





Self-Reported Head Trauma Predicts Poor Dual Task Gait in Retired National Football League Players

Brad Manor, PhD ^{1,2,3} Junhong Zhou, PhD ^{1,2,3} On-Yee Lo, PhD ^{1,2,3} Hao Zhu, MA,¹
Natalia A. Gouskova, PhD,^{1,2,3} Wanting Yu, ME,¹ Ross Zafonte, DO ^{3,4}
Lewis A. Lipsitz, MD,^{1,2,3} Thomas G. Trivison, PhD,^{1,2,3} and Alvaro Pascual-Leone, PhD^{1,3,5}

Objective: Symptomatic head trauma associated with American-style football (ASF) has been linked to brain pathology, along with physical and mental distress in later life. However, the longer-term effects of such trauma on objective metrics of cognitive–motor function remain poorly understood. We hypothesized that ASF-related symptomatic head trauma would predict worse gait performance, particularly during dual task conditions (ie, walking while performing an additional cognitive task), in later life.

Methods: Sixty-six retired professional ASF players aged 29 to 75 years completed a health and wellness questionnaire. They also completed a validated smartphone-based assessment in their own homes, during which gait was monitored while they walked normally and while they performed a verbalized serial-subtraction cognitive task.

Results: Participants who reported more symptomatic head trauma, defined as the total number of impacts to the head or neck followed by concussion-related symptoms, exhibited greater dual task cost (ie, percentage increase) to stride time variability (ie, the coefficient of variation of mean stride time). Those who reported ≥ 1 hit followed by loss of consciousness, compared to those who did not, also exhibited greater dual task costs to this metric. Relationships between reported trauma and dual task costs were independent of age, body mass index, National Football League career duration, and history of musculoskeletal surgery. Symptomatic head trauma was not correlated with average stride times in either walking condition.

Interpretation: Remote, smartphone-based assessments of dual task walking may be utilized to capture meaningful data sensitive to the long-term impact of symptomatic head trauma in former professional ASF players and other contact sport athletes.

ANN NEUROL 2020;87:75–83

Repeated exposure to biomechanical head trauma—especially during participation in contact sports such as American-style football (ASF)—has been linked to subjective complaints of physical, mental, and emotional distress in life,¹ as well as chronic traumatic encephalopathy upon autopsy.² However, the longer-term effects of such repeated head trauma on objective, clinically meaningful metrics of cognitive–motor function remains largely unknown.³ This gap in knowledge significantly hinders

current efforts to identify those at risk of developing chronic brain disease, as well as to design interventions aimed at assessing, preventing, and ultimately alleviating the potential clinical disability. There is thus an urgent need to identify and validate low-cost and widely accessible cognitive–motor assessment tools, and subsequently, characterize and prospectively track large numbers of individuals who have been exposed to repetitive head trauma in early life.

View this article online at wileyonlinelibrary.com. DOI: 10.1002/ana.25638

Received Apr 16, 2019, and in revised form Sep 7, 2019. Accepted for publication Nov 3, 2019.

Address correspondence to Dr Manor and Dr Zhou, Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife, Boston, MA 02131.
E-mail: bradmanor@hsl.harvard.edu and junhongzhou@hsl.harvard.edu

From the ¹Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife, Boston, MA; ²Division of Gerontology, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA; ³Harvard Medical School, Boston, MA; ⁴Spaulding Rehabilitation Hospital, Massachusetts General Hospital, and Department of Physical Medicine and Rehabilitation, Brigham and Women's Hospital, Boston, MA; and ⁵Guttmann Neurorehabilitation Institute, Autonomous University of Barcelona, Badalona, Spain

Assessment of walking provides clinically meaningful insights into cognitive–motor function and underlying brain health.⁴ In addition to the peripheral and spinal neuromuscular systems, the complex task of walking depends upon “higher-level” sensory–motor integration and various cognitive functions.⁵ Moreover, in daily life, walking is almost always performed in the context of cognitive tasks such as talking, reading signs, or making decisions. Within experimental paradigms, such dual tasking (eg, walking while counting backward) affects numerous metrics of gait.⁶ Acute, sport-related head trauma in younger adults has been linked to greater dual task cost (ie, percentage decrement) to gait performance.^{7,8} At the same time, worse dual task gait performance in older adults has been linked to executive cognitive dysfunction,⁹ chronic pain,¹⁰ increased likelihood of suffering a fall,¹¹ increased risk of converting from mild cognitive impairment to dementia,^{12,13} alterations in brain structure,¹⁴ and a reduced capacity to activate appropriate brain networks in response to cognitive–motor tasks.¹⁵

Based upon the above evidence, we hypothesized that metrics of dual task walking performance would be sensitive to chronic brain dysfunction induced by repeated sports-related head trauma in young adulthood, and therefore, could ultimately be useful for the detection of consequences of such head trauma, potentially before cognitive complaints and other clinical symptoms arise. To this end, we developed and validated a smartphone app that utilizes the phone’s internal movement sensors and offers multimedia instructions to enable remote assessment of dual task walking performance in larger numbers of individuals.¹⁶ The purpose of this study was to examine the cross-sectional relationship between dual task walking performance and self-reported history of football-related symptomatic head trauma during their professional playing careers in a subsample of former professional ASF players participating in the Football Players Health Study (FPHS) at Harvard University.

Subjects and Methods

Participants

The FPHS is a portfolio of studies intended to further our understanding of the benefits and risks of participation in ASF, identify risks that are potentially preventable or reversible, and develop interventions or approaches to improve the health and well-being of former professional ASF players. At the time of this study, the FPHS comprised 3,506 former professional ASF players who had completed a health and wellness questionnaire probing demographics, football exposure including history of football-related symptomatic head trauma, medical history, physical function, cognitive health, and mental well-being. A self-selected subset of this cohort (n = 66) of subjects who owned an

iPhone also participated in “TeamStudy,” which used an app designed for iPhones to gather health data that included a remote assessment of dual task walking performance.

Ethics Committee Approval

All TeamStudy procedures and its informed consent form were approved by the Beth Israel Deaconess Medical Center Institutional Review Board. The consent form was integrated into the app, and all participants reviewed the form, were quizzed on its content to ensure understanding, and consented to the study as part of the app’s setup procedures. Each participant completed the FPHS health and wellness questionnaire and the TeamStudy walking assessment within 1 year of one another.

Self-Reported Health, Wellness, and Football Exposures

Self-Reported Demographics, Medical History, and Health Status. We extracted data related to: (1) age at time of questionnaire completion; (2) race; (3) history of musculoskeletal surgery involving major joints that may significantly influence gait (neck, spine, hips, knees, or ankles); (4) report of physician-diagnosed hypertension, arthritis, diabetes, stroke, Parkinson disease, dementia, and depression; (5) chronic pain; (6) global physical function; and (7) global mental function. Chronic pain was assessed by the question, “In the past 7 days, how would you rate your pain on average on a scale of 0 (no pain) to 10 (worst pain imaginable).” Global physical health and global mental health were queried using the Patient-Reported Outcomes Measurement Information System (PROMIS) global health instrument and standard scoring procedures.¹⁷

Football-Related Exposures. We extracted the age at which participants first played organized football, the number of seasons played in the National Football League (NFL), and the position most often played professionally. For the latter, participants were classified as either linemen (including offensive or defensive line) or nonlinemen (including linebacker, defensive back, running back, wide receiver, tight end, quarterback, kicker/punter, special teams).

Players were asked to report the number (with choices of 0, 1, 2–5, 6–10, and 11 or more) of times they experienced a “hit or blow to the head, neck, or upper body followed by...” each of the following symptoms: headaches, nausea, dizziness, loss of consciousness, memory problems, disorientation, confusion, seizure, visual problems, weakness on one side of the body, and feeling unsteady on your feet. We then created a continuous “symptomatic head trauma” score for the total burden of hits followed by concussion-related symptoms (by coding each response as 0, 1, 3.5, 8, and 13, and then summing the responses for all 11 symptoms). We also created a yes/no dichotomous variable for at least 1 self-reported hit

followed by loss of consciousness, as we felt that this item in particular may be more reliably determined by self-report.

Remote Assessment of Dual Task Walking Performance

Data Acquisition. Dual task walking performance was measured remotely in the participant's home by the validated TeamStudy smartphone app, created in collaboration with Sage Bionetworks (Seattle, WA).¹⁶ Participants first watched an animation developed by Wondros (Los Angeles, CA) that provided a general overview of the assessment. The user was then presented with several on-screen text instructions. The gait assessment was designed to evaluate walking under normal conditions, and again while the subject performs verbalized serial subtractions of 3 from a random number between 200 and 999.

Participants were encouraged to complete the walking assessment in an empty room or hallways within their own home. Each assessment included one 45-second trial of normal walking followed by one 45-second trial of dual task walking. Trails were separated by at least 90 seconds. Trial start and end cues triggered acquisition of accelerometer, gyroscope, and magnetometer data, which was stored in the phone's internal storage. Kinematic and questionnaire data were then automatically uploaded via wi-fi to a remote, cloud-based data server for offline analyses.

Data Capturing and Preprocessing. We extracted 2 outcomes from each walking trial—average stride time and stride time variability—using procedures that have been shown to produce accurate results when compared to the GAITRite mat within the laboratory, and high test–retest reliability over multiple days in user homes.¹⁶

Walking trials completed within user homes typically included variable amounts of turning, which alters stride timing.¹⁸ Turning also influences z-axis accelerations derived from the phone and thus the ability to accurately detect heel strikes. We therefore utilized a method we previously developed and validated to identify and remove relatively sharp, rapid turns using rotated z-axis gyroscope data (ie, rotations about the global vertical axis). Stride times for the current analysis were thus calculated from all z-axis acceleration data that occurred outside of detected periods of turning. To ensure reliability of results, we excluded any trials that contained <10 identified strides.

Primary gait outcomes included the dual task cost to stride time and dual task cost to stride time variability; that is, the percentage change in each outcome from normal walking to dual task walking conditions. Secondary outcomes included stride time and stride time variability

derived from each walking condition separately. Only these specific metrics were chosen because each (1) can be accurately derived from smartphone motion data captured during walking with the phone in the pants pocket; and (2) is sensitive to cognitive status,^{9,12,13} chronic pain,¹⁰ falls,¹¹ and markers of brain health^{14,19} in older adults.

Statistical Analysis

Descriptive statistics were used to summarize cohort characteristics and gait outcomes, followed by model estimation and hypothesis testing. We examined relationships between self-reported burden of hits followed by concussion-related symptoms and primary and secondary gait outcomes using 3 separate approaches. First, 1-way analysis of variance (ANOVA) was used to examine the main effect of symptomatic head trauma score quartile on each gait outcome. Second, linear regression models were used to examine the correlation between the symptomatic head trauma score, modeled as a continuous variable (see above), and each gait outcome. Third, 1-way ANOVAs were used to examine the influence of self-report of at least 1 hit to the head or neck followed by loss of conscious on each gait outcome. In each of these 3 analyses, models were completed both with and without adjustments for age, body mass index (BMI), exposure to ASF defined as the number of NFL seasons played, and injuries unrelated to head trauma that may influence gait as defined by the total number of reported musculoskeletal injuries to the neck, spine, hips, knees, or ankles. Tests allowed for type I error probability of $\alpha = 0.05$. Analyses were performed using JMP software version 13 (SAS Institute, Cary, NC).

Results

Participant Characteristics

Sixty-six participants of the FPHS joined TeamStudy in response to a broadly publicized advertisement and used their smartphone to complete a remote dual task gait assessment. Two of these participants were excluded from analysis because, after removal of periods of turning during the assessment, <10 were identified in single and dual task trials. Within all trials of the included 64 participants, a mean of 3.5 (standard deviation [SD] = 2.1) periods of turning were detected and removed. Twenty-seven phone-side leg strides (SD = 8, range = 12–35 strides) were identified from the remaining, relatively straight periods of walking. Numbers of identified turns and strides did not differ between single and dual task conditions.

Compared to the entire FPHS cohort, the TeamStudy subsample was similar in age, height, and body mass, but had a greater proportion of white participants (Table 1). The TeamStudy subsample was similar to the FPHS cohort in age at first exposure to organized ASF, number of NFL seasons played, and proportion of linemen to nonlinemen. As compared to the FPHS cohort, TeamStudy participants reported greater symptomatic head trauma scores and were more likely

TABLE 1. Self-Reported Demographic, Health, and Football-Related Characteristics of the TeamStudy Subsample Compared to the Total Population of the FPHS at Harvard University

Characteristic	FPHS	TeamStudy Subsample
Sample size	3,506	64
Age, yr, mean (SD)	52.8 (14.2)	52.7 (12.4)
Height, in, mean (SD)	74.3 (2.5)	74.9 (2.7)
Body mass, lb, mean (SD)	239.6 (42.0)	240.7 (41.3)
Race, n (%) white	2,053 (58.6)	47 (73.4)
Age at first organized football, yr, mean (SD)	11.8 (3.1)	11.7 (3.0)
Professional seasons, n, mean (SD)	6.8 (3.8)	6.5 (4.5)
Primary position played, n (%)		
Lineman	1,248 (35.6)	28 (43.8)
Nonlineman	2,258 (64.4)	36 (56.2)
Concussion-related symptoms		
Symptomatic head trauma score, mean (SD) ^a	32.0 (29.2)	21.9 (14.8)
Loss of consciousness, n (%) ^b	1,763 (50.2)	31 (48.4)
Physician-diagnosed medical conditions, n (%)		
Hypertension	1,325 (37.8)	23 (35.9)
Diabetes	313 (8.9)	2 (3.1)
Parkinson disease	24 (0.7)	1 (1.6)
Stroke	99 (2.8)	2 (3.1)
Arthritis	1,785 (50.9)	30 (46.9)
Dementia	125 (3.6)	0 (0.0)
Depression	312 (8.9)	1 (1.6)
History of musculoskeletal surgery, n (%) ^c	2,115 (60.3)	42 (65.6)
Global pain, mean (SD) ^d	4.8 (2.5)	3.75 (2.3)
PROMIS physical health, mean (SD) ^e	48.4 (8.1)	51.8 (6.8)
PROMIS mental health, mean (SD) ^e	43.4 (11.3)	49.4 (9.5)

^aSymptomatic head trauma score: sum of reported number of hits to the head or neck followed by 1 of 11 concussion-related symptoms.

^bLoss of consciousness: report of at least 1 hit to the head or neck followed by loss of consciousness.

^cMusculoskeletal surgery: at least 1 reported surgery for the neck, spine, hips, knees, or ankles.

^dGlobal pain: response to the question, "In the past 7 days, how would you rate your pain on average on a scale of 0 (no pain) to 10 (worst pain imaginable)".

^ePROMIS global physical and mental health were *t*-scored using standard procedures.

FPHS = Football Players Health Study; PROMIS = Patient-Reported Outcomes Measurement Information System; SD = standard deviation.

to report depression as a medical condition. On the other hand, the TeamStudy and FPHS cohorts reported approximately similar PROMIS physical and mental health scores.

The range of symptomatic head trauma score was broad (4–75) across participants. This score was not related to participant age, number of NFL seasons played, or the PROMIS physical health score ($r^2 < 0.02$, $p = 0.30$ – 0.65). TeamStudy participants who reported greater symptomatic head trauma score reported worse PROMIS mental health score ($r^2 = 0.09$, $p = 0.01$).

Effects of Self-Reported Head Trauma on Gait Performance

We examined relationships between gait outcomes and self-reported burden of hits followed by concussion-related symptoms by separating TeamStudy participants into quartiles of symptomatic head trauma score (Table 2). An effect of quartile was observed for the dual task cost to stride time variability ($F = 6.9$, $p = 0.005$). This effect was independent of age, BMI, the number of NFL seasons, and the number of reported musculoskeletal surgeries ($F = 6.0$, $p = 0.001$). Tukey post hoc testing of the adjusted model indicated that those in the highest burden quartile exhibited greater dual task costs to stride time variability than the 2 quartiles with lowest burden (see

Table 2). The dual task cost to stride time variability in the highest quartile was 9.8 (95% confidence interval [CI] = 3.5–27.9) times higher than in the first quartile and 4.4 (95% CI = 2.0–9.4) times higher than in the second quartile. A significant effect of quartile was also present for stride time variability specifically within the dual task walking condition (unadjusted: $F = 4.6$, $p = 0.03$; adjusted: $F = 4.2$, $p = 0.03$). The highest 3 burden quartiles exhibited greater dual task stride time variability than the lowest burden quartile by 1.3 (95% CI = 1.1–1.6), 1.4 (95% CI = 1.2–1.7), and 1.8 (95% CI = 1.5–2.2) times, respectively. Symptomatic head trauma quartile was not associated with the dual task cost to stride time, stride time within the dual task walking condition, or either gait metric within the single task walking condition.

Linear regression analysis similarly revealed that participants with higher symptomatic head trauma scores exhibited greater dual task costs to stride time variability (Figs 1 and 2). This relationship remained significant when models were adjusted for age, BMI, the number of NFL seasons, and the number of reported musculoskeletal surgeries ($r^2 = 0.20$, $p = 0.003$). Relationships between higher symptomatic head trauma score and greater stride time variability specifically within the dual task walking condition trended toward significance in both unadjusted

TABLE 2. Relationship between Self-Reported Symptomatic Head Trauma Quartile and Remotely Assessed Walking Performance in Retired NFL Players

	Symptomatic Head Trauma Score (quartile thresholds)				<i>p</i>
	<11	11–19	20–28	>28	
Sample, n	16	16	16	16	
Stride time, s					
Single task	1.1 (0.1)	1.2 (0.1)	1.2 (0.1)	1.2 (0.1)	0.89
Dual task	1.2 (0.1)	1.2 (0.1)	1.3 (0.1)	1.3 (0.1)	0.87
Stride variability, COV					
Single task	2.6 (0.8)	3.4 (1.2)	3.2 (1.1)	3.1 (1.7)	0.06
Dual task	2.7 (0.6) ^a	3.6 (1.2) ^b	3.8 (1.2) ^b	4.9 (1.3) ^b	0.03*
Dual task cost, %					
Stride time	1.7 (4.6)	3.2 (4.2)	4.4 (6.2)	3.8 (5.1)	0.19
Stride variability	3.3 (6.8) ^a	7.4 (10.9) ^{a,b}	22.9 (13.4) ^{b,c}	32.4 (17.6) ^c	0.003*

All values reflect group mean (standard deviation). Probability values reflect 1-way analyses of variance adjusted for age, body mass index, number of NFL seasons, and number of reported musculoskeletal surgeries.

^{a,b,c}Within each row, quartile means with different superscript letters were significantly different from one another based on Tukey post hoc testing of adjusted models.

*Statistically significant.

COV = coefficient of variation; NFL = National Football League.

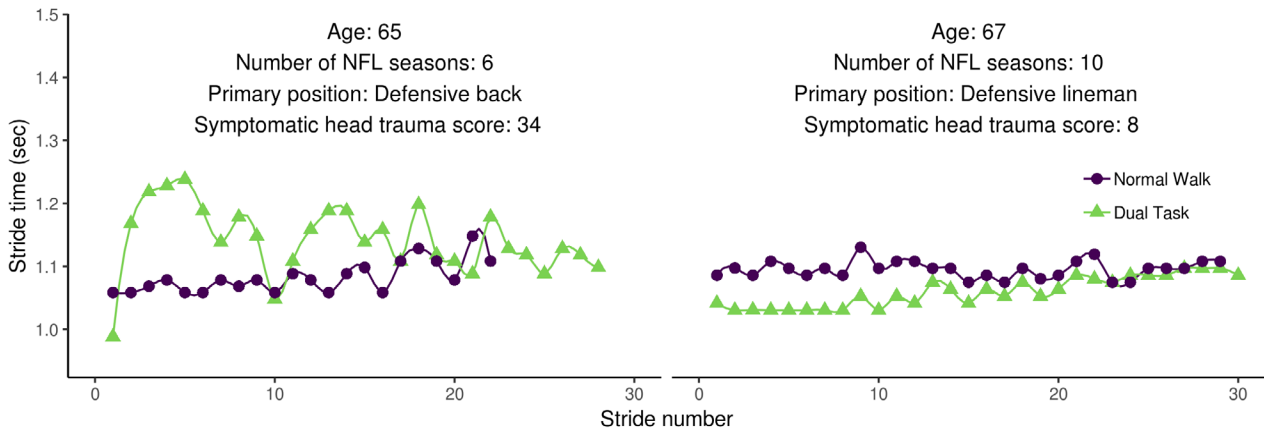


FIGURE 1: Stride times derived from remote smartphone-based dual task gait assessment for 2 retired National Football League (NFL) players. Symptomatic head trauma score was defined as the number of self-reported hits to the head or neck followed by 1 of 11 queried symptoms related to concussion (see Subjects and Methods). Each data point represents a validated stride time derived from consecutive heel strikes of the phone-side leg during all nonturning periods of walking within each 45-second trial. The dual task cost to stride time variability, as defined by the change (ie, percentage increase) from single to dual task walking conditions, was noticeably higher in the player who reported higher symptomatic head trauma.

($r^2 = 0.09$, $p = 0.09$) and adjusted ($r^2 = 0.06$, $p = 0.10$) regression models. The symptomatic head trauma score was not associated with the dual task cost to stride time or stride time within the dual task walking condition. Neither stride time nor its variability during the single task walking condition was related to self-reported symptomatic head trauma.

Self-report of experiencing hits to the head or neck specifically followed by loss of consciousness was also associated with worse gait performance. Participants who reported experiencing at least 1 hit followed by loss of consciousness had 2.5 times (95% CI = 1.6–3.9) greater dual task cost to stride time variability than those who did not report loss of consciousness (unadjusted: $F = 4.3$,

$p = 0.007$; adjusted: $F = 4.5$, $p = 0.001$; Table 3). Self-reported loss of consciousness did not have a significant effect on any other gait outcome.

Relationships between Gait Performance and Participant Demographics, ASF Exposure, and Health and Wellness

Older participants tended to have longer stride times when walking in both single task ($r^2 = 0.30$, $p = 0.04$) and dual task ($r^2 = 0.32$, $p = 0.03$) conditions. Those who reported at least 1 surgery to the neck, back, hips, knees, or ankles also tended to have longer stride times in both walking conditions (single task: $r^2 = 0.25$, $p = 0.02$; dual task: $r^2 = 0.18$, $p = 0.05$). Age and history of musculoskeletal surgery did not significantly

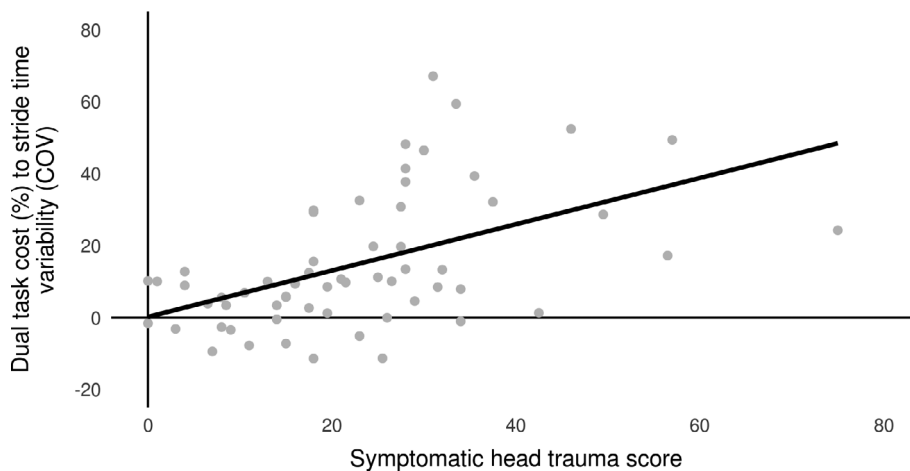


FIGURE 2: The relationship between self-reported symptomatic head trauma and the dual task cost to stride time variability. The symptomatic head trauma score was defined as the number of self-reported hits to the head or neck followed by 1 of 11 queried symptoms related to concussion (see Subjects and Methods). The dual task cost was calculated as the percentage change in the coefficient of variation (COV) in mean stride time from single to dual task walking conditions.

TABLE 3. Relationship between Self-Reported Loss of Consciousness following a Hit to the Head or Neck and Remotely Assessed Walking Performance in Retired NFL Players

	Loss of Consciousness		<i>p</i>
	No	Yes	
Sample, n	32	32	
Stride time, s			
Single task	1.2 (0.1)	1.2 (0.1)	0.80
Dual task	1.2 (0.1)	1.2 (0.1)	0.68
Stride variability, COV			
Single task	3.2 (1.1)	3.0 (1.1)	0.83
Dual task	3.5 (1.1)	3.7 (1.2)	0.41
Dual task cost, %			
Stride time	2.9 (5.7)	2.9 (5.4)	0.94
Stride variability	8.6 (10.2)	21.4 (12.7)	0.007 ^a

All values reflect group mean (standard deviation). Probability values reflect 1-way analyses of variance adjusted for age, body mass index, number of NFL seasons, and number of reported musculoskeletal surgeries.

^aStatistically significant.

COV = coefficient of variation; NFL = National Football League.

correlate with stride time variability or dual task cost metrics. Gait metrics were not significantly correlated with participant BMI, race, age at first exposure to organized football, number of NFL seasons played, or primary position played within the NFL. Participants who reported worse PROMIS global physical health walked with longer stride times in the single task condition ($r^2 = 0.19$, $p = 0.05$), but not during dual task walking. Gait metrics were not sensitive to general pain severity or PROMIS global mental health.

Discussion

This cross-sectional study utilized a validated smartphone app to remotely assess dual task walking performance in former professional ASF players participating in the FPHS at Harvard University. Participants who reported relatively high burden of hits followed by concussion-related symptoms during their professional playing careers exhibited significantly greater stride time variability when dual tasking, as well as greater dual task cost to this metric of gait performance. Those who reported suffering at least 1 hit to the head or neck followed by loss of consciousness also exhibited greater dual task costs to stride time variability. As each of these results were independent of

participant age, BMI, NFL career duration, and reported history of musculoskeletal surgery, this preliminary evidence indicates that remote assessments of dual task walking may be particularly sensitive to chronic brain dysfunction associated with repetitive sports-related head trauma.

Performance decrements associated with dual tasking are theorized to arise as the 2 tasks compete for shared brain resources.²⁰ The observation that participants who reported greater total symptomatic head trauma, or at least 1 hit followed by loss of consciousness, also exhibited greater dual task costs suggests that these individuals possessed diminished capacity to differentially recruit the required brain networks or enlist the alternative cognitive strategies needed to maintain performance in both tasks.²¹ Whereas symptomatic head trauma was linked to worse gait performance specifically during dual task walking, it was not correlated with gait performance during single task walking—a task that, as compared to dual-tasking, is less cognitively demanding and associated with relatively lower levels of cortical brain activation.²² The results of this study therefore suggest the possibility that the accumulation of biomechanical head trauma severe enough to induce concussionlike symptoms may manifest in later life as diminished “cognitive reserve.”²¹ However, future studies that assess and control for serial subtraction performance are needed. Such work should also consider capturing common proxies of cognitive reserve such as education,²³ examine compensatory strategies that may enable some individuals to maintain function in the presence of brain pathology, and consider the possible beneficial protective impact of cognitive remediation, physical exercise, and/or other interventions aimed at promoting cognitive reserve into senescence.²⁴

Although walking entails repetitive cyclical movements, no two gait cycles are exactly the same. In the current study, self-reported symptomatic head trauma did not influence single or dual task average stride time, a metric closely related to walking speed. However, participants within the 3 highest quartiles of symptomatic head trauma score, as compared to the lowest quartile, walked with elevated dual task stride time variability. Mounting evidence indicates that dual task stride time variability may be a sensitive predictor of even subtle changes in cognitive function.^{9,13,25} Beauchet et al,¹³ for example, reported in a sample of 56 nondemented older adults that those with greater dual task stride time variability at baseline were more likely to experience global cognitive decline as measured by the Mini-Mental State Examination over a 5-year follow-up period. Recently, Lo et al¹⁹ provided resting-state functional magnetic resonance imaging evidence from a small sample of older adults that greater

stride time variability correlated with weaker functional connectivity between 2 large-scale brain networks; namely, the dorsal attention and default networks. Intriguingly, the functional connectivity between these 2 networks has separately been linked to sustained attention defined as the capacity to maintain performance on a continuous cognitive task over time.²⁶ The observed link between symptomatic head trauma and stride time variability in the current study is thus supported by reports that retired NFL players who report a history of concussion, as compared to those who do not, tend to have difficulties in attentional control,²⁷ structural abnormalities within frontoparietal tracts and the corpus callosum,²⁸ and reduced global resting-state functional connectivity.²⁹ However, reported links between sports-related head trauma, brain structure, brain function, and/or health outcomes have been derived largely from cross-sectional studies and/or comparisons to suboptimal control groups. Longitudinal studies that include multimodal mobile imaging of numerous aspects of dual task gait performance³⁰ and/or habitual physical activity coupled with physiologic, biomarker, and neurocognitive testing are thus needed to establish whether a history of sports-related head trauma alters the time course of changes in brain health, and whether such changes underline reductions in gait and other cognitive–motor functions over time.

Metrics of gait performance were obtained via smartphone assessment without supervision from trained personnel in nonlaboratory environments that undoubtedly varied from participant to participant. Although it is thus impossible to confirm whether participants completed the assessment correctly in the absence of environment perturbations, only those steps identified from periods meeting specific validated criteria were included in analysis. Moreover, we observed that participant age, history of musculoskeletal surgery, and self-report of worse physical function were each correlated with longer average stride times under both single and dual task walking conditions. The presence of these relationships, which were expected and corroborated by several previous reports in other populations,^{15,31} provides additional support that gait assessments were completed successfully as directed.

Symptomatic head trauma scores were derived from self-report of events that occurred quite remote in time for many participants. The accuracy of such recall may also have been influenced by multiple factors, including participant age, NFL career duration, and current health status. Sampling biases may also have been present; for example, older players who were willing and able to participate in the study despite relatively high symptomatic head trauma scores may not be representative of all players of similar age and self-reported burden. Nevertheless, results of

adjusted analyses focused on symptomatic head trauma score quartiles—together with corroborating results of models focused on self-report of suffering at least 1 hit followed by loss of consciousness—provide preliminary evidence that suffering relatively large amounts of symptomatic head trauma during one’s professional playing career is associated with worse gait performance in later life. We therefore believe that a remote smartphone-based assessment of dual task walking may provide important information for the evaluation of present and incipient dysfunction in former professional ASF players and possibly others exposed to high-risk repetitive head trauma.

Acknowledgment

This work was primarily supported by the FPHS at Harvard University, the Harvard Catalyst | Harvard Clinical and Translational Science Center (NIH/National Center for Research Resources and National Center for Advancing Translation Sciences, UL1 RR025758), and the NIH/NIA Boston Claude D. Pepper Older Americans Independence Center (OAIC) (P30 AG031679). B.M. and J.Z. were also supported by grants from the NIH/NIA (R01 AG059089-01), the United States-Israel Binational Science Foundation, and the Marcus-Applebaum Foundation at Hebrew SeniorLife. A.P.-L. was also supported by grants from the NIH, National Science Foundation, Sidney R. Baer, Jr. Foundation, and Defense Advanced Research Projects Agency (DARPA; HR001117S0030). The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic health care centers, the National Institutes of Health, NeuroNEXT, the Sidney R. Baer, Jr. Foundation, the FPHS, or DARPA.

Author Contributions

B.M., R.Z., and A.P.-L. contributed to study concept and design. B.M., J.Z., O.-Y.L., H.Z., W.Y., N.A.G., and T.G.T. contributed to data acquisition and analysis. B.M., J.Z., O.-Y.L., H.Z., R.Z., L.A.L., T.G.T., and A.P.-L. contributed to manuscript and figure preparation.

Potential Conflicts of Interest

Nothing to report.

References

1. Montenigro PH, Alosco ML, Martin BM, et al. Cumulative head impact exposure predicts later-life depression, apathy, executive dysfunction, and cognitive impairment in former high school and college football players. *J Neurotrauma* 2017;34:328–340.

2. Mez J, Daneshvar DH, Kiernan PT, et al. Clinicopathological evaluation of chronic traumatic encephalopathy in players of American football. *JAMA* 2017;318:360–370.
3. Montenegro PH, Baugh CM, Daneshvar DH, et al. Clinical subtypes of chronic traumatic encephalopathy: literature review and proposed research diagnostic criteria for traumatic encephalopathy syndrome. *Alzheimers Res Ther* 2014;6:68.
4. Montero-Odasso M, Almeida QJ, Bherer L, et al. Consensus on shared measures of mobility and cognition: from the Canadian Consortium on Neurodegeneration in Aging (CCNA). *J Gerontol A Biol Sci Med Sci* 2019;74:897–909.
5. Yogev-Seligmann G, Hausdorff JM, Giladi N. The role of executive function and attention in gait. *Mov Disord* 2008;23:329–342; quiz 472.
6. Ruffieux J, Keller M, Lauber B, Taube W. Changes in Standing and Walking Performance Under Dual-Task Conditions Across the Lifespan. *Sports Med* 2015;45:1739–1758.
7. Parker TM, Osternig LR, Lee HJ, et al. The effect of divided attention on gait stability following concussion. *Clin Biomech (Bristol, Avon)* 2005;20:389–395.
8. Howell DR, Osternig LR, Chou LS. Detection of acute and long-term effects of concussion: dual-task gait balance control versus computerized neurocognitive test. *Arch Phys Med Rehabil* 2018;99:1318–1324.
9. Lee J, Park S. Effects of a priority-based dual task on gait velocity and variability in older adults with mild cognitive impairment. *J Exerc Rehabil* 2018;14:993–997.
10. Hamacher D, Hamacher D, Schega L. A cognitive dual task affects gait variability in patients suffering from chronic low back pain. *Exp Brain Res* 2014;232:3509–3513.
11. Herman T, Mirelman A, Giladi N, et al. Executive control deficits as a prodrome to falls in healthy older adults: a prospective study linking thinking, walking, and falling. *J Gerontol A Biol Sci Med Sci* 2010;65:1086–1092.
12. Montero-Odasso MM, Sarquis-Adamson Y, Speechley M, et al. Association of dual-task gait with incident dementia in mild cognitive impairment: results from the Gait and Brain Study. *JAMA Neurol* 2017;74:857–865.
13. Beauchet O, Launay CP, Sekhon H, et al. Association of increased gait variability while dual tasking and cognitive decline: results from a prospective longitudinal cohort pilot study. *Geroscience* 2017;39:439–445.
14. Allali G, Montembeault M, Brambati SM, et al. Brain structure covariance associated with gait control in aging. *J Gerontol A Biol Sci Med Sci* 2019;74:705–713.
15. Jor'dan AJ, Manor B, Illoputaife I, et al. Diminished locomotor control is associated with reduced neurovascular coupling in older adults. *J Gerontol A Biol Sci Med Sci* 2019; <https://doi.org/10.1093/gerona/glz006>.
16. Manor B, Yu W, Zhu H, et al. Smartphone app-based assessment of gait during normal and dual-task walking: demonstration of validity and reliability. *JMIR Mhealth Uhealth* 2018;6:e36.
17. Cella D, Riley W, Stone A, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. *J Clin Epidemiol* 2010;63:1179–1194.
18. Strike SC, Taylor MJ. The temporal-spatial and ground reaction impulses of turning gait: is turning symmetrical? *Gait Posture* 2009;29:597–602.
19. Lo OY, Halko MA, Zhou J, et al. Gait speed and gait variability are associated with different functional brain networks. *Front Aging Neurosci* 2017;9:390.
20. Pashler H. Dual-task interference in simple tasks: data and theory. *Psychol Bull* 1994;116:220–244.
21. Tucker AM, Stern Y. Cognitive reserve in aging. *Curr Alzheimer Res* 2011;8:354–360.
22. Mirelman A, Maidan I, Bernad-Elazari H, et al. Increased frontal brain activation during walking while dual tasking: an fNIRS study in healthy young adults. *J Neuroeng Rehabil* 2014;11:85.
23. Grotz C, Seron X, Van Wissen M, Adam S. How should proxies of cognitive reserve be evaluated in a population of healthy older adults? *Int Psychogeriatr* 2017;29:123–136.
24. Stern Y, Arenaza-Urquijo EM, Bartres-Faz D, et al. Whitepaper: Defining and investigating cognitive reserve, brain reserve, and brain maintenance. *Alzheimer Dement* 2018;pii:S1552-5260(18)33491-5.
25. Hausdorff JM, Schweiger A, Herman T, et al. Dual-task decrements in gait: contributing factors among healthy older adults. *J Gerontol A Biol Sci Med Sci* 2008;63:1335–1343.
26. Esterman M, Noonan SK, Rosenberg M, Degutis J. In the zone or zoning out? Tracking behavioral and neural fluctuations during sustained attention. *Cereb Cortex* 2013;23:2712–2723.
27. Alosco ML, Koerte IK, Tripodis Y, et al. White matter signal abnormalities in former National Football League players. *Alzheimers Dement (Amst)* 2018;10:56–65.
28. Tremblay S, Henry LC, Bedetti C, et al. Diffuse white matter tract abnormalities in clinically normal ageing retired athletes with a history of sports-related concussions. *Brain* 2014;137(pt 11):2997–3011.
29. Hampshire A, MacDonald A, Owen AM. Hypoconnectivity and hyperfrontality in retired American football players. *Sci Rep* 2013;3:2972.
30. Malcolm BR, Foxe JJ, Butler JS, De Sanctis P. The aging brain shows less flexible reallocation of cognitive resources during dual-task walking: a mobile brain/body imaging (MoBI) study. *Neuroimage* 2015;117:230–242.
31. Slater LV, Hart JM, Kelly AR, Kuenze CM. Progressive changes in walking kinematics and kinetics after anterior cruciate ligament injury and reconstruction: a review and meta-analysis. *J Athl Train* 2017;52:847–860.