Gait Measurement in Chronic Mild Traumatic Brain Injury: A Model Approach

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Abstract

Introduction

Mild traumatic brain injury (mTBI) can impact gait, with deficits linked to underlying neural disturbances in cognitive, motor and sensory systems. Gait is complex as it is comprised of multiple characteristics that are sensitive to underlying neural deficits. However, there is currently no clear framework to guide selection of gait characteristics in mTBI. This study developed a model of gait in chronic mTBI and replicated this in a separate group of controls, to provide a comprehensive and structured methodology on which to base gait assessment and analysis.

Methods

Fifty-two people with chronic mTBI and 59 controls completed a controlled laboratory gait assessment; walking for two minutes back and forth over a 13m distance while wearing five wirelessly synchronized inertial sensors. Thirteen gait characteristics derived from the inertial sensors were selected for entry into the principle component analysis based on previous literature, robustness and novelty. Principle component analysis was then used to derive domains (components) of gait.

Results

Four gait domains were derived for our chronic mTBI group (variability, rhythm, pace and turning) and this was replicated in a separate control cohort. Domains totaled 80.8% and 77.4% of variance in gait for chronic mTBI and controls, respectively. Gait characteristic loading was unambiguous for all features, with the exception of gait speed in controls that loaded on pace and rhythm domains.

Conclusion

This study contributes a four component model of gait in chronic mTBI and controls that can be used to comprehensively assess and analyze gait and underlying mechanisms involved in impairment, or examine the influence of interventions.

KEYWORDS: gait, mild traumatic brain injury, principle component analysis, inertial sensors

1. Introduction

Gait assessment is a simple marker for overall health, as it predicts quality of life, survival, cognitive decline and falls [1]. Gait becomes more difficult with age and neurological deficits, which cause transfer from automatic to cognitive (higher level) control to maintain performance, particularly with complex environments or tasks [2]. Gait is complex and multifactorial, and therefore cannot be captured by one characteristic, such as gait speed which is universally used to reflect gait due to its robust clinometric properties [3]. Gait is comprised of multiple characteristics including temporal, spatial and variability characteristics that can further discriminate pathological effects; therefore, measuring multiple gait characteristics is critical to examine specific features of disease or injury [2]. Despite this, most previous mild traumatic brain injury (mTBI) gait research has focused on singular gait characteristics (i.e. primarily gait speed) [4], likely due to the ease of measurement and to avoid multiple comparison statistical issues. Gait speed is an accumulation of many gait features and although it provides a measure of global performance and is sensitive to pathology and age [3], it is not specific and therefore may not reflect precise underlying deficits [5]. For example, gait speed is not discriminative or reflective of subtle and selective alterations in gait that occur due to injury or illness [6-8]. Selective identification of gait characteristics is vital for discrimination of pathology, identifying specific features of injury or disease progression and discerning the effect of pathology via detection of shared neural substrates for gait and other features (e.g. cognition, sensory function etc.) [2]. For example, different cognitive domains and brain regions have selective relationships to specific gait features (pace, variability, rhythm etc.) [2, 9], therefore examining multiple aspects of gait may help to uncover underpinning neural impairments due to mTBI. Additionally, those with chronic mTBI typically have persistent symptoms that do not relate to gait speed, but may relate to other discrete gait characteristics (i.e. turning performance) [10].

There are inconsistent reports of how gait is impaired in people with chronic mTBI. These mixed results could be due to the variable gait testing conditions (e.g. straight, turning, obstacle crossing, etc.), and gait characterization techniques (e.g. gait mats, camera-based motion capture, etc.), as well as limited cohorts involved (e.g. differing samples, small sample sizes, etc.). For chronic mTBI populations more than one year post injury, there are reports of no change or decrease of gait speed during straight gait and complex gait (e.g. obstacle crossing, uneven surfaces, crowded spaces etc.) under single and dual-task conditions [4]. Additionally, previous reports of increased double support time with chronic mTBI [4] has not been reproduced across two cohorts where age and mTBI history were matched [11, 12]. Similar trends for other spatiotemporal gait

characteristics, such as stride length, stride width, and stride time can be found throughout the chronic mTBI gait literature [4]. Some of the variability of these observations could be mitigated by comprehensively assessing gait through examination of gait domains accounting for many aspects of gait performance (e.g. pace, variability, rhythm, turning etc.) opposed to individual gait characteristics. Conceptual models of gait provide a simplified framework for grouping and selection of gait characteristics, which allow even small cohort studies to examine gait comprehensively through informed analysis of independent features of gait while avoiding redundancy.

A comprehensive range of gait characteristics is required to detect selective and specific neural substrate relationships [2]. However, an issue of measuring multiple gait characteristics is high covariance amongst the measures, suggesting redundancy of some characteristics and a need to identify key components for sensitivity and specificity of pathology. Therefore, conceptual gait models have been developed to eliminate redundancy by assisting with data reduction and interpretation, which group gait characteristics into domains [5, 7, 13-15]. Domains provide a useful structure to interpret underlying contributions of various pathological deficits to gait. Data reduction methods, such as exploratory factor analysis and principle component analysis (PCA), have previously been used to examine and explain other complex physiological processes (e.g. cardiovascular disease [16]), and have been used to derive statistically independent domains of gait in various cohorts. Development of a pathology specific gait model facilitates robust investigation into underlying mechanisms involved in gait impairment [8], which helps identify specific features that contribute to gait deficits and the influence of interventions or rehabilitation. To date, however, no model of gait has been developed for chronic mTBI, which limits the understanding of gait disturbance in this population. Previous studies have shown that depending on the population being studied (e.g. older adults, Parkinson's disease etc.) gait model domains may vary in terms of gait characteristics that load onto specific domains. For example, some gait characteristics (e.g. step and stance time variability) have been found to load onto multiple domains (e.g. Pace and Variability) in Parkinson's disease [13] but not in older adults [5]. Therefore, a specific gait model that contains key outcomes with respect to chronic mTBI pathology is required to reduce data to allow comprehensive gait analysis and direct comparison to control groups in future studies in this population.

This study builds on earlier work in different cohorts that include older adults and Parkinson's disease [5, 7, 13-15, 17, 18] and uses PCA to derive independent gait domains in chronic mTBI. Additionally, this study validates the derived model in a separate group of age matched healthy

controls. Our aim was to determine a gait model in chronic mTBI to allow robust understanding of the underlying construct of gait in this population and to guide variable selection for future research (data reduction).

2. Methods

2.1. Participants

Subjects who had an mTBI with self-reported balance instability >3 months after their initial injury were recruited as part of a larger study evaluating chronic mTBI. A total of 52 participants with chronic mTBI and 59 age matched healthy controls were included in this study. Full details of the mTBI classification, recruitment process and study can be found elsewhere [19]. Briefly, inclusion criteria consisted of (1) were >3 months post mTBI with persistent balance complaints for the mTBI group, or had no history of brain injury in the past year for the control group, (2) had no cognitive deficits as determined by the Short Blessed Test (score ≤8), and (3) were between the ages of 18 and 60 years. Exclusion criteria consisted of musculoskeletal injury in the previous year that could have seriously impacted gait or balance; current moderate or severe substance abuse; any peripheral vestibular or oculomotor pathology from before their reported mTBI; or refusal to abstain from medications that could impact their mobility for the duration of testing. Participants were asked to abstain from medications that could impact their mobility starting 24 hours prior to their first testing date. Prohibited medications included sedatives, benzodiazepines, narcotics pain medications and alcohol. All recruitment procedures were approved by the Oregon Health & Science University (OHSU) and Veterans Affairs Portland Health Care System (VAPORHCS) joint institutional review board and participants provided written informed consent prior to commencing the study.

2.2. Clinical Assessment

Age, sex, height (m) and mass (kg) were recorded for all of the participants. Symptom severity was measured using the Neurobehavioral Symptoms Index (NSI) [20]. Days since injury was also recorded for the mTBI group.

2.3. Gait Assessment

Participants wore five inertial sensors (Opals, v.1, APDM, Inc., 128Hz) strapped to their feet, lumbar (L5), sternum and head while they walked at their comfortable speed for two minutes back and forth over a 13m distance along a firm surfaced hallway.

2.4. Gait Characteristics for Principle Component Analysis

The rationale for inclusion of gait characteristics into our PCA was based upon the following;

1) **Metrics from MobilityLab:** To facilitate replication in future studies and in line with previous research [17, 18], only gait metrics that were automatically provided by MobilityLab (v.2) were included. Therefore, step length and asymmetry metrics were not included and standard deviations (SD) were used rather than coefficient of variability. SDs have also been used in previous gait models, as they are suggested to be easier for non-technical audiences to interpret [21].
2) **Metrics from Literature:** Earlier work that has investigated discrete aspects of gait in healthy controls and people with mTBI [4] highlighted that gait speed, stride length, stride time and double support time were the only variables widely examined in previous mTBI gait studies. We also examined previous gait models to include a sufficient number and range of gait characteristics and ensure the model accurately represented the underlying construct (gait) [14, 22, 23], while avoiding duplication and redundancy [5, 7, 13-15]. In line with other models we used single and double support time, rather than stance and swing time to avoid redundancy, as these features have been used in previous mTBI literature [4]. Additionally, we examined methodological factors and reliability of inertial sensor gait metrics to ensure robust metrics were included [24, 25].
3) **Metrics from Group Comparison:** Due to the limited range of gait metrics that have previously been assessed in mTBI populations, we examined the effect size of a comprehensive range of gait metrics between our chronic mTBI and control subjects to inform clinically useful metrics to enter into our gait model (Table 1). We also included several novel gait metrics, derived from the inertial sensors, which have not been included in previous gait models, such as foot angles and turning characteristics. Mean gait characteristics that had a $d>0.5$ effect size (i.e. medium effect size or greater) were considered for entry into the gait model, along with relevant SDs. All metrics that were considered for model entry are detailed above or shown in Table 1.

2.5. Data Analysis

Inertial sensor data were processed through MobilityLab (v.2, APDM, Inc.) [26] which provided the 16 gait characteristics included in statistical analysis. Data were analyzed in SPSS (v. 24, IBM, USA), checked for normality with Kolomogrov-Smirnov tests along with box-plots, with parametric analysis used. Means and SD described demographic data, with independent t-tests used for continuous data comparisons and Pearson Chi-square test used for frequency data

comparisons. Statistical tests were two-tailed with a $p<0.05$ considered significant. Gait data were described in terms of Mean and SD, with Cohen's effect sizes (*d*) used to examine the magnitude of differences between groups, and to inform gait variable entry into our PCA. Gait variability characteristics were log transformed to improve normality of distribution, in line with previous research [5].

2.5.1. Principle Component Analysis

Principle component analysis was used to identify independent gait domains for mTBI. A varimax rotation was applied to derive orthogonal factor scores with a minimum eigenvalue for extraction set to 1 [27]. Scree plots, component loadings, item loadings and cross-loadings were examined. In line with previous gait models developed with a similar sample size [15], items that met a minimum loading of 0.60 were considered relevant to each domain. To validate our mTBI gait model (i.e. examine model robustness), we replicated the PCA analysis in a group of age-matched healthy controls.

3. Results

3.1. Participants

Demographic and gait characteristics of the mTBI and control participants are provide in Table 1. The mTBI group were on average 551 days since injury, with a wide range from 283 to 1013 days since injury reported. The NSI score showed that the mTBI participants were symptomatic compared with normative values (e.g. 6-13 [20]), and significantly symptomatic compared with the controls ($p<.001$).

There were several impaired gait characteristics in mTBI compared with controls (Table 1), although some variability (SD) features had small (<0.40) effect sizes between the groups. Toe off angle ($d=0.07$) and number of steps performed when turning ($d=0.10$) had marginal effect sizes for differences between the groups, which highlighted that they may not be useful for mTBI populations and that we may need more sensitive or validated measures of these features. Therefore, toe off angle and number of steps when turning were not entered into the further PCA analysis.

3.2. Principle Component Analysis

Thirteen gait characteristics were entered into the PCA yielding four domains (Variability, Rhythm, Pace and Turning) that accounted for 80.8% of variance for mTBI gait and 77.4% of the variance for control gait. These findings highlighted that the mTBI gait model was replicated in the healthy

controls, with consistent between-component loadings between the groups. Within both groups, Variability accounted for the largest amount of variance in gait, followed by Rhythm, Pace and Turning (Table 2). The majority of gait characteristics loaded onto one domain (>0.600) for both groups, however gait speed cross-loaded onto both Rhythm (0.623) and Pace (0.630) domains for controls with higher loading onto Pace (Table 2). Cross-loading may indicate that gait speed and timing features of gait are linked.

4. Discussion

This is the first study to determine a conceptual gait model in those with chronic mTBI, which we replicated within a group of age-matched healthy controls. Such conceptual models of gait are useful to provide a simple framework for selecting and reducing gait characteristics for further analysis, which is particularly required when using wearable sensors that provide a plethora of gait outcomes. We confirmed the presence of four independent gait domains in chronic mTBI and controls, which supports the idea that gait is not a singular construct but is made up of independent characteristics. Previous studies have suggested that independence is due to different neural mechanisms (i.e. specific brain regions, processes or substrates) underpinning the separate gait domains [5, 9, 13]. Additionally, we demonstrated that when our gait model was applied to both mTBI and healthy controls, the domains remained the same, with similar levels of explained variance (i.e. mTBI 80.8% vs controls 77.4%), which is in line with previously developed gait models [5, 13]. This is vital to aid in examination of specific gait impairments with chronic mTBI.

4.1. Gait Model Development

Our gait model for chronic mTBI contained a comprehensive range of gait variables while avoiding redundancy. The selection of gait characteristics for the developed model was based on several factors, such as; a number of robust gait features, avoiding duplication and including measures previously reported in mTBI studies. We also included novel measures of gait (e.g. foot angles and turning) in our model, as these were available due to the use of multiple wearable inertial sensors (one on each foot and one at the waist) [26]. Of note, other studies have not been able to include turning or foot angle variables due reporting gait assessment with instrumented walkways or single inertial sensors [5, 7, 13-15, 17]. Likewise, measures not automatically exported through MobilityLab were not included. The use of inertial sensors, therefore, resulted in subtle but important differences in our gait model compared to previous models [5, 7, 13, 14]. For example, similar to some previous gait models [7, 17], we did not include asymmetry within

our model as this feature was not automatically exported from MobilityLab. Nonetheless, asymmetry is not known to be a key feature of mTBI gait, unlike other pathological gait disorders (e.g. Parkinson's disease or Stroke) [2, 13, 15], and may be interesting to examine in future studies.

4.2. Gait Model Domains

The gait domains identified in this study were similar to previous models in older adults [5, 7] and Parkinson's disease [13, 15, 17], with variability, rhythm and pace being common amongst previous models. However, we found that explained variance in gait was slightly different between our model and previous models, as Variability accounted for the largest variance in the model, followed by Rhythm and Pace (Figure 1). Whereas other models have highlighted that pace or rhythm explained the most variance in older adults and pathological cohorts [5, 7, 13, 14, 17]. Differences in explained variance compared to previous studies may have occurred due to our model involving a different pathology (i.e. mTBI vs Parkinson's disease [13, 15, 17]) and age range (i.e. previous studies were primarily in older adults [5, 7, 14]). Similarly, the current study involved a smaller cohort and used a lower number of gait characteristics in the model, i.e. 13 compared to previous studies of 14 [2], 16 [5, 13], 18 [17] or 23 [14] characteristics. With the ability to derive turning metrics from the inertial sensors, we were able to derive a further independent domain of turning which emerged in both mTBI and control groups. In contrast, our recent Parkinson's gait model showed that pace and turning gait characteristics loaded onto the same domain [18], which highlights the importance of distinguishing independent gait features in different neurological groups. Turning being an independent domain of gait is an important finding for an mTBI cohort, as turning has been shown to be sensitive to mTBI pathology in both acute [28, 29] and chronic stages [10]. Interestingly, turning explained the least amount of variance of gait in the groups (mTBI: 17.4%, control: 14.7%), which suggests that we may need more sensitive measures to reflect this complex aspect of gait.

4.3. Gait Model Validation

The validation of our developed mTBI gait model was performed by conducting the same PCA in a separate healthy control cohort. The model was well replicated in the separate group, which highlighted that our model is robust and stable across those with and without pathology. As a result, the model can be used in future studies to directly assess differences in comprehensive but independent gait domains, through analysis of domains scores or selection of gait characteristics from independent domains. Nevertheless, there were some unexpected findings. Specifically, we found that while gait speed primarily loaded onto the Pace domain in both groups,

it also loaded onto the Rhythm domain in healthy controls, which has not been previously reported [5, 7, 13, 14], but may be linked to the statistical relationship between speed and timing features of gait. Similarly, while the same gait features loaded onto the same domains in both chronic mTBI and control groups, the factor loading weights were different. These important differences highlighted that the gait model was more discrete (e.g. no cross-loading of gait characteristics onto different domains) within the pathological population than controls, similar to previous gait models [5, 7, 13, 14]. Differences in our findings compared to previous studies may relate to the different instruments used to derive gait metrics (i.e. inertial sensors compared to pressure sensor mats) and inclusion of different gait features (i.e. double and single support time instead of stance and swing time). Despite this, the domains found for our chronic mTBI cohort were replicated in a separate age-matched healthy control cohort, with very similar levels of explained variance.

4.4. Future Directions

In line with previous studies in other populations, our developed gait model simplifies gait measurement in mTBI, and demonstrates the independence of different gait characteristics [5, 7, 13-15, 17, 18], such as variability, rhythm, pace and turning, but also addresses redundancy of features. Gait is often used as an outcome for studies that address the efficacy of treatments or therapeutics in mTBI [30, 31]. Studies of mTBI often adopt a detailed measurement of gait using sophisticated technologies and protocols that result in a wide range of metrics to select from [4, 32-35], but despite this, gait is largely reported via a limited set of gait characteristics. Gait speed is primarily used across different neurological pathologies to report gait performance due to the ease and robustness of measurement [36], especially within clinical and laboratory settings for mTBI [37-39]. However, gait speed only reflect global gait performance and provides limited understanding of impairments seen in different pathologies [13], which is where a more comprehensive approach may add value. Similarly, gait characteristics, other than gait speed, may be useful for non-invasive discrimination between pathologies [40-42], with potential for gait to become a diagnostic tool for mTBI. Appropriate gait characteristics selection for mTBI studies would benefit from a more systematic and informed approach, which is where our developed gait model could add value to future studies. The primary benefit of a gait model for chronic mTBI is the reduced number of gait characteristics for further analysis, which avoids statistical issues with the number of variables examined (i.e. multiple comparisons) within cohorts of variable size. Researchers using the model can be confident that a wide range of characteristics are represented, while reducing analysis of redundant variables. Future studies can now use our developed gait model framework to select individual gait characteristics from independent gait

domains (e.g. double support time SD, double support time, stride length, turn duration) or combine gait characteristics within a domain using Z-scores for further analysis [8], or comparison to controls.

4.5. Study Strengths and Limitations

This study has several strengths and limitations that should be noted. The strengths of this study include the use of a commercially available inertial measurement units and MobilityLab software to record gait. This allowed simple, quick and easy collection of quantitative gait data that in the future could be performed in a variety of environments (e.g. clinics, research laboratories, home or community settings etc.). Additionally, inertial sensors allowed for the inclusion of novel and clinically relevant gait features (i.e. turning and foot angles). Another strength was the inclusion of a separate cohort of healthy controls to replicate the gait model that was derived for our mTBI cohort, which provided validation of the gait model. Only one previous study has examined a gait model within two separate cohorts in the same study [15], as other previous models have either only examined gait models within a single cohort [7, 14] or have replicated their model in a separate study [5, 13].

The limitations of this study include the relatively small number of participants in each group, as the majority of previous gait model studies have included n>100 participants [5, 7, 13, 14]. Previous statistical research has suggested large numbers (e.g. n>100) are required to adequately perform PCA [43], however it is recognized that in observational studies this sample size is challenging [44, 45]. Therefore, others have recommended that the variable to sample size ratio can be as low as 2-6 subjects for each variable (e.g. 2:1 ratio) [46-49], which will achieve appropriate component loadings if the structure of the model (and underlying concept) is strong. Additionally, in line with a previous gait model with a similar size cohort (n=60) [15], to ensure robust domains we only considered variables that had component loadings >0.60 as opposed to larger cohort studies that have used >0.50 loadings to define variables loaded onto specific domains [5, 7, 13]. Another limitation was the lack of asymmetry gait variables included in the model. While measures of asymmetry may not be relevant to an mTBI population, they may provide a more comprehensive evaluation of gait, and could be included in future gait models. Finally, our mTBI cohort consisted of people who were still symptomatic >3months following their injury, and it should be noted that the developed gait model (i.e. domains loadings) may change in those who are asymptomatic or at different mTBI stages (i.e. acute, sub-acute etc.), which could be examined in future studies.

5. Conclusion

This study presents a gait model to guide assessment and analysis of gait in chronic mTBI, which was replicated in a group of age-matched controls. We found that there were four domains of gait in chronic mTBI and controls, specifically Variability, Rhythm, Pace and Turning. The developed gait model provides a useful framework with which to assess the relationships between gait and the underlying mechanisms (or outcomes that represent these) of impairment. However, selection of gait characteristics in future analysis should be specific to pathology and the aims of investigation.

Author Contributions

SS was involved in: Conceptualization, Data Curation, Formal analysis, Investigation, Writing; original draft and all revisions, review and editing. LP, RM, DM and PCF were involved in: Data Collection, Methodology, Writing; review and editing. LAK was involved in: Obtaining Funding, Conceptualization, Methodology, Study Supervision, and Writing; review and editing.

Conflict of Interest

None to declare.

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References

1. Studenski, S., Perera, S., Patel, K., Rosano, C., Faulkner, K., Inzitari, M., Brach, J., Chandler, J., Cawthon, P., Connor, E.B., Nevitt, M., Visser, M., Kritchevsky, S., Badinelli, S., Harris, T., Newman, A.B., Cauley, J., Ferrucci, L., and Guralnik, J., *Gait Speed and Survival in Older Adults.* JAMA, 2011. **305**(1): p. 50-58.
2. Morris, R., Lord, S., Bunce, J., Burn, D., and Rochester, L., *Gait and cognition: Mapping the global and discrete relationships in ageing and neurodegenerative disease.* Neurosci Biobehav Rev, 2016. **64**: p. 326-45.

3. Wade, D.T., Collen, F.M., Robb, G.F., and Warlow, C.P., *Physiotherapy intervention late after stroke and mobility.* BMJ (Clinical research ed.), 1992. **304**(6827): p. 609-613.
4. Fino, P.C., Parrington, L., Pitt, W., Martini, D.N., Chesnutt, J.C., Chou, L.S., and King, L.A., *Detecting gait abnormalities after concussion or mild traumatic brain injury: A systematic review of single-task, dual-task, and complex gait.* Gait Posture, 2018. **62**: p. 157-166.
5. Lord, S., Galna, B., Verghese, J., Coleman, S., Burn, D., and Rochester, L., *Independent Domains of Gait in Older Adults and Associated Motor and Nonmotor Attributes: Validation of a Factor Analysis Approach.* The Journals of Gerontology: Series A, 2012. **68**(7): p. 820-827.
6. Stolze, H., Kuhtz-Buschbeck, J.P., Drucke, H., Johnk, K., Illert, M., and Deuschl, G., *Comparative analysis of the gait disorder of normal pressure hydrocephalus and Parkinson's disease.* J Neurol Neurosurg Psychiatry, 2001. **70**(3): p. 289-97.
7. Verghese, J., Wang, C., Lipton, R.B., Holtzer, R., and Xue, X., *Quantitative gait dysfunction and risk of cognitive decline and dementia.* J Neurol Neurosurg Psychiatry, 2007. **78**(9): p. 929-35.
8. Lord, S., Galna, B., Coleman, S., Yarnall, A., Burn, D., and Rochester, L., *Cognition and gait show a selective pattern of association dominated by phenotype in incident Parkinson's disease.* Front Aging Neurosci, 2014. **6**: p. 249.
9. Seidler, R.D., Bernard, J.A., Burutolu, T.B., Fling, B.W., Gordon, M.T., Gwin, J.T., Kwak, Y., and Lipps, D.B., *Motor control and aging: Links to age-related brain structural, functional, and biochemical effects.* Neuroscience & Biobehavioral Reviews, 2010. **34**(5): p. 721-733.
10. Fino, P.C., Parrington, L., Walls, M., Sippel, E., Hullar, T.E., Chesnutt, J.C., and King, L.A., *Abnormal Turning and Its Association with Self-Reported Symptoms in Chronic Mild Traumatic Brain Injury.* J Neurotrauma, 2018. **35**(10): p. 1167-1177.
11. Martini, D.N., Sabin, M.J., DePesa, S.A., Leal, E.W., Negrete, T.N., Sosnoff, J.J., and Broglio, S.P., *The Chronic Effects of Concussion on Gait.* Archives of Physical Medicine and Rehabilitation, 2011. **92**(4): p. 585-589.
12. Martini, D.N., Goulet, G.C., Gates, D.H., and Broglio, S.P., *Long-term effects of adolescent concussion history on gait, across age.* Gait & Posture, 2016. **49**: p. 264-270.
13. Lord, S., Galna, B., and Rochester, L., *Moving forward on gait measurement: Toward a more refined approach.* Movement Disorders, 2013. **28**(11): p. 1534-1543.

14. Hollman, J.H., McDade, E.M., and Petersen, R.C., *Normative spatiotemporal gait parameters in older adults.* Gait Posture, 2011. **34**(1): p. 111-8.
15. Morris, R., Hickey, A., Del Din, S., Godfrey, A., Lord, S., and Rochester, L., *A model of free-living gait: A factor analysis in Parkinson's disease.* Gait & Posture, 2017. **52**: p. 68-71.
16. Lakka, H.M., Laaksonen, D.E., Lakka, T.A., Niskanen, L.K., Kumpusalo, E., Tuomilehto, J., and Salonen, J.T., *The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men.* Jama, 2002. **288**(21): p. 2709-16.
17. Horak, F.B., Mancini, M., Carlson-Kuhta, P., Nutt, J.G., and Salarian, A., *Balance and Gait Represent Independent Domains of Mobility in Parkinson Disease.* Physical Therapy, 2016. **96**(9): p. 1364-1371.
18. Morris, R., Martini, D.N., Smulders, K., Kelly, V.E., Zabetian, C.P., Poston, K., Hiller, A., Chung, K.A., Yang, L., Hu, S.-C., Edwards, K.L., Cholerton, B., Grabowski, T.J., Montine, T.J., Quinn, J.F., and Horak, F., *Cognitive associations with comprehensive gait and static balance measures in Parkinson's disease.* Parkinsonism & Related Disorders, 2019.
19. Fino, P.C., Peterka, R.J., Hullar, T.E., Murchison, C., Horak, F.B., Chesnutt, J.C., and King, L.A., *Assessment and rehabilitation of central sensory impairments for balance in mTBI using auditory biofeedback: a randomized clinical trial.* J BMC Neurology, 2017. **17**(1): p. 41.
20. English, J., Miller, R.M., and Lee, A.J., *Normative Data for the Neurobehavioral Symptom Inventory AU - Meyers, John E.* Applied Neuropsychology: Adult, 2015. **22**(6): p. 427-434.
21. Lord, S., Howe, T., Greenland, J., Simpson, L., and Rochester, L., *Gait variability in older adults: a structured review of testing protocol and clinimetric properties.* Gait Posture, 2011. **34**(4): p. 443-50.
22. Brach, J.S., Perera, S., Studenski, S., Katz, M., Hall, C., and Verghese, J., *Meaningful change in measures of gait variability in older adults.* Gait Posture, 2010. **31**(2): p. 175-9.
23. Paterson, K.L., Hill, K.D., Lythgo, N.D., and Maschette, W., *The reliability of spatiotemporal gait data for young and older women during continuous overground walking.* Arch Phys Med Rehabil, 2008. **89**(12): p. 2360-5.
24. Del Din, S., Godfrey, A., and Rochester, L., *Validation of an Accelerometer to Quantify a Comprehensive Battery of Gait Characteristics in Healthy Older Adults and Parkinson's Disease: Toward Clinical and at Home Use.* IEEE J Biomed Health Inform, 2016. **20**(3): p. 838-847.

25. Schmitz-Hubsch, T., Brandt, A.U., Pfueller, C., Zange, L., Seidel, A., Kuhn, A.A., Paul, F., Minnerop, M., and Doss, S., *Accuracy and repeatability of two methods of gait analysis - GaitRite und Mobility Lab - in subjects with cerebellar ataxia.* Gait Posture, 2016. **48**: p. 194-201.
26. Mancini, M., King, L., Salarian, A., Holmstrom, L., McNames, J., and Horak, F.B., *Mobility Lab to Assess Balance and Gait with Synchronized Body-worn Sensors.* Journal of bioengineering & biomedical science, 2011. **Suppl 1**: p. 007-007.
27. Field, A., *Discovering statistics using IBM SPSS statistics*. 2013: sage.
28. Powers, K.C., Kalmar, J.M., and Cinelli, M.E., *Dynamic stability and steering control following a sport-induced concussion.* Gait Posture, 2014. **39**(2): p. 728-32.
29. Fino, P.C., Nussbaum, M.A., and Brolinson, P.G., *Locomotor deficits in recently concussed athletes and matched controls during single and dual-task turning gait: preliminary results.* Journal of NeuroEngineering and Rehabilitation, 2016. **13**(1): p. 65.
30. Sessoms, P.H., Gottshall, K.R., Collins, J.-D., Markham, A.E., Service, K.A., and Reini, S.A., *Improvements in gait speed and weight shift of persons with traumatic brain injury and vestibular dysfunction using a virtual reality computer-assisted rehabilitation environment.* Military medicine, 2015. **180**(suppl_3): p. 143-149.
31. Peters, D.M., Jain, S., Liuzzo, D.M., Middleton, A., Greene, J., Blanck, E., Sun, S., Raman, R., and Fritz, S.L., *Individuals with chronic traumatic brain injury improve walking speed and mobility with intensive mobility training.* Archives of physical medicine and rehabilitation, 2014. **95**(8): p. 1454-1460.
32. Lee, H., Sullivan, S.J., and Schneiders, A.G., *The use of the dual-task paradigm in detecting gait performance deficits following a sports-related concussion: a systematic review and meta-analysis.* Journal of Science and Medicine in Sport, 2013. **16**(1): p. 2-7.
33. Kleiner, M., Wong, L., Dubé, A., Wnuk, K., Hunter, S.W., and Graham, L.J., *Dual-task assessment protocols in concussion assessment: a systematic literature review.* journal of orthopaedic & sports physical therapy, 2018. **48**(2): p. 87-103.
34. Vienne, A., Barrois, R.P., Buffat, S., Ricard, D., and Vidal, P.-P., *Inertial sensors to assess gait quality in patients with neurological disorders: a systematic review of technical and analytical challenges.* Frontiers in psychology, 2017. **8**: p. 817.
35. Grants, L., Powell, B., Gessel, C., Hiser, F., and Hassen, A., *GAIT DEFICITS UNDER DUAL–TASK CONDITIONS IN THE CONCUSSED ADOLESCENT AND YOUNG ATHLETE POPULATION: A SYSTEMATIC REVIEW.* International journal of sports physical therapy, 2017. **12**(7): p. 1011.

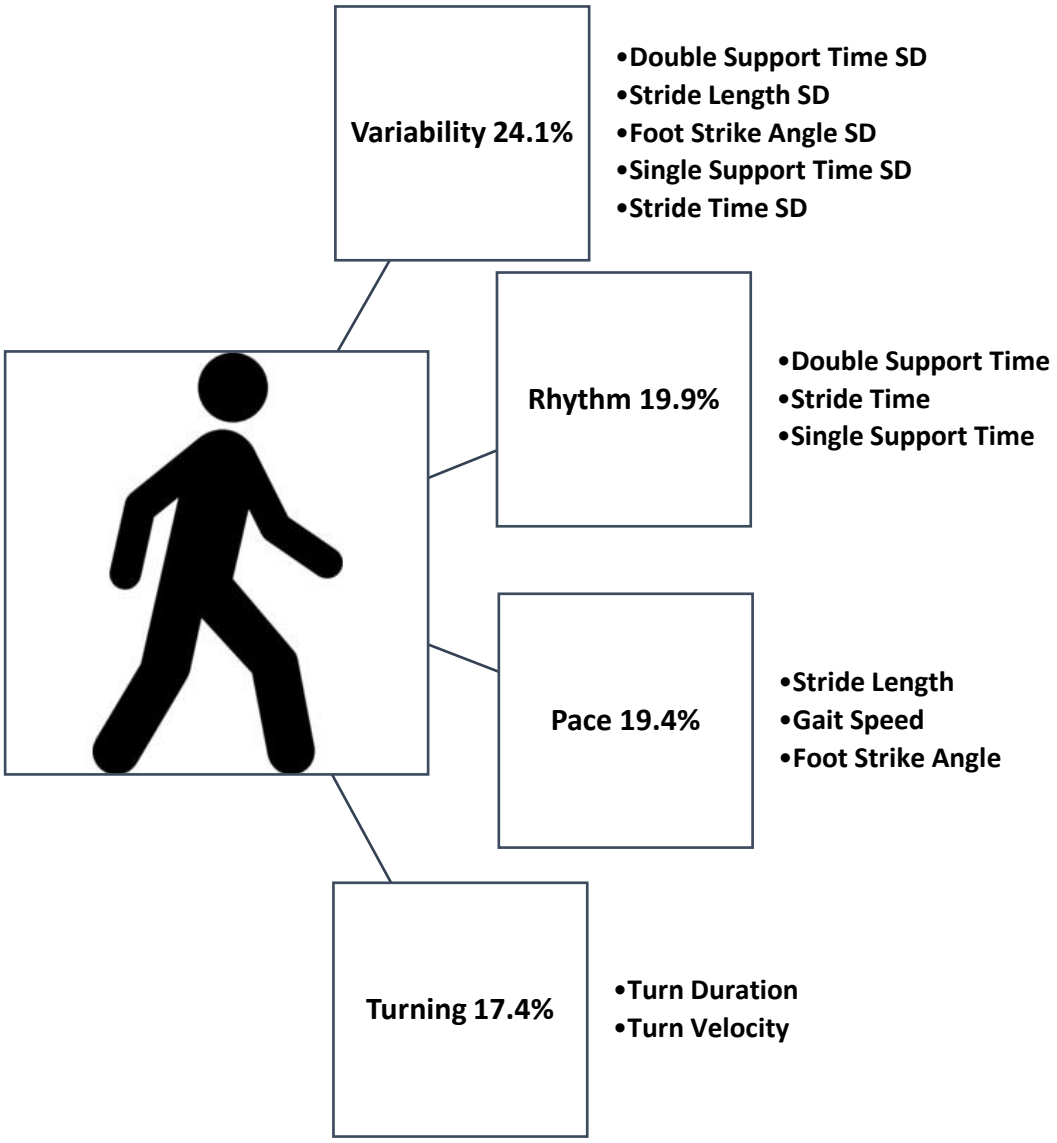
36. Wade, D.T., *Measurement in neurological rehabilitation.* Curr Opin Neurol Neurosurg, 1992. **5**(5): p. 682-6.
37. Cossette, I., Ouellet, M.-C., and McFadyen, B.J., *A preliminary study to identify locomotor-cognitive dual tasks that reveal persistent executive dysfunction after mild traumatic brain injury.* Archives of physical medicine and rehabilitation, 2014. **95**(8): p. 1594-1597.
38. Basford, J.R., Chou, L.-S., Kaufman, K.R., Brey, R.H., Walker, A., Malec, J.F., Moessner, A.M., and Brown, A.W., *An assessment of gait and balance deficits after traumatic brain injury.* Archives of physical medicine and rehabilitation, 2003. **84**(3): p. 343-349.
39. Williams, G., Morris, M.E., Schache, A., and McCrory, P.R., *Incidence of gait abnormalities after traumatic brain injury.* Archives of physical medicine and rehabilitation, 2009. **90**(4): p. 587-593.
40. Mc Ardle, R., Galna, B., Donaghy, P., Thomas, A., and Rochester, L., *Do Alzheimer's and Lewy body disease have discrete pathological signatures of gait?* Alzheimer's & Dementia, 2019.
41. Büttner, F., Howell, D.R., Ardern, C.L., Doherty, C., Blake, C., Ryan, J., Catena, R., Chou, L.-S., Fino, P., Rochefort, C., Sveistrup, H., Parker, T., and Delahunt, E., *Concussed athletes walk slower than non-concussed athletes during cognitive-motor dual-task assessments but not during single-task assessments 2 months after sports concussion: a systematic review and meta-analysis using individual participant data.* British Journal of Sports Medicine, 2019: p. bjsports-2018-100164.
42. Del Din, S., Elshehabi, M., Galna, B., Hobert, M.A., Warmerdam, E., Suenkel, U., Brockmann, K., Metzger, F., Hansen, C., Berg, D., Rochester, L., and Maetzler, W., *Gait analysis with wearables predicts conversion to parkinson disease.* Annals of Neurology, 2019. **86**(3): p. 357-367.
43. Comrey, A.L. and Lee, H.B., *A first course in factor analysis, 2nd ed*. A first course in factor analysis, 2nd ed. 1992, Hillsdale, NJ, US: Lawrence Erlbaum Associates, Inc. xii, 430-xii, 430.
44. Velicer, W.F. and Fava, J.L., *Affects of variable and subject sampling on factor pattern recovery.* Psychological Methods, 1998. **3**(2): p. 231-251.
45. MacCallum, R.C., Widaman, K.F., Zhang, S., and Hong, S., *Sample size in factor analysis.* Psychological Methods, 1999. **4**(1): p. 84-99.
46. Osborne, J.W. and Costello, A.B., *Sample Size and Subject to Item Ratio in Principal Components Analysis.* Practical Assessment, Research & Evaluation, 2004. **9**.

47. Bandalos, D.L. and Boehm-Kaufman, M.R., *Four common misconceptions in exploratory factor analysis*, in *Statistical and methodological myths and urban legends: Doctrine, verity and fable in the organizational and social sciences.*, C.E. Lance and R.J. Vandenberg, Editors. 2009, Routledge/Taylor & Francis Group: New York, NY, US. p. 61-87.
48. Dochtermann, N.A. and Jenkins, S.H., *Multivariate Methods and Small Sample Sizes.* Ethology, 2011. **117**(2): p. 95-101.
49. MacCallum, R.C., Widaman, K.F., Preacher, K.J., and Hong, S., *Sample Size in Factor Analysis: The Role of Model Error.* Multivariate Behav Res, 2001. **36**(4): p. 611-37.

Table 1 - Demographic and gait characteristics

	Chronic mTBI (n=52)	**Controls (n= 59)**	***t***	***df***	***p***
Age (years)	39.56 (11.34)	36.96 (12.68)	1.14	110	.255
Height (m)	171.08 (9.51)	171.60 (9.55)	-0.29	110	.776
Weight (kgs)	79.69 (19.51)	76.10 (19.39)	0.95	110	.347
NSI score	36.51 (14.82)	3.92 (4.07)	16.23	110	**<.001***
Gender (m/f)	16 M / 37 F	25 M / 34 F	1.79†	1†	.239†
Days since injuryɻ	551 (283, 1013)	-	-	-	-
	Mean (SD)	**Mean (SD)**			***d***
Stride Length (m)	1.22 (0.12)	1.30 (0.11)			0.70
Gait Speed (m/s)	1.09 (0.13)	1.21 (0.13)			0.93
Foot Strike Angle (°)	23.61 (3.61)	26.11 (3.76)			0.68
Toe off Angle (°)	39.35 (3.10)	39.56 (3.18)			0.07
Single Support Time (%GCT)	39.52 (1.33)	40.41 (1.40)			0.66
Double Support Time (%GCT)	10.49 (1.33)	9.61 (1.39)			0.65
Stride Time (s)	1.12 (0.07)	1.08 (0.07)			0.58
Foot Strike Angle SD (°)	1.66 (0.38)	1.56 (0.40)			0.26
Toe off Angle SD (°)	1.25 (0.36)	1.12 (0.53)			0.29
Stride Length SD (m)	0.04 (0.01)	0.04 (0.01)			0.00
Single Support Time SD (%GCT)	0.69 (0.16)	0.63 (0.13)			0.42
Double Support Time SD (%GCT)	1.07 (0.30)	0.96 (0.23)			0.42
Stride Time SD (s)	0.02 (0.01)	0.02 (0.01)			0.45
Turn Duration (s)	2.34 (0.44)	2.09 (0.37)			0.62
Turn Step Number (n)	3.61 (0.67)	3.54 (0.72)			0.10
Turn Velocity (°/s)	161.18 (33.68)	197.76 (43.55)			0.94

[ɻ= Median and Inter-quartile range: 25th and 75th percentiles, †Chi-square, mTBI = mild traumatic brain injury, m = meters, s = seconds, %GCT = percentage of gait cycle time, n = number, ROM = range of movement]



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540 ***Figure 1 - Gait Model for Chronic Mild Traumatic Brain Injury***

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Table 2 – Principle Component Analysis of Gait Characteristics

	Chronic mTBI (n=52)				Control (n=59)			
	Variability	**Rhythm**	**Pace**	**Turning**	**Variability**	**Rhythm**	**Pace**	**Turning**
Double Support Time SD	**0.813**	-0.004	-0.418	-0.133	**0.815**	0.182	-0.247	0.185
Stride Length SD	**0.789**	0.032	0.221	0.006	**0.823**	0.069	0.248	-0.212
Foot Strike Angle SD	**0.783**	0.117	-0.127	0.229	**0.726**	-0.032	0.051	0.105
Single Support Time SD	**0.777**	-0.033	-0.500	-0.146	**0.845**	0.167	-0.261	0.277
Stride Time SD	**0.722**	0.173	-0.425	0.120	**0.612**	-0.201	-0.364	-0.097
Double Support Time	0.070	**0.962**	-0.066	0.094	-0.195	**-0.905**	-0.063	-0.166
Stride Time	0.044	**0.602**	0.110	0.561	0.167	**-0.699**	0.059	-0.283
Single Support Time	-0.072	**-0.962**	0.077	-0.093	0.197	**0.907**	0.064	0.165
Stride Length	-0.197	-0.186	**0.910**	-0.099	-0.128	0.285	**0.846**	0.062
Gait Velocity	-0.187	-0.482	**0.695**	-0.373	-0.194	**0.623**	**0.630**	0.227
Foot Strike Angle	-0.132	0.173	**0.664**	-0.168	-0.010	-0.311	**0.739**	0.165
Turn Duration	-0.031	0.095	-0.162	**0.914**	-0.112	-0.252	-0.098	**-0.880**
Turn Velocity	-0.085	-0.136	0.228	**-0.898**	0.087	0.298	0.219	**0.864**
% Variance					% Variance			
(80.8% total)	24.1	19.9	19.4	17.4	(77.4% total)	24.1	22.8	15.8	14.7

[Bold text = component loading >0.60, m = meters, s = seconds, %GCT = percentage of gait cycle time, n = number, ROM = range of movement]