tree (3-5). The ranges for each hyperparameter and which hyperparameters were chosen for tuning were based off preliminary analysis and to further minimize the risk of overfitting. Model performance was evaluated by overall classification accuracy (OCA), precision, recall, and F1-score that were calculated overall and per-class as described in Appendix C.

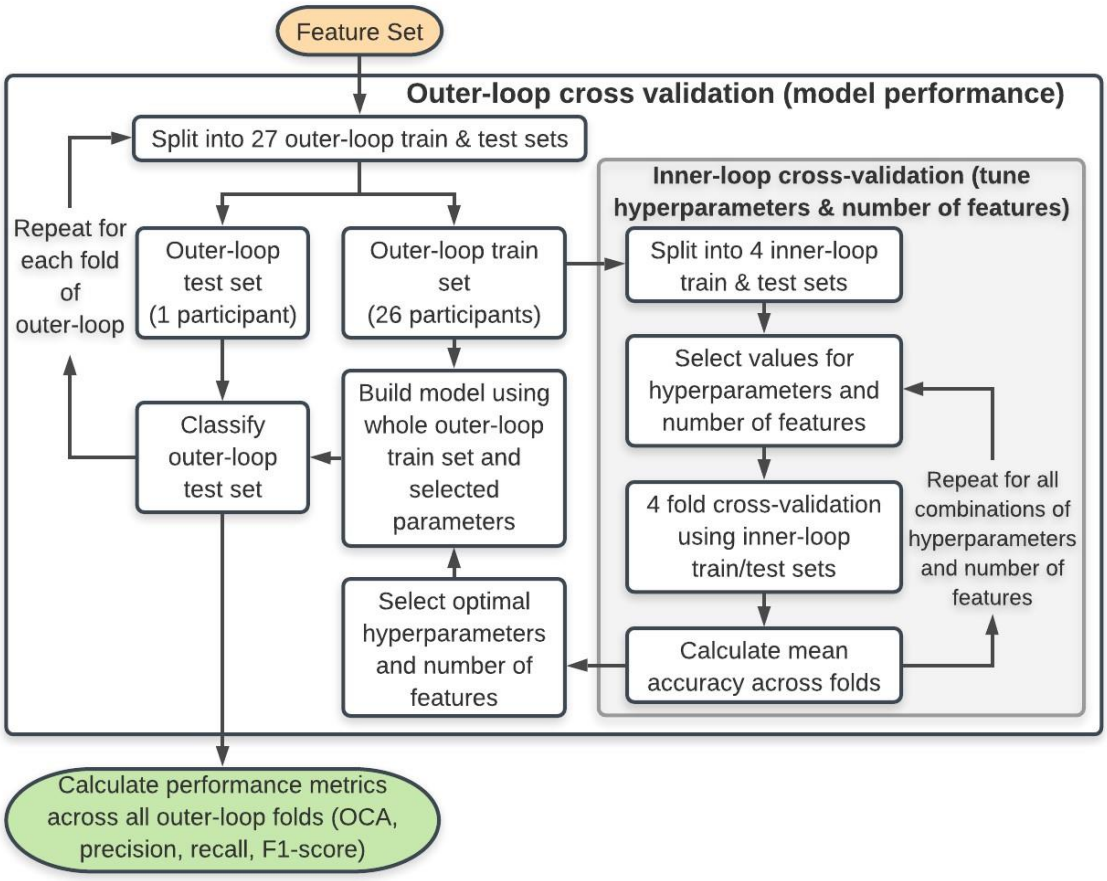


Figure 4.4: Flowchart showing leave-one-out nested cross-validation, with 27 outer-loop folds to estimate model performance and 4 inner-loop folds to optimize selection of hyperparameters and number of features.

4.4.3 **Results**

4.4.3.1 Participants

Thirty-four participants completed the study; 6 were excluded from the analysis because they self-reported no “typical” nights of sleep during the collection period and 1 was excluded because he reported the ability to ambulate but required bracing that wasn’t available during the study period. Two additional participants with motor incomplete SCI that were included in the

analysis Aim 1 were not included here, as they had been enrolled after this analysis was completed. The majority of analyzed participants (n=27, Table 4.5) were male, non-Hispanic White, Veterans, high school graduates, with paraplegia, attending adapted sporting events, who primarily used a manual wheelchair.

Table 4.5: Ambulatory outcomes and demographic information from participants with motor incomplete SCI included in the analysis (n=27).

Ambulatory Outcomes	N (%)
10m Walk Test (10mWT) [103, 212]	
Non-ambulatory (0 m/s)	11 (40.7)
Household ambulator (0.01-.44 m/s)	9 (33.3)
Community ambulator (>.44 m/s)	7 (25.9)
6-Minute Walk Test (6MWT) [213, 214]	
Non-ambulatory (0 m)	11 (40.7)
Household ambulator (1-204 m)	11 (40.7)
Community ambulator (> 204 m)	5 (18.5)
Categorical Demographics	**N (%)**
Sex	
Female	4 (14.8)
Male	23 (85.2)
Race/Ethnicity	
Non-Hispanic White	14 (51.9)
Non-Hispanic Black	8 (29.6)
Non-Hispanic Other Race	3 (11.1)
Hispanic (Any Race)	2 (7.4)
Veteran	
Not Veteran	4 (14.8)
Veteran	23 (85.2)
Annual Household Income	
<$25,000	8 (29.6)
$25,000-$49,999	3 (11.1)
$50,000-$74,999	5 (18.5)
≥$75,000	8 (29.6)
Decline to Answer or Unknown	3 (11.1)
Education	
High School Diploma/GED	14 (51.9)
Associate's Degree	7 (25.9)
Bachelor's Degree	4 (14.8)
Graduate Degree	2 (7.4)
SCI Injury Level	
Paraplegia	17 (63.0)
Tetraplegia	10 (37.0)
SCI AIS Classification (Calculated)	
C	13 (48.1)
D	14 (51.9)
Data Collection Location	
Local	6 (22.2)
Adapted Sporting Event	21 (77.8)
Primary Mode of Mobility	
Walk	4 (14.8)
Manual Wheelchair	19 (70.4)
Power Wheelchair/Scooter	3 (11.1)
Equally Walk and Wheel	1 (3.7)
Continuous Demographics	**Mean ± SD (Range)**
Age	53.4 ± 10.9 (25-70)
Years Since Injury	17.6 ± 12.0 (3.0-48.7)

4.4.3.2 10mWT

The random forest model using LA and clinical/demographic features resulted in the highest classification accuracy (OCA= 0.704), while the clinical/demographics only model had the lowest accuracy (OCA= 0.593, Table 4.6**,** Appendix Table E.2). The model using LA and clinical/demographic features correctly classified non-ambulatory participants 82% of the time (F1-score= 0.900), while household (F1-score= 0.632) and community ambulators (F1-score= 0.533) were more frequently misclassified.

The model using LA and clinical/demographic features selected 3 LA features that were representative of movement smoothness (Num Med Crossings- IQR/Med) and variation in local dynamic stability (Lyapunov Exp- IQR, Appendix Table E.3). Similarly, when given the opportunity to select any available features ("All" feature set), the 2 LA features describing movement smoothness were chosen slightly more frequently. PPEF features related to exercise, sleep medication, sleep quality, alcohol consumption, emotional role limitations, and pain interference with social activity were also chosen from the "All" model. Other features such as sensation at L2 and L4, knee flexors and L3 strength, having pain, and being a Veteran were frequently chosen in all models.

Table 4.6: Random forest model ambulatory ability classification accuracy for each feature set and ambulatory outcome. *†

	10mWT				6MWT			
Feature Set	OCA	Precision	Recall	F1-Score	OCA	Precision	Recall	F1-Score
Clinical & Demographics	0.593	0.576	0.593	0.581	0.667	0.670	0.667	0.667
LA, Clinical & Demographics	0.704	0.737	0.704	0.715	0.815	0.824	0.815	0.817
PPEF, Clinical & Demographics	0.667	0.689	0.667	0.669	0.741	0.744	0.741	0.740
All	0.630	0.637	0.630	0.626	0.741	0.739	0.741	0.739

* Model with the highest classification accuracy is highlighted grey per ambulatory outcome.
† Precision, recall, and F1-score represent the weight average of the per-class scores.

4.4.3.3 6MWT

The 6MWT also produced the highest classification accuracy with the LA and clinical/demographics feature set (OCA= 0.815, Table 4.6, Appendix Table E.2). Community ambulators were classified well (F1-score= 0.889); 2 participants each in the non-ambulatory (F1-score= 0.818) and household ambulator (F1-score= 0.783) groups were misclassified.

LA features of movement smoothness were frequently selected, while variations in local dynamic stability (Lyapunov Exp- IQR), movement timing (Start/End Move %- IQR/Med), and variation in positioning changes were selected less frequently (Grav Change Z- IQR, Appendix Table E.4). Commonly selected PPEF features from the "All" model included sleep medication use, exercise, and sleep quality. Frequently selected clinical/demographic features were similar to the 10mWT with the addition of presence of comorbidities.

4.4.4 **Discussion**

By including novel LA features in combination with clinical/demographic measures, random forest models exhibited higher classification accuracies, as compared to models that included only clinical/demographic features. Adding PPEF also enhanced the model, and may further increase model accuracy in a larger, more diverse sample with greater variability of responses. These findings indicate a likely benefit to using LA and potentially PPEF to improve prognosis for individuals with acute, incomplete SCI, a group whose mobility outcomes are currently not well predicted. Further, there is a demonstrated relationship between these features and functional measures of mobility. The added level of granularity from classifying multiple categories of each functional ambulation measure may increase clinical utility compared to CPRs that target only a binary walking/wheeling outcome.

Random forest models for the 10mWT exhibited higher accuracies when classifying non-ambulators, while the 6MWT models were slightly better at classifying community ambulators. This demonstrates that the current features selected to classify each outcome are sufficient for some groups, but may need further refinement to better differentiate others. Since household ambulators are likely to use a wheelchair for community mobility, require additional assistance, and/or have worse long-term outcomes than community ambulators, these groups are important to distinguish.[18] Previous work among individuals with SCI demonstrated differences in walking capacity can be detected using the 10mWT versus 6MWT and our results may further support the importance of using both outcome measures.[103]

For both the 10mWT and 6MWT, the feature set that produced the highest classification accuracy included LA and clinical/demographic features. LA features were more prominently selected for the 6MWT versus the 10mWT. Measures of movement smoothness (Num Med Crossings- IQR/Med) were the most commonly selected LA features for both outcomes. When an individual has decreased motor control over a limb or increased spasticity, movements may more frequently change speed as opposed to a smoother movement performed by someone who has better strength, motor control, and likely better ambulatory ability. A similar measure was found to be negatively correlated to 6MWT distances among children with muscular dystrophy, indicating that more frequent and less smooth movements were related to poorer walking endurance.[89] Greater smoothness has also been associated with improved gait quality when comparing health controls to those with Parkinson's disease and peripheral neuropathy.[146]

A benefit of using LA over common clinical predictors is the continuous nature of most LA features allows for a large amount of variability between participants, which provides greater responsiveness and ability to differentiate between ambulatory abilities. However, given the small

sample, some LA features may have been too variable to provide enough information about the ambulatory outcome to be useful in the models. Since unobtrusively wearing the accelerometers overnight allows for many LA features to be calculated with minimal data collection burden or computational cost, future analyses should not just be limited to the LA features selected in this analysis. LA features may be even better predictors in a larger sample or an acutely injured population.

PPEF features related to exercise, sleep medication use, and sleep quality were most frequently selected. Previous studies among those with SCI have shown the benefit that exercise can have in improving walking outcomes,[215, 216] even when walking was not included in the exercise program.[217] However, ambulatory individuals with SCI have been shown to participate in less and have more negative attitudes towards physical activity than manual wheelchair users.[218] Additionally, both exercise and sleep have been related to gait and physical functioning in other populations.[219-222] Thus, it can be inferred that individuals who have poorer sleep quality, and potentially rely on sleep medications, may have poorer ambulatory outcomes.

Frequently selected clinical features for both ambulatory outcomes included variables used in previous CPRs like sensation and strength at L3, and also variables that were not selected in previous models such as sensation at L2 and L4.[4, 5] Interestingly, knee flexors strength was consistently one of the most frequently selected features, but has not been included in previous prediction models since it isn't measured in the standard ISNCSCI. Sufficient quadriceps (L3) and plantarflexors (S1) strength are important for ambulation; although, weaknesses can be overcome through bracing. However, knee flexors strength needed during the swing phase of gait is difficult to compensate for weaknesses and should be considered as a predictor in future models.

4.4.4.1 Limitations

The present study utilized a cross-sectional cohort of individuals with chronic SCI. Although a study following individuals longitudinally after acute SCI is needed for future CPR development, collecting novel features and measuring mobility long-term is time and resource intensive. The current analysis was used as a preliminary step to determine which features are likely to be meaningful in a future CPR and the results are not intended to be used directly for longitudinal prediction. Since PPEF collected were stable over time and LA is likely to change in relation to neurological recovery, we expect that the results of this study are likely to be applicable when used with an acute SCI sample measured longitudinally.

Since many participants completed the study while at sporting events, several steps were taken to control for any abnormal activity or sleep. Participants recorded exercise, alcohol and caffeine use on a daily log and these covariates were included in the analysis. Additionally, only nights reported as "typical" to how the participant would sleep in their normal environment were used. It is possible that the demographics of our sample aren't representative of the population of people with SCI which may limit generalizability of the findings.

Although likely important in the description of functional ambulation, the WISCI-II that assesses an individual's need for assistance through the use of physical assistance, bracing, and assistive devices was not included as an outcome in the current analysis due to an insufficient distribution based upon our original categorization of the WISCI-II (using bracing as the determinant for individuals being classified into the middle category instead of assistive devices). The categorization used for the WISCI-II was changed after the completion of this. Given the improved classification of the 10mWT and 6MWT when utilizing LA features, we would expect that the WISCI-II would have improved results as well, but this should be further assessed.

Usually, small sample sizes could lead to model overfitting and inaccurately favorable results. Random forest algorithms have consistently demonstrated adequate classification accuracies in high-dimensional feature spaces with small samples containing complex, non-linear data.[223] Additionally, the nested, leave-one-out cross-validation technique was utilized to eliminate this risk and produce an unbiased estimate of the true performance, regardless of the small sample size.[185-187] Despite selecting ranges for feature selection and hyperparameter tuning to minimize the likelihood of overfitting, it's possible that the training set models overfit during the inner-loop cross-validation, but this would result in the current findings being a conservative estimate of the possible improved performance given a larger sample. Future studies could include the use of multiple machine learning algorithms, potentially combined using ensemble methods, to improve accuracy and further reduce bias and overfitting. Similarly, there may be additionally predictors that are beneficial to include in future prediction models, but were not captured here.[98, 203]

4.4.5 **Conclusions**

Models including diverse feature sets (LA/PPEF) better classified participants into categories of functional ambulation than clinical/demographic features alone. Targeting functional categories of ambulatory ability, based on gait speed and endurance, may guide clinicians, patients, and families towards more optimal rehabilitation goals and manage expectations for recovery better than a binary outcome of walking/wheeling. Using novel predictors and machine learning may lead to a better CPR to guide clinicians towards the right mobility training for the right patients at the right time to maximize long-term outcomes and independence after SCI.

4.5 **Cross-sectional Study Conclusions**

Aims 1 and 2 established that LA is related to clinical measures of neuromuscular impairment (strength, sensation, spasticity) and beneficial in the classification of ambulatory abilities (speed, endurance) among those with chronic, motor incomplete SCI. A variety of features such as those related to energy and power of movements, movement timing, and consistency were most strongly related to measures of impairment. Measures of movement smoothness, timing, and stability were most commonly selected in relation to measures of ambulatory ability. Compared to impairment, fewer LA features were selected as related to each classification for ambulatory ability; however, similar features were selected in both the analysis of neuromuscular impairment and ambulatory ability (Table 6.1 and Table 6.2). Limitations in the analysis of LA and impairment that were reported in Aim 1, including less responsive outcomes and stringent model validation, did not affect Aim 2 in the classification of functional ambulation using a strict leave-one-out nested cross-validation random forest model. This strengthens the findings from both Aims that LA is related to impairment and ambulation.

Lyapunov Exp is a measure of local dynamic stability or chaos which may be a measure of the motor system's ability to diminish perturbations and continue along a trajectory.[224, 225] This feature was found to be related to both measures of ambulatory ability assessed (10mWT, 6MWT) and 2 of the 3 measures of impairment (strength, sensation). This feature has been shown to be related to improvements in lower limb rehabilitation,[173] gait stability and changes in gait speed,[146, 225] and fall risk from measurements during gait.[224, 226] Thus, finding the Lyapunov Exp to be related to strength, sensation, and gait indicates that this features is strongly related to clinical measures and is likely useful in a CPR for ambulatory ability.

The Num Med Crossings which measures movement smoothness was also found to be related to both the 10mWT, 6MWT, and strength after being normalized by the movement duration. If an individual is frequently changing increasing or decreasing their rate of changes in speed throughout a movement, then they would have an increased number of times that the acceleration-time signal crosses the median acceleration for that movement (higher Num Med Crossings). A similar measure of acceleration crossings was found to be related to 6MWT and weakly correlated to knee extensor strength among a sample of children with Duchenne Muscular Dystrophy.[89] Additionally, other measures of movement smoothness have been associated with improved gait.[146] This also demonstrates that this feature has excellent potential to be useful in a future CPR among individuals with acute SCI. While they had weaker relationships, LA features describing movement timing (Move/hour, Time Asleep, Start Move %) and changes in positioning (Grav Change Z) were also shown to be related to both ambulatory and impairment measures.

Across nearly all models built using LA features, the majority of features selected were representing the IQR of the metric and a minority represented the median value. The only exception was the model for moderate spasticity, which had an equal proportion of LA features representing the IQR of the metric and median values. This indicates that the actual value of the feature is valuable, but the ability to have variability in movement characteristics may be more important.

These similarities in the findings between the measures of impairment and ambulatory ability among participants with chronic SCI lay the foundation for LA to be utilized in other contexts as a more descriptive measure of impairment. It also further emphasizes that LA would likely be a useful predictor of long-term ambulatory ability among those with acute SCI.

5.0 Longitudinal Study with Acute SCI Over the First Year Post-Injury

5.1 **Study Population**

Participants were approached during the first week of IPR at the UPMC Rehabilitation Institute Spinal Cord Injury Unit. We recruited adults (≥18 years) with a new, incomplete (AIS B, C, or D) SCI, based upon the neurological exam upon admission to IPR, or individuals for whom a mobility prognosis was unclear. At admission to IPR, individuals with AIS A injuries are unlikely to achieve ambulation; therefore, they were not included unless their primary physical therapist specifically noted that they had an unclear ambulatory prognosis (e.g. with a lower level of injury).[35] Although individuals with an AIS B SCI are unlikely to begin gait training at admission to rehab, approximately 50% convert to AIS C or D injuries within the first year, 20-65% achieve some degree of ambulation, and 18-33% achieve functional ambulation, thus, this population is important to consider.[4, 35, 36, 99, 109] Although we are not excluding individuals who have experienced a traumatic brain injury, we are excluding those with significant cognitive impairments as indicated by a score < 20/25 on the Modified Mini-Mental Status Exam (cutoff score was < 23/25 at the beginning of the study and was lowered mid-way through).[227] Participants were excluded if they do not live a reasonable driving distance from one of our centers to allow for follow-up. However, to gather pilot data in preparation for the planned multi-site expansion of this longitudinal study, research at the University of Washington Harborview Medical Center and Shepherd Center were also trained to complete the same data collection as is performed in Pittsburgh. One participant was included in the analyses the University of Washington site and has

completed all follow-ups remotely. All participants completed informed consent as approved by the University of Pittsburgh institutional review board and the appropriate other site as needed.

Follow-up data collections took place for approximately 1 week immediately prior to discharge from IPR and at 3-months, 6- months, and 1-year post-discharge from IPR. The 3-month follow-up was added mid-way through the study to increase the detail regarding changes over time and as such, limited data was collected at that time and it was not included in the analysis. Although, at admission to IPR, only participants with incomplete SCI or an unclear ambulatory prognosis were enrolled, participants with any severity of SCI could also be enrolled just prior to discharge from IPR as part of a separate analysis for a larger study; these participants are not be included in this dissertation. Data collection occurred during a 3-week window surrounding each follow-up time point (3-months, 6-months, and 1-year post-discharge).

5.1.1 **Sample Size Considerations**

This analysis was a pilot analysis as part of a larger study that aimed to enroll enough participants to build and evaluate a new clinical prediction model using LA and PPEF features collected at admission to IPR to predict 1-year ambulatory ability among a sample with acute, incomplete SCI. As such, these Aims were only intended to be exploratory and were not designed to be powered to detect statistical significance. We planned to recruit 25 participants for these analyses, assuming a 25% drop out rate and a final sample size of 20 participants that complete all time points through 1-year post-discharge from IPR.

To date, we have enrolled 39 participants with incomplete SCI, of which, 33 completed the admission time point (Figure 5.1). Due to difficulties with data collection due to COVID-19 and the subsequent IRB restrictions such as the inability to follow-up with participants in skilled

nursing facilities and other difficulties (e.g., participants medical complications or passing away) the follow-up rates for the study were lower than anticipated. Additionally, 100% of the 3-month, 68.8% of the 6-month, and 55.6% of the 1-year follow-ups were completed remotely due to COVID-19 restrictions, which resulted in collection of clinical and ambulatory measures being more sparse in those participants. To date, 23 participants have reached the 1-year time point, aligning with our original recruitment goals. The same overall sample is used in Aims 3 and 4, although for some analyses only a portion of the sample is utilized.

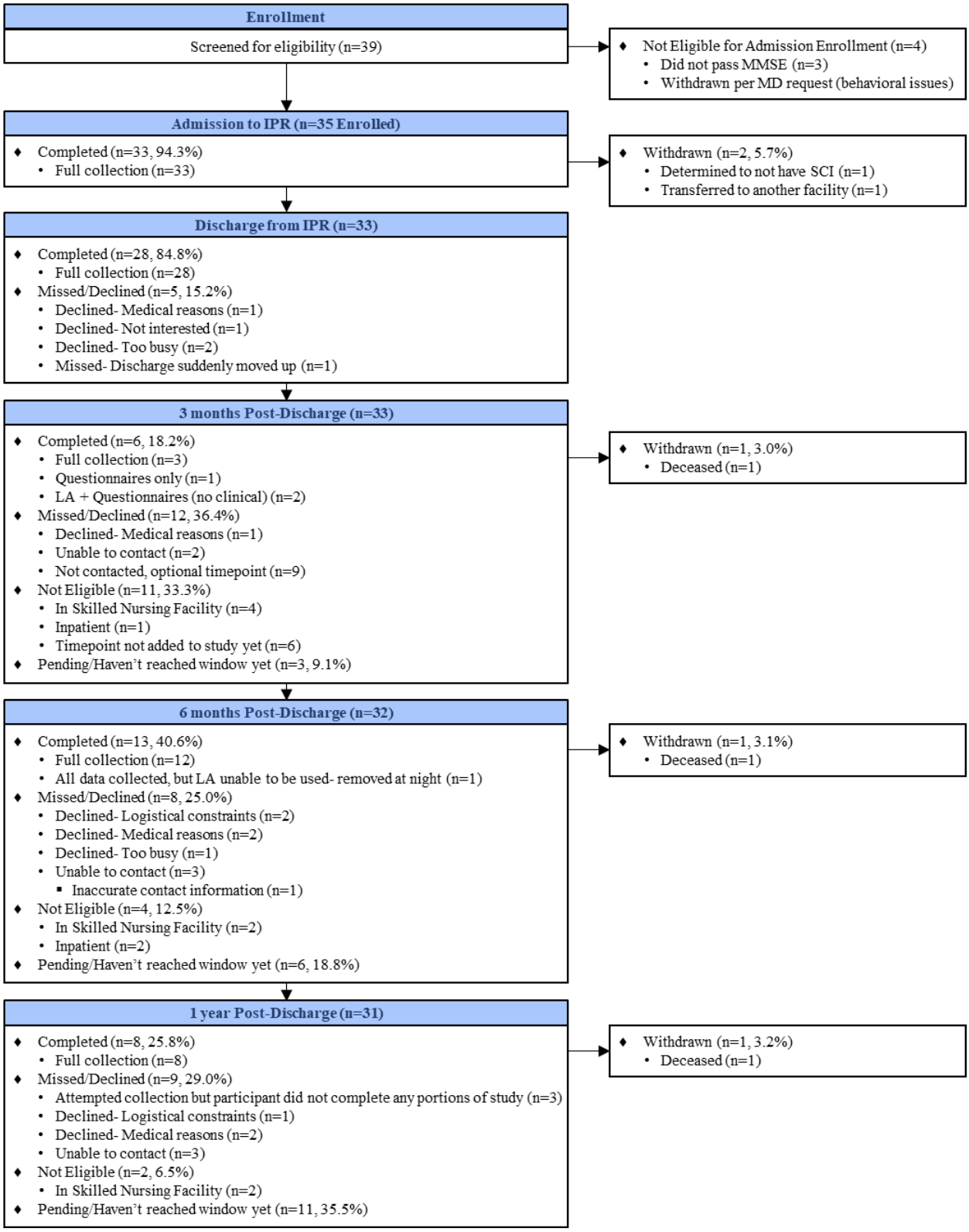


Figure 5.1: Flowchart of participant enrollment and follow-up from admission to IPR through 1-year post-discharge

5.2 **Longitudinal Study Analysis Overview**

Although still in the pilot phase, we were able to utilize the data from individuals with acute, incomplete SCI for multiple purposes with the goals to provide information about the psychometric properties of LA when measured acutely and determine which features of LA are most likely to be useful in a future CPR for ambulation. These goals were addressed over 4 analyses that were grouped in to 2 Aims that assess the psychometric properties of LA (Aims 3a and 3b) and related LA to clinical measures (Aims 4a and 4b). For clarity, the reasoning behind each analysis and how it will benefit a future CPR will be briefly described here, with additional details and specific methodologies provided in later sections.

For the purposes of a CPR, the most useful time point for prediction would be upon admission to IPR. Aim 3a assesses the reliability of LA features when measured within the first week after admission to IPR to determine the minimum number of typical nights needed to obtain a reliable, robust feature set. Only features that were determined to be reliable when measured at admission to IPR were used in the remainder of the analyses (Aims 3b, 4a and 4b). Additional information regarding validity, reliability, and responsiveness of predictors for use in a CPR was explained in Section 2.4.1.1).

Aim 3b assesses the change in LA from admission to IPR through the first 6-months post-discharge. Although LA features that are used in a CPR would be measured at admission to IPR, it is important to determine which features of LA are stable (Figure 5.2 a-c) or changing ("variable LA") over time (Figure 5.2 d-f). Stable LA features provide the benefit of being time invariant; thus, there would be more flexibility in when LA was measured and utilized in a CPR if the CPR consisted of all stable LA features. Variable LA features that change over time in relation to measures of ambulatory ability or impairment may also be important to include in a CPR. These

features may capture changes in strength, sensation, and spasticity that affect the ability to walk and perform many other functional tasks (Figure 5.2e). The score of these variable LA features at admission to IPR might be predictive of the individual's abilities and recovery potential. Additionally, variable LA may capture similar, but potentially more detailed and responsive, information to the clinical measures that CPRs frequently include currently.[4, 5, 53, 58-63] LA features that change over time, but not in relation to clinical measures (Figure 5.2f), are not likely to be useful in a CPR. The association between changes in variable LA features and changes in ambulatory ability and impairment is evaluated in Aim 4a. However, this analysis found that the changes in LA compared to ambulatory ability and impairment may be better determined in a large sample, so these findings provide a preliminary assessment of the change LA compared to clinical measures over time, but further evaluation is needed.

Aim 4b evaluates the relationship between LA measured at admission and ambulatory ability at 6-months to perform a preliminary assessment of which LA features are most likely to be beneficial in a future. Stable LA features may be useful as predictors in a CPR if they are able to differentiate between ambulatory abilities (Figure 5.2 b-c); thus, all stable LA features were evaluated. Variable LA may be useful if it changes over time in a clinically meaningful pattern, so variable LA features that were found to be related to ambulatory ability or impairment in Aim 4a were included. Because of the sample size limitations on the analysis for Aim 4a, variable LA features that were not significantly related to changes in ambulatory ability and impairment in Aim 4a were still included in the analysis for Aim 4b. These 3 features were specifically noted and additional information for them is provided in Appendix H.1, as their usefulness in a future CPR is less clear. The features from admission to IPR that were identified as being related to 6-month ambulatory ability in Aim 4b are most likely to be beneficial to improve CPR accuracy when

predicting long-term ambulatory ability among those with acute, incomplete SCI. All LA features identified as meaningful in each analysis are summarized in Table 6.1 and Table 6.2.

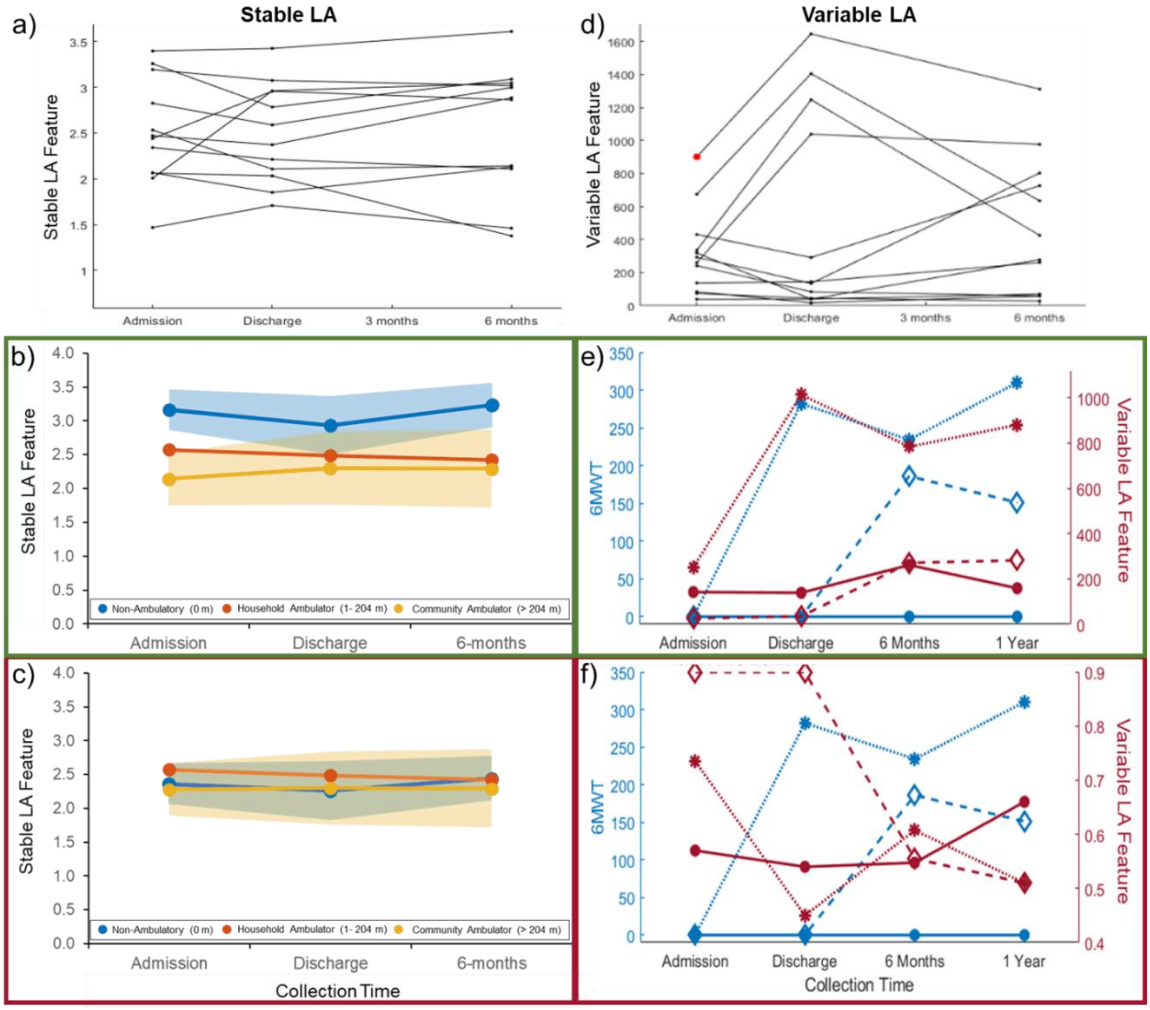


Figure 5.2: Examples of a-c) stable and d-f) variable LA features.a) Trajactoreies of a stable LA feature over time per participant; b) example of a stable LA feature that is visually different and c) not different between ambulatory ability groups. d) trajectories of each participant's variable LA feature over time; e) example of a variable feature (red) that is related to and f) not related to an ambulatory outcome (6MWT, blue) over time for 3 participants (corresponding LA and 6MWT scores for the each participant have the same marker shape and line pattern). Stable features that are related to measures of ambulatory ability (b, green outline) or variable features that change in relation to ambulaotry ability or impairment (e) are most likely to be useful in a CPR for ambulation, while features with little variance between ambulatory groups (c, red outline) or inconsistient changes (f) are unlikely to be useful in a CPR.

One major limitation of these analyses should be noted in advance as it affects Aims 3b, 4a, and 4b. In Aim 3a, it was found that measuring LA from the combination of 2 typical nights provided the best balance between obtaining numerous reliable LA features, minimizing collection burden to participants and clinicians, and maximizing clinical utility. However, due to sample size limitations in certain ambulatory ability groups, we decided to utilize any participants with at least 1 typical night measured for the remaining exploratory analyses. Two participants (16.7%) that were included in Aims 3b, 4a, and 4b only had one typical night collected at admission to IPR. However, 10 of 12 participants at admission and all participants at discharge and 6-months post-discharge had at least 2 typical nights included.

5.2.1 **Long-term outcome**

Although the longitudinal study outcome was intended to be 1-year post-discharge from IPR, only 23 participants reached the 1-year time point to date, of which only 8 participants completed the full collection. However, the rate of motor recovery has been shown to substantially decline by 6-months.[59, 228, 229] When assessing the Spearman's rank correlations between the ambulatory and impairment outcomes (strength, sensation) at 6-months and 1-year post-discharge (Table 5.1), we found that the outcomes were all highly correlated, except the sensation measurements. Due to restrictions from COVID-19, many of the follow-up collections occurred remotely and utilized the participant's own physical therapist (if still attending and willing to assist), which limited the small sample size for that measure. The low likelihood for the ambulatory and impairment outcomes to substantially change from 6-months to 1-year post-injury and the high correlation between 6-months and 1-year in our data, compounded with the larger sample collected at 6 months, led to the use of the 6-month assessments as the final outcome in these analyses.

Additional comparisons between the ambulatory categorization for each outcome (WISCI-II, 10mWT, 6MWT) at each time are shown in Appendix Table F.1 for all participants in the study, and Appendix Table H.2 for all participants included in the sample for Aims 3b and 4a.

Table 5.1: Spearman correlations between outcomes at 6 months and 1-year post -discharge

Outcome	n	r	p
WISCI-II	8	1.000	0.001
10mWT	8	0.952	0.001
6MWT	8	0.833	0.015
Strength (LEMS)	4	0.800	0.333
Sensation (Lower Limb LT)	4	0.211	0.833

5.3 **Aim 3: Reliability and Stability of LA Measured Acutely**

5.3.1 **Introduction**

In Aims 1 and 2, evidence was provided to support the validity of LA being related to neuromuscular impairment and ambulatory ability in a sample with chronic SCI. However, the primary proposed use for LA is in a CPR for a sample with acute SCI to predict ambulatory ability 1-year later. In the initial days after a SCI, the spinal cord is in shock and the individual may experience substantial impairments including flaccidity, loss of all sensation, and loss of reflexes caudal to their level of injury.[230] In the days to months that follow, an individual may experience substantial changes to their neurological system including the development of hyperreflexia and spasticity as well as possible motor and sensory recovery.[230] Additionally, sleep-disordered breathing, such as obstructive sleep apnea, can be highly prevalent after SCI and develops in up to 60% of individuals with a cervical SCI within 2 weeks after injury.[231] All of these changes,

compounded with data collection challenges innate to the inpatient setting, could potentially affect the measurement of LA among those with an acute SCI. Therefore, the psychometric properties of LA when measured acutely must be assessed, as individuals with acute SCI often present with very different characteristics than those in the chronic phase.

For a feature to be useful as a predictor in a CPR, one of the most important characteristics it must possess is being reliable.[232] Reliability refers to the extent to which a measure yields the same results each time it is administered, all other things being equal.[55, 233] As long as sleep characteristic are within the normal range for that participant and considered typical of how they have slept since their injury, we expect that features of LA across multiple days of data collection upon admission to IPR can be measured reliably. Understanding the intra-subject reliability of LA features between nights will also allow us to identify a minimum number of nights necessary for a reliable set of LA features to be collected.

Although patients begin physical and occupational therapy while in the acute care setting, intensive rehabilitation generally does not begin until the individual is admitted in to IPR. Patients typically spend a median of 11 days on acute care after SCI before being admitted to IPR, however this may vary substantially based upon an individual's injury level and other medical needs.[3] For LA to be a successful predictor in a CPR, it must be able to produce consistent and accurate predictions regardless of if the participant is a few days or a few weeks post-injury.[232, 234] Further, learning which LA features remain stable over time will provide a deeper understanding of how well the findings from Aims 1 and 2 in the sample with chronic SCI generalize to participants with acute injuries.

Therefore, this analysis had the following goals: Aim 3a) to establish which features of LA can be reliably measured across nights when collected at admission to IPR and Aim 3b) to evaluate

which features of LA remain stable from admission to IPR through 6-months post-discharge. We hypothesized that a set of LA features could be identified that produced at least moderate reliability when examining intra-subject reliability at admission to IPR and stability between time points through 6-months post-discharge.

5.3.2 **Methods**

For Aim 3a, participants were included if they had at least 2 nights of accelerometer data recorded from admission to IPR that they self-reported on the sleep log as being "typical" to how they have slept since their injury. For Aim 3b, participants were included if they had at least 1 typical night collected at admission to IPR, just prior to discharge, and 6-months post-discharge from IPR. Clinical and ambulatory assessments were collected and LA was pre-processed as described in Section 3.0 to extract 133 features (Table 3.4).

5.3.2.1 Analysis

5.3.2.1.1 LA Intra-subject Reliability at Admission to IPR (Aim 3a)

Intraclass correlation coefficients (ICCs) were calculated to assess the level of agreement between the first two typical nights recorded from each participant. Pearson correlations that only assess the trend of the data and may be misleading if data shows the same pattern but not the same values. In contrast, ICCs are able to assess both the trend and absolute agreement between sets of data. ICCs are calculated from the mean squares from the repeated measures analysis of variance. To assess intra-subject reliability between nights, we utilized a 2-way mixed effects ICC for absolute agreement of single and average nights.[234, 235] If the reliability is sufficient for single night

ICCs, then it would indicate that those LA features could be measured from any individual night collected during the first week of admission to IPR and be considered reliable when used in future applications. The average nights ICC was also included to compare the reliability if the first two typical nights when they were are combined. Although we utilized a median nights approach previously to combine the LA features from individual nights into one set of features per participant and collection (Section 3.3.2), our approach to using LA more closely resembles the average nights analysis. Both the single and average nights calculations are performed within the ICC model based upon the input data from individual nights collected per participant. We considered a feature to be "reliable" if had an intra-subject reliability defined as an ICC greater than 0.5.[235] Additionally, ICC values from 0.75 - 0.9 indicate good reliability and greater than 0.9 indicate excellent reliability.[235]

Since ICC calculations require a consistent number of nights to be included for each participant, only the first 2 typical nights were used to maximize our sample size. However, most participants wore the accelerometers for 2 - 7 days and many recorded more than 2 typical nights. Additional analyses were performed using all participants that had at least 3 and 5 typical nights to compare between the ICCs when using the first 2 nights and these increased numbers of nights. This was done to ensure that even though only the first 2 nights were utilized in the primary analysis, there were not substantial differences between the first 2 nights and additional nights collected. This also improves our ability to identify a minimum number of nights necessary to collect to result in a reliable set of LA features.

5.3.2.1.2 LA Stability Over Time (Aim 3b)

LA from multiple typical nights were combined as one set of features per collection by taking the median and IQR across all typical nights per participant as described in Section 3.3.2.

ICCs were again used to quantify the agreement between time points for all LA features that were found to be reliably measured at admission to IPR in Aim 3a. Since each time point is a separate sample and there is limited clinical value to combining time points, ICCs were only assessed for a single collection using a 2-way mixed, absolute agreement ICC analysis.[235] Additionally, boxplots of each LA feature across the collection times and line graphs of each participant's LA feature values for each time point were visually assessed to confirm the ICC findings since the ICCs may be affected by the smaller sample size. The general trends of the line plots as well as the variation in the range, IQR, and median for discharge and 6-months as compared to admission for the boxplots were used to classify a feature's stability over time (Figure 5.2). A LA feature was considered "stable" over time if it had a single collection ICC > 0.5 indicating moderate reliability and was visually confirmed to be stable when plotted.

5.3.3 **Results**

5.3.3.1 Participants

Thirty-one of 33 (93.9%) participants who had data collected at admission to IPR had at least 2 typical nights recorded and were used for the intra-subject reliability analysis (Aim 3a). Additionally, 24 (72.7%) and 11 (33.3%) participants had at least 3 or 5 typical nights recorded at admission, respectively, and were included in the supplemental analysis. Thirteen participants completed the admission, discharge, and 6-month collections; of these one had no ankle movements recorded across any night during the collection and was excluded as his ankle accelerometers were likely removed each night. Therefore, 12 participants were included in the stability analysis (Aim 3b). Categorical and continuous demographic information for the participants included in each analysis are shown in Table 5.2 and Table 5.3, respectively.

For both analyses, participants were primarily male, Non-Hispanic White, non-Veterans, with a variety of annual incomes, educational levels, and insurance providers. There was one participant with AIS A (complete) paraplegia who was included due to his low level of injury (L2) and unclear ambulatory prognosis. That participant had improved to a L4 AIS B injury by discharge from IPR. All other participants had an incomplete SCI (AIS B, C or D) and the majority had cervical injuries. By discharge from IPR one participant used in Aim 3b improved from AIS B to AIS C paraplegia, while all others stayed in the same category.

Demographics for participants who were included in the analysis and those who had reached the 6-month time point, but did not complete all necessary parts of the data collection to be included in the analysis for Aim 3b are described in Appendix Table G.1 and Appendix Table G.2. Compared to those who were included in the analysis, those who were excluded had a significantly longer length of stay in IPR (47 vs 34 days), and at discharge start the data collection later, have fewer individuals who could ambulate (7.7% could walk without physical assistance vs 58.3%, 25% were at least household ambulators vs 54.5% who were included), and have a slower gait speed (0.1 m/s vs 0.4 m/s).

For Aim 3b, by discharge, 3 (25%) participants were primarily ambulating for mobility and by 6-months post-discharge, 8 (66.7%) were primarily walking (1 additional participant was a limited ambulator and primarily used a manual wheelchair).

Table 5.2: Categorical participant demographics at admission to IPR for Aim 3

Categorical Demographics	Aim 3a N (% of total n=31)	Aim 3b N (% of total n=12)
Sex		
Female	10 (32.3%)	5 (41.7%)
Male	21 (67.7%)	7 (58.3%)
Race/Ethnicity		
Non-Hispanic White	23 (74.2%)	9 (75.0%)
Non-Hispanic Black	4 (12.9%)	1 (8.3%)
Non-Hispanic Other Race	1 (3.2%)	0 (0.0%)
Hispanic (Any Race)	3 (9.7%)	2 (16.7%)
Veteran		
Not A Veteran	27 (87.1%)	11 (91.7%)
Veteran	4 (12.9%)	1 (8.3%)
Annual Household Income		
< $25,000	7 (22.6%)	1 (8.3%)
$25,000 - $49,999	7 (22.6%)	3 (25.0%)
$50,000 -$74,999	4 (12.9%)	3 (25.0%)
≥ $75,000	5 (16.1%)	1 (8.3%)
Decline to Answer or Unknown	8 (25.8%)	4 (33.3%)
Education		
Less Than High School	4 (12.9%)	2 (16.7%)
High School Diploma/GED	13 (41.9%)	6 (50.0%)
Associate's Degree	6 (19.4%)	2 (16.7%)
Bachelor's Degree	3 (9.7%)	1 (8.3%)
Graduate Degree	1 (3.2%)	0 (0.0%)
Other	4 (12.9%)	1 (8.3%)
Medical Insurance		
Private	14 (45.2%)	3 (25.0%)
Medicaid	7 (22.6%)	3 (25.0%)
Medicare	1 (3.2%)	1 (8.3%)
VA	2 (6.5%)	0 (0.0%)
No Insurance	1 (3.2%)	1 (8.3%)
Other/Multiple	6 (19.4%)	4 (33.3%)
SCI Neurological Category at Admission to IPR		
Motor Complete (AIS A or B) Tetraplegia	2 (6.5%)	1 (8.3%)
Motor Complete (AIS A or B) Paraplegia	4 (12.9%)	3 (25.0%)
AIS C Tetraplegia	10 (32.3%)	1 (8.3%)
AIS C Paraplegia	2 (6.5%)	1 (8.3%)
AIS D Tetraplegia	11 (35.5%)	5 (41.7%)
AIS D Paraplegia	2 (6.5%)	1 (8.3%)
Primary Mode of Mobility at Admission to IPR		
Power Wheelchair	27 (87.1%)	9 (75.0%)
Manual Wheelchair	4 (12.9%)	3 (25.0%)

Table 5.3: Continuous participant demographics for Aim 3

Continuous Demographics	Aim 3a Mean ± SD (Range) (Total n=12)	Aim 3b Mean ± SD (Range) (Total n=12)
Age	51.0 ± 17.5 (18 - 82)	45.8 ± 17.8 (18 - 71)
BMI	28.8 ± 6.9 (15 - 47)	27.8 ± 3.4 (23 - 35)
LEMS (Strength)	22.5 ± 15.4 (0 - 47)	23.8 ± 16.0 (0 - 47)
Lower Limb LT (Sensation)	10.1 ± 6.6 (0 - 20)	10.5 ± 7.1 (0 - 20)
Number of Nights Collected	5.1 ± 2.1 (2 - 7)	4.6 ± 1.9 (2 - 7)
Number of Typical Nights Collected	4.6 ± 2.0 (2 - 7)	3.5 ± 2.0 (1 - 7)
Length of Stay in IPR (Days)	38.8 ± 11.2 (12 - 64)	32.6 ± 10.2 (12 - 43)
Days from Injury to Start of IPR	14.6 ± 7.7 (5 - 30)	14.8 ± 16.0 (5 - 62)
Days from Injury to Start of Data Collection	18.4 ± 8.5 (7 - 36)	17.5 ± 15.9 (9 - 65)

5.3.3.2 LA Intra-subject Reliability at Admission (Aim 3a)

An example of the consistency of LA between nights per participant is shown in Figure 5.3 and additional examples are provided in Appendix Figure G.1 and Appendix Figure G.2. Of the 133 LA features assessed, 72 (54.1%) features had at least moderate reliability and 6 (4.5%) had good reliability when averaged over the first 2 typical nights collected at admission to IPR (brief results in Table 5.5; full results shown in Appendix Table G.3). Using the single night ICCs, 25 (18.8%) features had moderate reliability and none had good reliability.

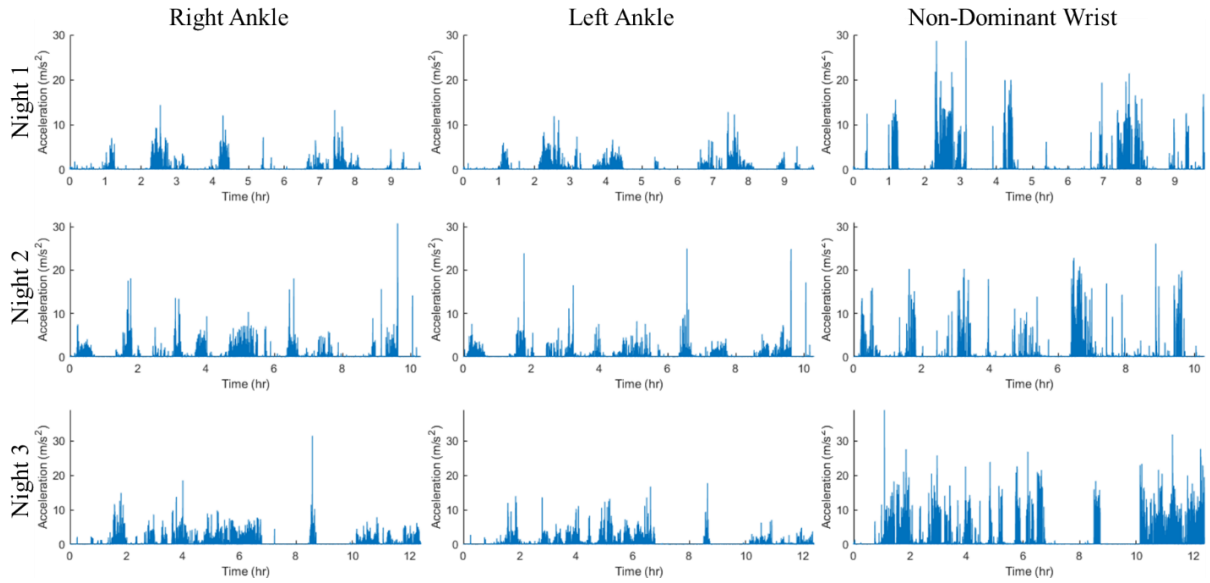


Figure 5.3: Example of LA across each accelerometer for 3 typical nights at admissionfor one participant with an L1 AIS D SCI

Table 5.4: ICCs of reliable LA features to assess intra-subject reliability (Aim 3a) and stability over time from admission to IPR through 6 months post-discharge (Aim 3b)

		LA Admission Intra-subject Reliability (Aim 3a) *		LA Stability Over Time (Aim 3b) †
Feature Category	Feature Name	Average Nights ICC	Single Night ICC	Single Collection ICC
Change in angle of inclination	Angle Net Change-Med	0.662	0.495	0.495
	Angle Rate Change-IQR	0.595	0.424	0.482
	Angle Rate Change-Med	0.738	0.585	0.427
	Angle Total Change-IQR	0.576	0.404	0.502
	Angle Total Change-Med	**0.816**	0.689	0.559
Change in gravitational acceleration	Grav Change X-IQR	0.571	0.400	0.538
	Grav Change Y-IQR	0.604	0.433	0.087
	Grav Change Z-IQR	**0.815**	0.688	0.424
	Grav Change Z-Med	0.618	0.447	0.158
Correlation coefficients between axes	Corr YZ-IQR	0.687	0.523	0.043
Frequency domain	Bandwidth-Med	0.572	0.401	**0.803**
	Centroid Freq-Med	0.501	0.334	0.727
	Dom Freq 1-Med	0.597	0.426	0.653
	Med Freq-IQR	0.721	0.563	0.575
	Med Freq-Med	0.634	0.464	0.746
	Power Dom Freq 1/Total-Med	0.609	0.438	**0.783**
	Power Dom Freq 1-Med	0.585	0.414	0.615
	Power Dom Freq 2-IQR	0.614	0.443	0.436
	Power Dom Freq 2-Med	0.704	0.543	0.647
	Power Dom Low Freq-IQR	0.566	0.395	0.527
	Power Dom Low Freq-Med	0.669	0.503	0.662
	Power High Freq/Total-Med	0.588	0.416	0.663
	Power Total-IQR	0.554	0.384	0.523
Limb movement percentages	Bilat Ankle %	0.600	0.429	0.299
	Unilat Ankle %	0.600	0.429	0.299
Median crossings	Num Med Crossings Norm-Med	0.644	0.474	0.545
	Num Med Crossings-IQR	0.629	0.459	0.264
	Num Med Crossings-Med	0.619	0.448	0.260
PLM	Num PLM Norm	**0.827**	0.706	0.302
	PLM %	0.716	0.557	0.579
	PLM Index	0.740	0.587	0.101
Relationship to recent movements	Close Cross Corr Peak-IQR	0.652	0.483	**0.756**
	Dom Freq Last 90s-Med	0.673	0.508	**0.762**
	Max Cross Cov-Med	0.511	0.343	0.612
	Move Last 90s-Med	0.581	0.409	0.181
	Move Next 90s-Med	0.581	0.409	0.181

Table 5.4 Continued

Feature Category	Feature Name	LA Admission Intra-subject Reliability (Aim 3a) *		LA Stability Over Time (Aim 3b) †
		Average Nights ICC	Single Night ICC	Single Collection ICC
Signal characteristics	Entropy Rate-IQR	0.640	0.471	0.748
	Entropy Rate-Med	0.600	0.429	0.410
	Lempel-Ziv Comp-Med	0.534	0.364	0.553
	Lyapunov Exp-IQR	0.618	0.448	0.676
	Wave Approx-Med	0.688	0.525	0.297
	Wave Energy 2-IQR	0.637	0.467	0.417
	Wave Energy 2-Med	0.716	0.558	0.392
	Wave Energy 3-IQR	**0.804**	0.672	0.269
	Wave Energy 3-Med	0.720	0.563	0.165
	Wave Entropy-Med	0.668	0.502	0.343
Statistical	AUC Acc Norm-IQR	0.568	0.396	0.649
	AUC Acc Norm-Med	0.694	0.531	0.674
	AUC Acc-IQR	0.669	0.503	0.586
	AUC Acc-Med	0.654	0.486	0.701
	Duration-IQR	0.55	0.379	0.413
	Duration-Max	0.576	0.404	0.143
	Duration-Med	0.631	0.46	0.726
	Kurtosis-Med	0.58	0.409	0.577
	Max Acc-IQR	0.638	0.468	0.723
	Max-RMS Acc-Med	0.613	0.441	0.596
	Med Acc-IQR	0.553	0.382	0.543
	Med Acc-Med	**0.782**	0.642	0.646
	Range Acc-IQR	0.641	0.472	0.725
	RMS Acc-Med	0.577	0.406	0.643
	SD Acc-IQR	0.513	0.345	0.701
	Skewness-Med	0.593	0.421	0.612
	SMA Acc-IQR	0.617	0.447	0.66
	SMA Acc-Med	0.704	0.544	0.661
Timing	Move/hour	0.693	0.530	0.129
	Move/night	0.608	0.437	0.147
	Time Asleep	0.721	0.564	0.302
Velocity and distance	Med Vel-IQR	0.588	0.417	0.535
	Med Vel-Med	**0.775**	0.633	0.350
	RMS Vel-Med	0.590	0.418	0.475
	Total Dist-IQR	0.706	0.546	0.552
	Total Dist-Med	0.673	0.507	0.702

* ICC values > 0.5 (moderate reliability) are highlighted grey and those > 0.75 (good reliability) are also bolded.
† If also visually confirmed, ICC values > 0.5 are highlighted grey and those > 0.75 are also bolded.

Table 5.5: Number of LA features that are reliable at admission using 1-5 typical nights

Number (%) of LA Features with…	Participants with ≥ 2 Typical Nights (n=31)		Participants with ≥ 3 Typical Nights (n=24)				Participants with ≥ 5 Typical Nights (n=11)			
	Nights 1-2		Nights 1-2		Nights 1-3		Nights 1-2		Nights 1-5	
	Ave Nights	Single Night	Ave Nights	Single Night	Ave Nights	Single Night	Ave Nights	Single Night	Ave Nights	Single Night
Moderate Reliability (ICC > 0.5)	72 (54.1%)	25 (18.8%)	77 (57.9%)	33 (24.8%)	97 (72.9%)	13 (9.8%)	86 (64.7%)	61 (45.9%)	98 (73.7%)	18 (13.5%)
Good Reliability (ICC > 0.75)	6 (4.5%)	0 (0.0%)	11 (8.3%)	1 (0.8%)	13 (9.8%)	0 (0.0%)	51 (38.3%)	16 (12.0%)	48 (36.1%)	0 (0.0%)

Appendix Table G.4 shows the ICC for average and single nights for participants with 2 (n=31), 3 (n=24), and 5 (n=11) typical nights. When using 3 or 5 typical nights, the number of LA features that have at least moderate reliability increased compared to only using the first 2 nights with the same participants. Additionally, when examining the ICCs for each feature, 97 of 133 (72.9%) LA features increased the average nights' ICC when using 3 nights compared to 2. Similarly, 74 (55.6%) features increased their average nights reliability when using 5 nights compared to 2. The average of 5 nights also produced the most features with good reliability (48/133, 36.1%). Using the average of 3 nights and 5 nights produced nearly the same number of reliable LA features (97 and 98, respectively). However, the smaller sample of participants with at least 5 typical nights collected at admission is likely biased towards having more consistent nights, as seen by the increased reliability when just using the first 2 nights in that sample. The proportion of features that were reliable when used as a single night decreased with each additional night included in the analysis.

5.3.3.3 LA Stability Over Time (Aim 3b)

The 72 LA features that had at least moderate reliability when measured using the average of the first 2 typical nights were assessed for stability from admission to IPR through 6-months post-discharge (Table 5.4 and full results in Appendix Table G.5). Forty-two (58.3%) LA features were initially classified as being stable due to having an ICC > 0.5. However, eight features were found to not be stable when assessed visually. Therefore, 34 (47.2%) LA features were determined by ICC and visual confirmation to be stable over time. Of the 38 features that were not stable over time (called "variable" features), 6 (15.8%) were consistently increasing, 4 (10.5%), were consistently decreasing, and 28 (73.7%) were changing inconsistently.

Mean ± SD plots were initially used to show the trajectory of LA features for all participants averaged per time point, but these were found to be misleading at times compared to the per participant line graphs. It was noted that for variable, inconsistently changing LA features, participants may change over time in opposite directions which may lead to the mean ± SD appearing stable. For example, in Figure 5.4, a slight increase of 0.21 can be appreciated in the mean ± SD plot (a), but this feature still appears relatively stable over time. However, in Figure 5.4b, it can be clearly seen that there are participants changing in various directions and in non-negligible amounts.

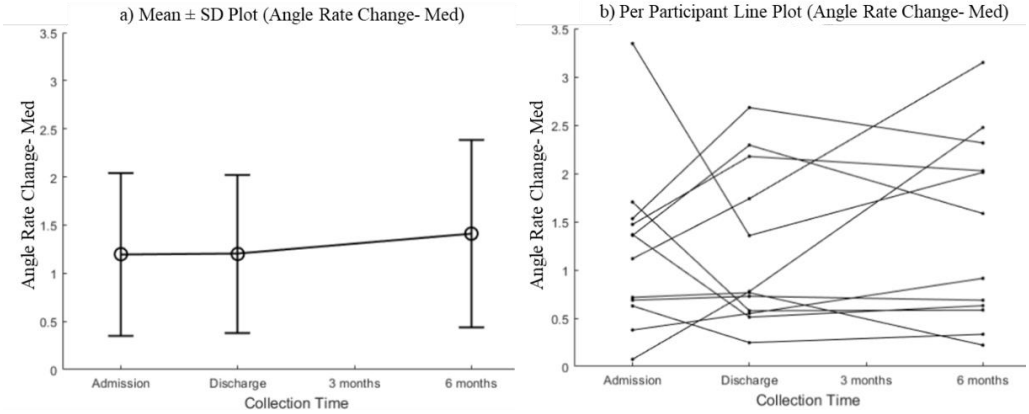


Figure 5.4: Examples of a) mean±SD plots versus b) individual line graphs per participant to assess LA stability over time. For reference, the feature shown had an ICC= 0.427.

After noting the misleading findings associated with the mean ± SD plots, the per participant line graphs and boxplots were used to guide visual analyses. An example of a visually classified stable and unstable feature are shown in Figure 5.5. Although some intra-subject variation is still noted in Figure 5.5a and the median of the boxplot for 6-months in Figure 5.5b is at the top of the 95% confidence interval for the median at admission, this feature was still noted to be stable since most participants showed little change over time. This is further confirmed by the very similar ranges and IQRs for each time point noted in the boxplots. Alternatively, for Power Dom Freq 1- Med the ICC values would have classified this feature as stable (ICC= 0.615), but the per participant line graphs (Figure 5.5c) demonstrate very large changes at each time for 4 participants and moderate changes between discharge and 6-months for an additional 2 participants. This inconsistency is also noted in the Figure 5.5d boxplot where the range of values substantially increases from admission to discharge and the median is just below of the 95% confidence interval at discharge and approaching the upper bound at 6-months. Although it is possible that this feature remains stable for a minority of participants, it was classified as being unstable overall.

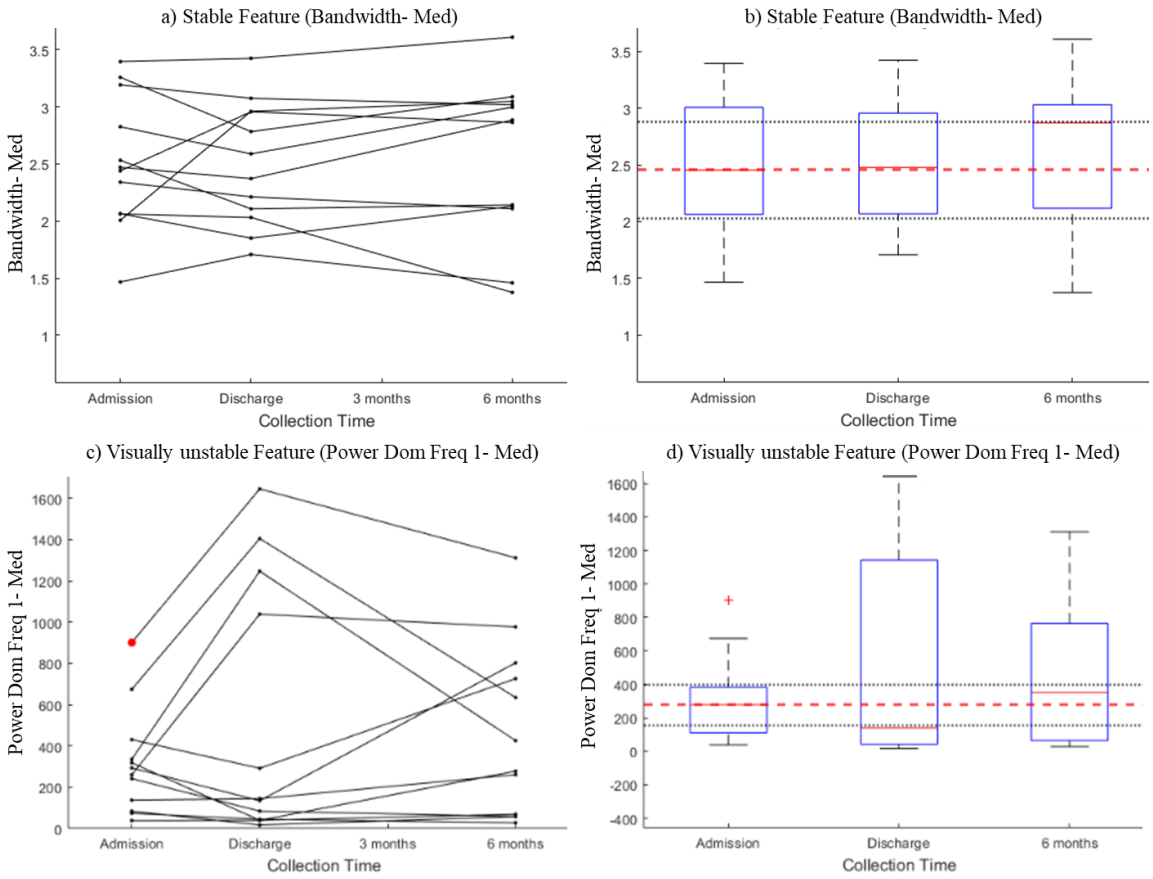


Figure 5.5: Examples of a visually stable feature (top) and a visually unstable feature (bottom) per participant line graphs (left) and per time point boxplots (right). The red dashed line on the boxplots shows the median and the black dotted lines are the 95% confidence interval of the median at admission. For reference the stable (Bandwidth- Med) and unstable (Power Dom Freq 1- Med) ICC values were 0.803 and 0.615, respectively.

Figure 5.5c also demonstrated another trend that was frequently seen during the analysis: the appearance of sub-grouped trajectories. As already mentioned, the Power Dom Freq 1- Med feature seems to consist of 3 groups that change in similar patterns to others in the group, but change differently than others not in the group. In Aim 4a, we will further explore these trajectories and how they relate to clinical measures of impairment and ambulation to see if participants with similar functional characteristics follow similar LA trajectories over time.

5.3.4 **Discussion**

Of 133 initial LA features, a subset of 72 features were found to be reliable when measured at admission over the first 2 typical nights and 34 of those were stable from admission to IPR through 6-months post-discharge. The knowledge that LA can be reliably measured in the inpatient setting among individuals with acute, incomplete SCI provides evidence that LA would be useful in a CPR for ambulation. Additionally, trends were noticed in the variable LA features that may be related to changes in impairment and ambulation and will be further explored in Aim 4.

When evaluating the intra-subject reliability of LA features measured at admission, it was found that the reliability increased when averaged across an increased number of nights, but the single night reliability decreased. This may indicate the LA can still be used reliably when measured over a single night, but the features available may be limited. Nearly the same number of features were reliably measured when using 3 or 5 nights; as such, using the combination of 3 typical nights may optimize the number of reliable LA features while minimizing data collection burden. However, measuring 2 nights still found over half of the assessed features to be reliable. In the context of CPRs, patients and clinicians would most benefit from a prediction provided as early in the IPR stay as possible and the CPR has a higher likelihood of being utilized if it is minimal burden to collect the necessary data.[236] Therefore, the 72 LA features collected over the first 2 typical nights with an at least moderately reliable average night ICC were utilized as the "reliable" features in further analyses in this dissertation.

A wide variety of LA features from every feature category were found to be reliable. This ensures that diverse characteristics of participant's movements would still be captured if only using reliable features in future analyses and this assortment of features should be more informative in a CPR than clinical measures primarily used in previous CPRs which represent single domains of

function.[4, 5, 53, 58-63] This is reinforced by 17 of the 35 (48.6%) LA features associated with impairment among a sample with chronic SCI in Aim 1 were found to be reliable when measured in a sample with acute, incomplete SCI (Table 6.2). Likewise, 4 of the 6 (66.7%) LA features found to be associated with ambulation in the sample with chronic, motor incomplete SCI in Aim 2 were also found to be reliable when measured acutely. The numerous features related to measures of impairment and ambulation in a sample with chronic SCI and able to be reliably measured in an acute population demonstrates versatility and the high potential for these features to be related to clinical measures and predictive of ambulation in an acute sample. These relationships will be further explored in Aim 4.

Alternatively, our findings indicate that 51.4% of the features associated with impairment (Aim 1) and 33.3% associated with ambulation (Aim 2) in the sample with chronic, primarily motor incomplete SCI were not found to be reliable in the acute, incomplete population. Although preliminary analyses to evaluate the intra- and inter-subject variability were assessed in the sample with chronic SCI using visual analyses of boxplots for each feature (described in 3.3.2), we did not perform a structured reliability analysis as performed here for the acute SCI sample. Therefore, the reliability should be formally assessed among those with chronic SCI, especially for the features that were found to be related to impairment or ambulatory ability in Aims 1 and 2, but were not reliable in the sample with acute SCI.

Another possible explanation for the discrepancy in reliability compared to the chronic SCI sample, is that some changes inherent to an acute SCI and the differences in data collection setting (IPR vs community setting) may have affected the ability to measure some LA features reliably at admission to IPR. For example, 5 of the 6 features representing the correlations between axes for each movement that describe the consistency of movement directions were associated with

impairment, but only 1 of those features was found to be reliable in the acute setting (Corr YZ-IQR). Since participants in an acute setting are more likely to be limited in their sleeping positions and may have less motor ability to voluntarily change positions within each night, these features may be too dependent on how the participant is initially positioned at night in the acute setting whereas participants with chronic SCI may have improved ability to vary their sleep positions throughout the night. Additionally, individuals with acute SCI are likely to be still developing spasticity at admission to IPR and may be in various stages of effectively managing the spasticity. Theses participants may present with more significant night-to-night fluctuations in the quantity and characteristics of spastic movements (Figure 4.2 and Section 4.3.4) and, thus, the consistency of movement directions, than we would expect in a chronic SCI population that is more likely to have consistent levels and treatments for spasticity.[74, 237] Therefore, some degree of difference in the reliable features between the chronic and acute settings is expected but should be further evaluated.

We have demonstrated that LA features can be reliably measured at admission to IPR which was anywhere from 7 to 36 days after injury in our sample. Nearly half of those reliable features from admission to IPR were found to be stable over the stay in IPR and through 6-months post discharge. The van Middendorp CPR was validated for when the predictor clinical measures were measured in the first 15 days post-injury.[4] However, due to various medical and logistical complications, providing a prediction that early may not always be possible or clinically appropriate especially for patients with tetraplegia who often have longer acute stays before being admitted to IPR compared to those with paraplegia.[3] Alternatively, some patients may be admitted to IPR within a few days after injury and it is important to have an accurate prediction available as soon as possible to maximize the clinical utility to inform decision-making and patient

expectations. If a new CPR exclusively utilized features that are stable over time, then this CPR will likely be useful when applied at any time after the initial injury has stabilized, generally 48-72 hours after SCI.[19, 238, 239] A CPR utilizing reliable and stable LA features may also be particularly useful because, since these LA features are not expected to change over time, it would likely be valid to re-predict a patient's ambulatory ability after an unexpected change in status later in the sub-acute phase after SCI.

5.3.4.1 Limitations

The ICC analysis was limited by the need for the number of typical nights included to be consistent across participants. For the first few participants, we had only collected 2 nights of accelerometer data before increasing the length of data collection briefly to 4 and then to 7 nights. Thus, 2 nights was the primary time period analyzed to maximize our available sample size. As we would want to use the shortest data collection window possible for prediction to maximize the clinical utility while still ensuring accurate results, we believe 2 nights has been shown to be reliable enough for this purpose. Additionally, the "moderate reliability" cutoff of 0.5 is lower than what is used in some other studies.[234, 235] Since this is a preliminary analysis as part of a larger study and we are still exploring the properties and uses of LA, it was thought that it would be more beneficial to include LA with potentially lower reliability for the present analyses and these features can be re-assessed with more stringent criteria in a future sample. Therefore, this study may also benefit from further assessment with a larger sample population with more typical nights recorded.

The ICC analysis is beneficial in the ability to assess the reliability of the nights used individually and when they are averaged. However, during our preliminary analysis we found that taking the median and IQR across nights provided an informative, yet more stable description of

an individual's LA across all of the nights collected that was less prone to outliers. It is then likely that the "average nights" ICC that was primarily utilized for the reliability analysis (Aim 3a) underestimated the reliability of LA features that may be more stable when the median analysis is implemented to combine nights. Other methods to assess reliability such as repeated measures analysis of variance or ICCs with a larger number of included nights and participants would improve the evaluation of reliability.

The small sample size was a major limitation of this study, especially when examining the stability of LA features over time. Due to challenges from COVID-19 and increased medical and related barriers, our long-term follow-up was limited. Additionally, it was likely biased since participants who participated in the follow-ups tended to be more ambulatory with likely less impairments and medical complications than those who did not participate (Appendix Table G.1 and Appendix Table G.2). Visual analyses were added to verify the ICC analyses and ensure that trends over time were captured appropriately.

Only 1 typical night was required for participants to be included in the analysis for Aim 3b, despite the knowledge that including more than one night improves reliability. All participants had 2 or more typical nights for the discharge and 6-month collections, but 2 participants only had 1 typical night recorded at admission (out of 4 or 7 nights collected). Due to the already limited sample size, these participants were still included in the analysis, but it should be acknowledged that it is possible their inclusion could have affected the stability analysis. Additionally, further analysis should be performed to evaluate the quantitative differences or lack thereof between participant reported "typical" and "non-typical" nights. Follow-up in a larger, more heterogeneous sample could be beneficial to address many of these of these questions.

5.3.5 **Conclusions**

LA features were identified that could be reliably measured in as little as 2 typical nights in an IPR setting among a population with acute, incomplete SCI and variable days since injury. Additionally, many of these features remained stable over time, allowing for them to be utilized nearly any time after injury with consistent results. Many of the features that were shown to be related to impairment or ambulatory ability in Aims 1 and 2 were also identified as being reliable when measured at admission, providing further support for the usefulness and clinical applicability of LA when measured acutely.

5.4 **Aim 4: Exploring Longitudinal LA in Relation to Ambulation and Impairment**

5.4.1 **Introduction**

As described previously, characteristics of a good predictor for use in a CPR include being reliable, valid, and responsive. This allows the predictor to be utilized consistently to measure a clinically valuable metric and recognize subtleties between different participant presentations and characteristics.[234, 235] LA features were found to be reliable in Aim 3a between nights when measured at admission to IPR and in Aim 3b, a subset of those features were identified as being stable over the first 6-months post-injury. Not yet investigated are "variable LA features" that change in relation to clinical measures of impairment and ambulation. These features may be more sensitive to neurorecovery and provide additional evidence of face, construct, and concurrent validity.

The primary purpose of our investigation of LA has been intended for use as a novel biomarker in a CPR to predict long-term ambulatory ability following incomplete SCI. As this study is only a pilot analysis as part of a larger, ongoing study we do not have a sufficient sample size to build and assess the machine learning model for prediction at this time. However, we do have sufficient pilot data to explore the predictive validity of LA as related to ambulatory ability at 6-months post-discharge from IPR. Findings from this analysis will support the continued longitudinal data collection and future plans to build and validate a CPR utilizing LA.

Aim 4a explores how variable LA features change in relation to measures of ambulatory ability and impairment over the IPR stay and first 6-months post-discharge. We hypothesized the change in variable LA features will be significantly correlated with the change in measures of impairment (strength, sensation) and ambulation (need for assistance, speed, endurance) between admission to IPR and 6-months post-discharge. Aim 4b explores the relationship between reliable LA features measured acutely at admission to IPR and ambulatory ability at 6-months post-discharge. We hypothesize that features of LA measured at admission to IPR will be significantly correlated or show clear visual relationships with ambulatory ability measured at 6-months post-discharge.

5.4.2 **Methods**

LA features were included that were identified as reliable but not stable (n=38) in Aims 3a and 3b. These 38 features were described in Table 5.4 with the full results in Appendix Table G.5. Clinical and ambulatory assessments were also collected (Section 3.2). The WISCI-II, 10mWT, and 6MWT were used as measures of ambulatory ability at 6-months post-discharge from IPR to

assess the need for assistance, speed, and endurance during ambulation (Section 3.2.2). Impairment at 6-month was assessed by the LEMS and lower limb LT for strength and sensation, respectively.

Participants were enrolled as described in Section 5.1. Participants were included in the analysis for Aim 4a if they had LA from at least 1 typical night and at least 1 outcome measure (WISCI-II, 10mWT, 6MWT, LEMS, lower limb LT) collected at admission to IPR, just prior to discharge from IPR, and 6-month post-discharge. Participants were included in Aim 4b if they had at least 1 typical night of LA collected from admission to IPR and at least 1 ambulatory ability outcome (WISCI-II, 10mWT, 6MWT) measured at 6-months post-discharge, but were not required to have LA or ambulatory outcomes from the remaining time points. As described previously (Sections 5.2 and 5.3.4.1), only including participants with at least 2 typical nights at admission would have been preferred given the results from Aim 3a, but due to sample size limitations, 2 participants were included that only had 1 typical night measured at admission.

5.4.2.1 Analysis

5.4.2.1.1 Change in Variable LA Related to Change in Outcomes (Aim 4a)

Spearman's rank correlations were used to quantify the relationship between the change in each variable LA feature and each ambulatory and impairment outcome between time points. Unlike Pearson correlations, Spearman correlations are more robust to outliers and do not require a normal distribution and were more appropriate for this exploratory analysis. The change in LA and the outcomes were calculated by subtracting the earlier time point from the later. Correlations were assessed separately for the change from admission to discharge from IPR and from discharge to 6-months post-discharge from IPR. Correlations were also assessed when combining both sets of changes to assess trends over the entire time period from admission to 6-months post discharge.

Correlations using the difference between admission and 6-months post-discharge were not used since this difference may mask the changes occurring at the discharge time point. Since this analysis is exploratory, correlations were considered to be significant if $p < 0.1$. Correlation coefficients were interpreted as: ρ from 0 - 0.3= negligible, 0.3 - 0.5= low, 0.5 - 0.7= moderate, 0.7 - 0.9= high, 0.9 - 1.0= very high.[240] Scatter plots were utilized to further evaluate the trends in the LA features with significant correlations.

As a supplemental analysis, the same per participant line plots used in Aim 3b to evaluate LA stability over time were examined after color-coding participants by their ambulatory ability category at the 6-month time point (ambulatory ability categories shown in Table 3.3). For the impairment outcomes, participants were categorized based on if they improved their LEMS or lower limb LT sensation score from admission to 6-months post-discharge by 6.9 or 4.16 points, respectively. The score of 6.9 points is the repeatability threshold for the LEMS when used for participants with motor incomplete SCI.[56] Similarly, a score of 23.3 (out of 112) was the repeatability threshold for the LT total score among those with motor incomplete SCI which was then scaled to 4.16 (out of 20) estimate the threshold for only the lower limb portion of the LT exam.[56]

5.4.2.1.2 Relationship between Admission LA and 6-month Ambulation (Aim 4b)

As in Aim 4a, a combination of correlations and visual analyses were used to explore the relationship between reliable LA features measured at admission to IPR and clinical assessments of ambulatory ability at 6-months post-discharge. Although stability over time affects the way the feature may be used in a CPR, it is possible for both stable and variable LA features to be beneficial. Since the results from Aim 4a would benefit from further assessment, variable LA features that were not related to changes in ambulatory ability or impairment were still included,

but it was noted that they may be less useful in a future CPR if the results of Aim 4a are confirmed in a larger, more diverse sample. Thus, all 72 LA features that were reliably measured at admission to IPR (Aim 3a) were included in this analysis, regardless of their stability over time.

The Pearson correlation coefficient was calculated to assess the linear relationship between each LA feature and ambulatory outcome. Again, $p< 0.1$ was used to indicate significance since this is an exploratory analysis.

A benefit of using machine learning algorithms to build a new CPR, is that relationships do not necessarily need to be linear to be useful. For example, the random forest classification model used in Aim 2 uses many decision trees to split the sample at nodes until all remaining samples at the bottom of each branch belong to the same class. The nodes that branch the samples are based on cutoff values from the features. Thus, if groups could be separated from each other by a threshold or hyperplane or samples within a group are otherwise distinctly identifiable from other groups, then they might be useful in a non-linear machine learning analysis (Figure 5.6).

To estimate which LA features demonstrate a visual relationship, scatter plots showing the ambulatory outcome vs LA feature were assessed. Participants were categorized by each ambulatory outcome at 6-months and the mean and SD of each ambulatory category were also plotted for reference. For a feature to be potentially useful in non-linear analyses, at least 2 of the 3 groups for each outcome had to be clearly separated from each other on the scatter plots. Features that either had a correlation $p< 0.1$, were visually confirmed to show a trend, or visually classified as being separable from other groups were recorded as being related to the ambulatory outcome.

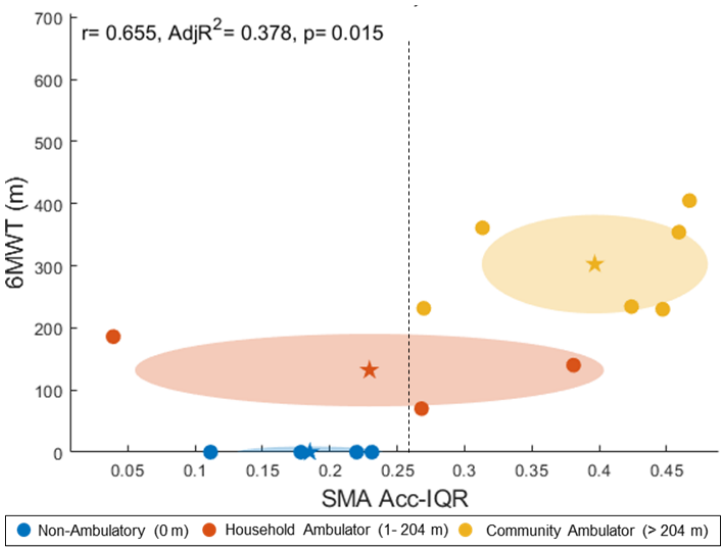


Figure 5.6: Example of visual separation in the LA feature between the non-ambulatory and community ambulator groups of the 6MWT at 6-months post-discharge from IPR. The stars represent the mean and the shading represents 1 SD from the mean per ambulatory group. The black dashed line was added to demonstrate the separability between the groups.

5.4.3 **Results**

5.4.3.1 Participants

The same 12 participants that were included in Aim 3b were also utilized for Aim 4a. An additional 2 participants are included in Aim 4b who had admission LA and 6-month ambulatory outcomes, but were missing 6-month LA thus excluding them from prior analyses. One of those participants did have accelerometer data collected at 6-months, but likely removed the devices for sleep each night which prevented the calculation of LA during sleep. Categorical demographics and ambulation assessments are shown in Table 5.6 for each time point and sample of participants. SCI Neurological category was only reported from admission and discharge because it was not formally assessed at 6-months. Continuous demographics, impairment, and data collection

measures from admission to IPR are shown in Table 5.7 and the measures from all times (including 1-year for reference) are shown in Appendix Table H.1. By 6-months post-discharge, approximately 2/3 of participants were primarily ambulating, 35.7 (Aim 4a) - 41.7% (Aim 4b) did not require an AD or physical assistance to walk, and about half were community ambulators are defined by the 10mWT or 6MWT. Confusion matrices that show the group assignment for each participant between ambulatory outcome are shown in Appendix Table H.2. At 6-months, only one participant was assigned at community ambulator by the 10mWT, but a household ambulator from the 6MWT.

The admission data collection began on average 18 days after injury, but ranged from 9 to 65 days post-injury. Demographics for participants who were included in the analysis and those who had reached the 6-month time point, but did not complete all necessary parts of the data collection to be included in the analysis for Aim 4a are the same as 3b described previously (Appendix Table G.1 and Appendix Table G.2) and are described in Appendix Table H.3 and Appendix Table H.4 for the sample from Aim 4b. The participants who were excluded from the analysis for Aim 4b had a longer length of stay in IPR, were mostly power wheelchair users at discharge, and walked with slower gait speeds than those who were included.

Table 5.6: Categorical participant demographics and ambulation assessments for Aim 4

	Aim 4a N (%) (Total n=12)*			Aim 4b N (%) (Total n=14)†		
Categorical Demographics	Admission	Discharge	6-months	Admission	Discharge	6-months
Sex						
Female	5 (41.7%)			6 (42.9%)		
Male	7 (58.3%)			8 (57.1%)		
Race/Ethnicity						
Non-Hispanic White	9 (75.0%)			11 (78.6%)		
Non-Hispanic Black	1 (8.3%)			1 (7.1%)		
Non-Hispanic Other Race	0 (0.0%)			0 (0.0%)		
Hispanic (Any Race)	2 (16.7%)			2 (14.3%)		
Veteran						
Not A Veteran	11 (91.7%)			12 (85.7%)		
Veteran	1 (8.3%)			2 (14.3%)		
Annual Household Income						
< $25,000	1 (8.3%)			2 (14.3%)		
$25,000 - $49,999	3 (25.0%)			3 (21.4%)		
$50,000 -$74,999	3 (25.0%)			3 (21.4%)		
≥ $75,000	1 (8.3%)			2 (14.3%)		
Decline to Answer or Unknown	4 (33.3%)			4 (28.6%)		
Education						
Less Than High School	2 (16.7%)			2 (14.3%)		
High School Diploma/GED	6 (50.0%)			7 (50.0%)		
Associate's Degree	2 (16.7%)			2 (14.3%)		
Bachelor's Degree	1 (8.3%)			1 (7.1%)		
Graduate Degree	0 (0.0%)			1 (7.1%)		
Other	1 (8.3%)			1 (7.1%)		
Medical Insurance						
Private	3 (25.0%)			5 (35.7%)		
Medicaid	3 (25.0%)			3 (21.4%)		
Medicare	1 (8.3%)			1 (7.1%)		
VA	0 (0.0%)			0 (0.0%)		
No Insurance	1 (8.3%)			1 (7.1%)		
Other/Multiple	4 (33.3%)			4 (28.6%)		
SCI Neurological Category						
Motor Complete (AIS A or B) Tetraplegia	1 (8.3%)	1 (8.3%)		1 (7.1%)	1 (7.1%)	
Motor Complete (AIS A or B) Paraplegia	3 (25.0%)	2 (16.7%)		4 (28.6%)	3 (21.4%)	
AIS C Tetraplegia	1 (8.3%)	1 (8.3%)		2 (14.3%)	1 (7.1%)	
AIS C Paraplegia	1 (8.3%)	2 (16.7%)		1 (7.1%)	2 (14.3%)	
AIS D Tetraplegia	5 (41.7%)	5 (41.7%)		5 (35.7%)	6 (42.9%)	
AIS D Paraplegia	1 (8.3%)	1 (8.3%)		1 (7.1%)	1 (7.1%)	
Primary Mode of Mobility						
Power Wheelchair	9 (75.0%)	4 (33.3%)	2 (16.7%)	11 (78.6%)	4 (28.6%)	2 (14.3%)
Manual Wheelchair	3 (25.0%)	5 (41.7%)	2 (16.7%)	3 (21.4%)	7 (50.0%)	3 (21.4%)
Ambulation	0 (0.0%)	3 (25.0%)	8 (66.7%)	0 (0.0%)	3 (21.4%)	9 (64.3%)

Table 5.6 Continued

Categorical Demographics	Aim 4a N (%) (Total n=12)*			Aim 4b N (%) (Total n=14)†		
	Admission	Discharge	6-months	Admission	Discharge	6-months
WISCI-II						
Requires Physical Assistance (or Non-Ambulatory)	12 (100%)	5 (41.7%)	3 (25.0%)	14 (100%)	7 (50.0%)	4 (28.6%)
Requires AD, but no Physical Assistance	0 (0.0%)	5 (41.7%)	4 (33.3%)	0 (0.0%)	5 (35.7%)	5 (35.7%)
Requires No AD or Physical Assistance	0 (0.0%)	2 (16.7%)	5 (41.7%)	0 (0.0%)	2 (14.3%)	5 (35.7%)
10mWT*†						
Non-ambulatory (0 m/s)	10 (83.3%)	5 (45.5%)	3 (25.0%)	12 (85.7%)	6 (46.2%)	4 (30.8%)
Household Ambulator (0.01- 0.44 m/s)	2 (16.7%)	1 (9.1%)	2 (16.7%)	2 (14.3%)	2 (15.4%)	2 (15.4%)
Community Ambulator (>0.44 m/s)	0 (0.0%)	5 (45.5%)	7 (58.3%)	0 (0.0%)	5 (38.5%)	7 (53.9%)
6MWT†						
Non-ambulatory (0 m)	10 (83.3%)	5 (41.7%)	3 (25.0%)	12 (85.7%)	6 (42.9%)	4 (30.8%)
Household Ambulator (1-204 m)	2 (16.7%)	4 (33.3%)	3 (25.0%)	2 (14.3%)	5 (35.7%)	3 (23.1%)
Community Ambulator (> 204 m)	0 (0.0%)	3 (25.0%)	6 (50.0%)	0 (0.0%)	3 (21.4%)	6 (46.2%)

* n=11 for the 10mWT at admission and discharge for Aim 4a
† n=13 for the 10mWT at discharge and for the 10mWT and 6MWT at 6-months

Table 5.7: Continuous participant demographics for Aim 4 from admission to IPR

Continuous Demographics	Aim 4a Mean ± SD (Range)	Aim 4b Mean ± SD (Range)
Age	45.8 ± 17.8 (18 - 71)	43.8 ± 17.5 (18 - 71)
BMI	27.8 ± 3.4 (23 - 35)	27.9 ± 3.5 (23 - 35)
LEMS (Strength)	23.8 ± 16.0 (0 - 47)	22.5 ± 16.1 (0 - 47)
Lower Limb LT (Sensation)	10.5 ± 7.1 (0 - 20)	10.3 ± 7.5 (0 - 20)
Number of Nights Collected	4.6 ± 1.9 (2 - 7)	4.4 ± 1.9 (2 - 7)
Number of Typical Nights Collected	3.5 ± 2.0 (1 - 7)	3.4 ± 1.9 (1 - 7)
Length of Stay in IPR (Days)	32.6 ± 10.2 (12 - 43)	35.0 ± 11.3 (12 - 51)
Days from Injury to Start of IPR	14.8 ± 16.0 (5 - 62)	15.9 ± 15.1 (5 - 62)
Days from Injury to Start of Data Collection	17.5 ± 15.9 (9 - 65)	19.0 ± 15.2 (9 - 65)

5.4.3.2 Change in Variable LA Related to Change in Outcomes (Aim 4a)

LA features with significant correlations between the change in the feature and the change in the ambulatory or impairment outcomes are shown in Table 5.8 and Table 5.9, respectively. Twenty-six of 38 (68.4%) variable LA features were found to have a significant correlation with at least one ambulatory or impairment outcome at least 1 set of collection times (e.g., admission to discharge from IPR).

Table 5.8: Significant correlations (ρ) between the change in variable LA features and the change in ambulation outcomes from admission to IPR to 6-months post-discharge*

		WISCI-II			10mWT			6MWT		
Feature Category	LA Feature	Adm - Dc (n=12)	Dc-6m (n=12)	Both (n=24)	Adm - Dc (n=11)	Dc-6m (n=11)	Both (n=22)	Adm - Dc (n=12)	Dc-6m (n=12)	Both (n=24)
Change in grav acc	Grav Change Z-IQR	0.182	0.523	0.264	0.225	-0.193	-0.063	0.236	0.011	0.052
Freq domain	Power Dom Freq 1-Med	0.349	0.343	0.365	0.124	-0.183	-0.068	0.189	-0.155	0.012
	Power Dom Freq 2-IQR	0.388	0.285	0.348	0.048	-0.312	-0.179	0.029	-0.099	-0.023
	Power Dom Freq 2-Med	0.356	0.519	0.424	0.076	-0.092	-0.072	0.094	0.070	0.088
	Power Dom Low Freq-Med	0.434	0.482	0.475	0.133	-0.092	-0.051	0.145	0.106	0.131
Limb move %	Bilat Ankle %	0.537	-0.102	0.192	0.434	-0.395	-0.037	0.424	-0.338	0.002
	Unilat Ankle %	-0.537	0.102	-0.192	-0.434	0.395	0.037	-0.424	0.338	-0.002
PLM	PLM %	-0.232	0.292	0.007	-0.029	0.459	0.184	-0.007	0.500	0.215
Signal char	Wave Approx-Med	0.623	0.117	0.315	0.715	-0.165	0.209	0.725	0.042	0.272
	Wave Energy 2-Med	-0.481	-0.073	-0.195	-0.677	0.239	-0.126	-0.761	-0.007	-0.222
	Wave Energy 3-IQR	-0.541	-0.073	-0.338	-0.543	0.266	-0.170	-0.544	0.081	-0.230
	Wave Energy 3-Med	-0.651	0.110	-0.249	-0.763	0.385	-0.127	-0.725	0.169	-0.161
	Wave Entropy-Med	-0.519	-0.139	-0.281	-0.597	0.138	-0.205	-0.628	-0.053	-0.270
Statistical	AUC Acc Norm-Med	0.502	0.431	0.476	0.305	-0.073	0.084	0.319	-0.056	0.120
	Duration-Max	0.306	0.380	0.251	0.019	0.275	0.151	0.036	0.500	0.283
	SMA Acc-Med	0.517	0.400	0.461	0.272	-0.078	0.042	0.287	-0.074	0.089
Velocity, distance	RMS Vel-Med	0.730	-0.068	0.367	0.474	-0.505	0.109	0.425	-0.391	0.117

* Correlations with $p < 0.1$ are highlighted grey

The WISCI-II had the most correlated features of any of the outcomes, particularly from admission to discharge from IPR. Most features for the WISCI-II had low to moderate correlation coefficients, while most features for the 10mWT and 6MWT had moderate to high correlations. Visually, there were a few features for the WISCI-II, primarily in the frequency domain and signal characteristics categories, that showed weak to moderate trends (Figure 5.7a). However, most other features for the WISCI-II and all features for the 10mWT and 6MWT showed weak visual correlations (Figure 5.7b) and at times conflicting trends (Figure 5.7c and Figure 5.7d).

Some interesting trends were noted when examining the per participant line graphs by ambulation or impairment outcome (Appendix Figure H.1), such as the participants with more prominent variability tended to have better ambulatory ability while those who had more stable measurements over time tended to be non-ambulatory or more limited ambulators. However, most of these trends were inconsistent and would be better assessed in a larger, more variable sample.

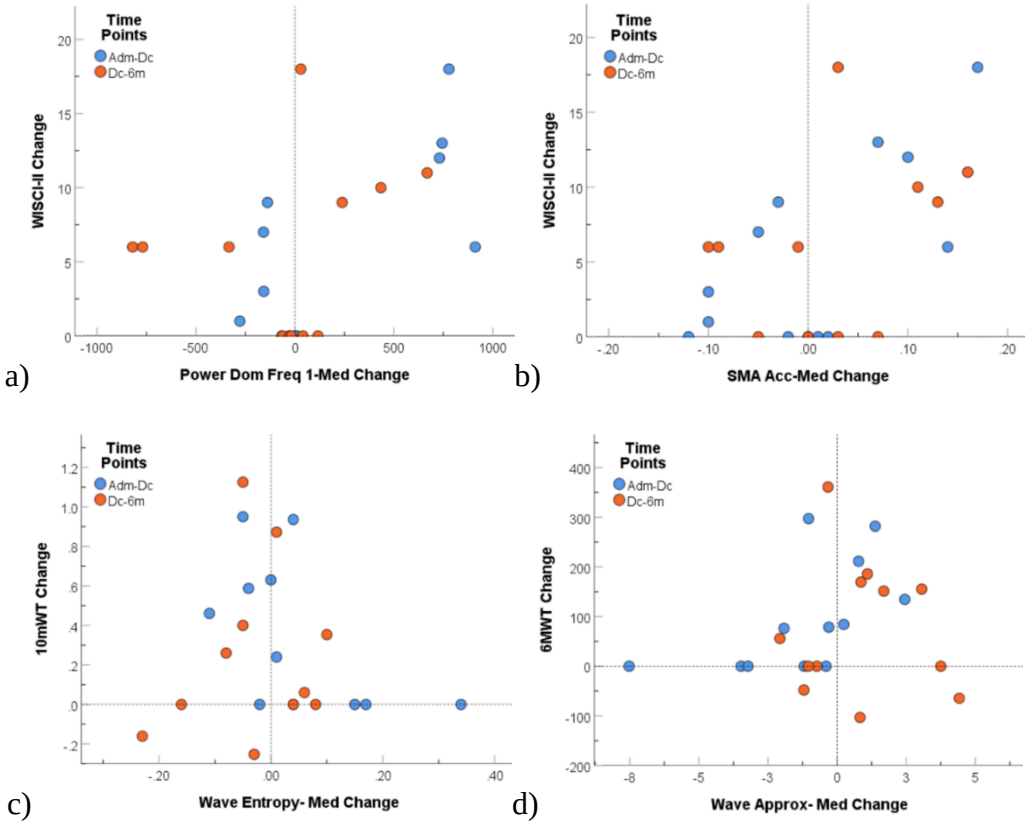


Figure 5.7: Examples of significant, but relatively weak changes in LA features and ambulatory outcomes. a) Power Dom Freq 1- Med has a moderate visual trend with the WISCI-II particularly from admission to discharge. b) SMA Acc- Med has a weak-moderate visual trend with the WISCI-II that is stronger between discharge and 6-months. c) Wave Entropy- Med has a weak trend with the 10mWT that is negative form admission to discharge and positive from discharge to 6-months. d) Wave Approx- Med Change has a weak trend with the 6MWT that is positive from admission to discharge but negative from discharge to 6-months.

Table 5.9: Significant correlations (ρ) between the change in variable LA features and the change in impairment outcomes from admission to IPR to 6-months post-discharge*

		LEMS			Lower Limb LT		
Feature Category	LA Feature	Adm - Dc (n=12)	Dc-6m (n=9)	Both (n=21)	Adm - Dc (n=11)	Dc-6m (n=7)	Both (n=18)
Change in angle of inclination	Angle Net Change-Med	-0.141	-0.333	-0.228	-0.055	0.883	0.213
	Angle Rate Change-Med	-0.058	-0.067	-0.050	-0.097	0.829	0.249
	Angle Total Change-IQR	0.134	-0.167	-0.048	-0.220	0.685	0.189
	Angle Total Change-Med	-0.042	-0.050	-0.014	-0.110	0.829	0.301
Change in gravitational acceleration	Grav Change Y-IQR	-0.179	-0.267	-0.294	-0.046	0.883	0.232
	Grav Change Z-Med	0.095	-0.559	-0.193	0.468	0.645	0.493
Correlation coefficients between axes	Corr YZ-IQR	-0.341	0.217	-0.076	-0.248	0.793	0.175
Frequency domain	Power Dom Freq 2-IQR	0.046	-0.250	-0.158	-0.105	0.739	0.166
	Power Dom Freq 2-Med	0.127	-0.267	-0.112	0.087	0.901	0.373
	Power Dom Low Freq-Med	0.105	-0.250	-0.109	0.027	0.901	0.363
Median crossings	Num Med Crossings-IQR	0.606	0.051	0.297	0.173	-0.075	0.063
Statistical	Duration-Max	0.545	0.183	0.353	0.430	0.018	0.235
Velocity and distance	Med Vel-Med	0.588	0.548	0.504	0.195	0.206	0.291

* Correlations with p< 0.1 are highlighted grey

Three LA features had significant correlations to LEMS, but only one of them (Num Med Crossings- IQR) had a moderate positive trend to the change in LEMS from admission to discharge (Figure 5.8a, Appendix Figure H.2). Only weak visual trends were found related to lower limb LT; however, one feature (Corr YZ- IQR, variability in movement directions) had an unusual difference in the direction of change with nearly all participants decreasing the variability of their movement directions from admission to discharge and then increasing from discharge to 6-months.

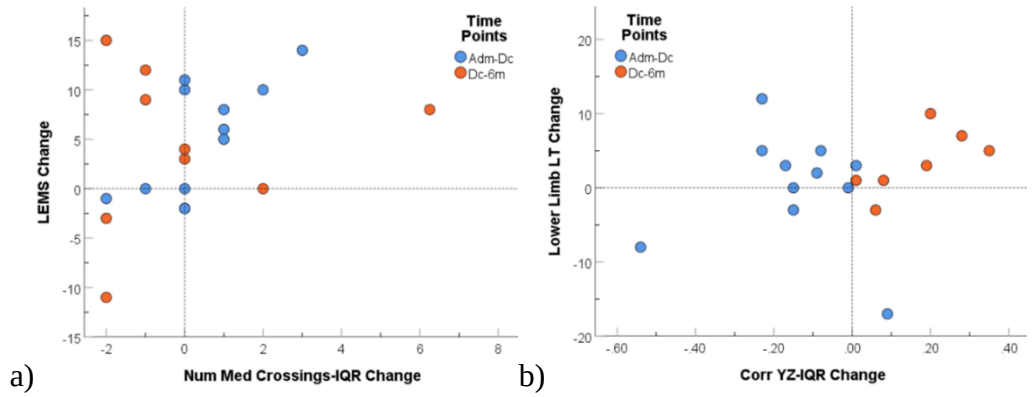


Figure 5.8: Examples of the change in LA features and impairment outcomes a) Moderate positive trend noted from admission to discharge between the Num Med Crossings- IQR and LEMS. b) Unusual finding with Corr YZ- IQR where from admission to discharge nearly all participants decreased their variability in movement directions, but from discharge to 6-months nearly all participants increased their variability in movement directions with a positive trend to lower limb LT sensation noted.

5.4.3.3 Relationship between Admission LA and 6-month Ambulation (Aim 4b)

Of the 72 features that were reliably measured at admission to IPR, 41 (56.9%) were related to one of the measures of ambulatory ability at 6-months post-discharge. Ten of the 25 (40%, 24% of the 41 related features) features that were reliable when measured using a single night at admission were also found to be related to ambulatory ability at 6-months.

Table 5.10 summarizes the number of features found to be related to each ambulatory outcome, Table 5.11 summarizes the findings from the correlation, and visual analyses for each ambulatory outcome and the full results for all reliable features are shown in Appendix Table H.5. Most features that were related to each outcome had both significant correlations and a supporting visual relationship. Overall, 11 (15.3%) reliable LA features were related to only one ambulatory outcome, while 15 (20.8%) features each were associated with 2 and all 3 ambulatory outcomes. LA features from all categories were reliable and associated with 6-month ambulatory ability except change in gravitational acceleration, correlation coefficients between axes, and timing.

Twenty-five out of 34 (73.5%) features found to be stable over time in Aim 3b were also related to an ambulatory outcome at 6-months (Table 6.1). Of the 38 features that were variable over time in Aim 3b, 16 (42.1%) were associated with 6-month ambulation, with 13 (81.3%, 34.2% of 38 variable features) of those features also significantly changing with measures of ambulation or impairment over time in Aim 4a. The 3 variable LA features that were related to ambulatory ability at 6-months but not to changes in ambulatory ability or impairment over time from Aim 4a (Angle Rate Change-IQR, Wave Energy 2-IQR, Duration-IQR) were further visually examined in Appendix H.1. It is possible these features would have a significant association between change in the feature and change in ambulatory ability or impairment in a larger sample, but none had clear associations when visually examined. Angle Rate Change- IQR had one of the most distinct separation of groups for the 10mWT and 6MWT in the visual analyses of any admission feature. Wave Energy 2- IQR had a smaller separation between the non-ambulatory and household ambulator groups for the 6MWT and Duration- IQR showed a weak-moderate correlation between the admission LA feature and the 6-month WISCI-II and 10mWT outcomes.

Table 5.10: Number of reliable admission LA features related to each measure of ambulatory ability at 6-months post-discharge from IPR

Association to 6-month Ambulatory Ability	WISCI-II	10mWT	6MWT	Total
Significant Correlation Only	9 (12.5%)	1 (1.4%)	2 (2.8%)	12 (16.7%)
Visual Association Only	0 (0.0%)	5 (6.9%)	9 (12.5%)	14 (19.4%)
Both Correlation and Visual Association	25 (34.7%)	17 (23.6%)	17 (23.6%)	59 (81.9%)
Total	34 (47.2%)	23 (31.9%)	28 (38.9%)	41 (56.9%)

Table 5.11: Reliable LA features measured at admission to IPR that are related to ambulation outcomes at 6-months*†‡

Feature Category	LA Feature	WISCI-II	10mWT	6MWT
Change in angle of inclination	Angle Rate Change-IQR §	0.324	0.452	0.399
	Angle Rate Change-Med	**0.513**	0.421	0.460
	Angle Total Change-IQR	**0.468**	**0.651**	**0.580**
	Angle Total Change-Med	**0.471**	0.382	0.432
Frequency domain	*Bandwidth-Med*	**-0.662**	-0.421	-0.424
	Centroid Freq-Med	**-0.657**	-0.445	**-0.491**
	Power Dom Freq 1/Total-Med	**0.499**	0.305	0.386
	Dom Freq 1-Med	**-0.641**	**-0.506**	**-0.520**
	Power Dom Freq 1-Med	**0.489**	0.277	0.292
	Power Dom Freq 2-IQR	**0.652**	**0.755**	**0.651**
	Power Dom Freq 2-Med	**0.596**	0.369	0.376
	Power Dom Low Freq-IQR	**0.698**	**0.776**	**0.664**
	Power Dom Low Freq-Med	**0.547**	0.332	0.334
	Power High Freq/Total-Med	**-0.511**	-0.338	-0.359
	Power Total-IQR	**0.712**	**0.768**	**0.614**
Limb movement percentages	Bilat Ankle %	-0.247	-0.300	**-0.487**
	Unilat Ankle %	0.247	0.300	**0.487**
Median crossings	*Num Med Crossings Norm-Med*	**-0.708**	**-0.570**	**-0.546**
Relationship to recent movements	*Close Cross Corr Peak-IQR*	**0.691**	**0.562**	**0.482**
Signal characteristics	*Lempel-Ziv Comp-Med*	-0.089	-0.090	0.041
	Lyapunov Exp-IQR	**0.620**	0.407	0.417
	Wave Energy 2-IQR §	0.378	0.092	0.079
Statistical	*AUC Acc Norm-IQR*	**0.747**	**0.733**	**0.681**
	AUC Acc-IQR	**0.699**	**0.735**	**0.679**
	AUC Acc-Med	**0.537**	0.424	0.426
	Duration-IQR §	**0.517**	**0.569**	0.465
	Duration-Max	**0.622**	0.425	**0.503**
	Duration-Med	**0.521**	**0.546**	**0.529**
	Max Acc-IQR	**0.611**	**0.668**	0.443
	Med Acc-IQR	**0.703**	**0.673**	**0.701**
	Med Acc-Med	0.391	0.282	0.344
	Range Acc-IQR	**0.612**	**0.669**	0.444
	RMS Acc-Med	**0.472**	0.256	0.230
	SD Acc-IQR	**0.741**	**0.694**	**0.556**
	SMA Acc-IQR	**0.710**	**0.720**	**0.655**
	SMA Acc-Med	**0.504**	0.340	0.327
Velocity and distance	*Med Vel-IQR*	**0.699**	**0.672**	**0.701**
	Med Vel-Med	0.358	0.256	0.302
	RMS Vel-Med	**0.476**	0.257	0.231
	Total Dist-IQR	**0.687**	**0.776**	**0.701**
	Total Dist-Med	**0.574**	0.448	0.468

* Outcomes that had a correlation p< 0.1 are bolded
† Outcomes found to have visual trends or at least 2 groups were visually separable are highlighted grey
‡ LA features that were found to be stable over time in Aim 3b are italicized
§ Indicates a feature that was variable over time in Aim 3b, but not related to changes in ambulatory ability or impairment in Aim 4a

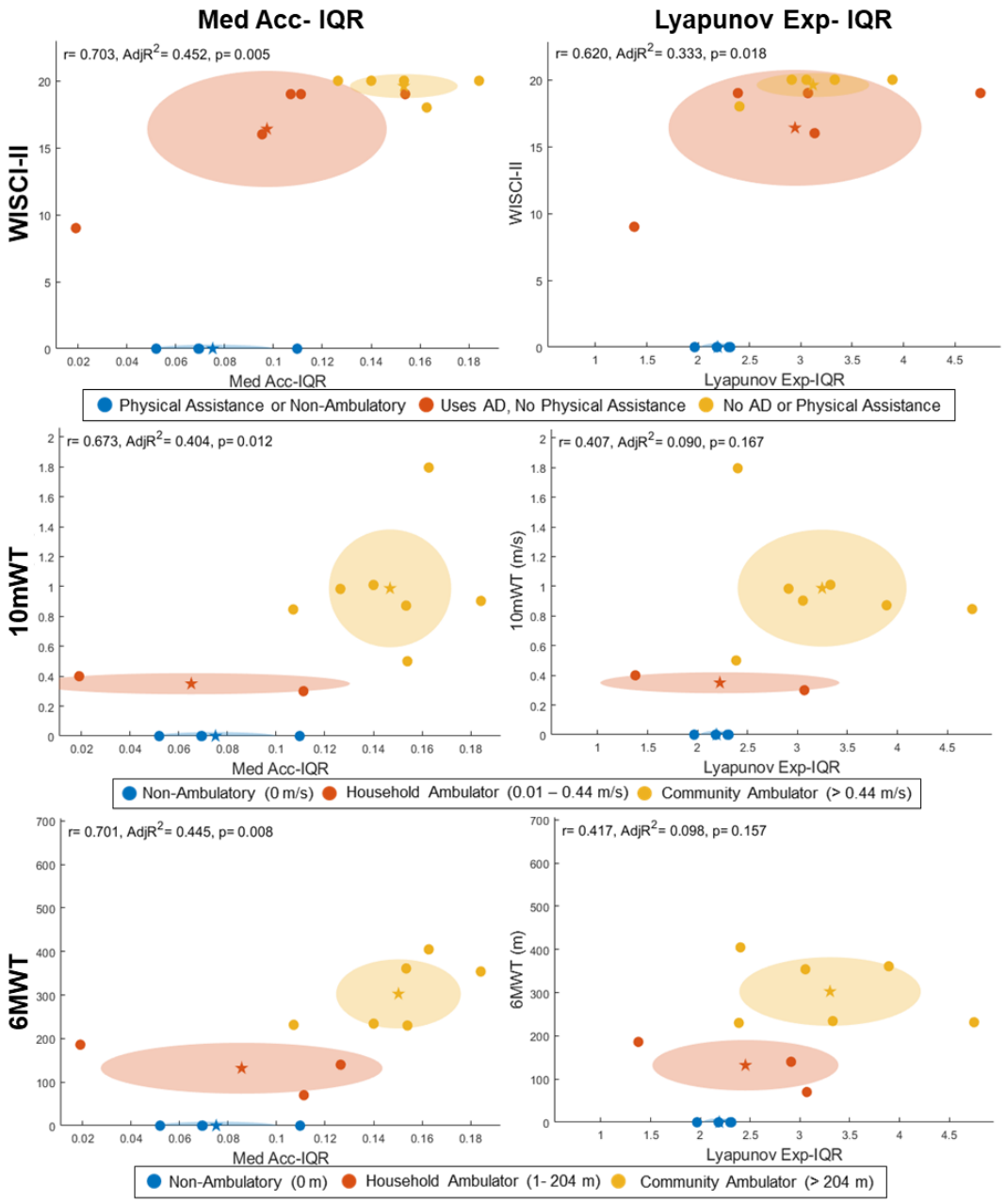


Figure 5.9: Examples of the relationship between 2 LA features from admission and each ambulatory outcome at 6-months post-discharge from IPR. The stars represent the mean values and the shading represents 1 SD from the mean per group. The LA features Med Acc- IQR (left) and Lyapunov Exp- IQR (right) demonstrate positive correlations that are most prominent for the 6MWT. Additionally, there is no overlap in the LA feature values between participants in the lowest and highest ambulatory groups for each outcome, demonstrating the visual separation of the groups.

5.4.4 **Discussion**

Although exploratory in nature, these findings provide further evidence that LA is valid as a clinically meaningful metric when assessed in acute, incomplete SCI and would be likely to be successful if utilized in a CPR for functional, long-term ambulatory ability.

More than 2/3 of the variable LA features were found to significantly change in relation to changes in impairment or ambulatory ability. However, when visually examined, many of these correlations were relatively weak. The small sample size, especially for the impairment measures, may have led to the LA features appearing more variable when in a larger sample the correlation may be stronger. Because of the many variable LA features with significant correlations but minimal visual trends, a larger sample is likely needed to confirm the results found in this exploratory analysis. Because of this, all variable features were included in the analysis for Aim 4b with the understanding that features that are confirmed in a larger, more diverse sample are not likely to be useful in a CPR. Although the correlations may be weak in the current sample, these findings still provide evidence of face and construct validity of LA when measured acutely as well as demonstrating the responsiveness and robustness of this measure to still be able to detect trends in a small sample.

The findings noted when examining the per participant changes in relation to ambulation and impairment groups indicate that there may be additional associations between LA and the outcomes that were not fully captured by the correlation analysis. For example, participants who are better ambulators may be extremely variable in a measure over time, while those who are non-ambulatory may remain relatively stable. This finding would not be noticed by correlational analyses, but may still be helpful because the direction and amount of change between repeated measurements of that feature may provide information about future changes in ambulatory ability.

Understanding how these features change over time and the nuances in their associations to clinical measures of ambulation and impairment will assist in informing a future CPR and clinical outcomes.

Care should be taken when utilizing the 3 LA features (Angle Rate Change-IQR, Wave Energy 2-IQR, Duration-IQR) that were found to be related to ambulatory ability at 6-months, but were variable and not related to changes in ambulatory ability or impairment over time. These features may be inconsistently measured in which case they may add noise to future models and increase the variability in LA in an unpredictable manor which would decrease prediction accuracy of the CPR. Additional analyses to further evaluate how these features change over time and ensure that they change in a predictable and meaningful way before including them in a CPR or other applications.

Over 20% of the LA features measured at admission to IPR were related to all 3 ambulatory outcomes at 6-months post-discharge. An additional 15% were related to only outcome; these features may provide unique information about specific aspects of ambulatory ability that influence an individual's performance in one assessment, but not another. As demonstrated by the participant classifications in Appendix Table F.1 (for all participants) and Appendix Table H.2 (for only participants in Aim 4a), the WISCI-II provides unique that may inform clinical care differently than the 10mWT and 6MWT. Even though the majority of participants did fall in to the same categories for the 10mWT and 6MWT, the differences between these outcomes can still be recognized by not all participants be classified identically into these groups. This reinforces the importance of utilizing multiple non-dichotomous ambulatory outcomes to produce a comprehensive prediction of an individual's functional abilities.[102-104, 109]

Visually it was seen that the middle ambulatory ability category (uses AD but no physical assistance for WISCI-II, household ambulator for 10mWT and 6MWT) was less separable from the other two. This trend was also detected when classifying individuals with chronic SCI into those ambulatory categories in Aim 2. Since this group may possess characteristics of both the lowest and highest ambulatory groups, it makes sense that this group may have the most overlap and may be most differentiate in a population with acute, incomplete SCI. However, some LA features were able to show significant correlations or clear visual separation of this group (Figure 5.6). Thus, it is possible that this group may have the lowest accuracy for the 3 groups for each outcome when predicted in a future CPR utilizing LA, but we believe that LA consists of enough unique features to cumulatively still differentiate this group well. This was supported by the findings from Aim 2 in the sample with chronic, motor incomplete where the household ambulator group was the most commonly misclassified of the 3 ambulatory groups, but still was correctly classified with an F1-score of 0.632 and 0.783 and is likely to improve in a larger, longitudinal sample.[241] Further, the middle ambulatory ability groups generally had the smallest sample size of the 3 groups for each outcome, so the increased variability may be influenced by the smaller number of participants.

Many traditional statistical models used in previous CPRs assess a predictor's relationship to the outcome linearly or using log-odds,[4-6] but machine learning models have the ability to identify non-linear associations between the predictor and outcome, as well as associations between predictors.[210, 211, 223] Additionally, machine learning models can generally utilize many more features or autonomously identify sets of important features that traditional statistical models with the same sample size cannot.[107] Phan et al. has suggested that including a greater number of predictors and using less traditional statistical analyses like logistic regression could improve the

accuracy of future prediction models.[109] Our findings demonstrate that a wide variety of different movement characteristics captured by LA are related to ambulatory ability and a CPR would likely perform best by utilizing predictors that embody this diversity.

Although the current sample was too small to use machine learning techniques, the use of both correlational and visual analyses to identify trends that are not easily captured by statistical techniques allowed for a deeper understanding of the relationship and potential predictive ability of LA for long-term ambulatory ability. This also provides increased confidence that these features would be useful in a CPR for ambulatory ability. Machine learning models may pick up additional or different non-linear relationships between LA features or the features and outcomes that could not be visually assessed.

5.4.4.1 Limitations

Nearly all of the challenges regarding the sample size and other limitations that were discussed in Aim 3 (Section 5.3.4.1) are applicable to Aim 4 as well. The decision to use 1 typical night despite the finding that 2 typical nights provide the best reliability was a substantial limitation of these analyses. Due to the exploratory nature of these analyses and the limited sample size and distribution of ambulatory abilities, participants were not excluded if they did not have at least 2 typical nights collected at admission to IPR (all participants did have ≥2 typical nights for the follow-ups). Since 24% of the features that were related to 6-month outcomes in Aim 4b were reliable when using a single night of LA (Aim 3a), we believe these findings are accurate despite the inclusion of those 2 participants with less reliable LA. Future analyses should assess the differences between "typical" and "non-typical" nights, as well as ensure that only participants with reliable LA are included.

Limitations unique to is aim, include the clinical and ambulatory assessments not being consistently performed by clinicians trained by the research team which may decrease the reliability of these assessments. However, one of the reasons that these ambulatory and clinical outcomes were utilized, is that they are frequently performed, common assessments that most clinicians would previously have been trained to complete and utilize regularly.[102, 104] Additionally, the ambulatory assessments have demonstrated excellent test-retest and inter-rater reliability which indicates that these measures would likely still be consistently measured in these circumstances.[102, 242]

For both impairment outcomes, but especially lower limb LT, the sample size decreased at 6-months secondary to limitations from remote follow-up collections (assessments could not be completed for impairment outcomes if participants weren't attending physical therapy and were not consistently collected from those attending therapy). This sample size limits the interpretation of the findings and likely led to the larger number of features with correlations to the change in lower limb LT from discharge to 6-months post-discharge. For these reasons and the large number of missing data, the MAS had limited follow-up measurements and could not be included in this analysis.

Although the 3 ambulatory outcomes assessed provide a comprehensive understanding of an individual's ability to walk (capacity), they do not provide a measure of how much the participants actually do walk (performance). A person may be more likely to functionally ambulate if they walk with a better quality and speed, but other factors may also affect their primary mode of mobility and daily activity. The current findings make it likely that LA would also be related to measures of walking performance such as daily steps.[214, 243] Additionally, the relationship between person, psychosocial, and environmental factors (PPEF) such as an individual's coping strategies,

pain, environmental barriers, and social support may all influence an individual's ambulation capacity and performance.[11, 12, 90, 91, 244] Measures of daily steps, time and use of a wheelchair versus ambulation, and PPEF were all collected in this longitudinal sample and should be assessed in future analyses.

Lastly, the visual analyses performed for this aim were subjective to some extent, although efforts were made to minimize the effects of subjectivity. These efforts include, one researcher performed all of the analyses with predetermined guidelines and checked the findings a second time to ensure that all visual classifications were consistent. Because of the aforementioned efforts taken to decrease subjectivity, compounded with the fact that these analyses are exploratory with a small sample size, the findings are still meaningful and will be further evaluated in future analyses.

5.4.5 **Conclusions**

Changes over time in variable features of LA were significantly correlated with and may be related to changes over time in each measure of ambulatory ability and impairment, though further analysis is needed. Additionally, 41 features that were reliable when measured at admission to IPR among a sample with acute, incomplete SCI were found to be related to the need for assistance, speed, and endurance during ambulation at 6-months post discharge. These features capture a variety of different aspects of movements representing a diverse understanding of a participant's movement characteristics and abilities. These findings provide evidence that LA measured at admission to IPR would likely be beneficial in a CPR to predict a comprehensive description of ambulatory ability among a sample with acute, incomplete SCI who would benefit from this prediction the most.

5.5 **Longitudinal Study Conclusions**

In Aim 3a, LA were established as reliable when measured over the first two typical nights soon after admission to IPR (number of selected features=72). Further, we identified LA features that are stable over the first 6-months post-discharge (Aim 3b) as well as features that were not stable (variable) over time and were related to changes in ambulatory ability and impairment (Aim 4a). LA features stable over time (n=25) may be able to differentiate between different levels of impairment and ambulatory ability using measurements from a few days to a several months after injury. LA features that are variable over time and related to ambulation or impairment (n=26) represent baseline measures of characteristics that would only substantially change if the individual's level of impairment or functional abilities improve. These measures are similar to clinical predictors such as MMT and LT scores that are commonly used in current CPRs and are likely to change with neurorecovery.[4, 5, 53, 58-63] But unlike those clinical measures, the LA features capture much more information about an individual's movement and should be more useful in a CPR.

This work culminates in Aim 4b which shows LA features (both stable and variable) are related to ambulatory ability at 6-months. Each of these features demonstrated either a significant correlation with or visual separation of long-term ambulatory groups based on LA measurements from admission to IPR. They indicate diverse movement characteristics are important including movement magnitude, power, energy distribution, frequency, smoothness, stability, duration, similarity to recent movements, directions, velocity, and distance traveled. Further, they show that it is important to consider both the actual values of the movement characteristics (median values) and the ability to produce a variety of movement characteristics (IQR).

While a machine learning model may identify features most useful for prediction differently than the current analyses, our results provide strong pilot data evidence that LA, measured acutely after injury, is related to ambulatory ability following SCI and important to consider in future CPRs. Collectively, these analyses provide evidence of reliability and face, construct, concurrent, and predictive validity of LA when measured in a sample with acute, incomplete SCI. This makes a strong case for the future use of LA as a measure of impairment and predictor of functional, long-term ambulatory ability.

6.0 Overall Conclusions and Future Directions

This dissertation established LA as a meaningful clinical metric that is related to measures of impairment (strength, sensation, spasticity; Aim 1) and ambulation (speed, endurance; Aim 2) in a cross-sectional analysis of individuals with chronic, primarily motor incomplete SCI. These findings established the face, construct, and concurrent validity of LA in a diverse sample. Then using a longitudinal analysis of individuals with acute, incomplete SCI from admission to IPR through 6-months post-discharge, we were able to evaluate the reliability, validity, and relationship to clinical outcomes. These results determined that LA can be reliably measured in an acute setting, includes features that can be identified as stable over time or changing in relation to measures of impairment and ambulation, and are likely predictive of 6-month ambulatory ability when measured at admission to IPR.

Summary findings of which LA features were determined to be supportive of the goals for each aim (e.g., related to ambulatory ability, reliable, etc.) are shown in Table 6.1. Additionally, a summary table describing the number of features selected for each aim is shown in Table 6.2. While many LA features were selected for each aim that represent a diverse set of movement characteristics, the only feature that was selected in every applicable analysis was Lyapunov Exp-IQR. The Lyapunov exponent is a measure of local dynamic stability or chaos which may be a measure of the motor system's ability to diminish perturbations and continue along a trajectory with higher values representing increased divergence/chaos and less stability.[224, 225] It has been shown to prevuously be related to measues of sleep apnea, brain activity during sleep,[245] gait,[146, 225] fall risk,[224, 226] and improvements in lower limb rehabilitation.[173] The variability in this measure may represent an individual's ability to produce consistent, stable movements and unpredictable

movements. Individuals with limited strength or severe spasticity may have limited ability to move in a variety of directions and speeds, thus their movements are more likely to be predictable with less variability. Therefore, the finding that individuals with better strength and ambulatory ability would exhibit more variability in movement stability.

Seven other features were selected in 4 of the analyses: speed of positional changes (Angle Rate Change-Med), variability of position changes (Grav Change Z-IQR), movement frequency (Dom Freq 1-Med), power (Power Dom Freq 2-Med), movement smoothness (Num Med Crossings Norm-Med), and variability in similarity of recent movements (Close Cross Corr Peak-IQR). All of those features were found to be related to a measure of impairment among those with chronic SCI, were reliable to measure at admission to IPR in acute, incomplete SCI, and were related to 6-month ambulatory ability when measured at admission in acute, incomplete SCI (except Grav Change Z- IQR which was related to ambulatory ability in chronic SCI).

Both Angle Rate Change-Med and Grav Change Z-IQR describe different aspects related to the changes in position throughout the night. Angle Rate Change-Med describes the total change in the angle of inclination (resultant angle between 3 gravitational axes) divided by the time to complete the movement as a measure of angular velocity.[154, 159, 162] Having a faster rotational movements was associated with greater strength in Aim 1 and was positively correlated with both the WISCI-II and 6MWT at 6-months post-discharge in Aim 4b. The Z axis of the accelerometer runs medial-lateral (Figure 3.2) and would experience the greatest changes when the participant rotates side to side, such as when rolling from the right to the left side. Grav Change Z- IQR was associated with mild spasticity in Aim 1 and the 6MWT in Aim 2 among those with chronic SCI and was correlated with changes in the WISCI-II over time in participants with acute SCI in Aim 4a. Participants who are able to rotate positions more quickly and complete a variety of rotational

position changes throughout the night likely have improved strength to perform such movements, which may be related to improved walking endurance and less assistance for ambulation. Thus, these features may capture reliable and useful measures of how an individual moves throughout the night and are related to measures of strength and ambulatory ability which could be useful in a CPR.

Dom Freq 1-Med represents the dominant frequency of the signal (frequency at the maximum spectral power) and provides of measure of periodicity. Someone with a higher dominant frequency would likely have many fluctuations in their movements and a noisier signal compared to someone with a lower dominant frequency. Power Dom Freq 2-Med represents the power at the second local maxima and will be higher for movements with higher intensities. It also could be higher if a larger amount of the total power is at the second dominant frequency as compared to other movements where the power might be highly concentrated at the dominant frequency. A higher Dom Freq 1-Med was associated with worse sensation, worse spasticity, and worse ambulatory ability in all 3 outcomes. Higher Power Dom Freq 2- Med values were associated with having worse sensation, more spasticity and better ambulatory outcomes for the WISCI-II and 10mWT. It makes intuitive sense that having noisier, higher frequency movements may be associated with more spasticity and worse outcomes and more intense movements being associated with better walking outcomes. However, the association between power and worse sensation and spasticity warrant further investigation.

Num Med Crossings Norm-Med is a measure of movement smoothness that is calculated by counting the number of times that the acceleration magnitude crosses the median of the acceleration over the whole movement normalized by the duration of the movement. A participant with many changes in acceleration per second of movement would have a higher Num Med

Crossings Norm-Med and less smooth movement and was associated with worse walking outcomes for the WISCI-II, 10mWT, and 6MWT at 6-months post-injury. It would be expected that someone with poorer motor control and strength would have more difficulty performing a movement smoothly, thus it makes sense that Num Med Crossings Norm-Med was also associated with lower strength among those with chronic SCI. A similar measure was also found to be negatively correlated to 6MWT distances among children with muscular dystrophy, and greater smoothness has also been associated with improved gait quality when comparing health controls to those with Parkinson's disease and peripheral neuropathy.[89, 146]

Having movements in series with similar characteristics was common of movements that were more likely spastic or PLM (Figure 4.2). This was demonstrated by the finding that lower Close Cross Corr Peak-IQR which is a measure of similarity to recent movements was associated with a lower probability of having no spasticity. Additionally, having more variable recent movements was associated with all 3 ambulatory outcomes at 6-months post-injury.

These features are a likely to be useful in a CPR for ambulation and other potential purposes such as improved measures of impairment. With the exception of the 2 features from the frequency domain, these features all represent different categories of movement information, which emphasizes the benefits of a diverse feature set.

Both Aims 1 and 2 utilize machine learning models to assess the relationship between LA and measures of impairment and ambulatory ability. A benefit from those analyses is that feature selection steps were embedded in the analysis to minimize bias and overfitting in the results. The feature selection is designed to choose features that are likely to improve model performance and decrease collinearity, which would likely result in only one feature out of a group of highly correlated feature to be included in the model. Thus, it is likely that other highly correlated features

to those described above that were reliable when measured acutely (Aim 3a) and related to a 6-month measure of ambulatory ability (Aim 4b), are also likely to be particularly useful in future applications.

Future work in this area should include evaluating the reliability of LA features in the chronic SCI population and further validation of the findings in Aims 3 and 4 should in a larger, more diverse sample. Additionally, the differences between participant reported "typical" and "non-typical" nights should be evaluated. It would be beneficial to have a better understanding of what makes a participant identify a night as "non-typical" and if non-typical nights can be utilized in analyses if similar LA can be extracted to self-reported "typical" nights. It would also be beneficial to assess LA in relation to an ambulatory outcome that evaluates performance, such as daily steps, as well as the use of personal, psychosocial, and environmental factors (PPEF) as a predictor of all outcomes. Further, LA may be applicable as a movement biomarker that could be used to predict the response to rehabilitation interventions in other populations and for other activities.

Given the many diverse, informative, and reliable features that can be extracted from limb movements during sleep with low collection burden in both acute and chronic populations with incomplete SCI, LA has the potential to be a widely utilized clinical metric. LA that is reliably measured at admission to IPR and used in a machine learning model to accurately predict long-term functional ambulation among those with acute, incomplete SCI may lead to optimized use of therapy time, more realistic patient expectations, and improved long-term outcomes for patients.

Table 6.1: Summary of LA features selected from each analysis*†

Feature Category	LA Feature	Related to Impairment (Aim 1)	Related to Ambulation (Aim 2)	Reliable at Admission (Aim 3a)	Stable from Admission to 6m (Aim 3b)	LA Change Related to Outcome Change (Aim 4a)	Admission Related to 6m Ambulation (Aim 4b)	Number of Related Aims
Change in angle of inclination	Angle Net Change-IQR	×	×	×				0
	Angle Net Change-Med	×	×	✓	×	✓	×	2
	Angle Rate Change-IQR	×	×	✓	×	×	✓	2
	Angle Rate Change-Med	✓	×	✓	×	✓	✓	4
	Angle Total Change-IQR	×	×	✓	×	✓	✓	3
	Angle Total Change-Med	×	×	✓	×	✓	✓	3
Change in gravitational acceleration	Grav Change X-IQR	×	×	✓	✓		×	2
	Grav Change X-Med	×	×	×				0
	Grav Change Y-IQR	✓	×	✓	×	✓	×	3
	Grav Change Y-Med	×	×	×				0
	Grav Change Z-IQR	✓	✓	✓	×	✓	×	4
	Grav Change Z-Med	×	×	✓	×	✓	×	2
Correlation coefficients between axes	Corr XY-IQR	✓	×	×				1
	Corr XY-Med	✓	×	×				1
	Corr XZ-IQR	✓	×	×				1
	Corr XZ-Med	×	×	×				0
	Corr YZ-IQR	×	×	✓	×	✓	×	2
	Corr YZ-Med	✓	×	×				1
Frequency domain	Bandwidth-IQR	×	×	×				0
	Bandwidth-Med	×	×	✓	✓		✓	3
	Centroid Freq-IQR	×	×	×				0
	Centroid Freq-Med	×	×	✓	✓		✓	3
	Dom Freq 1-IQR	✓	×	×				1
	Dom Freq 1-Med	✓	×	✓	✓		✓	4
	Dom Freq 2-IQR	✓	×	×				1
	Dom Freq 2-Med	×	×	×				0
	Dom Low Freq-IQR	×	×	×				0
	Dom Low Freq-Med	×	×	×				0
	Mean Freq-IQR	✓	×	×				1
	Mean Freq-Med	×	×	×				0

Table 6.1 Continued

Feature Category	LA Feature	Related to Impairment (Aim 1)	Related to Ambulation (Aim 2)	Reliable at Admission (Aim 3a)	Stable from Admission to 6m (Aim 3b)	LA Change Related to Outcome Change (Aim 4a)	Admission Related to 6m Ambulation (Aim 4b)	Number of Related Aims
Frequency domain	Med Freq-IQR	✓	×	✓	✓		×	**3**
	Med Freq-Med	✓	×	✓	✓		×	**3**
	Power Dom Freq 1/Total-IQR	✓	×	×				**1**
	Power Dom Freq 1/Total-Med	×	×	✓	✓		✓	**3**
	Power Dom Freq 1-IQR	✓	×	×				**1**
	Power Dom Freq 1-Med	×	×	✓	×	✓	✓	**3**
	Power Dom Freq 2-IQR	×	×	✓	×	✓	✓	**3**
	Power Dom Freq 2-Med	✓	×	✓	×	✓	✓	**4**
	Power Dom Low Freq-IQR	×	×	✓	✓		✓	**3**
	Power Dom Low Freq-Med	×	×	✓	×	✓	✓	**3**
	Power High Freq/Total-IQR	×	×	×				0
	Power High Freq/Total-Med	×	×	✓	✓		✓	**3**
	Power Total-IQR	×	×	✓	✓		✓	**3**
	Power Total-Med	×	×	×				0
Limb movement percentages	**Bilat Ankle %**	×	×	✓	×	✓	✓	**3**
	Unilat Ankle %	×	×	✓	×	✓	✓	**3**
	Whole Body %	×	×	×				0
	Wrist Ankle %	×	×	×				0
Median crossings	Num Med Crossings Norm-IQR	×	×	×				0
	Num Med Crossings Norm-Med	✓	×	✓	✓		✓	**4**
	Num Med Crossings-IQR	×	✓	✓	×	✓	×	**3**
	Num Med Crossings-Med	×	✓	✓	×	×	×	**2**
PLM	Num PLM Norm	×	×	✓	×	×	×	**1**
	PLM %	✓	×	✓	×	✓	×	**3**
	PLM Index	✓	×	✓	×	×	×	**2**

Table 6.1 Continued

Feature Category	LA Feature	Related to Impairment (Aim 1)	Related to Ambulation (Aim 2)	Reliable at Admission (Aim 3a)	Stable from Admission to 6m (Aim 3b)	LA Change Related to Outcome Change (Aim 4a)	Admission Related to 6m Ambulation (Aim 4b)	Number of Related Aims
Relationship to recent movements	**Close Cross Corr Peak-IQR**	✓	×	✓	✓		✓	**4**
	Close Cross Corr Peak-Med	×	×	×				0
	Close Cross Cov Peak-IQR	✓	×	×				**1**
	Close Cross Cov Peak-Med	×	×	×				0
	Dom Freq Last 90s-IQR	✓	×	×				**1**
	Dom Freq Last 90s-Med	×	×	✓	✓		×	**2**
	Max Cross Corr-IQR	×	×	×				0
	Max Cross Corr-Med	×	×	×				0
	Max Cross Cov-IQR	✓	×	×				**1**
	Max Cross Cov-Med	×	×	✓	✓		×	**2**
	Mean Cross Corr Peaks-IQR	×	×	×				0
	Mean Cross Corr Peaks-Med	×	×	×				0
	Mean Cross Cov Peaks-IQR	×	×	×				0
	Mean Cross Cov Peaks-Med	×	×	×				0
	Move Last 90s-IQR	×	×	×				0
	Move Last 90s-Med	✓	×	✓	×	×	×	**2**
	Move Next 90s-IQR	×	×	×				0
	Move Next 90s-Med	×	×	✓	×	×	×	**1**
	Num Cross Corr Peaks-IQR	✓	×	×				**1**
	Num Cross Corr Peaks-Med	×	×	×				0
	Num Cross Cov Peaks-IQR	✓	×	×				**1**
	Num Cross Cov Peaks-Med	×	×	×				0
	Time Since Prev-IQR	✓	×	×				**1**
	Time Since Prev-Med	×	×	×				0
Signal character-istics	Entropy Rate-IQR	×	×	✓	✓		×	**2**
	Entropy Rate-Med	×	×	✓	×	×	×	**1**
	Lempel-Ziv Comp-IQR	×	×	×				0
	Lempel-Ziv Comp-Med	×	×	✓	✓		✓	**3**
	Lyapunov Exp-IQR	✓	✓	✓	✓		✓	**5**
	Lyapunov Exp-Med	✓	×	×				**1**
	Wave Approx-IQR	✓	×	×				**1**
	Wave Approx-Med	×	×	✓	×	✓	×	**2**

Table 6.1 Continued

Feature Category	LA Feature	Related to Impairment (Aim 1)	Related to Ambulation (Aim 2)	Reliable at Admission (Aim 3a)	Stable from Admission to 6m (Aim 3b)	LA Change Related to Outcome Change (Aim 4a)	Admission Related to 6m Ambulation (Aim 4b)	Number of Related Aims
Signal character-istics	Wave Energy 1-IQR	×	×	×				0
	Wave Energy 1-Med	×	×	×				0
	Wave Energy 2-IQR	×	×	✓	×	×	✓	**2**
	Wave Energy 2-Med	✓	×	✓	×	✓	×	**3**
	Wave Energy 3-IQR	×	×	✓	×	✓	×	**2**
	Wave Energy 3-Med	×	×	✓	×	✓	×	**2**
	Wave Entropy-IQR	✓	×	×				**1**
	Wave Entropy-Med	×	×	✓	×	✓	×	**2**
Statistical	**AUC Acc Norm-IQR**	×	×	✓	✓		✓	**3**
	AUC Acc Norm-Med	×	×	✓	×	✓	×	**2**
	AUC Acc-IQR	×	×	✓	✓		✓	**3**
	AUC Acc-Med	×	×	✓	✓		✓	**3**
	Duration-IQR	×	×	×				0
	Duration-Max	×	×	✓	✓		×	**2**
	Duration-Med	×	×	✓	✓		✓	**3**
	Kurtosis-IQR	×	×	×				0
	Kurtosis-Med	×	×	×				0
	Max Acc-IQR	×	×	✓	✓		×	**2**
	Max Acc-Med	×	×	✓	✓		✓	**3**
	Max-RMS Acc-IQR	×	×	✓	✓		✓	**3**
	Max-RMS Acc-Med	×	×	✓	×	×	✓	**2**
	Med Acc-IQR	×	×	✓	×	✓	✓	**3**
	Med Acc-Med	×	×	✓	✓		✓	**3**
	Range Acc-IQR	×	×	✓	✓		✓	**3**
	Range Acc-Med	×	×	×				0
	RMS Acc-IQR	×	×	×				0
	RMS Acc-Med	×	×	✓	✓		✓	**3**
	SD Acc-IQR	×	×	✓	✓		✓	**3**
	SD Acc-Med	×	×	×				0
	Skewness-IQR	×	×	×				0
	Skewness-Med	✓	×	✓	✓		×	**3**

Table 6.1 Continued

Feature Category	LA Feature	Related to Impairment (Aim 1)	Related to Ambulation (Aim 2)	Reliable at Admission (Aim 3a)	Stable from Admission to 6m (Aim 3b)	LA Change Related to Outcome Change (Aim 4a)	Admission Related to 6m Ambulation (Aim 4b)	Number of Related Aims
Statistical	**SMA Acc-IQR**	×	×	✓	✓		✓	**3**
	SMA Acc-Med	×	×	✓	×	✓	✓	**3**
Timing	End Move %-IQR	×	×	×				0
	End Move %-Med	×	×	×				0
	Move/hour	✓	×	✓	×	×	×	**2**
	Move/night	×	×	✓	×	×	×	**1**
	Start Move %-IQR	×	✓	×				**1**
	Start Move %-Med	×	✓	×				**1**
	Time Asleep	✓	×	✓	×	×	×	**2**
Velocity and distance	**Med Vel-IQR**	×	×	✓	✓		✓	**3**
	Med Vel-Med	×	×	✓	×	✓	✓	**3**
	RMS Vel-IQR	×	×	×				0
	RMS Vel-Med	×	×	✓	×	✓	✓	**3**
	Total Dist-IQR	×	×	✓	✓		✓	**3**
	Total Dist-Med	×	×	✓	✓		✓	**3**
Total Number of LA Features Selected		35 (26.3%)	6 (4.5%)	72 (54.1%)	34 (47.2%)	26 (68.4%)	41 (56.9%)	92 (69.2%)

* ✓ = Feature was chosen/related, × = Feature was not chosen/related, Blank= Feature was not applicable for analysis. † Feature names are highlighted grey if that feature is reliably measured at admission to IPR (Aim 3a) and bolded if also related to ambulatory ability at 6 months post-discharge (Aim 4b).

Table 6.2: Summary of the number of LA features selected from each analysis (% of maximum number of features included in anlaysis, % of maximum number of features that could be selected)

Aim	Related to Impairment (Aim 1)	Related to Ambulation (Aim 2)	Reliable at Admission (Aim 3a)	Stable from Admission to 6m (Aim 3b)	LA Change Related to Outcome Change (Aim 4a)	Admission Related to 6m Ambulation (Aim 4b)
Related to Impairment (Aim 1)	**35 (26.3% of 133)**	2 (1.5% of 133, 33.3% of 6)	17 (12.8% of 133, 48.6% of 35)	7 (9.7% of 72, 20.6% of 34)	6 (15.8% of 38, 23.1% of 26)	6 (8.3% of 72, 17.1% of 35)
Related to Ambulation (Aim 2)	2 (1.5% of 133, 33.3% of 6)	**6 (4.5% of 133)**	4 (3.0% of 133, 66.7% of 6)	1 (1.4% of 72, 16.7% of 6)	2 (5.3% of 38, 33.3% of 6)	1 (1.4% of 72, 16.7% of 6)
Reliable at Admission (Aim 3a)	17 (12.8% of 133, 48.6% of 35)	4 (3.0% of 133, 66.7% of 6)	**72 (54.1% of 133)**	34 (47.2% of 72, 100.0% of 34)	26 (68.4% of 38, 100.0% of 26)	41 (56.9% of 72, 100.0% of 41)
Stable from Admission to 6m (Aim 3b)	7 (9.7% of 72, 20.6% of 34)	1 (1.4% of 72, 16.7% of 6)	34 (47.2% of 72, 100.0% of 34)	**34 (47.2% of 72)**	N/A	25 (34.7% of 72, 73.5% of 34)
LA Change related to Outcome Change (Aim 4a)	6 (15.8% of 38, 23.1% of 26)	2 (5.3% of 38, 33.3% of 6)	26 (68.4% of 38, 100.0% of 26)	N/A	**26 (68.4% of 38)**	13 (34.2% of 38, 50.0% of 26)
Admission Related to 6m Ambulation (Aim 4b)	6 (8.3% of 72, 17.1% of 35)	1 (1.4% of 72, 16.7% of 6)	41 (56.9% of 72, 100.0% of 41)	25 (34.7% of 72, 73.5% of 34)	13 (34.2% of 38, 50.0% of 26)	**41 (56.9% of 72)**

Appendix A List of Abbreviations

AD= Assistive device

AIS= American Spinal Injury Association impairment scale

AUC= Area under the curve

BMI= Body mass index

CPR= Clinical prediction rule

FIM= Functional Independence Measure

ICC= Intraclass correlation coefficient

ISNCSCI= International Standards for Neurological Classification of Spinal Cord Injury

IPR= Inpatient rehabilitation

IQR= Interquartile range

LA= Limb accelerations

LARS= Least angle regression

LASSO=Least absolute shrinkage and selection operator

LEMS= Lower extremity motor score

LT= Light touch

MAS= Modified Ashworth Scale

MMT= Manual muscle test

OCA= Overall classification accuracy

PLM= Periodic limb movement

PSQI= Pittsburgh Sleep Quality Index

RMS= Root mean square

SCI= Spinal cord injury

SD= Standard deviation

SF-36= Medical Outcomes Study 36-Item Short-Form Health Survey

WISCI-II= Walking Index for Spinal Cord Injury II

6MWT= 6 minute walk test

10mWT= 10 meter walk test

Appendix B Additional CPRs for Ambulation

Although the van Middendorp CPR is the most widely cited CPR, there are many others that have sought to improve upon this CPR or approach prediction from a different angle. The Hicks CPR was created as a simpler version of the van Middendorp CPR and uses only age (≥65 years), the MMT motor score at L3, and LT sensation score at S1 to predict the probability of independent ambulation at 1-year post-injury as measured by the FIM.[5] Like the van Middendorp CPR, it has demonstrated high accuracy (AUC= 0.866, overall classification accuracy= 84%), but also suffers from a biased sample population that may have led to overly-favorable results.[52]

Belliveau at al. predicted the self-reported ability to walk 150 feet in their home, 1 street block outside, and 1 flight of stairs (with or without mobility aids) using artificial neural networks. Predictors included age ≥65 years, maximal motor scores for each myotome that were dichotomized into having against gravity strength or not (MMT ≥ 3), and lower and upper extremity motor scores.[36] The artificial neural network prediction models using age and dichotomized motor scores from L2, L3, and S1 had AUC= .880 - .902 from OCA= 85 - 88% in the validation test set which were comparable to prediction accuracies from similar models made using logistic regression using the entire dataset (no validation).[36] These models demonstrated that machine learning methods can be used for ambulatory prediction at least as well as traditional statistics. Additionally, this study was one of the first to use more functional ambulatory outcomes, but still limited those outcomes to dichotomized groups of those who could or could not complete the ambulation task.

The prediction models by Zörner et al. were some of the only prediction models that focused only on individuals with motor incomplete SCI (AIS C and D) and used a variety of

predictors (gender, age, lower and upper extremity motor, LT, and pinprick sensation scores, AIS grade, tibial somatosensory evoked potentials) to predict more descriptive and functional outcome measures at 6-months after injury (dichotomized Walking Index for SCI II [WISCI-II] and 6 Minute Walk Test [6MWT] scores into categories of independent or dependent and functional and non-functional ambulators, respectively).[53] They found that the models performed best when calculated separately for individuals with tetraplegia and paraplegia. Lower extremity motor score (LEMS) was consistently included in all models. Although these models produced high classification accuracies among individuals with motor incomplete SCI (OCA= 82.1 - 92.2% for the WISCI-II and OCA= 84.2 - 100% for the 6MWT), the models were not validated, which, given the small sample size (n= 51 with tetraplegia, n= 39 with paraplegia) and feature selection steps prior to fitting the model, may lead to models that are not generalizable and perform poorly on unseen test sets. These models had much smaller proportions of individuals with paraplegia in the lower ambulatory groups that may have affected model performance. This is demonstrated by the lower prediction accuracies for individuals with paraplegia who were dependent walkers (n= 14, accuracy= 64.3% vs independent walkers n= 25, accuracy= 92.0%) and non-functional walkers (n=8, accuracy= 37.5% vs functional walkers n= 30, accuracy= 96.7%).[53] These results also demonstrate the problematic use of only metrics such as OCA and AUC for model evaluation as skewed sample populations could cover up prediction inaccuracies among certain sub-populations that could be clinically useful to detect.[109] This study addresses the importance of focusing CPRs for ambulation on individuals with motor incomplete injuries and using a combination of more descriptive and functional measures of ambulation as model outcomes, but is likely not as clinically useful due to flaws in the sample population and model building and validation.

Appendix C Model Evaluation Metrics

The overall classification accuracy (OCA), precision, recall, and F1-score were used to describe classification model performance. For the present analyses, those performance metrics are defined as follows:

$$OCA = \frac{number\ of\ participants\ correctly\ classified}{total\ number\ of\ participants}$$

Appendix Equation C.1: Overall Classification Accuracy (OCA)

$$Precision\ (per\ class\ i) = \frac{True\ Positives}{True\ Positives + False\ Positives}$$

$$= \frac{number\ of\ participants\ correctly\ classified\ as\ class\ i}{total\ number\ of\ participants\ classified\ as\ class\ i}$$

Appendix Equation C.2: Precision

$$Recall\ (per\ class\ i) = \frac{True\ Positives}{True\ Positives + False\ Negatives}$$

$$= \frac{number\ of\ participants\ correctly\ classified\ as\ class\ i}{total\ number\ of\ participants\ actually\ class\ i}$$

Appendix Equation C.3: Recall

$$F1 - Score\ (per\ class\ i) = 2 * \frac{Precision_i * Recall_i}{Precision_i + Recall_i}$$

Appendix Equation C.4: F1-Score

Precision represents the proportion of an outcome class that was labeled as a given class and actually in that class (i.e., ability not to label a negative sample as positive, positive predictive value). Recall is defined as the proportion of classifications that were correct out of the total number of classifications for a given class (i.e., ability of the classifier to find all positive samples, true positive rate). Precision is focused on minimizing false positives, while recall is focused on minimizing false negatives. Recall can also be referred to as sensitivity when used in binary classification. Measures such as specificity (true negative rate) are not applicable for multiclass

classification. F1-score is able to provide a more comprehensive view of model performance by calculating the weighted harmonic mean of precision and recall and is particularly useful for imbalanced classification problems where accuracy may be misleading.[177, 178] For all metrics, a higher score (range=0-1) is indicative of higher accuracy and better model performance.

The macro and weighted averages of the precision, recall, and F1-scores across classes were calculated to best evaluate the model performance when all classes are treated equally or when each class contribution is adjusted for the relative number of samples in that class, respectively.[177] Each averaging method is calculated as:

$$Macro\ Average = \frac{\sum_i metric_i}{total\ number\ of\ classes}$$

Appendix Equation C.5: Macro Average

$$Weighted\ Average = \frac{\sum_i metric_i * number\ of\ participants\ in\ class\ i}{total\ number\ of\ participants}$$

Appendix Equation C.6: Weighted Average

Appendix D Aim 1 Supplemental Material

Appendix Table D.1: Description of covariates included in feature sets for Aim 1

Covariate Type	Covariates Included in Analysis
Demographics[54, 97]	• Age • Sex • BMI • Years since injury
Pain[120, 121, 123]	• If pain present • Average pain intensity • Number of pain locations • Pain Domain Score

Sleep Quality[138]	• Global score (sum of 7 components)
	• Poor sleep quality (global score >5 [poor sleep quality] or ≤5)
	• Components:
	  ○ Daytime dysfunction
	  ○ Disturbances
	  ○ Duration
	  ○ Efficiency
	  ○ Latency
	  ○ Sleep quality
	• Averaged over nights collected (score 0-10)
	  ○ Fatigue rating
	  ○ Sleep rating

Factors Affecting Sleep[120, 121, 132-134, 136, 137]	• Pain interference with sleep
	• Dichotomized to if it occurred over the collection period (yes/no):
	  ○ Alcohol use (in 6 hours prior to sleep)
	  ○ Caffeine use (in 6 hours prior to sleep)
	  ○ Exercise
	  ○ Sleep medication use

Appendix D.1 Assessment of Limb Independence

To increase the sample size, it was proposed to treat the right and left lower limbs as independent samples since LA and each impairment outcome are measured separately for each limb. Although SCI can often lead to asymmetric impairments, it was still assumed that there will be some level of relation between the sides. Therefore, Pearson correlations were calculated for each outcome and LA feature between the stronger and weaker lower limbs for each participant.

The impairment outcome correlations are shown in Appendix Table D.2 and the LA correlations are shown in Appendix Table D.3. For the participants with motor complete SCI, all strength scores were 0, so the correlation between sides was not applicable. For both the impairment outcomes and the LA features, participants with motor complete SCI generally had higher correlations than those with motor incomplete SCI. Due to these high correlations between both the input and output variables assessed in the analysis, the limbs were determined to be not independent and only one sample per participant was used that combined both limbs.

Appendix Table D.2: Correlations coefficients (r) for each impairment outcome between the stronger and weaker lower limbs*

Impairment Outcome	Motor Incomplete (n=30, 28 for Spasticity)	Motor Complete (n=10)	All (n=40, 38 for Spasticity)
Strength (LEMS)	**0.770**	N/A	**0.857**
Sensation (Lower Extremity LT)	**0.810**	**1.00**	**0.884**
Spasticity (MAS from knee flexors and plantarflexors)†	0.530	**0.832**	0.625

* Correlation coefficients ≥ 0.7 are bolded; Coefficients ≥ 0.9 are in grey
† MAS was treated as continuous with a score of 1+ as 1.5

Appendix Table D.3: Correlations coefficients (r) for each LA feature between the stronger and weaker lower limbs*

Feature Category	LA Feature	Motor Incomplete (n=30)	Motor Complete (n=10)	All (n=40)
Change in angle of inclination	Angle Net Change-IQR	0.497	**0.980**	0.543
	Angle Net Change-Med	0.343	0.629	0.377
	Angle Rate Change-IQR	0.353	**0.938**	0.438
	Angle Rate Change-Med	0.386	**0.867**	0.483
	Angle Total Change-IQR	0.603	**0.976**	0.662
	Angle Total Change-Med	0.642	**0.779**	0.652
Change in gravitational acceleration	Grav Change X-IQR	0.599	**0.873**	0.640
	Grav Change X-Med	0.110	-0.067	0.025
	Grav Change Y-IQR	0.220	**0.913**	0.263
	Grav Change Y-Med	0.076	**0.774**	0.035
	Grav Change Z-IQR	0.352	0.349	0.356
	Grav Change Z-Med	-0.091	-0.699	-0.104
Correlation coefficients between axes	Corr XY-IQR	0.320	0.502	0.374
	Corr XY-Med	-0.106	0.587	0.074
	Corr XZ-IQR	0.417	-0.006	0.414
	Corr XZ-Med	0.052	-0.149	0.007
	Corr YZ-IQR	0.555	0.462	0.526
	Corr YZ-Med	-0.189	0.021	-0.206

Appendix Table D.3 Continued

Feature Category	LA Feature	Motor Incomplete (n=30)	Motor Complete (n=10)	All (n=40)
Frequency domain	Bandwidth-IQR	0.542	0.272	0.484
	Bandwidth-Med	0.593	**0.867**	0.687
	Centroid Freq-IQR	**0.754**	-0.242	0.673
	Centroid Freq-Med	0.641	**0.840**	0.695
	Dom Freq 1-IQR	0.510	**0.874**	0.607
	Dom Freq 1-Med	**0.757**	**0.953**	**0.851**
	Dom Freq 2-IQR	0.180	0.559	0.186
	Dom Freq 2-Med	0.582	**0.947**	0.483
	Dom Low Freq-IQR	0.080	**0.804**	0.307
	Dom Low Freq-Med	0.658	**0.813**	**0.740**
	Mean Freq-IQR	**0.706**	0.235	0.625
	Mean Freq-Med	0.693	**0.778**	**0.734**
	Med Freq-IQR	0.578	**0.872**	**0.718**
	Med Freq-Med	0.693	**0.915**	**0.794**
	Power Dom Freq 1/Total-IQR	**0.708**	**0.828**	**0.716**
	Power Dom Freq 1/Total-Med	**0.700**	0.663	0.698
	Power Dom Freq 1-IQR	0.327	**0.968**	0.373
	Power Dom Freq 1-Med	0.431	0.677	0.433
	Power Dom Freq 2-IQR	0.558	**0.994**	0.664
	Power Dom Freq 2-Med	0.353	**0.891**	0.366
	Power Dom Low Freq-IQR	0.610	**0.952**	0.663
	Power Dom Low Freq-Med	0.326	**0.932**	0.351
	Power High Freq/Total-IQR	0.679	**0.837**	**0.700**
	Power High Freq/Total-Med	0.576	**0.708**	0.621
	Power Total-IQR	0.419	**0.976**	0.467
	Power Total-Med	0.355	**0.779**	0.366
Limb movement percentages	Bilat Ankle %	0.590	-0.038	0.512
	Unilat Ankle %	0.590	-0.038	0.512
	Whole Body %	**0.795**	**0.708**	**0.781**
	Wrist Ankle %	**0.734**	**0.757**	**0.749**
Median crossings	Num Med Crossings Norm-IQR	0.641	**0.743**	0.652
	Num Med Crossings Norm-Med	0.697	**0.956**	**0.759**
	Num Med Crossings-IQR	0.516	**0.931**	0.605
	Num Med Crossings-Med	0.636	0.580	0.618
Periodic limb movements (PLM)	Num PLM Norm	0.571	**0.921**	**0.745**
	PLM %	**0.780**	**0.927**	**0.811**
	PLM Index	**0.953**	**0.988**	**0.958**
Relationship to recent movements	Close Cross Corr Peak-IQR	0.617	0.272	0.586
	Close Cross Corr Peak-Med	0.537	0.495	0.534
	Close Cross Cov Peak-IQR	0.616	0.175	0.549
	Close Cross Cov Peak-Med	**0.739**	**0.919**	**0.725**
	Dom Freq Last 90s-IQR	0.284	**0.862**	0.241
	Dom Freq Last 90s-Med	**0.796**	**0.930**	**0.839**
	Max Cross Corr-IQR	0.639	0.296	0.550
	Max Cross Corr-Med	**0.728**	**0.786**	**0.732**
	Max Cross Cov-IQR	0.696	0.463	0.643
	Max Cross Cov-Med	**0.845**	**0.862**	**0.827**
	Mean Cross Corr Peaks-IQR	0.468	0.629	0.496
	Mean Cross Corr Peaks-Med	0.644	**0.714**	0.650
	Mean Cross Cov Peaks-IQR	0.451	0.227	0.411
	Mean Cross Cov Peaks-Med	**0.840**	**0.749**	**0.810**

Appendix Table D.3 Continued

Feature Category	LA Feature	Motor Incomplete (n=30)	Motor Complete (n=10)	All (n=40)
Relationship to recent movements	Move Last 90s-IQR	0.425	0.372	0.394
	Move Last 90s-Med	**0.924**	**0.821**	**0.903**
	Move Next 90s-IQR	0.425	0.372	0.394
	Move Next 90s-Med	**0.924**	**0.821**	**0.903**
	Num Cross Corr Peaks-IQR	0.416	0.308	0.434
	Num Cross Corr Peaks-Med	**0.848**	**0.893**	**0.853**
	Num Cross Cov Peaks-IQR	0.501	0.456	0.465
	Num Cross Cov Peaks-Med	**0.787**	**0.869**	**0.809**
	Time Since Prev-IQR	0.632	**0.910**	0.684
	Time Since Prev-Med	0.394	**0.976**	0.579
Signal characteristics	Entropy Rate-IQR	0.515	0.429	0.501
	Entropy Rate-Med	0.665	0.645	0.655
	Lempel-Ziv Comp-IQR	0.549	**0.831**	0.617
	Lempel-Ziv Comp-Med	0.618	**0.757**	0.631
	Lyapunov Exp-IQR	0.493	0.252	0.450
	Lyapunov Exp-Med	0.652	**0.882**	**0.726**
	Wave Approx-IQR	0.545	0.303	0.541
	Wave Approx-Med	0.673	0.606	0.661
	Wave Energy 1-IQR	0.633	0.546	0.606
	Wave Energy 1-Med	**0.748**	**0.862**	**0.789**
	Wave Energy 2-IQR	0.250	0.274	0.267
	Wave Energy 2-Med	0.507	**0.765**	0.554
	Wave Energy 3-IQR	0.465	**0.808**	0.569
	Wave Energy 3-Med	0.525	**0.722**	0.593
	Wave Entropy-IQR	0.490	0.018	0.488
	Wave Entropy-Med	0.664	0.636	0.657
Statistical	AUC Acc Norm-IQR	0.532	**0.855**	0.554
	AUC Acc Norm-Med	0.592	**0.778**	0.611
	AUC Acc-IQR	**0.876**	**0.982**	**0.853**
	AUC Acc-Med	0.535	**0.851**	0.574
	Duration-IQR	**0.817**	**0.985**	**0.847**
	Duration-Max	**0.880**	**0.991**	**0.891**
	Duration-Med	**0.837**	**0.951**	**0.854**
	Kurtosis-IQR	0.604	0.493	0.558
	Kurtosis-Med	0.431	0.568	0.447
	Max Acc-IQR	**0.801**	**0.937**	**0.812**
	Max Acc-Med	0.628	**0.913**	0.632
	Max-RMS Acc-IQR	**0.706**	**0.775**	0.684
	Max-RMS Acc-Med	0.683	**0.760**	0.686
	Med Acc-IQR	**0.713**	**0.877**	**0.749**
	Med Acc-Med	**0.757**	**0.848**	**0.779**
	Range Acc-IQR	**0.801**	**0.937**	**0.812**
	Range Acc-Med	0.630	**0.911**	0.633
	RMS Acc-IQR	0.517	**0.847**	0.537
	RMS Acc-Med	0.602	**0.803**	0.615
	SD Acc-IQR	0.529	**0.866**	0.551
	SD Acc-Med	0.540	**0.794**	0.558
	Skewness-IQR	0.349	0.675	0.439
	Skewness-Med	0.437	**0.707**	0.489
	SMA Acc-IQR	0.537	**0.829**	0.554
	SMA Acc-Med	0.583	**0.792**	0.605

Appendix Table D.3 Continued

Feature Category	LA Feature	Motor Incomplete (n=30)	Motor Complete (n=10)	All (n=40)
Timing	End Move %-IQR	0.571	0.482	0.553
	End Move %-Med	**0.905**	**0.927**	**0.909**
	Move/hour	**0.940**	**0.991**	**0.949**
	Move/night	**0.945**	**0.961**	**0.946**
	Start Move %-IQR	0.571	0.480	0.552
	Start Move %-Med	**0.907**	**0.927**	**0.910**
	Time Asleep	**1.000**	**1.000**	**1.000**
Velocity and distance	Med Vel-IQR	**0.720**	**0.833**	**0.751**
	Med Vel-Med	**0.753**	**0.826**	**0.764**
	RMS Vel-IQR	0.507	**0.846**	0.529
	RMS Vel-Med	0.611	**0.807**	0.624
	Total Dist-IQR	**0.859**	**0.985**	**0.851**
	Total Dist-Med	0.518	**0.827**	0.563

* Correlation coefficients ≥ 0.7 are bolded; Coefficients ≥ 0.9 are in grey

Appendix D.1.1 Machine Learning Algorithm Descriptions

The LASSO algorithm is a linear regression model with embedded feature selection that favors more sparse solutions (fewer non-zero coefficients) using ℓ_1 regularization. The ℓ_1 regularization uses coordinate descent which minimizes the objective function of the residual sum of squares plus the sum of the absolute value of the coefficients which creates a trade-off between accuracy and simplicity. The regularization parameter, λ, can be used to influence the simplicity of the solution, with larger values of λ decreasing the number of features included in the model.[176, 246, 247]

The LASSO model can be implemented using the LARS algorithm which determines the features to be included in the model for all values of λ along the regularization path. It does this by finding the feature with the highest correlation to the residual and then continuing along that regression line until another variable is found that has the same or a higher correlation. It then continues equiangular to those features until no more features are added. In this way it produces

an exact value for the optimal λ in as few steps as forwards stepwise regression. Thus, the LASSO LARS algorithm is particularly useful when there are many more features than samples and provides an efficient and more automated method for feature selection and model fitting.[176, 246, 247]

To provide consistency between the models for the continuous and categorical outcomes, the ℓ_1 regularization was also used in the multinomial logistic regression model. A range of regularization parameters were used to ensure an appropriate value was used. The saga solver in sklearn in Python[248] is a variation of the stochastic average gradient descent and was used as it supports both ℓ_1 regularization and multinomial logistic regression.[249] The output in multinomial logistic regression is separate equations that evaluate the probability that the sample belongs to a given class. The class with the highest probability is chosen as the predicted class.

Appendix D.2 Impairment Models Full Results

Appendix Table D.4: Features included in the strength LASSO LARS models per feature set, sorted by the absolute value of the coefficient.

LA Features (16 features)		**Covariates Features** (19 features)	
Feature Name	Coeff	Feature Name	Coeff
Wave Approx- IQR	20.99	SF-36: Pain	-29.98
Num Cross Corr Peaks- IQR	-19.81	BMI	23.66
Lyapunov Exp- IQR	13.90	Number if Pain Locations	-21.56
Angle Rate Change- Med	13.22	PSQI: Poor Sleep Quality	17.00
Power Dom Freq 1/Total- IQR	11.64	PSQI: Sleep Duration	-15.20
Corr XY- IQR	8.83	Pain Interference: Sleep	-13.67
Move Next 90s- Med	8.67	PSQI: Sleep Meds	-11.26
Med Freq- Med	-6.08	Exercised During Collection	10.18
Max Cross Cov- IQR	-5.74	Sex	6.84
Corr XY- Med	-5.73	PSQI: Sleep Efficiency	-6.36
PLM %	5.42	Pain Present	2.40
Time Since Prev- IQR	-4.61	PSQI: Sleep Latency	-1.65
Time Asleep	2.09	Sleep Meds During Collection	-1.05
Mean Freq- IQR	0.70	Age	0.99
Num Med Crossings Norm- Med	-0.64	Ave Sleep Rating	0.83
Skewness- Med	-0.51	Alcohol During Collection	-0.79
		Years Since Injury	0.56
		PSQI: Sleep Disturbance	0.40
		Caffeine During Collection	0.09

Abbreviations: Coeff= Model Coefficient
Covariates are in grey; LA features are in white.

Appendix Table D.5: Features included in the strength linear regression models per feature set, sorted by the absolute value of the coefficient.

LA Features (16 features)		Covariates Features (19 features)		LA + Covariates Features (35 features)	
Feature Name	Coeff	Feature Name	Coeff	Feature Name	Coeff
Max Cross Cov- IQR	-37.57	SF-36: Pain	-35.30	Corr XY- IQR	77.84
Wave Approx- IQR	30.98	BMI	31.97	Angle Rate Change- Med	71.32
Num Med Crossings Norm- Med	-30.33	Number if Pain Locations	-30.44	Max Cross Cov- IQR	-69.68
Lyapunov Exp- IQR	26.42	PSQI: Poor Sleep Quality	21.94	Years Since Injury	59.43
Num Cross Corr Peaks- IQR	-23.93	PSQI: Sleep Duration	-20.75	PSQI: Sleep Disturbance	-54.71
Angle Rate Change- Med	17.75	Pain Interference: Sleep	-20.32	Ave Sleep Rating	51.83
Corr XY- IQR	13.35	PSQI: Sleep Meds	-16.48	Num Med Crossings Norm- Med	49.94
Time Asleep	11.20	Sex	11.74	Number if Pain Locations	-44.14
Mean Freq- IQR	11.16	Exercised During Collection	11.54	Skewness- Med	32.20
Time Since Prev- IQR	-10.39	Pain Present	9.06	PSQI: Poor Sleep Quality	29.64
PLM %	8.74	PSQI: Sleep Efficiency	-5.43	Med Freq- Med	-28.90
Corr XY- Med	-6.54	Age	5.19	PLM %	28.51
Skewness- Med	4.82	Sleep Meds During Collection	-4.48	Age	-27.69
Move Next 90s- Med	4.47	Years Since Injury	4.21	Lyapunov Exp- IQR	26.38
Med Freq- Med	-3.30	Ave Sleep Rating	4.18	Mean Freq- IQR	-24.91
Power Dom Freq 1/Total- IQR	0.84	PSQI: Sleep Latency	-2.14	Move Next 90s- Med	-24.42
		Caffeine During Collection	0.91	PSQI: Sleep Meds	-23.91
		PSQI: Sleep Disturbance	-0.15	Num Cross Corr Peaks- IQR	18.21
		Alcohol During Collection	0.04	Wave Approx- IQR	15.51
				Sleep Meds During Collection	-12.67
				Time Since Prev- IQR	-12.50
				BMI	11.57
				PSQI: Sleep Duration	-10.74
				Time Asleep	-9.58
				PSQI: Sleep Latency	-8.62
				Pain Interference: Sleep	-7.61
				Alcohol During Collection	6.62
				Sex	4.33
				Caffeine During Collection	3.96
				SF-36: Pain	-3.38
				Corr XY- Med	2.21
				Exercised During Collection	1.96
				Pain Present	0.93
				Power Dom Freq 1/Total- IQR	-0.82
				PSQI: Sleep Efficiency	0.77

Abbreviations: Coeff= Model Coefficient
Covariates are in grey; LA features are in white.

Appendix Table D.6: Features included in the sensation LASSO LARS models per feature set, sorted by the absolute value of the coefficient.

LA Features (15 features)		**Covariates Features** (2 features)	
Feature Name	Coeff	Feature Name	Coeff
Time Since Prev- IQR	-9.62	Number if Pain Locations	-2.76
Corr YZ- Med	8.34	PSQI: Sleep Efficiency	-2.38
Dom Freq 1- Med	-8.10		
Num Cross Cov Peaks- IQR	-7.15		
Time Asleep	6.92		
Wave Entropy- IQR	5.67		
Num Cross Corr Peaks- IQR	-4.85		
Power Dom Freq 2- Med	-3.72		
Dom Freq 1- IQR	3.48		
Grav Change Y- IQR	3.17		
Power Dom Freq 1/Total- IQR	2.08		
Mean Freq- IQR	1.18		
Lyapunov Exp- Med	1.12		
Corr XZ- IQR	-0.59		
PLM Index	0.11		

Abbreviations: Coeff= Model Coefficient
Covariates are in grey; LA features are in white.

Appendix Table D.7: Features included in the sensation linear regression models per feature set, sorted by the absolute value of the coefficient.

LA Features (15 features)		**Covariates Features** (2 features)		**LA + Covariates Features** (17 features)	
Feature Name	Coeff	Feature Name	Coeff	Feature Name	Coeff
Time Since Prev- IQR	-11.23	Number if Pain Locations	-9.08	Dom Freq 1- Med	-12.34
Dom Freq 1- Med	-10.89	PSQI: Sleep Efficiency	-5.08	Power Dom Freq 2- Med	-10.42
Corr YZ- Med	10.39			Time Since Prev- IQR	-10.34
Power Dom Freq 2- Med	-10.19			Corr YZ- Med	10.33
Grav Change Y- IQR	9.90			Grav Change Y- IQR	9.64
Num Cross Cov Peaks- IQR	-8.97			Time Asleep	8.95
Time Asleep	8.79			Wave Entropy- IQR	8.06
Wave Entropy- IQR	8.40			Dom Freq 1- IQR	7.94
Dom Freq 1- IQR	8.26			Num Cross Cov Peaks- IQR	-6.29
Lyapunov Exp- Med	4.63			PLM Index	4.72
PLM Index	4.55			Num Cross Corr Peaks- IQR	-4.07
Num Cross Corr Peaks- IQR	-3.73			Number if Pain Locations	-3.43
Corr XZ- IQR	-3.21			Power Dom Freq 1/Total- IQR	2.72
Power Dom Freq 1/Total- IQR	3.06			Corr XZ- IQR	-2.42
Mean Freq- IQR	1.62			Mean Freq- IQR	2.13
				Lyapunov Exp- Med	1.52
				PSQI: Sleep Efficiency	-0.56

Abbreviations: Coeff= Model Coefficient
Covariates are in grey; LA features are in white.

Appendix Table D.8: Spasticity logistic regression with ℓ_1 regularization model overall and per-class statistics per feature set.*

Spasticity: LA, Number of Initial Features= 133							
Actual/Predicted Class	No Spasticity	Mild Spasticity	Moderate Spasticity	Number of Features Selected	F1- Score	Precision	Recall
No Spasticity	**14**	1	0	10	0.848	0.778	0.933
Mild Spasticity	3	**11**	0	7	0.786	0.786	0.786
Moderate Spasticity	1	2	**6**	10	0.800	1.000	0.667
Macro Average	Overall Classification Accuracy= 0.816				0.854	0.795	0.811
Weighted Average					0.833	0.816	0.814
Spasticity: Covariates, Number of Initial Features= 24							
Actual/Predicted Class	No Spasticity	Mild Spasticity	Moderate Spasticity	Number of Features Selected	F1- Score	Precision	Recall
No Spasticity	**13**	2	0	5	0.765	0.684	0.867
Mild Spasticity	4	**10**	0	5	0.741	0.769	0.714
Moderate Spasticity	2	1	**6**	6	0.800	1.000	0.667
Macro Average	Overall Classification Accuracy= 0.763				0.818	0.749	0.768
Weighted Average					0.790	0.763	0.764

* The number of participants correctly classified per ambulation category are bolded.

Appendix Table D.9: Spasticity logistic regression without regularization model overall and per-class statistics per feature set.*

Spasticity: LA							
Actual/Predicted Class	No Spasticity	Mild Spasticity	Moderate Spasticity	Number of Features Selected	F1- Score	Precision	Recall
No Spasticity	**9**	6	0	10	0.765	0.684	0.867
Mild Spasticity	1	**13**	0	7	0.741	0.769	0.714
Moderate Spasticity	0	2	**7**	10	0.800	1.000	0.667
Macro Average	Overall Classification Accuracy= 0.763				0.769	0.779	0.840
Weighted Average					0.763	0.765	0.820
Spasticity: Covariates							
Actual/Predicted Class	No Spasticity	Mild Spasticity	Moderate Spasticity	Number of Features in Model	F1- Score	Precision	Recall
No Spasticity	**12**	3	0	5	0.750	0.706	0.800
Mild Spasticity	3	**11**	0	5	0.688	0.611	0.786
Moderate Spasticity	2	4	**3**	6	0.500	1.000	0.333
Macro Average	Overall Classification Accuracy= 0.684				0.640	0.646	0.772
Weighted Average					0.684	0.668	0.741
Spasticity: LA + Covariates							
Actual/Predicted Class	No Spasticity	Mild Spasticity	Moderate Spasticity	Number of Features in Model	F1- Score	Precision	Recall
No Spasticity	**12**	3	0	15	0.889	1.000	0.800
Mild Spasticity	0	**14**	0	12	0.875	0.778	1.000
Moderate Spasticity	0	1	**8**	16	0.941	1.000	0.889
Macro Average	Overall Classification Accuracy= 0.895				0.926	0.896	0.902
Weighted Average					0.918	0.895	0.896

* The number of participants correctly classified per ambulation category are bolded.

Appendix Table D.10: Features included in the spasticity logistic regression with ℓ_1 regularization models per category and feature set, sorted by the absolute value of the coefficient.

LA Features					
No Spasticity		Mild Spasticity		Moderate Spasticity	
Corr YZ- Med	-0.95	Time Asleep	1.38	Wave Entropy- IQR	-2.26
Skewness- IQR	0.93	Num Cross Cov Peaks- IQR	-0.74	Move/hour	1.70
Power Dom Freq 2- Med	-0.62	Power Dom Freq 1- IQR	0.48	Skewness- IQR	-1.03
Close Cross Cov Peak- IQR	0.59	Grav Change Z- IQR	-0.37	Wave Energy 2- Med	-0.91
Close Cross Corr Peak- IQR	0.58	Corr XY- Med	-0.27	Med Freq- Med	0.60
Wave Energy 2- Med	0.54	Dom Freq Last 90s- IQR	-0.06	Corr YZ- Med	0.38
Dom Freq 2- IQR	0.39	Dom Freq 1- Med	-0.04	Wave Approx- IQR	-0.27
PLM %	-0.34			Med Freq- IQR	0.17
Wave Approx- IQR	0.15			PLM Index	0.17
Num Cross Cov Peaks- IQR	0.06			Dom Freq 1- Med	0.04
Corr YZ- Med	-0.95	Time Asleep	1.38	Wave Entropy- IQR	-2.26
Covariates Features					
No Spasticity		Mild Spasticity		Moderate Spasticity	
Feature Name	Coeff	Feature Name	Coeff	Feature Name	Coeff
PSQI: Sleep Quality	1.86	Ave Fatigue Rating	0.82	Ave Sleep Rating	-1.40
Years Since Injury	1.10	PSQI: Sleep Meds	-0.63	PSQI: Sleep Duration	0.87
PSQI: Poor Sleep Quality	-0.87	Age	-0.52	PSQI: Sleep Disturbance	-0.72
Pain Interfere: Sleep	0.81	Caffeine During Collection	0.38	Pain Present	0.70
Sleep Meds During Collection	-0.35	Exercised During Collection	-0.21	Sleep Meds During Collection	0.30
				Caffeine During Collection	-0.26

Abbreviations: Coeff= Model Coefficient
Covariates are in grey; LA features are in white.

Appendix Table D.11: Features included in the spasticity logistic regression without regularization models per category and feature set, sorted by the absolute value of the coefficient.

LA Features					
No Spasticity		Mild Spasticity		Moderate Spasticity	
Feature Name	Coeff	Feature Name	Coeff	Feature Name	Coeff
Power Dom Freq 2- Med	-2.50	Time Asleep	2.51	Wave Approx- IQR	-2.26
PLM %	-2.38	Grav Change Z- IQR	-1.95	Wave Entropy- IQR	-2.07
Corr YZ- Med	-2.28	Power Dom Freq 1- IQR	1.87	Corr YZ- Med	2.07
Wave Approx- IQR	2.18	Num Cross Cov Peaks- IQR	-1.41	Skewness- IQR	-1.55
Num Cross Cov Peaks- IQR	1.60	Dom Freq Last 90s- IQR	-1.13	Move/hour	1.40
Skewness- IQR	1.49	Corr XY- Med	-1.03	Wave Energy 2- Med	-1.31
Close Cross Cov Peak- IQR	1.35	Dom Freq 1- Med	-0.67	PLM Index	1.07
Dom Freq 2- IQR	1.27			Med Freq- IQR	0.66
Wave Energy 2- Med	1.18			Dom Freq 1- Med	0.63
Close Cross Corr Peak- IQR	0.98			Med Freq- Med	0.59
Covariates Features					
No Spasticity		Mild Spasticity		Moderate Spasticity	
Feature Name	Coeff	Feature Name	Coeff	Feature Name	Coeff
Years Since Injury	2.69	Ave Fatigue Rating	1.93	PSQI: Sleep Disturbance	-2.22
PSQI: Sleep Quality	1.64	Age	-1.85	Ave Sleep Rating	-2.11
Sleep Meds During Collection	-0.90	Exercised During Collection	-1.02	Sleep Meds During Collection	1.54
PSQI: Poor Sleep Quality	-0.79	Caffeine During Collection	0.96	Pain Present	1.02
Pain Interfere: Sleep	0.48	PSQI: Sleep Meds	-0.39	Caffeine During Collection	-0.98
				PSQI: Sleep Duration	0.77
LA + Covariates Features					
No Spasticity		Mild Spasticity		Moderate Spasticity	
Feature Name	Coeff	Feature Name	Coeff	Feature Name	Coeff
PLM %	-2.08	Time Asleep	2.20	Wave Approx- IQR	-1.57
Years Since Injury	1.59	Ave Fatigue Rating	1.99	Wave Entropy- IQR	-1.56
Wave Approx- IQR	1.37	Age	-1.83	Corr YZ- Med	1.48
Corr YZ- Med	-1.25	Grav Change Z- IQR	-1.83	Sleep Meds During Collection	1.30
Skewness- IQR	1.24	Corr XY- Med	-1.28	Skewness- IQR	-1.29
PSQI: Poor Sleep Quality	-1.03	Power Dom Freq 1- IQR	1.18	Move/hour	1.28
Power Dom Freq 2- Med	-1.02	Num Cross Cov Peaks- IQR	-0.89	Wave Energy 2- Med	-1.25
PSQI: Sleep Quality	0.97	Dom Freq Last 90s- IQR	-0.85	Ave Sleep Rating	-1.04
Num Cross Cov Peaks- IQR	-0.91	Dom Freq 1- Med	-0.71	PSQI: Sleep Duration	1.01
Sleep Meds During Collection	0.79	Exercised During Collection	-0.66	PLM Index	1.00
Dom Freq 2- IQR	0.67	Caffeine During Collection	0.52	PSQI: Sleep Disturbance	-0.98
Close Cross Cov Peak- IQR	0.62	PSQI: Sleep Meds	0.14	Dom Freq 1- Med	0.57
Close Cross Corr Peak- IQR	0.61			Caffeine During Collection	-0.50
Wave Energy 2- Med	0.58			Med Freq- IQR	0.44
Pain Interfere: Sleep	0.47			Med Freq- Med	0.41
				Pain Present	0.40

Abbreviations: Coeff= Model Coefficient
Covariates are in grey; LA features are in white.

Appendix D.3 Supplemental Analysis for Sensation Models

When evaluating the relationship between the covariates feature set and lower limb LT sensation, it was found that higher sensation scores were associated with 2 covariates: fewer pain locations and better sleep efficiency (lower PSQI: Sleep efficiency). This model resulted in much lower R^2 values than would have been expected (i.e., a slightly lower R^2 than when using only LA as seen in the other models). Thus, further analysis was completed to assess if an irregularity in the data was leading to the overly reduced feature selection and model instability or whether the covariates truly had a poorer relationship than expected.

The LASSO LARS model is effective in reducing multicollinearity by only including 1 of the highly correlated features in the model, which is in a beneficial characteristic. However, the model effectively chooses between highly correlated features at random which can introduce problems in the model.[176, 246] Although some covariate features were expected to have high correlations to other covariates, only 2 features had a correlation coefficient greater than 0.7: PSQI: Poor Sleep Quality and PSQI: Sleep Duration (r= .729) and PSQI: Poor Sleep Quality and PSQI: Sleep Quality (r= 0.718; Poor Sleep Quality is the dichotomized version of the PSQI Sleep Quality measure of the PSQI).

Although there was not evidence of substantial correlation between covariate features, models were assessed that manually removed features that either conceptually measured similar information or were highly correlated. When determining which features to remove, features were kept that were more clinically meaningful, decreased the number of other features that were highly correlated, and were easier to calculate. A set of 19 covariate features after the repetitive/correlated features were removed was assessed in the LASSO LARS models and compared to the original model with all covariate features (24 initial features). The model with the non-repetitive features

produced essentially the same results as when no prior feature selection was performed, with the R^2= 0.157 and the 2 same covariate features (number of pain problems, PSQI: Sleep Efficiency) selected.

Feature selection was also performed algorithmically so that features with the highest mutual information scores with respect to the outcome were included in the model while other highly correlated features were removed. Mutual information measures the dependency between the LA feature and the outcome using nonparametric methods based on entropy estimations from k-nearest neighbors distances. Higher mutual information values indicate higher dependency between the variables.[250] In addition to using mutual information to remove repetitive features, it was also used for further feature selection. The model containing all original covariate features (All) was compared to models using the following feature sets: only non-repetitive features after repetitive features with lower mutual information scores removed, only features with mutual information scores greater than zero, the top 50% of features based off mutual information score, top 25% and top 10%. Model performance is the same or worse than when all features were used until the features were restricted to the top 25% or less. Since it was determined that this method introduces too much bias to select features based off their relationship to the outcome and restricts features too much prior to when feature selection should occur in the LASSO LARS model, these methods were not further used.

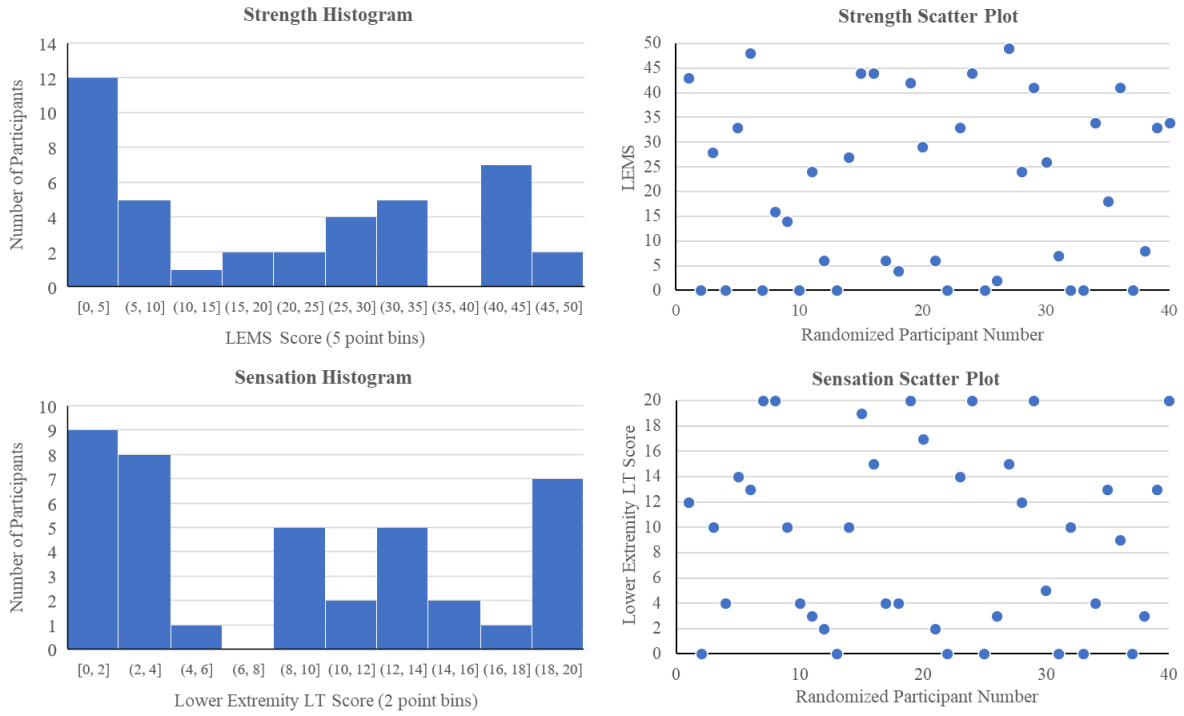
These results indicate that highly correlated features were not affecting the results. Since any feature selection prior to the machine learning model introduces bias, all future models did not have any feature selection performed prior.

It was still thought that there was an interaction between covariates that was interfering with proper model building. The LASSO LARS model was run with all LA features and 1

covariate at a time to attempt to isolate the problematic covariate. All models performed essentially as expected with R^2= 0.706 – 0.839 and 15-22 features selected for each model. Of the 24 models, 10 included the covariate in the model, 13 did not select the covariate and produced the same model as when LA features only were included, and 1 covariate (Caffeine During Collection) was not selected in the model but produced a different model than when only LA features were included. Thinking that this covariate could be the source of the model instability, another model was assessed that included all LA and covariate features except for caffeine during the collection, but this again resulted in only the same 2 covariate features being selected and a poor model performance.

A similar analysis was performed by including all LA features and all covariates except 1 at a time. Each of these models selected only the same 2 covariate features when they were both available. When PSQI: Sleep Efficiency was excluded then only number of pain problems remained (R^2= 0.067). However, when number of pain problems or both the PSQI: Sleep Efficiency and number of pain problems were excluded, then no variables were selected for the model).

Since this finding with the covariate features resulting in an over-reduction in the number of features included in the model was only occurring with respect to the sensation outcome and not strength, the distributions of the outcomes were more closely assessed. Although neither outcome exhibited a normal distribution, this is not required for machine learning models and neither was vastly skewed (Appendix Figure D.1).



Appendix Figure D.1: Histograms and scatter plots for the Aim 1 participant distribution for the strength (top) and sensation (bottom) outcomes.

Therefore, after evaluating correlations between features, manual feature reduction, algorithmic feature reduction, and individual covariate models there was not strong support for a data irregularity to be the primary cause of the poor sensation model performance. While it is still possible that a data issue may be present, this potential issue is unlikely to affect the study results or interpretation and it was determined that it was more likely that the covariates are just not strongly associated with sensation.

Appendix E Aim 2 Supplemental Material

Appendix Table E.1: 10mWT confusion matrices and per-class and overall evaluation metrics for each feature set.*

Actual/Predicted Class	Non-Ambulatory	Household Ambulator	Community Ambulator	Precision	Recall	F1-Score
10mWT: Clinical & Demographics						
Non-Ambulatory (0 m/s)	**9**	1	1	0.750	0.818	0.783
Household Ambulator (0.01-.44 m/s)	2	**5**	2	0.500	0.556	0.526
Community Ambulator (>.44 m/s)	1	4	**2**	0.400	0.286	0.333
Macro Average	Overall Classification Accuracy= 0.593			0.550	0.553	0.547
Weighted Average				0.576	0.593	0.581
10mWT: LA, Clinical & Demographics						
Non-Ambulatory (0 m/s)	**9**	1	1	1.000	0.818	0.900
Household Ambulator (0.01-.44 m/s)	0	**6**	3	0.600	0.667	0.632
Community Ambulator (>.44 m/s)	0	3	**4**	0.500	0.571	0.533
Macro Average	Overall Classification Accuracy= 0.704			0.700	0.685	0.688
Weighted Average				0.737	0.704	0.715
10mWT: PPEF, Clinical & Demographics						
Non-Ambulatory (0 m/s)	**9**	2	0	0.900	0.818	0.857
Household Ambulator (0.01-.44 m/s)	1	**6**	2	0.500	0.667	0.571
Community Ambulator (>.44 m/s)	0	4	**3**	0.600	0.429	0.500
Macro Average	Overall Classification Accuracy= 0.667			0.667	0.638	0.643
Weighted Average				0.689	0.667	0.669
10mWT: All (LA, PPEF, Clinical & Demographics)						
Non-Ambulatory (0 m/s)	**9**	1	1	0.900	0.818	0.857
Household Ambulator (0.01-.44 m/s)	1	**6**	2	0.500	0.667	0.571
Community Ambulator (>.44 m/s)	0	5	**2**	0.400	0.286	0.333
Macro Average	Overall Classification Accuracy= 0.630			0.600	0.590	0.587
Weighted Average				0.637	0.630	0.626

* The feature set with the highest classification accuracy per outcome is highlighted grey. The number of participants correctly classified per ambulation category are bolded.

Appendix Table E.2: 6MWT confusion matrices and per-class and overall evaluation metrics for each feature set. *

6MWT: Clinical & Demographics						
Actual/Predicted Class	Non-Ambulatory	Household Ambulator	Community Ambulator	Precision	Recall	F1-Score
Non-Ambulatory (0 m)	**9**	2	0	0.818	0.818	0.818
Household Ambulator (1-204 m)	2	**6**	3	0.600	0.545	0.571
Community Ambulator (> 204 m)	0	2	**3**	0.500	0.600	0.545
Macro Average	Overall Classification Accuracy= 0.667			0.639	0.655	0.645
Weighted Average				0.670	0.667	0.667
6MWT: LA, Clinical & Demographics						
Actual/Predicted Class	Non-Ambulatory	Household Ambulator	Community Ambulator	Precision	Recall	F1-Score
Non-Ambulatory (0 m)	**9**	2	0	0.818	0.818	0.818
Household Ambulator (1-204 m)	2	**9**	0	0.750	0.818	0.783
Community Ambulator (> 204 m)	0	1	**4**	1.000	0.800	0.889
Macro Average	Overall Classification Accuracy= 0.815			0.856	0.812	0.830
Weighted Average				0.824	0.815	0.817
6MWT: PPEF, Clinical & Demographics						
Actual/Predicted Class	Non-Ambulatory	Household Ambulator	Community Ambulator	Precision	Recall	F1-Score
Non-Ambulatory (0 m)	**9**	2	0	0.818	0.818	0.818
Household Ambulator (1-204 m)	2	**8**	1	0.667	0.727	0.696
Community Ambulator (> 204 m)	0	2	**3**	0.750	0.600	0.667
Macro Average	Overall Classification Accuracy= 0.741			0.745	0.715	0.727
Weighted Average				0.744	0.741	0.740
6MWT: All (LA, PPEF, Clinical & Demographics)						
Actual/Predicted Class	Non-Ambulatory	Household Ambulator	Community Ambulator	Precision	Recall	F1-Score
Non-Ambulatory (0 m)	**9**	2	0	0.750	0.818	0.783
Household Ambulator (1-204 m)	3	**7**	1	0.700	0.636	0.667
Community Ambulator (> 204 m)	0	1	**4**	0.800	0.800	0.800
Macro Average	Overall Classification Accuracy= 0.741			0.750	0.752	0.750
Weighted Average				0.739	0.741	0.739

* The feature set with the highest classification accuracy per outcome is highlighted grey. The number of participants correctly classified per ambulation category are bolded.

Appendix Table E.3: Features selected per 10mWT model and feature set (features selected 27 times maximum per model).

	Clinical & Demographic Features		LA, Clinical & Demographic Features		PPEF, Clinical & Demographic Features		All Features (LA, PPEF, Clinical & Demographic)	
	Name	Times Select	Name	Times Select	Name	Times Select	Name	Times Select
Clinical	LT: L4 (Best)	25	LT: L4 (Best)	24	MMT: Knee Flexion (Bilateral)	26	LT: L4 (Best)	27
	MMT: Knee Flexion (Best)	21	MMT: Knee Flexion (Best)	24	LT: L4 (Bilateral)	23	MMT: Knee Flexion (Best)	23
	LT: L2 (Best)	17	LT: L2 (Best)	18	LT: L2 (Best)	22	LT: L2 (Best)	18
	LT: L3 (Best)	15	MMT: L3 (Best)	16	MMT: L3 (Best)	19	AIS Classification	16
	AIS Classification	15	MMT: L5 (Best)	15	LT: L5 (Best)	19	LT: L5 (Best)	12
	MMT: L5 (Best)	12	LT: L3 (Best)	12	MMT: S1 (Best)	18	MMT: L3 (Best)	11
	LT: S1 (Best)	12	AIS Classification	11	AIS Classification	17	MMT: S1 (Best)	9
	LT: L5 (Best)	12	LT: L5 (Best)	11	MMT: L5 (Best)	16	MMT: L5 (Best)	8
	MMT: S1 (Best)	10	LT: S1 (Best)	9	LT: S1 (Bilateral)	15	MMT: L4 (Best)	7
	MMT: L3 (Bilateral)	10	MMT: L4 (Best)	7	LT: L3 (Best)	15	LT: S1 (Best)	7
	MMT: L4 (Best)	9	LT: Lower Extremity Score (Best)	6	MMT: L4 (Best)	13	LT: L3 (Bilateral)	4
	LT: Lower Extremity Score (Best)	4	MMT: Upper Extremity Score (Best)	4	LT: Lower Extremity Score (Best)	6	MMT: L2 (Best)	2
	MMT: Lower Extremity Score (Best)	3	MMT: L2 (Best)	4	MMT: Lower Extremity Score (Best)	5	LT: Lower Extremity Score (Best)	1
	MMT: Upper Extremity Score (Bilateral)	3	SCI Level of Injury	3	SCI Level of Injury	4	SCI Level of Injury	1
	MMT: L2 (Best)	3	MMT: Lower Extremity Score (Best)	3	MMT: Upper Extremity Score (Bilateral)	3	LT: Upper Extremity Score (Best)	1
	SCI Level of Injury	2	LT: Upper Extremity Score (Bilateral)	1	LT: Upper Extremity Score (Bilateral)	1	MMT: Upper Extremity Score (Bilateral)	1
	LT: Upper Extremity Score (Best)	2			MMT: L2 (Bilateral)	1		
Demographics	Veteran	20	Pain Present	19	Pain Present	25	Veteran	16
	Pain Present	17	Veteran	14	Veteran	22	Pain Present	11
	Medical Insurance	12	Medical Insurance	8	Comorbidities Present	14	Medical Insurance	7
	Number of Pain Locations	6	Number of Pain Locations	6	Number of Pain Locations	12	Comorbidities Present	4
	Marital Status	4	Marital Status	4	Medical Insurance	12	Number of Pain Locations	3
	Comorbidities Present	3	Comorbidities Present	4	Marital Status	6		
	Years Since Injury	1	Race/Ethnicity	1	Race/Ethnicity	3		
	Race/Ethnicity	1						
LA	N/A		Num Med Crossings- Med	2	N/A		Num Med Crossings- Med	4
			Num Med Crossings- IQR	1			Num Med Crossings- IQR	1
			Lyapunov Exp- IQR	1				

Appendix Table E.3 Continued

	Clinical & Demographic Features		LA, Clinical & Demographic Features		PPEF, Clinical & Demographic Features		All Features (LA, PPEF, Clinical & Demographic)	
	Name	Times Select	Name	Times Select	Name	Times Select	Name	Times Select
PPEF	N/A		N/A		Took Sleep Medication During Collection	26	Exercised During Collection	22
					Exercised During Collection	26	Took Sleep Medication During Collection	17
					PSQI: Sleep Quality	19	PSQI: Poor Sleep Quality	7
					PSQI: Poor Sleep Quality	18	Consumed Alcohol During Collection	6
					Consumed Alcohol During Collection	18	PSQI: Sleep Quality	5
					Pain Interference: Social Activity	11	SF-36: Emotional Role Limitations	2
					PSQI: Sleep Duration	5	Pain Interference: Social Activity	2
					SF-36: Emotional Role Limitations	5		
					Consumed Caffeine During Collection	3		
					Resilience	2		

Abbreviations: N/A= Not applicable

Appendix Table E.4: Features selected per 6MWT model and feature set (features selected 27 times maximum per model).

	Clinical & Demographic Features		LA, Clinical & Demographic Features		PPEF, Clinical & Demographic Features		All Features (LA, PPEF, Clinical & Demographic)	
	Name	Times Selected	Name	Times Selected	Name	Times Selected	Name	Times Selected
Clinical	MMT: Knee Flexion (Bilateral)	27	MMT: Knee Flexion (Bilateral)	27	MMT: Knee Flexion (Best)	27	LT: L4 (Best)	26
	LT: L4 (Best)	25	LT: L4 (Best)	26	LT: L4 (Best)	24	MMT: Knee Flexion (Best)	24
	MMT: L3 (Bilateral)	22	MMT: L3 (Bilateral)	19	MMT: L3 (Best)	23	MMT: L3 (Best)	21
	LT: L3 (Bilateral)	16	LT: L3 (Bilateral)	18	LT: L3 (Bilateral)	13	LT: L3 (Bilateral)	11
	MMT: Lower Extremity Score (Best)	14	MMT: Lower Extremity Score (Best)	12	MMT: Lower Extremity Score (Best)	13	MMT: Lower Extremity Score (Best)	9
	LT: Lower Extremity Score (Bilateral)	11	LT: Lower Extremity Score (Best)	10	MMT: L5 (Best)	12	MMT: L5 (Best)	9
	MMT: L2 (Bilateral)	10	MMT: S1 (Best)	10	LT: Lower Extremity Score (Best)	11	MMT: S1 (Best)	7
	MMT: L5 (Best)	7	MMT: L5 (Best)	9	MMT: L4 (Best)	10	LT: Lower Extremity Score (Best)	7
	LT: S1 (Best)	6	MMT: L2 (Bilateral)	5	MMT: L2 (Bilateral)	8	MMT: L2 (Best)	6
	MMT: S1 (Best)	6	MMT: L4 (Best)	5	MMT: S1 (Best)	5	MMT: L4 (Best)	4
	LT: L2 (Best)	4	LT: Upper Extremity Score (Best)	5	LT: Upper Extremity Score (Bilateral)	4	LT: L5 (Best)	4
	MMT: L4 (Bilateral)	3	LT: S1 (Best)	2	LT: S1 (Best)	4	LT: Upper Extremity Score (Best)	3
	LT: L5 (Best)	2	AIS Classification	2	LT: L2 (Best)	3	LT: L2 (Best)	2
	LT: Upper Extremity Score (Best)	1	LT: L2 (Best)	1	LT: L5 (Bilateral)	2		
	MMT: Upper Extremity Score (Bilateral)	1	LT: L5 (Bilateral)	1				
Demographics	Comorbidities Present	25	Comorbidities Present	20	Pain Present	21	Comorbidities Present	17
	Pain Present	19	Pain Present	17	Comorbidities Present	20	Pain Present	16
	Veteran	10	Race/Ethnicity	10	Veteran	12	Veteran	11
	Race/Ethnicity	9	Veteran	9	Race/Ethnicity	5	Race/Ethnicity	6
	Annual Income	1						
LA	N/A		Num Med Crossings- Med	18	N/A		Num Med Crossings- Med	24
			Lyapunov Exp- IQR	7			Lyapunov Exp- IQR	6
			Start Move %- Med	2			End Move %- Med	2
			Start Move %- IQR	1			End Move %- IQR	2
			Grav Change Z- IQR	1				

Appendix Table E.4 Continued

	Clinical & Demographic Features		LA, Clinical & Demographic Features		PPEF, Clinical & Demographic Features		All Features (LA, PPEF, Clinical & Demographic)	
	Name	Times Selected	Name	Times Selected	Name	Times Selected	Name	Times Selected
PPEF	N/A		N/A		Exercised During Collection	20	Took Sleep Medication During Collection	18
					Took Sleep Medication During Collection	18	Exercised During Collection	14
					PSQI: Poor Sleep Quality	9	PSQI: Sleep Quality	9
					Consumed Caffeine During Collection	9	PSQI: Poor Sleep Quality	9
					PSQI: Sleep Quality	6	Consumed Caffeine During Collection	3
					SF-36: Physical Functioning	5	SF-36: Emotional Role Limitations	1
					SF-36: Emotional Role Limitations	3	SF-36: Energy/Fatigue	1
					SF-36: Energy/Fatigue	1	SF-36: Physical Functioning	1
					Self-Efficacy	1		

Abbreviations: N/A= Not applicable

Appendix F Longitudinal Ambulatory and Clinical Assessments

Appendix Table F.1: Confusion matrices of ambulatory categoizations for all participants and time points

		Admission to IPR							
		WISCI-II Category				6MWT Category			
	Ambulatory Ability Category	Physical Assist or Non-Amb	AD, No Physical Assist	No AD or Assist	Total (% of column)	Non-Amb	Household Amb	Community Amb	Total (% of column)
10mWT Category	Non-Amb (0m/s)	31	0	0	31 (93.9%)	31	0	0	31 (93.9%)
	Household Amb (0.01-.44m/s)	2	0	0	2 (6.1%)	0	2	0	2 (6.1%)
	Community Amb (>0.44m/s)	0	0	0	0 (0.0%)	0	0	0	0 (0.0%)
	Total (% of row)	33 (100%)	0 (0.0%)	0 (0.0%)	33 (100%)	31 (93.9%)	2 (6.1%)	0 (0.0%)	33 (100%)
6MWT Category	Non-Amb (0m)	31	0	0	31 (93.9%)				
	Household Amb (1-204m)	2	0	0	2 (6.1%)				
	Community Amb (>204m)	0	0	0	0 (0.0%)				
	Total (% of row)	33 (100%)	0 (0.0%)	0 (0.0%)	33 (100%)				
		Discharge from IPR							
		WISCI-II Category				6MWT Category			
	Ambulatory Ability Category	Physical Assist or Non-Amb	AD, No Physical Assist	No AD or Assist	Total (% of column)	Non-Amb	Household Amb	Community Amb	Total (% of column)
10mWT Category	Non-Amb (0m/s)	19	0	0	19 (63.3%)	19	0	0	19 (63.3%)
	Household Amb (0.01-.44m/s)	3	1	0	4 (13.3%)	0	4	0	4 (13.3%)
	Community Amb (>0.44m/s)	0	5	2	7 (23.3%)	0	4	3	7 (23.3%)
	Total (% of row)	22 (73.3%)	6 (20.0%)	2 (6.7%)	30 (100%)	19 (63.3%)	8 (26.7%)	3 (10.0%)	30 (100%)
6MWT Category	Non-Amb (0m)	19	0	0	19 (57.6%)				
	Household Amb (1-204m)	4	7	0	11 (33.3%)				
	Community Amb (>204m)	0	1	2	3 (9.1%)				
	Total (% of row)	23 (69.7%)	8 (24.2%)	2 (6.1%)	33 (100%)				

Appendix Table F.1 Continued

6-months Post-Discharge from IPR								
		WISCI-II Category				6MWT Category			
Ambulatory Ability Category		Physical Assist or Non-Amb	AD, No Physical Assist	No AD or Assist	Total (% of column)	Non-Amb	Household Amb	Community Amb	Total (% of column)
10mWT Category	Non-Amb (0m/s)	4	0	0	4 (30.8%)	4	0	0	4 (30.8%)
	Household Amb (0.01-.44m/s)	0	2	0	2 (15.4%)	0	2	0	2 (15.4%)
	Community Amb (>0.44m/s)	0	2	5	7 (53.8%)	0	1	6	7 (53.8%)
	Total (% of row)	4 (30.8%)	4 (30.8%)	5 (38.5%)	13 (100%)	4 (30.8%)	3 (23.1%)	6 (46.2%)	13 (100%)
6MWT Category	Non-Amb (0m)	4	0	0	4 (30.8%)				
	Household Amb (1-204m)	0	2	1	3 (23.1%)				
	Community Amb (>204m)	0	2	4	6 (46.2%)				
	Total (% of row)	4 (30.8%)	4 (30.8%)	5 (38.5%)	13 (100%)				
1-year Post-Discharge from IPR									
		WISCI-II Category				6MWT Category			
Ambulatory Ability Category		Physical Assist or Non-Amb	AD, No Physical Assist	No AD or Assist	Total (% of column)	Non-Amb	Household Amb	Community Amb	Total (% of column)
10mWT Category	Non-Amb (0m/s)	2	0	0	2 (22.2%)	2	0	0	2 (22.2%)
	Household Amb (0.01-.44m/s)	0	0	0	0 (0.0%)	0	0	0	0 (0.0%)
	Community Amb (>0.44m/s)	0	3	4	7 (77.8%)	0	2	5	7 (77.8%)
	Total (% of row)	2 (22.2%)	3 (33.3%)	4 (44.4%)	9 (100%)	2 (22.2%)	2 (22.2%)	5 (55.6%)	9 (100%)
6MWT Category	Non-Amb (0m)	2	0	0	2 (22.2%)				
	Household Amb (1-204m)	0	2	0	2 (22.2%)				
	Community Amb (>204m)	0	1	4	5 (55.6%)				
	Total (% of row)	2 (22.2%)	3 (33.3%)	4 (44.4%)	9 (100%)				

Abbreviations: AD= Assistive Device, Amb= Ambulatory/Ambulation

Appendix G Aim 3 Supplemental Material

Appendix Table G.1: Categorical demographics from participants included and excluded from Aims 3b/4a*

	Aims 3b and 4a N (%)											
	Included in Analysis		Excluded From Analysis								t test	
	Collected and Usable (n=12)		Partially Collected/Not Usable (n=2)		Missed (n=9)		Not Eligible (n=2)		Total Not Included (n=13)		Sig	
Categorical Demographics	Adm	Dc	Adm	Dc	Adm	Dc	Adm	Dc	Adm	Dc	Adm	Dc
Sex											0.319	
Female	7 (58.3%)		1 (50.0%)		8 (88.9%)		1 (50.0%)		10 (76.9%)			
Male	5 (41.7%)		1 (50.0%)		1 (11.1%)		1 (50.0%)		3 (23.1%)			
Race/Ethnicity											0.716	
Non-Hispanic White	9 (75.0%)		2 (100%)		5 (55.6%)		1 (50.0%)		8 (61.5%)			
Non-Hispanic Black	1 (8.3%)		0 (0.0%)		1 (11.1%)		1 (50.0%)		2 (15.4%)			
Non-Hispanic Other Race	0 (0.0%)		0 (0.0%)		1 (11.1%)		0 (0.0%)		1 (7.7%)			
Hispanic (Any Race)	2 (16.7%)		0 (0.0%)		2 (22.2%)		0 (0.0%)		2 (15.4%)			
Veteran											0.953	
Not A Veteran	11 (91.7%)		1 (50.0%)		9 (100%)		2 (100%)		12 (92.3%)			
Veteran	1 (8.3%)		1 (50.0%)		0 (0.0%)		0 (0.0%)		1 (7.7%)			
Annual Household Income											0.240	
< $25,000	1 (8.3%)		1 (50.0%)		4 (44.4%)		0 (0.0%)		5 (38.5%)			
$25,000 - $49,999	3 (25.0%)		0 (0.0%)		2 (22.2%)		0 (0.0%)		2 (15.4%)			
$50,000 -$74,999	3 (25.0%)		0 (0.0%)		1 (11.1%)		0 (0.0%)		1 (7.7%)			
≥ $75,000	1 (8.3%)		1 (50.0%)		2 (22.2%)		0 (0.0%)		3 (23.1%)			
Declined/ Unknown	4 (33.3%)		0 (0.0%)		0 (0.0%)		2 (100%)		2 (15.4%)			
Education											0.541	
Less Than High School	2 (16.7%)		0 (0.0%)		0 (0.0%)		0 (0.0%)		0 (0.0%)			
High School Diploma/GED	6 (50.0%)		1 (50.0%)		3 (33.3%)		1 (50.0%)		5 (38.5%)			
Associate's Degree	2 (16.7%)		0 (0.0%)		3 (33.3%)		1 (50.0%)		4 (30.8%)			
Bachelor's Degree	1 (8.3%)		0 (0.0%)		1 (11.1%)		0 (0.0%)		1 (7.7%)			
Graduate Degree	0 (0.0%)		1 (50.0%)		0 (0.0%)		0 (0.0%)		1 (7.7%)			
Other	1 (8.3%)		0 (0.0%)		2 (22.2%)		0 (0.0%)		2 (15.4%)			

Appendix Table G.1 Continued

	Aims 3b and 4a N (%)											
	Included in Analysis		Excluded From Analysis								t test	
	Collected and Usable (n=12)		Partially Collected/ Not Usable (n=2)		Missed (n=9)		Not Eligible (n=2)		Total Not Included (n=13)		Sig	
Categorical Demographics	Adm	Dc	Adm	Dc	Adm	Dc	Adm	Dc	Adm	Dc	Adm	Dc
Medical Insurance											0.447	
Private	3 (25.0%)		2 (100%)		5 (55.6%)		0 (0.0%)		7 (53.8%)			
Medicaid	3 (25.0%)		0 (0.0%)		3 (33.3%)		0 (0.0%)		3 (23.1%)			
Medicare	1 (8.3%)		0 (0.0%)		0 (0.0%)		0 (0.0%)		0 (0.0%)			
No Insurance	1 (8.3%)		0 (0.0%)		0 (0.0%)		0 (0.0%)		0 (0.0%)			
Other/Multiple	4 (33.3%)		0 (0.0%)		1 (11.1%)		2 (100%)		3 (23.1%)			
SCI Neurological Category											0.387	0.620
Motor Complete (AIS A/B) Tetraplegia	1 (8.3%)	1 (8.3%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	0 (0.0%)		
Motor Complete (AIS A/B) Paraplegia	3 (25.0%)	2 (16.7%)	1 (50.0%)	1 (50%)	1 (11.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (15.4%)	1 (7.7%)		
AIS C Tetraplegia	1 (8.3%)	1 (8.3%)	1 (50.0%)	0 (0.0%)	4 (44.4%)	3 (33.3%)	1 (50.0%)	1 (50.0%)	6 (46.2%)	4 (30.8%)		
AIS C Paraplegia	1 (8.3%)	2 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.7%)		
AIS D Tetraplegia	5 (41.7%)	5 (41.7%)	0 (0.0%)	1 (50%)	2 (22.2%)	4 (44.4%)	1 (50.0%)	1 (50.0%)	3 (23.1%)	6 (46.2%)		
AIS D Paraplegia	1 (8.3%)	1 (8.3%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	1 (11.1%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	1 (7.7%)		
Primary Mode of Mobility											0.055	0.090
Power Wheelchair	9 (75.0%)	4 (33.3%)	2 (100%)	0 (0.0%)	9 (100%)	8 (88.9%)	2 (100%)	2 (100%)	13 (100%)	10 (76.9%)		
Manual Wheelchair	3 (25.0%)	5 (41.7%)	0 (0.0%)	2 (100%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (15.4%)		
Ambulation	0 (0.0%)	3 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.7%)		
WISCI-II											N/A	0.023
Physical Assistance (or Non-Ambulatory)	12 (100%)	5 (41.7%)	2 (100%)	2 (100%)	9 (100%)	8 (88.9%)	2 (100%)	2 (100%)	13 (100%)	12 (92.3%)		
Requires AD, but no Physical Assistance	0 (0.0%)	5 (41.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.7%)		
Requires No AD or Physical Assistance	0 (0.0%)	2 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		
10mWT											0.125	0.029
Non-ambulatory (0m/s)	10 (83.3%)	5 (45.5%)	2 (100%)	1 (50%)	9 (100%)	6 (75.0%)	2 (100%)	2 (100%)	13 (100%)	9 (75.0%)		
Household Ambulator (0.01-.44m/s)	2 (16.7%)	1 (9.1%)	0 (0.0%)	1 (50%)	0 (0.0%)	2 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (25.0%)		
Community Ambulator (>.44m/s)	0 (0.0%)	5 (45.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		
6MWT											0.125	0.128
Non-ambulatory (0m)	10 (83.3%)	5 (41.7%)	2 (100%)	1 (50%)	9 (100%)	6 (66.7%)	2 (100%)	2 (100%)	13 (100%)	9 (69.2%)		
Household Ambulator (1-204m)	2 (16.7%)	4 (33.3%)	0 (0.0%)	1 (50%)	0 (0.0%)	3 (33.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (30.8%)		
Community Ambulator (>204m)	0 (0.0%)	3 (25.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		

Abbreviations: Adm= Admission, Dc= Discharge

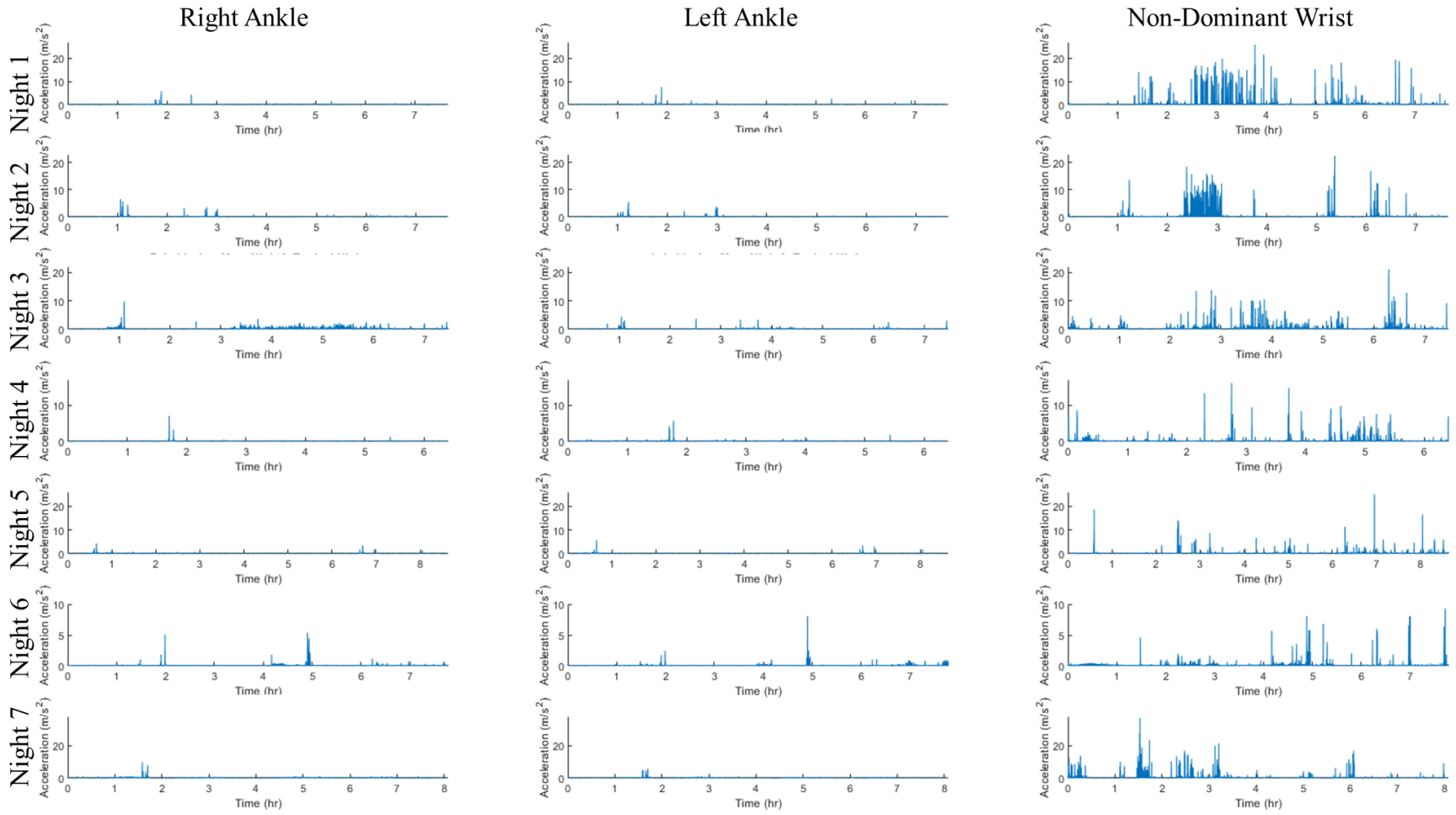
* Significant differences between those included and excluded from the analysis ($p < 0.05$) are highlighted grey

Appendix Table G.2: Continuous demographics from participants included and excluded from Aims 3b/4a*

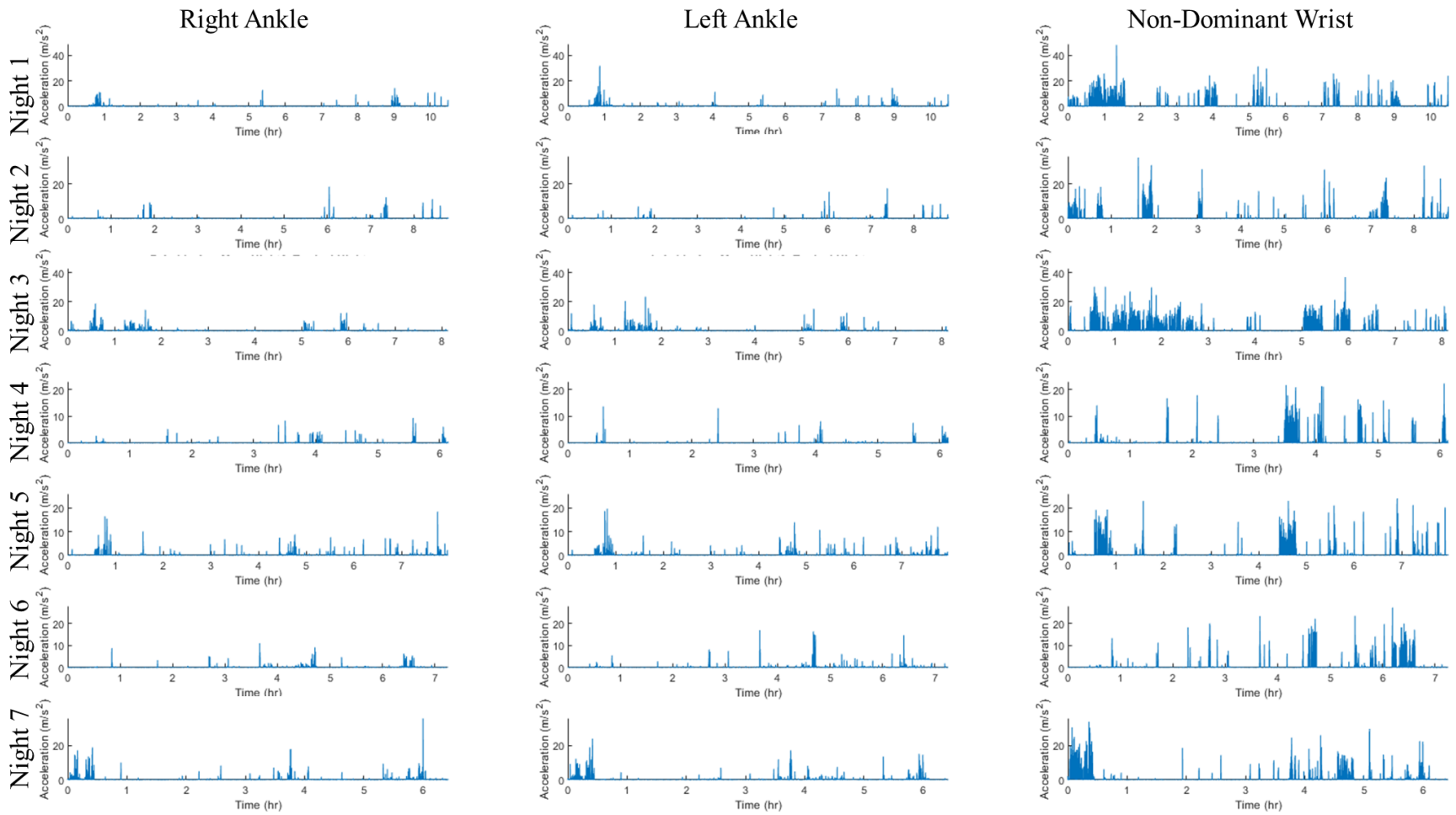
	Aims 3b and 4a Mean±SD (Range)											
	Included in Analysis		Excluded From Analysis								t test	
Continuous Demographics	Collected and Usable (n=12)		Partially Collected/Not Usable (n=2)		Missed (n=9)		Not Eligible (n=2)		Total Not Included (n=13)		Sig	
	Adm	Dc	Adm	Dc	Adm	Dc	Adm	Dc	Adm	Dc	Adm	Dc
Age	45.8±17.8 (18-71)		32.0±12.8 (23-41)		52.6±15.2 (36-82)		63.7±4.0 (61-67)		51.1±16.0 (23-82)		0.442	
BMI	27.8±3.4 (23-35)		28.8±5.4 (25-33)		29.2±9.9 (15-47)		30.4±4.3 (27-33)		29.3±8.3 (15-47)		0.549	
Length of Stay in IPR (Days)	33.8±10.7 (17-53)		49.5±2.1 (48-51)		47.3±10.9 (30-64)		44.0±12.7 (35-53)		47.2±9.8 (30-64)		0.002	
Days from Injury to Start of IPR	14.8±16.0 (5-62)		23.0±7.1 (18-28)		18.1±8.7 (8-30)		12.5±0.7 (12-13)		18.0±8.0 (8-30)		0.521	
Days from Injury to Start of Data Collection	17.5 ± 15.9 (9 - 65)	39.7 ± 16.5 (18 - 76)	28.0 ± 5.7 (24 - 32)	63.0 ± 4.2 (60 - 66)	22.8 ± 9.8 (10 - 36)	57.2 ± 11.0 (41 - 72)	17.5 ± 2.1 (16 - 19)	53.0 ± 9.9 (46 - 60)	22.8 ± 8.8 (10 - 36)	57.5 ± 9.5 (41 - 72)	0.311	0.007
LEMS	23.8±16.0 (0-47)	28.7±16.0 (0-45)	15.0±21.2 (0-30)	22.5±31.8 (0-45)	20.0±14.6 (0-36)	29.1±20.0 (0-48)	21.0±12.7 (12-30)	25.5±0.7 (25-26)	19.4±14.0 (0-36)	27.5±18.9 (0-48)	0.474	0.874
LELTS	10.5±7.1 (0-20)	10.7±6.5 (0-18)	9.0±12.7 (0-18)	9.0±12.7 (0-18)	11.0±6.7 (0-18)	9.1±5.8 (0-17)	10.0±0.0 (10-10)	16.0±5.7 (12-20)	10.5±6.6 (0-18)	10.2±6.8 (0-20)	0.998	0.835
WISCI-II	2.4±4.9 (0-17)	8.2±7.7 (0-20)	0±0 (0-0)	4.0±5.7 (0-8)	0.2±0.4 (0-1)	4.2±6.7 (0-17)	0±0 (0-0)	0±0 (0-0)	0.2±0.4 (0-1)	3.5±5.9 (0-17)	0.139	0.104
10mWT (m/s)	0.0±0.1 (0-0)	0.4±0.4 (0-1)	0±0 (0-0)	0.1±0.1 (0-0)	0±0 (0-0)	0.1±0.2 (0-0)	0±0 (0-0)	0±0 (0-0)	0±0 (0-0)	0.1±0.1 (0-0)	0.211	0.043
6WMT (m)	15.3±46.1 (0-160)	112.3±144.5 (0-457)	0±0 (0-0)	32.3±45.7 (0-65)	0±0 (0-0)	37.2±60.6 (0-161)	0±0 (0-0)	0±0 (0-0)	0±0 (0-0)	30.7±53.0 (0-161)	0.273	0.087

Abbreviations: Adm= Admission, Dc= Discharge

* Significant differences between those included and excluded from the analysis ($p < 0.05$) are highlighted grey



Appendix Figure G.1: Examples of LA collected from the right ankle, left ankle, and wrist across 7 typical nights at admission to IPR. This participant had an C5 AIS B SCI and non-ambulatory at admission to IPR.



Appendix Figure G.2: Examples of LA collected from the right ankle, left ankle, and wrist across 7 typical nights at admission to IPR. This participant had an L2 AIS A and primarily power wheelchia user but also uses a manual wheelchair and walks up to 45.7m with moderate assistance, a wheeled walker, and bilateral bracing (1 AFO, 1 KAFO) ambulatory with at admission to IPR.

Appendix Table G.3: ICC between nights of collection from admission to IPR*

Feature Category	Feature Name	Average Nights			Single Night			F Test with True Value 0	
			95% Confidence Interval			95% Confidence Interval			
		ICC	Lower Bound	Upper Bound	ICC	Lower Bound	Upper Bound	F Value	Sig
Change in angle of inclination	Angle Net Change-IQR	0.481	-0.083	0.751	0.317	-0.040	0.601	1.91	0.040
	Angle Net Change-Med	0.662	0.291	0.838	0.495	0.170	0.721	2.90	0.002
	Angle Rate Change-IQR	0.595	0.161	0.805	0.424	0.088	0.674	2.46	0.008
	Angle Rate Change-Med	0.738	0.453	0.874	0.585	0.293	0.776	3.74	<0.001
	Angle Total Change-IQR	0.576	0.124	0.795	0.404	0.066	0.660	2.35	0.011
	Angle Total Change-Med	**0.816**	**0.617**	**0.911**	0.689	0.446	0.837	5.31	<0.001
Change in gravitational acceleration	Grav Change X-IQR	0.571	0.107	0.794	0.400	0.056	0.658	2.31	0.013
	Grav Change X-Med	0.467	-0.104	0.743	0.305	-0.049	0.591	1.87	0.046
	Grav Change Y-IQR	0.604	0.180	0.809	0.433	0.099	0.679	2.51	0.007
	Grav Change Y-Med	0.439	-0.098	0.722	0.282	-0.047	0.565	1.86	0.047
	Grav Change Z-IQR	**0.815**	**0.616**	**0.911**	0.688	0.445	0.837	5.29	<0.001
	Grav Change Z-Med	0.618	0.211	0.815	0.447	0.118	0.688	2.61	0.005
Correlation coefficients between axes	Corr XY-IQR	0.232	-0.494	0.618	0.131	-0.198	0.447	1.33	0.223
	Corr XY-Med	0.195	-0.646	0.609	0.108	-0.244	0.438	1.24	0.276
	Corr XZ-IQR	0.221	-0.628	0.626	0.124	-0.239	0.456	1.28	0.251
	Corr XZ-Med	0.223	-0.640	0.628	0.125	-0.242	0.458	1.28	0.251
	Corr YZ-IQR	0.687	0.346	0.849	0.523	0.209	0.738	3.13	0.001
	Corr YZ-Med	0.162	-0.777	0.600	0.088	-0.280	0.429	1.19	0.319
Frequency domain	Bandwidth-IQR	-0.136	-1.436	0.461	-0.063	-0.418	0.300	0.88	0.631
	Bandwidth-Med	0.572	0.101	0.795	0.401	0.053	0.660	2.30	0.013
	Centroid Freq-IQR	0.135	-0.767	0.579	0.072	-0.277	0.408	1.16	0.345
	Centroid Freq-Med	0.501	-0.044	0.760	0.334	-0.021	0.614	1.98	0.033
	Dom Freq 1-IQR	0.272	-0.546	0.653	0.157	-0.214	0.485	1.36	0.201
	Dom Freq 1-Med	0.597	0.153	0.807	0.426	0.083	0.677	2.44	0.009
	Dom Freq 2-IQR	0.015	-0.962	0.515	0.007	-0.325	0.347	1.02	0.483
	Dom Freq 2-Med	0.469	-0.122	0.746	0.306	-0.057	0.595	1.86	0.048
	Dom Low Freq-IQR	0.340	-0.392	0.685	0.205	-0.164	0.520	1.50	0.135
	Dom Low Freq-Med	-0.095	-1.278	0.472	-0.046	-0.390	0.309	0.91	0.598
	Mean Freq-IQR	0.286	-0.431	0.650	0.167	-0.177	0.481	1.42	0.173
	Mean Freq-Med	0.469	-0.111	0.745	0.306	-0.052	0.594	1.87	0.046

Appendix Table G.3 Continued

Feature Category	Feature Name	Average Nights			Single Night			F Test with True Value 0	
			95% Confidence Interval			95% Confidence Interval			
		ICC	Lower Bound	Upper Bound	ICC	Lower Bound	Upper Bound	F Value	Sig
Frequency Domain	Med Freq-IQR	0.721	0.422	0.865	0.563	0.267	0.763	3.55	<0.001
	Med Freq-Med	0.634	0.231	0.824	0.464	0.131	0.701	2.68	0.004
	Power Dom Freq 1/Total-IQR	0.349	-0.297	0.680	0.211	-0.129	0.515	1.56	0.114
	Power Dom Freq 1/Total-Med	0.609	0.179	0.813	0.438	0.098	0.685	2.51	0.007
	Power Dom Freq 1-IQR	0.448	-0.112	0.730	0.289	-0.053	0.575	1.84	0.050
	Power Dom Freq 1-Med	0.585	0.132	0.801	0.414	0.071	0.668	2.38	0.010
	Power Dom Freq 2-IQR	0.614	0.208	0.813	0.443	0.116	0.684	2.60	0.005
	Power Dom Freq 2-Med	0.704	0.380	0.858	0.543	0.235	0.751	3.30	<0.001
	Power Dom Low Freq-IQR	0.566	0.132	0.787	0.395	0.071	0.649	2.41	0.009
	Power Dom Low Freq-Med	0.669	0.312	0.841	0.503	0.185	0.725	2.99	0.002
	Power High Freq/Total-IQR	0.079	-0.952	0.560	0.041	-0.322	0.389	1.08	0.414
	Power High Freq/Total-Med	0.588	0.143	0.802	0.416	0.077	0.669	2.40	0.010
	Power Total-IQR	0.554	0.088	0.784	0.384	0.046	0.645	2.26	0.014
	Power Total-Med	0.492	-0.071	0.757	0.327	-0.034	0.609	1.94	0.037
Limb movement percentages	Bilat Ankle %	0.600	0.196	0.804	0.429	0.108	0.673	2.72	0.004
	Unilat Ankle %	0.600	0.196	0.804	0.429	0.108	0.673	2.72	0.004
	Whole Body %	0.393	-0.166	0.696	0.245	-0.077	0.534	1.74	0.068
	Wrist Ankle %	0.122	-0.706	0.562	0.065	-0.261	0.391	1.15	0.354
Median crossings	Num Med Crossings Norm-IQR	0.441	-0.148	0.729	0.283	-0.069	0.574	1.79	0.058
	Num Med Crossings Norm-Med	0.644	0.265	0.828	0.474	0.153	0.706	2.80	0.003
	Num Med Crossings-IQR	0.629	0.250	0.819	0.459	0.143	0.693	2.79	0.003
	Num Med Crossings-Med	0.619	0.206	0.817	0.448	0.115	0.690	2.59	0.006
PLM	**Num PLM Norm**	**0.827**	**0.643**	**0.917**	0.706	0.474	0.846	5.72	<0.001
	PLM %	0.716	0.406	0.863	0.557	0.255	0.759	3.45	<0.001
	PLM Index	0.740	0.455	0.875	0.587	0.295	0.778	3.75	<0.001
Relationship to recent movements	Close Cross Corr Peak-IQR	0.652	0.295	0.830	0.483	0.173	0.710	2.99	0.002
	Close Cross Corr Peak-Med	0.086	-0.777	0.545	0.045	-0.280	0.374	1.10	0.397
	Close Cross Cov Peak-IQR	0.450	-0.133	0.734	0.290	-0.062	0.580	1.82	0.053
	Close Cross Cov Peak-Med	0.247	-0.519	0.632	0.141	-0.206	0.462	1.34	0.216
	Dom Freq Last 90s-IQR	-0.002	-1.074	0.516	-0.001	-0.349	0.348	1.00	0.502
	Dom Freq Last 90s-Med	0.673	0.332	0.841	0.508	0.199	0.726	3.10	0.001

Appendix Table G.3 Continued

Feature Category	Feature Name	Average Nights			Single Night			F Test with True Value 0	
			95% Confidence Interval			95% Confidence Interval			
		ICC	Lower Bound	Upper Bound	ICC	Lower Bound	Upper Bound	F Value	Sig
Relationship to recent movements	Max Cross Corr-IQR	0.254	-0.587	0.645	0.145	-0.227	0.476	1.33	0.220
	Max Cross Corr-Med	-0.019	-1.179	0.516	-0.009	-0.371	0.348	0.98	0.520
	Max Cross Cov-IQR	0.460	-0.140	0.742	0.299	-0.066	0.590	1.83	0.052
	Max Cross Cov-Med	0.511	-0.021	0.765	0.343	-0.010	0.619	2.03	0.029
	Mean Cross Corr Peaks-IQR	0.409	-0.205	0.713	0.257	-0.093	0.554	1.70	0.075
	Mean Cross Corr Peaks-Med	-0.559	-2.142	0.238	-0.219	-0.517	0.135	0.63	0.896
	Mean Cross Cov Peaks-IQR	0.179	-0.689	0.602	0.098	-0.256	0.431	1.22	0.295
	Mean Cross Cov Peaks-Med	0.434	-0.136	0.722	0.277	-0.064	0.566	1.80	0.057
	Move Last 90s-IQR	0.225	-0.598	0.625	0.127	-0.230	0.455	1.29	0.244
	Move Last 90s-Med	0.581	0.146	0.796	0.409	0.079	0.661	2.42	0.009
	Move Next 90s-IQR	0.225	-0.598	0.625	0.127	-0.230	0.455	1.29	0.244
	Move Next 90s-Med	0.581	0.146	0.796	0.409	0.079	0.661	2.42	0.009
	Num Cross Corr Peaks-IQR	0.294	-0.490	0.663	0.173	-0.197	0.495	1.41	0.177
	Num Cross Corr Peaks-Med	0.398	-0.220	0.707	0.249	-0.099	0.546	1.68	0.081
	Num Cross Cov Peaks-IQR	-0.042	-1.240	0.506	-0.021	-0.383	0.339	0.96	0.543
	Num Cross Cov Peaks-Med	0.471	-0.077	0.743	0.308	-0.037	0.591	1.91	0.041
	Time Since Prev-IQR	-0.021	-1.137	0.510	-0.010	-0.363	0.342	0.98	0.522
	Time Since Prev-Med	0.029	-1.086	0.540	0.015	-0.352	0.369	1.03	0.469
Signal characteristics	Entropy Rate-IQR	0.640	0.272	0.824	0.471	0.158	0.701	2.97	0.002
	Entropy Rate-Med	0.600	0.167	0.808	0.429	0.091	0.677	2.47	0.008
	Lempel-Ziv Comp-IQR	0.171	-0.548	0.578	0.093	-0.215	0.406	1.23	0.285
	Lempel-Ziv Comp-Med	0.534	0.050	0.773	0.364	0.026	0.630	2.17	0.019
	Lyapunov Exp-IQR	0.618	0.201	0.817	0.448	0.112	0.690	2.58	0.006
	Lyapunov Exp-Med	0.319	-0.326	0.661	0.190	-0.140	0.494	1.51	0.133
	Wave Approx-IQR	-0.010	-1.007	0.502	-0.005	-0.335	0.336	0.99	0.511
	Wave Approx-Med	0.688	0.352	0.850	0.525	0.214	0.739	3.57	<0.001
	Wave Energy 1-IQR	0.309	-0.406	0.663	0.182	-0.169	0.496	1.45	0.155
	Wave Energy 1-Med	0.209	-0.684	0.623	0.117	-0.255	0.453	1.26	0.268
	Wave Energy 2-IQR	0.637	0.240	0.826	0.467	0.136	0.703	2.71	0.004
	Wave Energy 2-Med	0.716	0.421	0.862	0.558	0.267	0.758	3.73	<0.001

Appendix Table G.3 Continued

Feature Category	Feature Name	Average Nights			Single Night			F Test with True Value 0	
			95% Confidence Interval			95% Confidence Interval			
		ICC	Lower Bound	Upper Bound	ICC	Lower Bound	Upper Bound	F Value	Sig
Signal Characteristics	**Wave Energy 3-IQR**	**0.804**	**0.598**	**0.905**	0.672	0.426	0.826	5.22	<0.001
	Wave Energy 3-Med	0.720	0.402	0.867	0.563	0.252	0.765	4.06	<0.001
	Wave Entropy-IQR	-1.117	-3.608	0.002	-0.358	-0.643	0.001	0.48	0.976
	Wave Entropy-Med	0.668	0.317	0.840	0.502	0.188	0.724	3.33	<0.001
Statistical	AUC Acc Norm-IQR	0.568	0.099	0.792	0.396	0.052	0.656	2.29	0.013
	AUC Acc Norm-Med	0.694	0.359	0.853	0.531	0.218	0.744	3.20	0.001
	AUC Acc-IQR	0.669	0.323	0.839	0.503	0.192	0.723	3.05	0.002
	AUC Acc-Med	0.654	0.282	0.833	0.486	0.164	0.714	2.86	0.003
	Duration-IQR	0.550	0.055	0.784	0.379	0.028	0.645	2.19	0.018
	Duration-Max	0.576	0.108	0.797	0.404	0.057	0.662	2.32	0.012
	Duration-Med	0.631	0.228	0.823	0.460	0.129	0.699	2.67	0.004
	Kurtosis-IQR	0.221	-0.321	0.579	0.124	-0.138	0.408	1.39	0.184
	Kurtosis-Med	0.580	0.160	0.794	0.409	0.087	0.658	2.55	0.006
	Max Acc-IQR	0.638	0.248	0.825	0.468	0.141	0.703	2.73	0.004
	Max Acc-Med	0.408	-0.239	0.715	0.256	-0.107	0.557	1.68	0.081
	Max-RMS Acc-IQR	0.161	-0.468	0.556	0.088	-0.190	0.385	1.24	0.280
	Max-RMS Acc-Med	0.613	0.220	0.810	0.441	0.124	0.681	2.75	0.004
	Med Acc-IQR	0.553	0.059	0.786	0.382	0.030	0.647	2.20	0.017
	Med Acc-Med	**0.782**	**0.544**	**0.895**	0.642	0.374	0.810	4.47	<0.001
	Range Acc-IQR	0.641	0.255	0.827	0.472	0.146	0.705	2.76	0.003
	Range Acc-Med	0.403	-0.249	0.714	0.253	-0.111	0.555	1.66	0.085
	RMS Acc-IQR	0.499	-0.048	0.759	0.332	-0.023	0.612	1.98	0.033
	RMS Acc-Med	0.577	0.110	0.798	0.406	0.058	0.663	2.32	0.012
	SD Acc-IQR	0.513	-0.016	0.766	0.345	-0.008	0.620	2.03	0.028
	SD Acc-Med	0.459	-0.137	0.741	0.298	-0.064	0.589	1.83	0.052
	Skewness-IQR	0.000	-0.757	0.472	0.000	-0.275	0.309	1.00	0.500
	Skewness-Med	0.593	0.184	0.800	0.421	0.101	0.667	2.61	0.005
	SMA Acc-IQR	0.617	0.203	0.816	0.447	0.113	0.689	2.58	0.006
	SMA Acc-Med	0.704	0.380	0.858	0.544	0.235	0.751	3.31	<0.001

Appendix Table G.3 Continued

Feature Category	Feature Name	Average Nights			Single Night			F Test with True Value 0	
			95% Confidence Interval			95% Confidence Interval			
		ICC	Lower Bound	Upper Bound	ICC	Lower Bound	Upper Bound	F Value	Sig
Timing	End Move %-IQR	0.329	-0.390	0.676	0.197	-0.163	0.511	1.49	0.141
	End Move %-Med	-0.623	-2.466	0.228	-0.237	-0.552	0.129	0.62	0.901
	Move/hour	0.693	0.358	0.853	0.530	0.218	0.743	3.19	0.001
	Move/night	0.608	0.175	0.812	0.437	0.096	0.684	2.50	0.007
	Start Move %-IQR	0.329	-0.391	0.676	0.197	-0.163	0.511	1.49	0.141
	Start Move %-Med	-0.625	-2.470	0.227	-0.238	-0.553	0.128	0.62	0.902
	Time Asleep	0.721	0.419	0.866	0.564	0.265	0.764	3.52	<0.001
Velocity and distance	Med Vel-IQR	0.588	0.134	0.803	0.417	0.072	0.671	2.38	0.010
	Med Vel-Med	**0.775**	**0.531**	**0.892**	0.633	0.362	0.805	4.35	<0.001
	RMS Vel-IQR	0.488	-0.071	0.754	0.322	-0.034	0.605	1.93	0.038
	RMS Vel-Med	0.590	0.137	0.804	0.418	0.074	0.672	2.39	0.010
	Total Dist-IQR	0.706	0.396	0.858	0.546	0.247	0.751	3.41	<0.001
	Total Dist-Med	0.673	0.321	0.842	0.507	0.191	0.728	3.02	0.002

* ICC values > 0.5 (moderate reliability) are highlighted grey and those > 0.75 (good reliability) are also bolded.

Appendix Table G.4: ICCs for intra-subject reliability with 1-5 typical nights collected at admission to IPR

		Participants with ≥ 2 Typical Nights (n=31)		Participants with ≥ 3 Typical Nights (n=24)				Participants with ≥ 5 Typical Nights (n=11)			
		Typical Nights 1-2		Typical Nights 1-2		Typical Nights 1-3		Typical Nights 1-2		Typical Nights 1-5	
Feature Category	Feature Name	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night
Change in angle of inclination	Angle Net Change-IQR	0.481	0.317	0.417	0.263	0.552	0.292	0.747	0.597	0.609	0.237
	Angle Net Change-Med	0.662	0.495	0.698	0.536	**0.759**	0.512	0.336	0.202	0.238	0.059
	Angle Rate Change-IQR	0.595	0.424	0.675	0.509	0.560	0.298	**0.818**	0.692	0.609	0.237
	Angle Rate Change-Med	0.738	0.585	**0.782**	0.642	**0.812**	0.591	0.679	0.514	0.620	0.246
	Angle Total Change-IQR	0.576	0.404	0.562	0.391	0.535	0.277	**0.822**	0.697	0.632	0.256
	Angle Total Change-Med	**0.816**	0.689	**0.826**	0.704	**0.820**	0.603	0.708	0.548	0.680	0.298
Change in gravitational acceleration	Grav Change X-IQR	0.571	0.400	0.623	0.452	0.636	0.368	0.498	0.331	0.201	0.048
	Grav Change X-Med	0.467	0.305	0.417	0.263	0.608	0.340	0.649	0.481	-1.170	-0.121
	Grav Change Y-IQR	0.604	0.433	0.588	0.417	0.726	0.469	**0.795**	0.660	0.489	0.161
	Grav Change Y-Med	0.439	0.282	0.443	0.284	0.469	0.227	-0.017	-0.009	0.599	0.230
	Grav Change Z-IQR	**0.815**	0.688	**0.831**	0.711	**0.767**	0.523	-0.404	-0.168	0.326	0.088
	Grav Change Z-Med	0.618	0.447	0.622	0.452	-1.791	-0.272	-0.009	-0.004	-0.191	-0.033
Correlation coefficients between axes	Corr XY-IQR	0.232	0.131	0.174	0.095	-0.161	-0.049	0.360	0.220	-0.230	-0.039
	Corr XY-Med	0.195	0.108	0.501	0.334	0.442	0.209	0.265	0.153	-1.228	-0.124
	Corr XZ-IQR	0.221	0.124	0.359	0.219	0.433	0.203	0.312	0.185	0.441	0.136
	Corr XZ-Med	0.223	0.125	0.482	0.318	0.251	0.101	0.278	0.161	0.405	0.120
	Corr YZ-IQR	0.687	0.523	0.682	0.518	0.265	0.107	0.613	0.442	0.409	0.122
	Corr YZ-Med	0.162	0.088	-0.212	-0.096	0.312	0.131	-1.209	-0.377	0.702	0.320
Frequency domain	Bandwidth-IQR	-0.136	-0.063	-0.276	-0.121	0.019	0.006	-2.650	-0.570	0.319	0.086
	Bandwidth-Med	0.572	0.401	0.644	0.475	0.649	0.381	0.587	0.415	0.595	0.227
	Centroid Freq-IQR	0.135	0.072	0.009	0.004	0.400	0.182	-2.073	-0.509	0.361	0.102
	Centroid Freq-Med	0.501	0.334	0.590	0.419	0.655	0.387	0.327	0.195	0.610	0.239
	Dom Freq 1-IQR	0.272	0.157	0.155	0.084	0.561	0.299	0.206	0.115	0.595	0.227
	Dom Freq 1-Med	0.597	0.426	0.604	0.433	0.629	0.361	0.614	0.443	**0.763**	0.391
	Dom Freq 2-IQR	0.015	0.007	0.049	0.025	0.189	0.072	0.052	0.026	0.706	0.325
	Dom Freq 2-Med	0.469	0.306	0.504	0.337	0.381	0.170	0.379	0.234	0.622	0.247
	Dom Low Freq-IQR	0.340	0.205	0.275	0.160	0.538	0.279	0.557	0.386	0.637	0.260
	Dom Low Freq-Med	-0.095	-0.046	-0.283	-0.124	0.397	0.180	-0.419	-0.173	0.449	0.140
	Mean Freq-IQR	0.286	0.167	0.198	0.110	0.527	0.271	-0.979	-0.329	0.675	0.293
	Mean Freq-Med	0.469	0.306	0.496	0.330	0.557	0.295	0.287	0.167	0.553	0.199

Appendix Table G.4 Continued

		Participants with ≥ 2 Typical Nights		Participants with ≥ 3 Typical Nights				Participants with ≥ 5 Typical Nights			
		Typical Nights 1-2		Typical Nights 1-2		Typical Nights 1-3		Typical Nights 1-2		Typical Nights 1-5	
Feature Category	Feature Name	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night
Frequency Domain	Med Freq-IQR	0.721	0.563	0.740	0.587	0.645	0.377	**0.857**	**0.751**	**0.820**	0.478
	Med Freq-Med	0.634	0.464	0.641	0.472	0.530	0.273	0.615	0.444	0.641	0.263
	Power Dom Freq 1/Total-IQR	0.349	0.211	0.359	0.219	0.570	0.306	**0.756**	0.608	0.718	0.337
	Power Dom Freq 1/Total-Med	0.609	0.438	0.404	0.253	0.663	0.396	0.065	0.034	0.636	0.259
	Power Dom Freq 1-IQR	0.448	0.289	0.402	0.251	0.619	0.352	**0.879**	**0.785**	**0.791**	0.432
	Power Dom Freq 1-Med	0.585	0.414	0.551	0.380	0.616	0.349	0.702	0.541	0.614	0.241
	Power Dom Freq 2-IQR	0.614	0.443	0.567	0.395	0.642	0.374	**0.829**	0.708	**0.756**	0.382
	Power Dom Freq 2-Med	0.704	0.543	0.727	0.571	0.648	0.380	0.590	0.418	0.619	0.245
	Power Dom Low Freq-IQR	0.566	0.395	0.544	0.373	0.695	0.431	**0.883**	**0.790**	**0.778**	0.413
	Power Dom Low Freq-Med	0.669	0.503	0.633	0.463	0.749	0.498	0.678	0.512	0.695	0.313
	Power High Freq/Total-IQR	0.079	0.041	-0.173	-0.079	0.491	0.243	-1.469	-0.423	0.162	0.037
	Power High Freq/Total-Med	0.588	0.416	0.700	0.538	0.739	0.486	0.356	0.217	0.423	0.128
	Power Total-IQR	0.554	0.384	0.556	0.385	0.708	0.448	**0.910**	**0.835**	**0.835**	0.504
	Power Total-Med	0.492	0.327	0.530	0.361	0.652	0.385	0.731	0.576	0.703	0.322
Limb movement percentages	Bilat Ankle %	0.600	0.429	0.635	0.465	0.723	0.465	**0.774**	0.631	**0.859**	0.549
	Unilat Ankle %	0.600	0.429	0.635	0.465	0.723	0.465	**0.774**	0.631	**0.859**	0.549
	Whole Body %	0.393	0.245	0.362	0.221	0.636	0.368	0.512	0.344	0.736	0.357
	Wrist Ankle %	0.122	0.065	0.131	0.070	0.354	0.155	0.551	0.381	0.583	0.218
Median crossings	Num Med Crossings Norm-IQR	0.441	0.283	0.458	0.297	0.281	0.115	0.614	0.444	0.633	0.257
	Num Med Crossings Norm-Med	0.644	0.474	0.664	0.497	**0.753**	0.504	0.667	0.501	**0.792**	0.433
	Num Med Crossings-IQR	0.629	0.459	0.667	0.500	0.674	0.408	**0.770**	0.626	**0.883**	0.603
	Num Med Crossings-Med	0.619	0.448	0.726	0.569	0.584	0.318	**0.828**	0.706	**0.897**	0.636
PLM	Num PLM Norm	**0.827**	0.706	**0.831**	0.712	0.640	0.373	**0.832**	0.712	**0.778**	0.412
	PLM %	0.716	0.557	**0.757**	0.609	0.747	0.497	0.520	0.352	0.742	0.365
	PLM Index	0.740	0.587	**0.771**	0.628	**0.786**	0.550	**0.804**	0.672	**0.766**	0.396

Appendix Table G.4 Continued

		Participants with ≥ 2 Typical Nights		Participants with ≥ 3 Typical Nights				Participants with ≥ 5 Typical Nights			
		Typical Nights 1-2		Typical Nights 1-2		Typical Nights 1-3		Typical Nights 1-2		Typical Nights 1-5	
Feature Category	Feature Name	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night
Relationship to recent movements	Close Cross Corr Peak-IQR	0.652	0.483	0.613	0.442	0.396	0.179	0.347	0.210	0.657	0.277
	Close Cross Corr Peak-Med	0.086	0.045	0.491	0.326	0.512	0.259	0.552	0.381	0.624	0.249
	Close Cross Cov Peak-IQR	0.450	0.290	0.427	0.271	0.622	0.355	**0.763**	0.617	**0.856**	0.544
	Close Cross Cov Peak-Med	0.247	0.141	0.337	0.203	0.702	0.440	0.598	0.426	**0.760**	0.388
	Dom Freq Last 90s-IQR	-0.002	-0.001	-0.004	-0.002	-0.035	-0.012	-0.456	-0.186	0.071	0.015
	Dom Freq Last 90s-Med	0.673	0.508	0.640	0.471	0.626	0.358	0.603	0.432	0.054	0.011
	Max Cross Corr-IQR	0.254	0.145	0.216	0.121	0.408	0.187	0.193	0.107	0.642	0.264
	Max Cross Corr-Med	-0.019	-0.009	0.302	0.178	0.525	0.269	0.345	0.209	0.701	0.319
	Max Cross Cov-IQR	0.460	0.299	0.413	0.260	0.562	0.300	0.739	0.586	**0.849**	0.529
	Max Cross Cov-Med	0.511	0.343	0.685	0.521	**0.765**	0.520	**0.821**	0.697	**0.830**	0.495
	Mean Cross Corr Peaks-IQR	0.409	0.257	0.160	0.087	0.269	0.109	-0.096	-0.046	0.472	0.152
	Mean Cross Corr Peaks-Med	-0.559	-0.219	-0.103	-0.049	0.382	0.171	0.246	0.140	0.703	0.321
	Mean Cross Cov Peaks-IQR	0.179	0.098	-0.115	-0.054	0.436	0.205	0.318	0.189	0.741	0.364
	Mean Cross Cov Peaks-Med	0.434	0.277	0.591	0.420	0.741	0.488	**0.792**	0.655	**0.840**	0.512
	Move Last 90s-IQR	0.225	0.127	0.334	0.200	0.388	0.175	0.309	0.183	0.413	0.123
	Move Last 90s-Med	0.581	0.409	0.629	0.459	0.746	0.495	0.473	0.310	0.617	0.244
	Move Next 90s-IQR	0.225	0.127	0.334	0.200	0.388	0.175	0.309	0.183	0.413	0.123
	Move Next 90s-Med	0.581	0.409	0.629	0.459	0.746	0.495	0.473	0.310	0.617	0.244
	Num Cross Corr Peaks-IQR	0.294	0.173	0.411	0.258	0.436	0.205	0.364	0.222	-0.091	-0.017
	Num Cross Corr Peaks-Med	0.398	0.249	0.276	0.160	0.516	0.262	-0.333	-0.143	0.333	0.091
	Num Cross Cov Peaks-IQR	-0.042	-0.021	-0.214	-0.097	0.415	0.191	**0.816**	0.689	0.294	0.077
	Num Cross Cov Peaks-Med	0.471	0.308	0.401	0.251	0.549	0.289	-0.421	-0.174	0.293	0.077
	Time Since Prev-IQR	-0.021	-0.010	-0.004	-0.002	0.597	0.331	0.391	0.243	0.694	0.312
	Time Since Prev-Med	0.029	0.015	0.245	0.139	0.488	0.241	-0.064	-0.031	0.616	0.243
Signal characteristics	Entropy Rate-IQR	0.516	0.348	0.495	0.329	0.650	0.383	0.568	0.397	**0.789**	0.428
	Entropy Rate-Med	0.517	0.349	0.587	0.416	0.585	0.319	**0.795**	0.659	**0.839**	0.510
	Lempel-Ziv Comp-IQR	0.171	0.093	0.192	0.106	0.536	0.278	0.549	0.379	**0.861**	0.554
	Lempel-Ziv Comp-Med	0.534	0.364	0.603	0.432	0.659	0.392	**0.865**	**0.762**	**0.851**	0.532
	Lyapunov Exp-IQR	0.618	0.448	0.685	0.521	0.620	0.352	0.612	0.441	0.515	0.175
	Lyapunov Exp-Med	0.319	0.190	0.294	0.172	0.536	0.278	0.546	0.375	**0.803**	0.449

Appendix Table G.4 Continued

		Participants with ≥ 2 Typical Nights		Participants with ≥ 3 Typical Nights				Participants with ≥ 5 Typical Nights			
		Typical Nights 1-2		Typical Nights 1-2		Typical Nights 1-3		Typical Nights 1-2		Typical Nights 1-5	
Feature Category	Feature Name	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night
Signal characteristics	Wave Approx-IQR	-0.010	-0.005	0.105	0.055	0.315	0.133	0.108	0.057	0.735	0.357
	Wave Approx-Med	0.688	0.525	0.697	0.535	0.737	0.483	**0.752**	0.602	0.690	0.308
	Wave Energy 1-IQR	0.309	0.182	0.435	0.278	0.595	0.328	-0.177	-0.081	0.323	0.087
	Wave Energy 1-Med	0.209	0.117	0.385	0.239	0.584	0.318	0.313	0.186	0.348	0.097
	Wave Energy 2-IQR	0.637	0.467	0.661	0.493	0.650	0.382	**0.857**	0.750	**0.763**	0.392
	Wave Energy 2-Med	0.716	0.558	0.738	0.585	0.718	0.459	**0.811**	0.682	0.600	0.231
	Wave Energy 3-IQR	**0.804**	0.672	**0.817**	0.690	0.624	0.356	**0.959**	**0.921**	**0.910**	0.668
	Wave Energy 3-Med	0.720	0.563	0.749	0.599	0.736	0.481	**0.755**	0.606	**0.762**	0.391
	Wave Entropy-IQR	-1.117	-0.358	-0.792	-0.284	0.043	0.015	-1.832	-0.478	0.500	0.167
	Wave Entropy-Med	0.668	0.502	0.679	0.514	0.727	0.471	**0.790**	0.653	0.658	0.278
Statistical	AUC Acc Norm-IQR	0.568	0.396	0.616	0.445	0.670	0.404	**0.861**	**0.756**	**0.760**	0.388
	AUC Acc Norm-Med	0.694	0.531	0.696	0.533	0.725	0.467	**0.843**	0.728	**0.791**	0.430
	AUC Acc-IQR	0.669	0.503	0.659	0.492	0.679	0.413	**0.818**	0.693	0.750	0.375
	AUC Acc-Med	0.654	0.486	0.659	0.492	0.726	0.469	**0.833**	0.714	**0.802**	0.448
	Kurtosis-IQR	0.221	0.124	0.248	0.142	0.363	0.160	0.199	0.111	0.371	0.106
	Kurtosis-Med	0.580	0.409	0.523	0.354	0.624	0.356	0.581	0.410	0.691	0.309
	Max Acc-IQR	0.638	0.468	0.700	0.539	**0.782**	0.545	**0.924**	**0.859**	**0.865**	0.562
	Max Acc-Med	0.408	0.256	0.503	0.336	0.683	0.418	**0.865**	**0.762**	**0.851**	0.534
	Max-RMS Acc-IQR	0.161	0.088	0.091	0.047	0.473	0.230	-0.365	-0.154	0.447	0.139
	Max-RMS Acc-Med	0.613	0.441	0.656	0.488	0.630	0.363	0.590	0.419	0.728	0.349
	Med Acc-IQR	0.553	0.382	0.567	0.395	0.560	0.298	0.655	0.487	0.506	0.170
	Med Acc-Med	**0.782**	0.642	**0.767**	0.622	0.692	0.428	**0.771**	0.628	**0.790**	0.430
	Duration-IQR	0.550	0.379	0.474	0.310	0.535	0.277	0.529	0.360	0.641	0.263
	Duration-Max	0.576	0.404	**0.776**	0.634	**0.826**	0.613	0.678	0.513	**0.835**	0.504
	Duration-Med	0.631	0.460	0.604	0.432	0.685	0.420	0.618	0.448	**0.792**	0.433
	Range Acc-IQR	0.641	0.472	0.704	0.543	**0.784**	0.548	**0.926**	**0.862**	**0.867**	0.565
	Range Acc-Med	0.403	0.253	0.499	0.333	0.683	0.417	**0.868**	**0.767**	**0.852**	0.536
	RMS Acc-IQR	0.499	0.332	0.547	0.376	0.701	0.439	**0.872**	**0.773**	**0.817**	0.471
	RMS Acc-Med	0.577	0.406	0.591	0.420	0.726	0.468	**0.815**	0.688	**0.809**	0.458
	SD Acc-IQR	0.513	0.345	0.562	0.391	0.729	0.472	**0.929**	**0.867**	**0.849**	0.529
	SD Acc-Med	0.459	0.298	0.486	0.321	0.676	0.410	**0.856**	0.748	**0.821**	0.479

Appendix Table G.4 Continued

		Participants with ≥ 2 Typical Nights		Participants with ≥ 3 Typical Nights				Participants with ≥ 5 Typical Nights			
		Typical Nights 1-2		Typical Nights 1-2		Typical Nights 1-3		Typical Nights 1-2		Typical Nights 1-5	
Feature Category	Feature Name	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night	Average Nights	Single Night
Statistical	Skewness-IQR	0.000	0.000	-0.006	-0.003	0.240	0.095	-0.211	-0.095	0.310	0.082
	Skewness-Med	0.593	0.421	0.569	0.398	0.663	0.397	0.708	0.548	0.749	0.374
	SMA Acc-IQR	0.617	0.447	0.669	0.502	0.692	0.429	**0.876**	**0.779**	**0.776**	0.409
	SMA Acc-Med	0.704	0.544	0.736	0.583	0.731	0.475	**0.853**	0.744	**0.778**	0.412
Timing	End Move %-IQR	0.329	0.197	0.501	0.334	-0.444	-0.114	**0.825**	0.701	-0.031	-0.006
	End Move %-Med	-0.623	-0.237	-0.820	-0.291	-0.301	-0.083	0.231	0.131	-0.233	-0.039
	Move/hour	0.693	0.530	**0.896**	**0.812**	**0.814**	0.594	**0.945**	**0.896**	**0.751**	0.376
	Move/night	0.608	0.437	**0.796**	0.662	**0.811**	0.588	**0.771**	0.627	0.672	0.291
	Start Move %-IQR	0.329	0.197	0.500	0.334	-0.445	-0.114	**0.824**	0.701	-0.033	-0.006
	Start Move %-Med	-0.625	-0.238	-0.823	-0.291	-0.302	-0.084	0.230	0.130	-0.235	-0.040
	Time Asleep	0.721	0.564	0.710	0.551	**0.775**	0.535	0.618	0.447	0.681	0.299
Velocity and distance	Med Vel-IQR	0.588	0.417	0.618	0.447	0.589	0.323	0.647	0.478	0.507	0.170
	Med Vel-Med	**0.775**	0.633	0.748	0.597	0.677	0.412	**0.805**	0.673	**0.792**	0.432
	RMS Vel-IQR	0.488	0.322	0.531	0.362	0.695	0.431	**0.862**	**0.757**	**0.815**	0.468
	RMS Vel-Med	0.590	0.418	0.599	0.428	0.726	0.469	**0.796**	0.661	**0.802**	0.448
	Total Dist-IQR	0.706	0.546	0.728	0.572	0.725	0.468	**0.811**	0.682	**0.751**	0.377
	Total Dist-Med	0.673	0.507	0.674	0.508	0.722	0.464	**0.807**	0.676	**0.788**	0.426

* ICC values > 0.5 (moderate reliability) are highlighted grey and those > 0.75 (good reliability) are also bolded.

Appendix Table G.5: ICC for stability and direction of change for reliable LA features measured at admission, discharge, and 6-months

			95% Confidence Interval		F Test with True Value 0		
Feature Category	Feature Name	ICC	Lower Bound	Upper Bound	F Value	Sig	Direction of Change
Change in angle of inclination	Angle Net Change-Med	0.495	0.127	0.797	3.704	0.004	Inconsistent
	Angle Rate Change-IQR	0.482	0.133	0.786	3.783	0.004	Inconsistent
	Angle Rate Change-Med	0.427	0.064	0.759	3.125	0.011	Inconsistent
	Angle Total Change-IQR	0.502	0.146	0.798	3.893	0.003	Inconsistent
	Angle Total Change-Med	0.559	0.216	0.827	4.681	0.001	Inconsistent
Change in gravitational acceleration	Grav Change X-IQR	0.538	0.180	0.818	4.244	0.002	Stable
	Grav Change Y-IQR	0.087	-0.224	0.518	1.269	0.304	Inconsistent
	Grav Change Z-IQR	0.424	0.051	0.759	3.033	0.013	Decreasing
	Grav Change Z-Med	0.158	-0.153	0.570	1.565	0.178	Decreasing
Correlation coefficients between axes	Corr YZ-IQR	0.043	-0.174	0.421	1.167	0.363	Inconsistent
Frequency domain	**Bandwidth-Med**	**0.803**	**0.570**	**0.932**	**12.351**	**< 0.001**	**Stable**
	Centroid Freq-Med	0.727	0.445	0.902	8.559	< 0.001	Stable
	Dom Freq 1-Med	0.653	0.335	0.871	6.364	< 0.001	Stable
	Med Freq-IQR	0.575	0.229	0.836	4.815	< 0.001	Stable
	Med Freq-Med	0.746	0.481	0.909	9.722	< 0.001	Stable
	Power Dom Freq 1/Total-Med	**0.783**	**0.532**	**0.925**	**10.925**	**< 0.001**	**Stable**
	Power Dom Freq 1-Med	0.615	0.296	0.852	6.024	< 0.001	Inconsistent
	Power Dom Freq 2-IQR	0.436	0.072	0.764	3.197	0.010	Inconsistent
	Power Dom Freq 2-Med	0.647	0.337	0.867	6.660	< 0.001	Inconsistent
	Power Dom Low Freq-IQR	0.527	0.185	0.809	4.363	0.002	Stable
	Power Dom Low Freq-Med	0.662	0.357	0.874	7.021	< 0.001	Inconsistent
	Power High Freq/Total-Med	0.663	0.351	0.875	6.657	< 0.001	Stable
	Power Total-IQR	0.523	0.169	0.810	4.131	0.002	Stable
Limb movement percentages	Bilat Ankle %	0.299	-0.032	0.672	2.339	0.043	Decreasing
	Unilat Ankle %	0.299	-0.032	0.672	2.339	0.043	Increasing
Median crossings	Num Med Crossings Norm-Med	0.545	0.206	0.819	4.609	0.001	Stable
	Num Med Crossings-IQR	0.264	-0.080	0.654	2.048	0.073	Inconsistent
	Num Med Crossings-Med	0.260	-0.065	0.644	2.097	0.067	Inconsistent
PLM	Num PLM Norm	0.302	-0.052	0.682	2.246	0.051	Inconsistent
	PLM %	0.579	0.248	0.836	5.171	< 0.001	Inconsistent
	PLM Index	0.101	-0.194	0.520	1.338	0.269	Increasing

Appendix Table G.5 Continued

Feature Category	Feature Name	ICC	95% Confidence Interval		F Test with True Value 0		Direction of Change
			Lower Bound	Upper Bound	F Value	Sig	
Relationship to recent movements	**Close Cross Corr Peak-IQR**	**0.756**	**0.498**	**0.914**	**10.199**	**< 0.001**	**Stable**
	Dom Freq Last 90s-Med	**0.762**	**0.508**	**0.916**	**10.607**	**< 0.001**	**Stable**
	Max Cross Cov-Med	0.612	0.284	0.852	5.622	< 0.001	Stable
	Move Last 90s-Med	0.181	-0.162	0.599	1.614	0.163	Inconsistent
	Move Next 90s-Med	0.181	-0.162	0.599	1.614	0.163	Inconsistent
Signal characteristics	Entropy Rate-IQR	0.748	0.479	0.911	9.459	< 0.001	Stable
	Entropy Rate-Med	0.410	0.073	0.742	3.251	0.009	Increasing
	Lempel-Ziv Comp-Med	0.553	0.219	0.822	4.834	< 0.001	Stable
	Lyapunov Exp-IQR	0.676	0.369	0.881	6.960	< 0.001	Stable
	Wave Approx-Med	0.297	-0.037	0.672	2.306	0.046	Inconsistent
	Wave Energy 2-IQR	0.417	0.075	0.748	3.246	0.009	Inconsistent
	Wave Energy 2-Med	0.392	0.047	0.733	2.979	0.014	Inconsistent
	Wave Energy 3-IQR	0.269	-0.050	0.648	2.187	0.057	Increasing
	Wave Energy 3-Med	0.165	-0.113	0.557	1.683	0.144	Inconsistent
	Wave Entropy-Med	0.343	0.000	0.703	2.590	0.028	Increasing
Statistical	AUC Acc Norm-IQR	0.649	0.331	0.869	6.300	< 0.001	Stable
	AUC Acc Norm-Med	0.674	0.371	0.880	7.088	< 0.001	Inconsistent
	AUC Acc-IQR	0.586	0.246	0.840	5.052	< 0.001	Stable
	AUC Acc-Med	0.701	0.408	0.891	7.797	< 0.001	Stable
	Kurtosis-Med	0.577	0.228	0.837	4.799	< 0.001	Stable
	Max Acc-IQR	0.723	0.447	0.900	9.050	< 0.001	Stable
	Max-RMS Acc-Med	0.596	0.256	0.845	5.159	< 0.001	Stable
	Med Acc-IQR	0.543	0.201	0.818	4.536	0.001	Stable
	Med Acc-Med	0.646	0.328	0.867	6.285	< 0.001	Stable
	Duration-IQR	0.413	0.041	0.752	2.949	0.015	Decreasing
	Duration-Max	0.143	-0.128	0.537	1.575	0.176	Increasing
	Duration-Med	0.726	0.437	0.902	8.313	< 0.001	Stable
	Range Acc-IQR	0.725	0.451	0.901	9.142	< 0.001	Stable
	RMS Acc-Med	0.643	0.325	0.866	6.257	< 0.001	Stable
	SD Acc-IQR	0.701	0.413	0.891	8.054	< 0.001	Stable
	Skewness-Med	0.612	0.270	0.854	5.340	< 0.001	Stable
	SMA Acc-IQR	0.660	0.349	0.874	6.657	< 0.001	Stable
	SMA Acc-Med	0.661	0.352	0.874	6.745	< 0.001	Inconsistent

Appendix Table G.5 Continued

Feature Category	Feature Name	ICC	95% Confidence Interval		F Test with True Value 0		Direction of Change
			Lower Bound	Upper Bound	F Value	Sig	
Timing	Move/hour	0.129	-0.171	0.543	1.449	0.221	Inconsistent
	Move/night	0.147	-0.158	0.558	1.525	0.192	Inconsistent
	Time Asleep	0.302	-0.031	0.675	2.346	0.043	Inconsistent
Velocity and distance	Med Vel-IQR	0.535	0.180	0.816	4.244	0.002	Stable
	Med Vel-Med	0.350	0.015	0.705	2.711	0.022	Inconsistent
	RMS Vel-Med	0.475	0.142	0.779	4.254	0.002	Inconsistent
	Total Dist-IQR	0.552	0.203	0.824	4.510	0.001	Stable
	Total Dist-Med	0.702	0.412	0.892	7.923	< 0.001	Stable

* If also visually confirmed, ICC values > 0.5 (moderate reliability) are highlighted grey and those > 0.75 (good reliability) are also bolded.

Appendix H Aim 4 Supplemental Material

Appendix Table H.1: Continous impairment, ambulation, and data collection measures for Aim 4 from admission to IPR through 6-months post-discharge with 1-year outcomes added for reference.

	Aim 4a							
Continuous	Admission		Discharge		6-months		1-year	
Demographics	n	Mean ± SD (Range)	n	Mean ± SD (Range)	n	Mean ± SD (Range)	n	Mean ± SD (Range)
LEMS (Strength)	12	23.8 ± 16.0 (0 - 47)	12	28.7 ± 16.0 (0 - 45)	9	38.9 ± 11.5 (15 - 50)	6	35.0 ± 18.1 (0 - 49)
Lower Limb LT (Sensation)	11	10.5 ± 7.1 (0 - 20)	11	10.7 ± 6.5 (0 - 18)	8	16.0 ± 5.6 (3 - 20)	6	17.8 ± 3.1 (13 - 20)
WISCI-II	12	2.4 ± 4.9 (0 - 17)	12	8.2 ± 7.7 (0 - 20)	12	13.7 ± 8.8 (0 - 20)	8	15.6 ± 7.3 (0 - 20)
10mWT (m/s)	12	0.03 ± 0.07 (0.00 - 0.22)	11	0.37 ± 0.43 (0.00 - 1.16)	12	0.63 ± 0.54 (0.00 - 1.80)	8	0.70 ± 0.36 (0.00 - 1.08)
6MWT (m)	12	15.3 ± 46.1 (0.0 - 160.0)	12	112.3 ± 144.5 (0.0 - 457.2)	12	184.3 ± 145.3 (0.0 - 404.8)	8	262.1 ± 175.4 (0.0 - 614.5)
Number of Nights Collected	12	4.6 ± 1.9 (2 - 7)	12	5.3 ± 2.2 (2 - 7)	12	6.2 ± 1.3 (4 - 7)	8	6.6 ± 1.1 (4 - 7)
Number of Typical Nights Collected	12	3.5 ± 2.0 (1 - 7)	12	4.4 ± 2.1 (2 - 7)	12	4.8 ± 1.7 (2 - 7)	8	4.5 ± 1.8 (2 - 7)
Days from Injury to Start of Data Collection	12	17.5 ± 15.9 (9 - 65)	12	39.7 ± 16.5 (18 - 76)	12	229.3 ± 24.2 (184 - 274)	8	414.5 ± 21.9 (390 - 448)
	Aim 4b							
Continuous	Admission		Discharge		6-months		1-year	
Demographics	n	Mean ± SD (Range)	n	Mean ± SD (Range)	n	Mean ± SD (Range)	n	Mean ± SD (Range)
LEMS	14	22.5 ± 16.1 (0 - 47)	14	27.8 ± 17.3 (0 - 45)	10	39.0 ± 10.9 (15 - 50)	6	35.0 ± 18.1 (0 - 49)
Lower Limb LT	13	10.3 ± 7.5 (0 - 20)	13	10.5 ± 7.0 (0 - 18)	8	16.0 ± 5.6 (3 - 20)	6	17.8 ± 3.1 (13 - 20)
WISCI-II	14	2.1 ± 4.6 (0 - 17)	14	7.6 ± 7.4 (0 - 20)	14	12.9 ± 8.9 (0 - 20)	8	15.6 ± 7.3 (0 - 20)
10mWT (m/s)	14	0.02 ± 0.06 (0.00 - 0.22)	13	0.33 ± 0.41 (0.00 - 1.16)	13	0.59 ± 0.54 (0.00 - 1.80)	8	0.70 ± 0.36 (0.00 - 1.08)
6MWT (m)	14	13.1 ± 42.8 (0.0 - 160.0)	14	100.9 ± 136.6 (0.0 - 457.2)	13	170.1 ± 148.2 (0.0 - 404.8)	8	262.1 ± 175.4 (0.0 - 614.5)
Number of Nights Collected	14	4.4 ± 1.9 (2 - 7)	14	5.1 ± 2.3 (2 - 7)	13	6.2 ± 1.3 (4 - 7)	8	6.6 ± 1.1 (4 - 7)
Number of Typical Nights Collected	14	3.4 ± 1.9 (1 - 7)	14	4.4 ± 2.1 (2 - 7)	13	4.9 ± 1.7 (2 - 7)	8	4.5 ± 1.8 (2 - 7)
Days from Injury to Start of Data Collection	14	19.0 ± 15.2 (9 - 65)	14	43.0 ± 17.4 (18 - 76)	13	230.8 ± 23.9 (184 - 274)	8	414.5 ± 21.9 (390 - 448)

Appendix Table H.2: Confusion matrices of ambulatory categoizations for participants included in Aims 3b and 4a across each time point

Admission to IPR									
		WISCI-II Category				6MWT Category			
Ambulatory Ability Category		Physical Assist or Non-Amb	AD, No Physical Assist	No AD or Assist	Total (% of column)	Non-Amb	Household Amb	Community Amb	Total (% of column)
10mWT Category	Non-Amb (0m/s)	10	0	0	10 (83.3%)	10	0	0	10 (83.3%)
	Household Amb (0.01-.44m/s)	2	0	0	2 (16.7%)	0	2	0	2 (16.7%)
	Community Amb (>0.44m/s)	0	0	0	0 (0.0%)	0	0	0	0 (0.0%)
	Total (% of row)	12 (100%)	0 (0.0%)	0 (0.0%)	12 (100%)	10 (83.3%)	2 (16.7%)	0 (0.0%)	12 (100%)
6MWT Category	Non-Amb (0m)	10	0	0	10 (83.3%)				
	Household Amb (1-204m)	2	0	0	2 (16.7%)				
	Community Amb (>204m)	0	0	0	0 (0.0%)				
	Total (% of row)	12 (100%)	0 (0.0%)	0 (0.0%)	12 (100%)				
Discharge from IPR									
		WISCI-II Category				6MWT Category			
Ambulatory Ability Category		Physical Assist or Non-Amb	AD, No Physical Assist	No AD or Assist	Total (% of column)	Non-Amb	Household Amb	Community Amb	Total (% of column)
10mWT Category	Non-Amb (0m/s)	5	0	0	5 (45.5%)	5	0	0	5 (45.5%)
	Household Amb (0.01-.44m/s)	0	1	0	1 (9.1%)	0	1	0	1 (9.1%)
	Community Amb (>0.44m/s)	0	3	2	5 (45.5%)	0	2	3	5 (45.5%)
	Total (% of row)	5 (45.5%)	4 (36.4%)	2 (18.2%)	11 (100%)	5 (45.5%)	3 (27.3%)	3 (27.3%)	11 (100%)
6MWT Category	Non-Amb (0m)	5	0	0	5 (41.7%)				
	Household Amb (1-204m)	0	4	0	4 (33.3%)				
	Community Amb (>204m)	0	1	2	3 (25.0%)				
	Total (% of row)	5 (41.7%)	5 (41.7%)	2 (16.7%)	12 (100%)				
6-months Post-Discharge from IPR									
		WISCI-II Category				6MWT Category			
Ambulatory Ability Category		Physical Assist or Non-Amb	AD, No Physical Assist	No AD or Assist	Total (% of column)	Non-Amb	Household Amb	Community Amb	Total (% of column)
10mWT Category	Non-Amb (0m/s)	3	0	0	3 (25.0%)	3	0	0	3 (25.0%)
	Household Amb (0.01-.44m/s)	0	2	0	2 (16.7%)	0	2	0	2 (16.7%)
	Community Amb (>0.44m/s)	0	2	5	7 (58.3%)	0	1	6	7 (58.3%)
	Total (% of row)	3 (25.0%)	4 (33.3%)	5 (41.7%)	12 (100%)	3 (25.0%)	3 (25.0%)	6 (50.0%)	12 (100%)
6MWT Category	Non-Amb (0m)	3	0	0	3 (25.0%)				
	Household Amb (1-204m)	0	2	1	3 (25.0%)				
	Community Amb (>204m)	0	2	4	6 (50.0%)				
	Total (% of row)	3 (25.0%)	4 (33.3%)	5 (41.7%)	12 (100%)				

Abbreviations: AD= Assistive Device, Amb= Ambulatory/Ambulation

Appendix Table H.3: Categorical demographics from participants included and excluded from Aim 4b*†

	Aim 4b N (%)					
	Included in Analysis (n=14)		**Excluded From Analysis** (n=11)		**t test Sig**	
Categorical Demographics	Admission	Discharge	Admission	Discharge	Admission	Discharge
Sex					0.189	
Female	8 (57.1%)		9 (81.8%)			
Male	6 (42.9%)		2 (18.2%)			
Race/Ethnicity					0.479	
Non-Hispanic White	11 (78.6%)		6 (54.5%)			
Non-Hispanic Black	1 (7.1%)		2 (18.2%)			
Non-Hispanic Other Race	0 (0.0%)		1 (9.1%)			
Hispanic (Any Race)	2 (14.3%)		2 (18.2%)			
Veteran					0.191	
Not A Veteran	12 (85.7%)		11 (100%)			
Veteran	2 (14.3%)		0 (0.0%)			
Annual Household Income					0.698	
< $25,000	2 (14.3%)		4 (36.4%)			
$25,000 - $49,999	3 (21.4%)		2 (18.2%)			
$50,000 -$74,999	3 (21.4%)		1 (9.1%)			
≥ $75,000	2 (14.3%)		2 (18.2%)			
Decline to Answer or Unknown	4 (28.6%)		2 (18.2%)			
Education					0.477	
Less Than High School	2 (14.3%)		0 (0.0%)			
High School Diploma/GED	7 (50.0%)		4 (36.4%)			
Associate's Degree	2 (14.3%)		4 (36.4%)			
Bachelor's Degree	1 (7.1%)		1 (9.1%)			
Graduate Degree	1 (7.1%)		0 (0.0%)			
Other	1 (7.1%)		2 (18.2%)			
Medical Insurance					0.771	
Private	5 (35.7%)		5 (45.5%)			
Medicaid	3 (21.4%)		3 (27.3%)			
Medicare	1 (7.1%)		0 (0.0%)			
No Insurance	1 (7.1%)		0 (0.0%)			
Other/Multiple	4 (28.6%)		3 (27.3%)			

Appendix Table H.3 Continued

	Aim 4b N (%)					
	Included in Analysis (n=14)		**Excluded From Analysis** (n=11)		**t test Sig**	
Categorical Demographics	Admission	Discharge	Admission	Discharge	Admission	Discharge
SCI Neurological Category					0.509	0.311
Motor Complete (AIS A or B) Tetraplegia	1 (7.1%)	1 (7.1%)	1 (9.1%)	0 (0.0%)		
Motor Complete (AIS A or B) Paraplegia	4 (28.6%)	3 (21.4%)	1 (9.1%)	0 (0.0%)		
AIS C Tetraplegia	2 (14.3%)	1 (7.1%)	5 (45.5%)	4 (36.4%)		
AIS C Paraplegia	1 (7.1%)	2 (14.3%)	0 (0.0%)	1 (9.1%)		
AIS D Tetraplegia	5 (35.7%)	6 (42.9%)	3 (27.3%)	5 (45.5%)		
AIS D Paraplegia	1 (7.1%)	1 (7.1%)	1 (9.1%)	1 (9.1%)		
Primary Mode of Mobility					0.102	0.006
Power Wheelchair	11 (78.6%)	4 (28.6%)	11 (100%)	10 (90.9%)		
Manual Wheelchair	3 (21.4%)	7 (50.0%)	0 (0.0%)	0 (0.0%)		
Ambulation	0 (0.0%)	3 (21.4%)	0 (0.0%)	1 (9.1%)		
WISCI-II					N/A	0.086
Requires Physical Assistance (or Non-Ambulatory)	14 (100%)	7 (50.0%)	11 (100%)	10 (90.9%)		
Requires AD, but no Physical Assistance	0 (0.0%)	5 (35.7%)	0 (0.0%)	1 (9.1%)		
Requires No AD or Physical Assistance	0 (0.0%)	2 (14.3%)	0 (0.0%)	0 (0.0%)		
10mWT					0.191	0.083
Non-ambulatory (0 m/s)	12 (85.7%)	6 (46.2%)	11 (100%)	8 (80.0%)		
Household Ambulator (0.01-.44 m/s)	2 (14.3%)	2 (15.4%)	0 (0.0%)	2 (20.0%)		
Community Ambulator (>.44 m/s)	0 (0.0%)	5 (38.5%)	0 (0.0%)	0 (0.0%)		
6MWT					0.191	0.176
Non-ambulatory (0 m)	12 (85.7%)	6 (42.9%)	11 (100%)	8 (72.7%)		
Household Ambulator (1-204 m)	2 (14.3%)	5 (35.7%)	0 (0.0%)	3 (27.3%)		
Community Ambulator (> 204 m)	0 (0.0%)	3 (21.4%)	0 (0.0%)	0 (0.0%)		

* Significant differences between those included and excluded from the analysis ($p < 0.05$) are highlighted grey

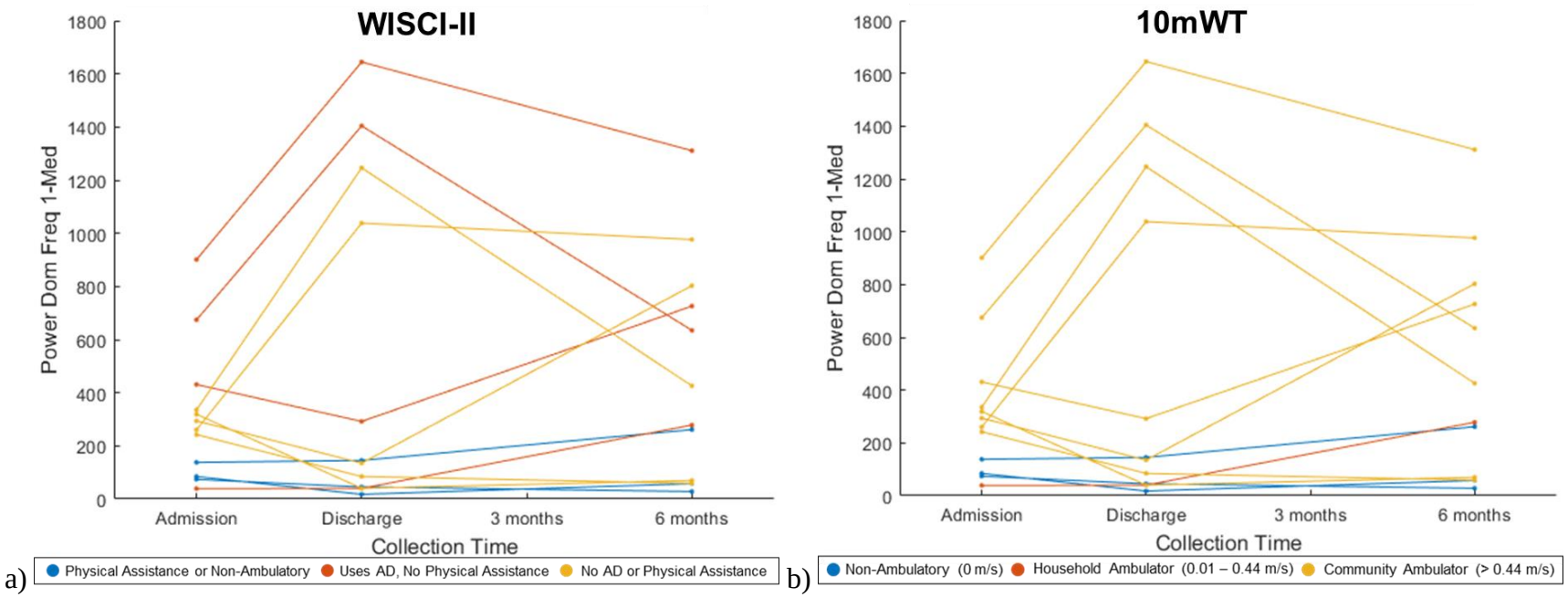
† Missing and not eligible participants are the same as in Appendix Table G.1 and Appendix Table G.2, and not repeated here

Appendix Table H.4: Continuous demographics from participants included and excluded from Aim 4b*†

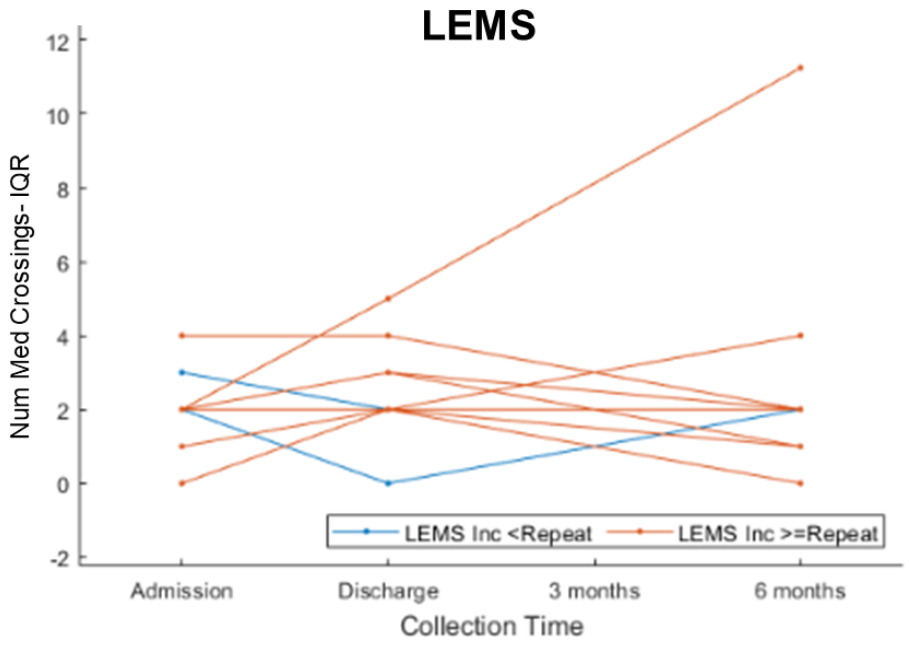
	Aim 4b Mean ± SD (Range)					
	Included in Analysis (n=14)		**Excluded From Analysis** (n=11)		**t test Sig**	
Continuous Demographics	Admission	Discharge	Admission	Discharge	Admission	Discharge
Age	43.8 ± 17.5 (18 - 71)		43.8 ± 17.5 (18 - 71)		0.113	
BMI	27.9 ± 3.5 (23 - 35)		27.9 ± 3.5 (23 - 35)		0.610	
Length of Stay in IPR (Days)	36.1 ± 11.4 (17 - 53)		46.7 ± 10.6 (30 - 64)		0.021	
Days from Injury to Start of IPR	15.9 ± 15.1 (5 - 62)		17.1 ± 8.1 (8 - 30)		0.820	
Days from Injury to Data Collection	19.0 ± 15.2 (9 - 65)	43.0 ± 17.4 (18 - 76)	21.8 ± 9.1 (10 - 36)	56.1 ± 10.2 (41 - 72)	0.593	0.067
LEMS	22.5 ± 16.1 (0 - 47)	27.8 ± 17.3 (0 - 45)	20.2 ± 13.7 (0 - 36)	28.5 ± 17.9 (0 - 48)	0.707	0.926
LELTS	10.3 ± 7.5 (0 - 20)	10.5 ± 7.0 (0 - 18)	10.8 ± 6.0 (0 - 18)	10.4 ± 6.2 (0 - 20)	0.857	0.972
WISCI-II	2.1 ± 4.6 (0 - 17)	7.6 ± 7.4 (0 - 20)	0.2 ± 0.4 (0 - 1)	3.5 ± 6.3 (0 - 17)	0.150	0.153
10mWT (m/s)	0.0 ± 0.1 (0 - 0)	0.3 ± 0.4 (0 - 1)	0.0 ± 0.0 (0 - 0)	0.1 ± 0.1 (0 - 0)	0.209	0.044
6MWT (m)	13.1 ± 42.8 (0 - 160)	100.9 ± 136.6 (0 - 457)	0.0 ± 0.0 (0 - 0)	30.4 ± 56.2 (0 - 161)	0.271	0.123

* Significant differences between those included and excluded from the analysis ($p < 0.05$) are highlighted grey

† Missing and not eligible participants are the same as in Appendix Table G.2, and not repeated here



Appendix Figure H.1: Per participant line graphs of LA over time for Power Dom Freq 1-Med colored by a) WISCI-II and b) 10mWT category by 6-months post-discharge from IPR. In a) it can be seen that participants who require physical assistance or are non-ambulatory do not change much over time, compared to those who can ambulate with or without an AD. In b) it can be seen that only community ambulators are widely variable over time, while those who are non-ambulatory or household ambulators stay relatively stable.



Appendix Figure H.2: Changes in Num Med Crossings- IQR over time categorized by if the participant increased their LEMS greater than the repeatability threshold of 6.9 points. This feature which was found to be significnatly correlated with the change in LEMS from admission to discharge (ρ= .606) but not from discharge to 6-months (likely influenced by outlier). From admission to discharge it can be seen that all participants who increase their LEMS score past the threshold (organge) also increased their variability in movement smoothness, however the participants that did not increase their LEMS past the repeatability threshold (blue) were the only participants to decrease their varaibility in movement smoothness.

Appendix Table H.5: Correlations between all reliable LA features measured at admission and ambulation outcomes at 6-months*†‡§

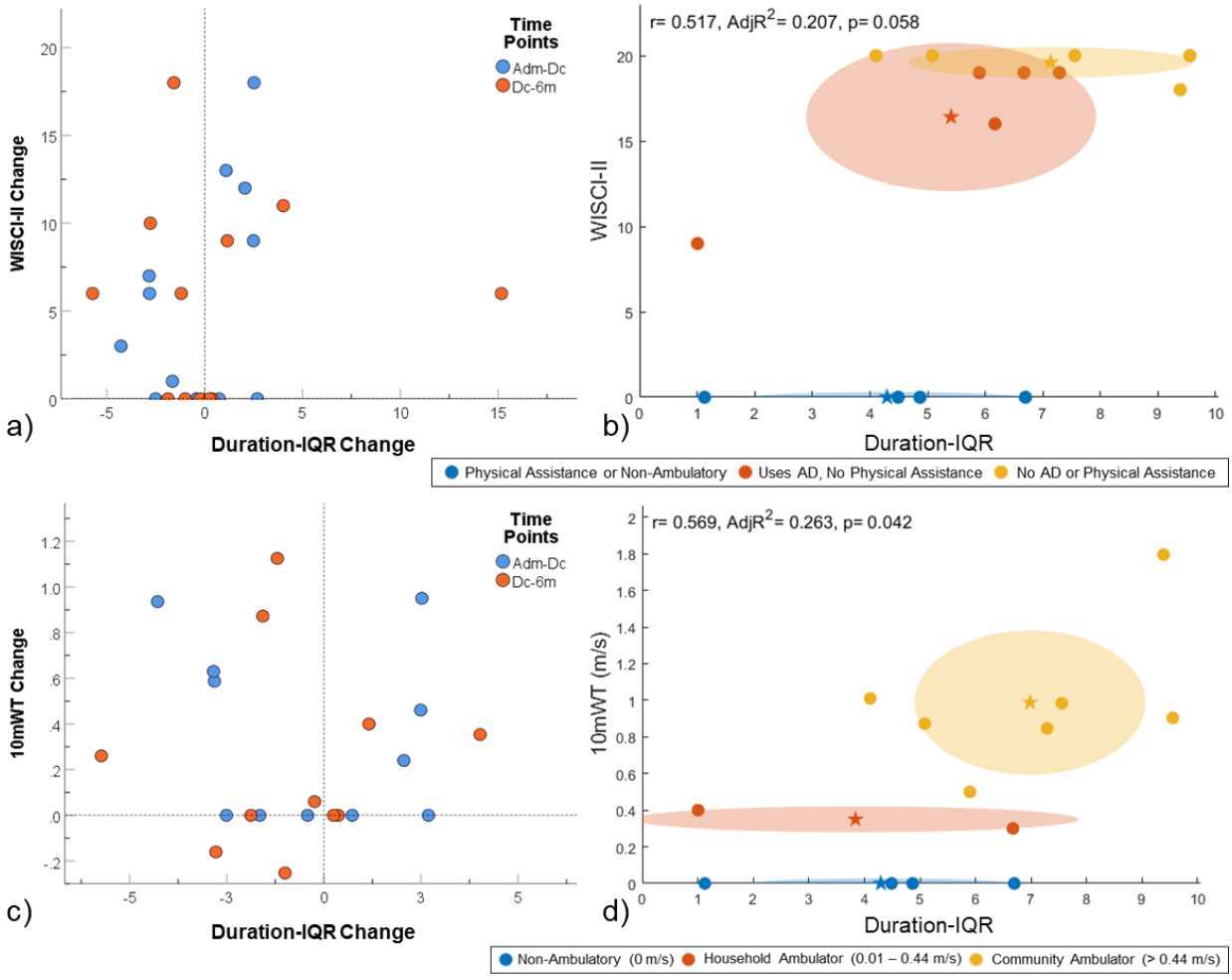
		WISCI-II		10mWT		6MWT	
Feature Category	LA Feature	r	p	r	p	r	p
Change in angle of inclination	Angle Net Change-Med	0.318	0.268	0.369	0.214	0.324	0.281
	Angle Rate Change-IQR §	0.324	0.258	0.452	0.121	0.399	0.176
	Angle Rate Change-Med	**0.513**	**0.061**	0.421	0.152	0.460	0.114
	Angle Total Change-IQR	**0.468**	**0.092**	**0.651**	**0.016**	**0.580**	**0.038**
	Angle Total Change-Med	**0.471**	**0.089**	0.382	0.197	0.432	0.141
Change in gravitational acceleration	*Grav Change X-IQR*	-0.004	0.990	0.150	0.624	0.120	0.696
	Grav Change Y-IQR	0.103	0.727	0.326	0.278	0.184	0.548
	Grav Change Z-IQR	0.341	0.233	0.316	0.294	0.292	0.333
	Grav Change Z-Med	-0.212	0.467	-0.167	0.586	-0.141	0.647
Correlation coefficients between axes	Corr YZ-IQR	0.204	0.485	-0.001	0.999	-0.128	0.677
Frequency domain	*Bandwidth-Med*	**-0.662**	**0.010**	-0.421	0.152	-0.424	0.149
	Centroid Freq-Med	**-0.657**	**0.011**	-0.445	0.128	**-0.491**	**0.088**
	Power Dom Freq 1/Total-Med	**0.499**	**0.069**	0.305	0.310	0.386	0.192
	Dom Freq 1-Med	**-0.641**	**0.013**	**-0.506**	**0.078**	**-0.520**	**0.069**
	Med Freq-IQR	0.094	0.749	0.032	0.916	0.102	0.740
	Med Freq-Med	-0.445	0.111	-0.387	0.192	-0.451	0.122
	Power Dom Freq 1-Med	**0.489**	**0.076**	0.277	0.359	0.292	0.333
	Power Dom Freq 2-IQR	**0.652**	**0.011**	**0.755**	**0.003**	**0.651**	**0.016**
	Power Dom Freq 2-Med	**0.596**	**0.024**	0.369	0.215	0.376	0.206
	Power Dom Low Freq-IQR	**0.698**	**0.006**	**0.776**	**0.002**	**0.664**	**0.013**
	Power Dom Low Freq-Med	**0.547**	**0.043**	0.332	0.267	0.334	0.264
	Power High Freq/Total-Med	**-0.511**	**0.062**	-0.338	0.259	-0.359	0.228
	Power Total-IQR	**0.712**	**0.004**	**0.768**	**0.002**	**0.614**	**0.025**
Limb movement percentages	Bilat Ankle %	-0.247	0.395	-0.300	0.320	**-0.487**	**0.092**
	Unilat Ankle %	0.247	0.395	0.300	0.320	**0.487**	**0.092**
Median crossings	*Num Med Crossings Norm-Med*	**-0.708**	**0.005**	**-0.570**	**0.042**	**-0.546**	**0.054**
	Num Med Crossings-IQR	0.048	0.869	-0.160	0.602	-0.156	0.611
	Num Med Crossings-Med §	0.065	0.826	-0.096	0.755	-0.006	0.984
PLM	Num PLM Norm §	0.230	0.429	-0.047	0.879	0.067	0.829
	PLM %	-0.066	0.824	-0.164	0.592	-0.109	0.722
	PLM Index §	-0.208	0.476	-0.265	0.381	-0.220	0.470
Relationship to recent movements	*Close Cross Corr Peak-IQR*	**0.691**	**0.006**	**0.562**	**0.046**	**0.482**	**0.095**
	Dom Freq Last 90s-Med	-0.151	0.607	-0.237	0.435	-0.072	0.816
	Max Cross Cov-Med	0.087	0.766	-0.018	0.952	0.039	0.899
	Move Last 90s-Med §	-0.059	0.841	-0.164	0.591	-0.057	0.853
	Move Next 90s-Med §	-0.059	0.841	-0.164	0.591	-0.057	0.853

Appendix Table H.5 Continued

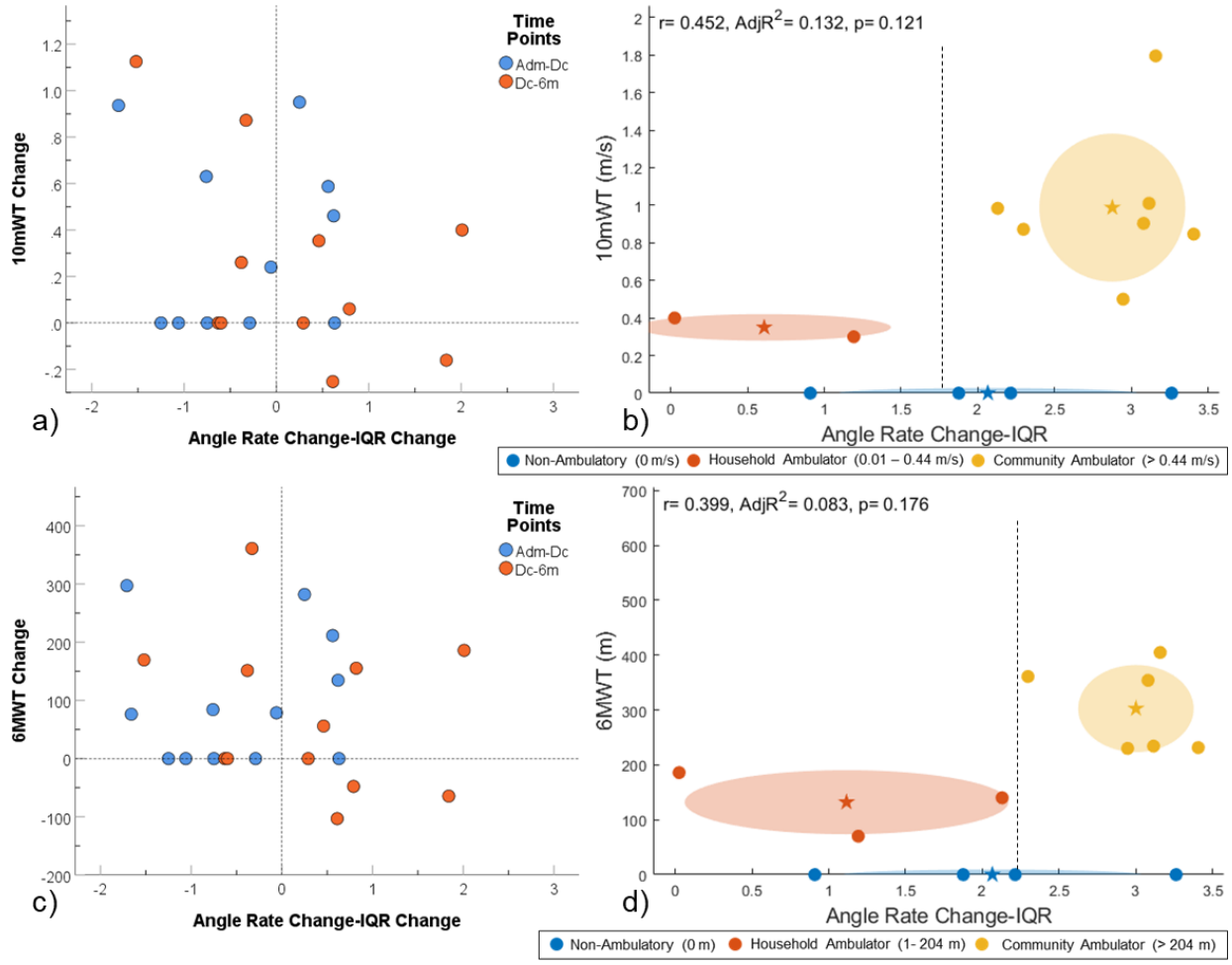
		WISCI-II		10mWT		6MWT	
Feature Category	LA Feature	r	p	r	p	r	p
Signal characteristics	*Entropy Rate-IQR*	0.329	0.251	0.416	0.157	0.186	0.543
	Entropy Rate-Med §	0.382	0.178	0.184	0.548	0.134	0.663
	Lempel-Ziv Comp-Med	-0.089	0.762	-0.090	0.771	0.041	0.895
	Lyapunov Exp-IQR	**0.620**	**0.018**	0.407	0.167	0.417	0.157
	Wave Approx-Med	-0.185	0.526	-0.115	0.709	-0.021	0.946
	Wave Energy 2-IQR §	0.378	0.182	0.092	0.765	0.079	0.798
	Wave Energy 2-Med	0.270	0.350	0.184	0.548	0.089	0.772
	Wave Energy 3-IQR	0.025	0.932	-0.090	0.771	-0.192	0.530
	Wave Energy 3-Med	0.201	0.492	0.115	0.708	-0.010	0.973
	Wave Entropy-Med	0.103	0.726	0.072	0.815	-0.011	0.972
Statistical	*AUC Acc Norm-IQR*	**0.747**	**0.002**	**0.733**	**0.004**	**0.681**	**0.010**
	AUC Acc Norm-Med	0.455	0.102	0.268	0.376	0.245	0.420
	AUC Acc-IQR	**0.699**	**0.005**	**0.735**	**0.004**	**0.679**	**0.011**
	AUC Acc-Med	**0.537**	**0.048**	0.424	0.149	0.426	0.147
	Duration-IQR §	**0.517**	**0.058**	**0.569**	**0.042**	0.465	0.110
	Duration-Max	**0.622**	**0.018**	0.425	0.148	**0.503**	**0.080**
	Duration-Med	**0.521**	**0.056**	**0.546**	**0.053**	**0.529**	**0.063**
	Kurtosis-Med	-0.008	0.978	0.172	0.575	0.039	0.899
	Max Acc-IQR	**0.611**	**0.020**	**0.668**	**0.013**	0.443	0.130
	Max-RMS Acc-Med	0.145	0.620	0.220	0.470	0.085	0.783
	Med Acc-IQR	**0.703**	**0.005**	**0.673**	**0.012**	**0.701**	**0.008**
	Med Acc-Med	0.391	0.167	0.282	0.351	0.344	0.250
	Range Acc-IQR	**0.612**	**0.020**	**0.669**	**0.012**	0.444	0.128
	RMS Acc-Med	**0.472**	**0.089**	0.256	0.399	0.230	0.450
	SD Acc-IQR	**0.741**	**0.002**	**0.694**	**0.009**	**0.556**	**0.049**
	Skewness-Med	0.003	0.992	0.155	0.614	0.014	0.963
	SMA Acc-IQR	**0.710**	**0.004**	**0.720**	**0.006**	**0.655**	**0.015**
	SMA Acc-Med	**0.504**	**0.066**	0.340	0.256	0.327	0.275
Timing	Move/hour §	0.163	0.578	-0.053	0.863	0.031	0.920
	Move/night §	0.141	0.631	-0.074	0.811	0.020	0.948
	Time Asleep §	0.268	0.354	0.099	0.748	0.132	0.668
	Med Vel-IQR	**0.699**	**0.005**	**0.672**	**0.012**	**0.701**	**0.008**
Velocity and distance	Med Vel-Med	0.358	0.209	0.256	0.398	0.302	0.316
	RMS Vel-Med	**0.476**	**0.085**	0.257	0.397	0.231	0.447
	Total Dist-IQR	**0.687**	**0.007**	**0.776**	**0.002**	**0.701**	**0.008**
	Total Dist-Med	**0.574**	**0.032**	0.448	0.125	0.468	0.107

* Outcomes that had a correlation p< 0.1 are bolded
† Outcomes where at least 2 groups could be visually well isolated when plotted are highlighted grey
‡ LA features that were found to be stable over time in Aim 3b are italicized
§ Indicates a feature that was variable over time in Aim 3b, but not related to changes in ambulatory ability or impairment in Aim 4a

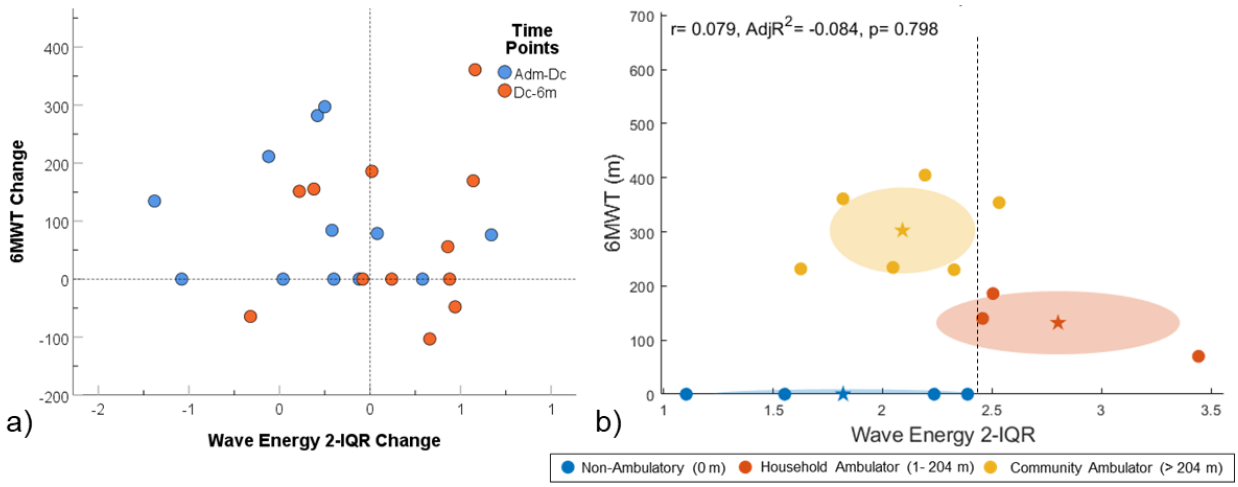
Appendix H.1 Supplemental Visual Analyses for Features Significant in Aim 4b, but Not Aim 4a



Appendix Figure H.3: Duration-IQR supplemental visual analysis (variable LA feature that was related to 6-month WISCI-II and 10mWT when measured at admission [Aim 4b], but not change in any outcomes over time [Aim 4a]). a) Shows no trend to change in WISCI-II over time, b) admission feature has significant correlation to WISCI-II at 6-months, c) no trend to change in 10mWT over time, b) admission feature has significant correlation to 10mWT at 6-months.



Appendix Figure H.4: Angle Rate Change-IQR supplemental visual analysis (variable LA feature that was related to 6-month 10mWT and 6MWT when measured at admission [Aim 4b], but not change in any outcomes over time [Aim 4a]). a) Shows no trend to change in 10mWT over time, b) admission feature is visually separable between the household and community ambulator groups for the 10mWT at 6-months, c) no trend to change in 6MWT over time, b) admission feature is visually separable between the household and community ambulator groups for the 6MWT at 6-months.



Appendix Figure H.5: Wave Energy 2-IQR supplemental visual analysis (variable LA feature that was related to 6-month 6MWT when measured at admission [Aim 4b], but not change in any outcomes over time [Aim 4a]). a) Shows no trend to change in 6MWT over time, b) admission feature is visually separable between the household ambulator and non-ambulatory groups for the 6MWT at 6-months.

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