Published in final edited form as:

Neurosci Lett. 2019 January 23; 692: 150–158. doi:10.1016/j.neulet.2018.10.022.

Stride-time variability is related to sensorimotor cortical activation during forward and backward walking

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Abstract

Previous research has used functional near-infrared spectroscopy (fNIRS) to show that motor areas of the cortex are activated more while walking backward compared to walking forward. It is also known that head movement creates motion artifacts in fNIRS data. The aim of this study was to investigate cortical activation during forward and backward walking, while also measuring head movement. We hypothesized that greater activation in motor areas while walking backward would be concurrent with increased head movement. Participants performed forward and backward walking on a treadmill. Participants wore motion capture markers on their head to quantify head movement and pressure sensors on their feet to calculate stride-time. fNIRS was placed over motor areas of the cortex to measure cortical activation. Measurements were compared for forward and backward walking conditions. No significant differences in body movement or head movement were observed between forward and backward walking conditions, suggesting that conditional differences in movement did not influence fNIRS results. Stride-time was significantly shorter during backward walking than during forward walking, but not more variable. There were no differences in activation for motor areas of the cortex when outliers were removed. However, there was a positive correlation between stride-time variability and activation in the primary motor cortex. This positive correlation between motor cortex activation and stride-time variability suggests that forward walking variability may be represented in the primary motor cortex.

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Conflict of Interest

The authors have no conflict of interest to declare.

Keywords

fNIRS; hemodynamic response; primary motor area; gait; cortex

Introduction

Past research has shown that structured, yet variable walking patterns are a characteristic of healthy young adults [1–3]. Deviations from these patterns are seen in older adults with increased fall risk, Parkinson’s disease, and other movement-related disorders [2–15]. Although changes in the variability present during walking have been reported in neurological and movement-related disorders, the precise relationship between cortical activity and this variability has not been studied in detail. Understanding how neural activity is related with walking variability may provide valuable insight into movement-related disorders and their respective treatment.

Studying human neural activity during movement and especially walking has proven to be a challenge in the past. Widely implemented imaging techniques, such as functional magnetic resonance imaging (fMRI) and positron emission topography (PET), are limited to foot movement as a proxy of walking or are used following a period of walking. Such studies have indicated the importance of the cerebellum, basal ganglia, and medial sensorimotor cortices in the task of walking [16–21]. However, isolated foot movement does not necessarily involve the complexities, or essential neural activity, of healthy walking. Thus, measuring cortical response following movement does not provide information on dynamic neural changes during the actual task of walking.

More recently, functional near infrared spectroscopy (fNIRS) and electroencephalography (EEG) have been used to record neural activity during movement tasks [22–26]. Both devices can be worn on the head during walking allowing for an immediate measure of cortical response [22–26]. Previous studies using fNIRS have corroborated the importance of medial motor, sensory, and supplementary motor areas in walking dynamics [23–29]. Specifically, Kurz et al. [23] utilized fNIRS to examine the relationship between sensorimotor cortical activity and stride-time (the time to complete a stride) variability during forward and backward walking. They reported that both stride-time variability and hemodynamic cortical activation in motor areas were greater while walking backwards compared to walking forwards [23]. In addition, a positive correlation was found between stride-time variability and primary motor cortex activation during forward walking [23]. They concluded that backward walking is more variable because it is practiced less than forward walking, and increased movement variability may require greater cortical resources [23]. However, previous studies, including Kurz et al. [23] did not consider in their conclusions that fNIRS data is highly susceptible to motion contamination, which is a shortcoming for its use in walking research [24–26]. Specifically, Cui et al. [30] has shown that motion artifacts in fNIRS data correlate to the magnitude of head movement. Although an increasing number of experiments are utilizing fNIRS to study cortical activation during walking, few studies have attempted to quantify head motion [30,31]. If fNIRS data is used

to examine cortical activation in walking studies, it is then necessary to account for differences in head motion between conditions.

The purpose of the current study was to investigate the relationship between stride-time variability and sensorimotor cortical activation during forward and backward walking, while also providing novel information about how head movement during walking may relate to hemodynamic cortical measurements. Using fNIRS, we measured oxygenated hemoglobin (oxyHb) and deoxygenated hemoglobin (deoxyHb) concentrations in the superior parietal lobule, post-central gyrus, pre-central gyrus, and supplementary motor area during walking conditions. Motion-capture markers were placed on the head and neck to account for head motion. We hypothesized that greater cortical activation and movement variability would be seen during backward walking and sensorimotor response would correlate with stride-time variability. Since previous research has reported greater stride-time variability during backward walking [23], we also hypothesized that there would be increased head movement during backward walking, and this would be concurrent with a greater hemodynamic response.

Material and methods

Participants

Ten healthy young adults (4 females, 6 males; age = 22.1 ± 1.4 years; mass = 71.1 ± 6.9 kg; height = 1.76 ± 6.9 m) participated in this study. The study was approved by the University of Nebraska Medical Center Institutional Review Board and all participants were required to give their written informed consent prior to the commencement of the study.

Experimental Procedure

Experimental procedures were based on the procedures of Kurz et al. [23]. Participants were asked to complete a forward and a backward walking session on a treadmill for this experiment (AMTI Force Sensing Tandem Treadmill; AMTI, Watertown, Massachusetts). There were five trials in each session, where each trial consisted of standing still for 30 seconds and walking at 0.45 m/s for 30 seconds. Since there were no breaks in between trials, each session lasted exactly five minutes. The order of the forward walking session and backward walking session was randomized for each participant. In order to maintain head position, participants held onto handrails and kept their gaze fixed on a fixation cross at eye-level throughout the trials.

Data analysis

A continuous-wave fNIRS system (ETG-4000 Optical System; Hitachi Medical Corporation, Tokyo, Japan) with two different wavelengths (~ 695 and ~ 830 nm) was used in this study to measure changes in near-infrared light absorption sampled at 10 Hz. Based on the modified Beer-Lambert approach [32,33] changes in near-infrared light absorption were converted to changes in oxygenated hemoglobin (oxyHb) and deoxygenated hemoglobin (deoxyHb). The fNIRS probe consisted of 8 emitter and 8 detector optodes affixed in a cap. Optodes were 3 cm apart and arranged into a 4×4 grid to create 24 channels for measuring hemodynamic cortical response. The fNIRS probe was placed on the participants' head

based on the International 10/20 System for EEG [34] and positioned so that Cz was located between the front two rows of optodes (between channels 19 and 20; Fig. 1). Cz was defined as halfway between the nasion and inion and halfway between preauricular points. Based on transformations from the International 10/20 EEG locations to MNI coordinates [35,36], the probe covered medial regions of the frontal and parietal lobes. Regions of interest were defined as the supplementary motor area (SMA; ch 19-20, 22-24), pre-central gyrus (PreCG; ch 12-13, 15-17), post-central gyrus (PostCG; ch 8-10, 12-13), and superior parietal lobule (SPL; ch 1-3, 5-6; Fig. 1). Infrared-light was transferred from optodes to the Hitachi ETG-4000 workstation through fiber optic cables. These cables were secured to a support system to reduce cap movement during walking trials (Fig. 2).

The fNIRS data were processed as follows [23]. A 5.0 s moving average and 0.01 Hz high pass filter were applied to the oxyHb and deoxyHb concentration waveforms for each channel. Principal component analyses were then implemented to remove biological noise and increase the signal-to-noise ratio [37,38]. Components for each trial were compared to a reference waveform: a trapezoidal function with a 5 second increase in concentration at the start of walking, a 25 second sustained peak concentration, and a 5 second decrease in concentration following the trial. If the correlation between the component and reference waveform was greater than 0.25, the component was incorporated into the final reconstruction of the oxyHb and deoxyHb time series for individual channels. Components with a correlation to the reference waveform of less than 0.25 were excluded from reconstruction. Following reconstruction, data were averaged across trials for each channel and participant. Thus, average deoxyHb and oxyHb waveforms were generated to represent the average hemodynamic activity for individual channels during forward and backward walking trials. The average waveforms consisted of a 10 second baseline, 30 second stimulus, 10 second post stimulus, and 10 second recovery period. For each channel and condition, oxyHb and deoxyHb concentrations were assessed relative to the 2.5 seconds prior to the onset of walking. Average maximum oxyHb and average minimum deoxyHb calculated for each region of interest and participant were compared for forward and backward walking.

Pressure sensors were used to measure heel-strikes and toe-offs of each foot during walking. Sensors were taped to the heel and first metatarsal of participants' feet. Data was collected at 148 Hz using footswitch sensors and a portable data collector (Trigno Mobile; Delsys Incorporated, Natick, Massachusetts). Raw data was used to calculate inter-stride intervals (ISI). The ISI, in relation to walking, is defined as the period of time between when the heel of one foot strikes the ground, weight is transferred to the other foot, and then the heel of the first foot hits the ground again. In this study, the time between heel strikes of the left foot was measured as the ISI. The ISI from the 30-second resting periods was removed to create a single series of ISI for each walking session. ISI mean, standard deviation, and coefficient of variation (CoV; standard deviation/mean $\times$ 100) were calculated and compared for walking conditions.

A 12-camera motion capture system (Raptor-E Digital RealTime System; Motion Analysis Corporation, Santa Rosa, California) was utilized to quantify head movement during forward and backward walking. Markers were placed participants' temples, adjacent regions on the

back of the head, 7th cervical vertebra (C7), and the sternum. An additional marker was placed directly above Cz on the fNIRS probe. Data was collected at 60 Hz and tracked using Cortex software (Cortex 5.3, Motion Analysis Corporation, Santa Rosa, California). Motion capture data from the five, 30-second walking periods was extracted for both the forward and backward walking sessions. Data from the motion capture marker on the sternum was analyzed to measure body movement. Importantly, data from the motion capture marker on the left temple was analyzed relative to the sternum marker in order to provide a measure of head movement relative to body movement (left temple - sternum). For both the sternum marker and left temple marker relative to the sternum marker, range of motion, path length, and root mean square were calculated for the anterior-posterior, medial-lateral, and vertical directions. For range of motion, the range of values for each of the five walking periods was calculated for the anterior-posterior, medial-lateral, and vertical directions. These five ranges were then averaged together to provide an average range of head movement in the anterior-posterior, medial-lateral, and vertical directions per session (forward or backward walking) and participant. Similarly, differential path length of the motion capture marker was calculated for each of the five walking periods. Differential path length was calculated by determining the distance a motion capture marker had moved between one time point and the next. These distances were then summed for each walking trial, and the sums for the five walking trials were then averaged together. This resulted in average anterior-posterior, medial-lateral, vertical, and composite path lengths for each session (forward and backward walking) and participant. Root mean square was calculated similarly. Range of motion, root mean square, and path length for each direction were compared across conditions for the sternum marker (body movement) and for the left temple marker relative to the sternum marker (relative head movement). One participant was excluded from motion capture analyses due to a missing sternum marker.

Statistics

Non-parametric statistical tests were used for analysis, because Shapiro-Wilk tests of normality indicated that the majority of the fNIRS data were not normally distributed. Wilcoxon sign-ranked tests were performed to determine if there was a difference in maximum oxyHb, minimum deoxyHb, ISI mean, ISI standard deviation, ISI CoV, range of marker movement, root mean square of marker movement, and marker line path between forward and backward walking conditions. Spearman's rank correlations were used to determine if average maximum oxyHb correlated with ISI coefficient of variation, mean, or standard deviation for forward or backward walking conditions. Spearman's rank correlations were performed to determine if there was a relationship between the amount of variability during walking and hemodynamic cortical activation in the SMA, PreCG, PostCG, or SPL. Significance was set at 0.05. Results are reported as median and interquartile range.

Results

No significant differences in body movement or relative head movement were observed between forward and backward walking conditions. The range of body movement in the anterior-posterior was greater by 27.423 mm during backward walking compared to forward

walking, but this difference was not significant ($P = 0.050$; Fig. 3). There were no significant differences in body movement for the medial-lateral ($P = 0.489$) or vertical ($P = 0.077$) directions. No significant differences in the range of relative head movement were observed for the anterior-posterior ($P = 0.340$), medial-lateral ($P = 1.00$) or vertical ($P = 0.931$; Fig. 4) directions. Similarly, there were no significant differences in the root mean square for body movement in the anterior-posterior, medial-lateral or vertical directions (Table 1). Root mean square for relative head movement did not show significant differences in any of the three directions (Table 1). The total line paths of the sternum marker and head marker relative to the sternum marker were not significantly different between walking trials for any of the three directions (Table 2).

There were no significant differences in maximum oxyHb concentration in the SMA ($P = 0.695$), PreCG ($P = 0.922$), PostCG ($P = 0.695$), or SPL ($P = 0.625$; Fig. 5). Compared to forward walking, minimum deoxyHb concentration in the SMA was significantly lower during backward walking ($P = 0.020$; Fig. 6). There were no significant differences in minimum deoxyHb concentrations for the PreCG ($P = 0.375$), PostCG ($P = 0.846$), or SPL ($P = 0.375$; Fig. 6).

ISI coefficient of variation was significantly greater during backward walking compared to forward walking ($P = 0.004$; Fig. 7). Mean ISI was significantly greater during forward walking (Backward: 1.463, 1.405 to 1.515 s; Forward: 1.841, 1.679 to 1.981 s; $P = 0.004$), but there was no significant difference in ISI standard deviation (Backward: 0.070, 0.063 to 0.075 s; Forward: 0.064, 0.049 to 0.075 s; $P = 0.113$).

Coefficient of variation, mean, standard deviation of ISI for backward walking did not correlate with maximum oxyHb concentration in any regions of interest. However, there was a significant positive correlation between maximum oxyHb concentration in the PreCG and ISI standard deviation during forward walking ($R = 0.66$, $P = 0.044$; Fig. 8). In addition, there was a positive correlation between ISI coefficient of variation during forward walking and maximum oxyHb concentration in the PreCG, but this relationship was not significant ($R = 0.55$, $P = 0.104$). There was also a significant correlation between maximum oxyHb in the SPL and ISI mean for forward walking ($R = 0.66$, $P = 0.044$).

Discussion

The current study investigated sensorimotor cortical activation, stride-time variability, and head movement between forward and backward walking conditions. Participants were instructed to walk forward and backward on a treadmill while hemodynamic response was measured by fNIRS. Results did not indicate differences in head movement, stride-time variability, or sensorimotor activation between forward and backward walking conditions. However, a significant positive correlation between hemodynamic sensorimotor cortical activity and stride-time variability was found, indicating the importance of the medial motor cortices in stride-time variability.

There were no differences in the range of body movement, relative head movement range, total path length for body movement, or total path length for relative head movement.

Similarly, there were no conditional differences in the root mean square for relative head movement. However, some differences in the motion capture data may not have been significant possibly due to the small sample size for this analysis. Therefore, conditional differences with a $P = 0.100$ are still described. Specifically, the range of anterior-posterior body movement during backward walking was 48.68% greater relative to the forward walking condition, but this difference did not reach significance ($P = 0.050$). These findings can be interpreted to mean participants may have had an increased range of anterior-posterior body movement while walking backward, but the range and magnitude of relative head movement did not significantly differ between forward and backward walking conditions. Since the increased range of movement while walking backward was not specific to the head, it is more likely that participants had an increased range of anterior-posterior movement due to difficulty maintaining a constant speed while walking backwards on a treadmill. Although slow and rapid head movements have been found to correlate with motion artifacts in fNIRS data [30], differences in the range of anterior-posterior body movement between forward and backward walking conditions would not influence fNIRS results, since relative head movement did not differ between conditions. Holding onto the treadmill handrails and visual fixation in this experiment may have prevented larger conditional differences in head movement.

Although stride-time coefficient of variation was greater during backward walking, further analyses indicated this finding did not correspond with increased stride-time variability. Mean stride-time was significantly greater during backward walking, but there were no conditional differences in standard deviation of stride-time. This indicates that conditional differences in coefficient of variation were influenced by differences in mean stride-time and not standard deviation. Decreases in stride-time during backward walking may have been caused by discomfort or lack of practice with backward walking. These findings did not correspond with Kurz et al. [23] and other previous studies [39–41], where stride-time variability was reported to be greater during backward walking. It is possible that Kurz et al. [23] showed a similar pattern of results for stride-time mean and standard deviation. However, this cannot be proven, because mean and standard deviation of stride-time were not reported as separate variables by Kurz et al. [23]. A different study reported reduced stride-length and increased stride-length variability during backward walking compared to forward walking [40]. This finding indicates that mean stride-length and variability are both altered during backward walking.

OxyHb concentration in regions of interest did not differ significantly between forward and backward walking conditions. In contrast, Kurz et al. [23] found increased oxyHb concentrations in the supplementary motor area, pre-central gyrus, and superior parietal lobule during backward walking. A number of reasons may explain why the findings of this study do not correspond with Kurz et al. [23]. In a more recent fNIRS walking study, Koenraadt et al. [28] found that more challenging walking conditions (i.e. precision stepping) did not correspond with increased sensorimotor cortical activation. These findings suggest that neural differences due to walking task difficulty are more discernable in subcortical regions and not in cortical areas [26]. In addition, Koenraadt et al. [28], unlike Kurz et al. [23] and the current study, utilized reference channels to correct for superficial blood flow. The authors suggest that the differences in sensorimotor activity found by Kurz

et al. [23] may have been influenced by differences in blood pressure between forward and backward walking conditions [28]. Respiration and superficial blood flow are known to interfere with measures of hemodynamic cortical activity [42–46]. Therefore, variable interference from superficial blood flow may explain why the results of the current study do not replicate the conditional differences in hemodynamic cortical activity observed in Kurz et al. [23]. On another note, the motor cortex may have an increased metabolic demand when processing efferent signals that result in more variable motor output. In line with this concept, Kurz et al. [23] suggests that the increased stride-time variability during backward walking in their study may have primarily been due to increased metabolic demands on the motor cortex, resulting in an increased hemodynamic response. Our results are in-line with this logic, such that oxyHb concentration did not differ between forward and backward walking and there were no conditional differences in stride-time variability (i.e. ISI standard deviation). However, for both Kurz et al. [23] and the current study, the directionality of relationship between stride-time variability and hemodynamic cortical activity cannot be effectively established. Lastly, large ranges of oxyHb concentration may have prevented conditional differences from reaching significance in this study.

Similar to Kurz et al. [23], deoxyHb concentration in the supplementary motor area was found to be reduced during backward walking. The reproducibility of these results may speak to the importance of the supplementary motor area in backward walking control [23]. However, corresponding differences in oxyHb in the supplementary motor area were not found in this study. The deoxyHb concentration has a reduced signal-to-noise ratio compared to oxyHb and has been found to be inconsistent during walking tasks [23,24,47]. Further research examining cortical deoxyHb activity would be necessary to confirm the importance of the deoxyHb response in backward walking.

A significant positive correlation between stride-time variability (standard deviation of stride-time) and activation in the precentral gyrus during forward walking is similar to the findings of Kurz et al. [23]. This finding further indicates the importance of the pre-central gyrus in stride-time variability. Stride-to-stride variation may be produced by dynamic changes in motor control, leading to increased oxygen consumption in the primary motor cortex. In addition, mean stride-time was found to positively correlate with activation in the superior parietal lobule. This finding indicates that the timing of steps may be associated with parietal cortex activation. Lastly, similar to Kurz et al. [23], no relationships between stride-time variability and sensorimotor activation during backward walking were found.

The current study has limitations. First, due to size limitations of the fNIRS probe, only medial sensorimotor cortical areas were examined in this study. However, other regions of the cortex are likely involved in forward and backward walking. For example, the dorso-lateral-prefrontal cortex is associated with motor control [48], making it a region of potential importance for novel tasks like backward walking. Examining a broader range of cortical regions should be a focus of future research studying the neural correlates of walking variability. Previous studies have also shown the importance of the cerebellum, basal ganglia, and spinal cord in motor control [19,39,49]. Although these areas were not measured in this study, their activity may have differed between forward and backward walking conditions. Finally, this study was conducted using ten healthy young adults. In

terms of numbers and lack of variability in participants, this limitation can restrict generalizability of results, and lack of statistical significance for some differences may be a result of being underpowered to detect those differences rather than the lack of important differences. Ten participants do provide 80% power to detect a standardized effect size of 1.1 (larger than a large effect, as defined by Cohen) with a 0.05 significance level for a two-sided Wilcoxon test. While we realize there will not be sufficient power to detect smaller effects, these results can inform future research directions. In addition, this study did find significant differences in stride-time and hemodynamic activity between forward and backward walking conditions, as well a significant correlation between stride-time variability and hemodynamic cortical activation. Some comparisons, such as head movement during forward and backward walking, have very similar distributions so it is not likely that meaningful differences were missed due to a lack of statistical power. Other comparisons, while not found statistically significant in the current study, reveal important information on what differences are likely to exist and give new insights for further research.

The current study was consistent with some findings of Kurz et al. [23], while also providing novel measurements of relative head movement in an fNIRS walking study. These results further indicate the importance of the pre-central gyrus in movement variability and the potential for using fNIRS to study cortical regions associated with walking. Although fNIRS is being used increasingly to study cortical activity during walking, most studies have only attempted to correct for motion artifacts. Alternatively, quantifying head movement during walking will allow for it to be measured as a covariate during analysis. If fNIRS is to successfully be used to study hemodynamic activity during walking, it may be necessary for future studies to measure head movement as an additional variable.

Conclusions

Cortical activation and stride-time variability did not differ between forward and backward walking. However, supporting previous results, we found that hemodynamic response in the precentral gyrus correlates with stride-time variability while walking forward. This finding further supports the association between stride-time variability and the function of the motor cortex in the control of walking. Although differences in head movement did not appear to influence the results of this study, quantifying head motion in future fNIRS walking experiments may provide additional insight into fNIRS data. Overall, the methods of the current study lay a framework for better accounting for head movement during fNIRS walking studies, the findings provide insights for future fNIRS studies examining hemodynamic cortical activity during different walking tasks, and the results support the findings of Kurz et al. [23], further indicating that stride-time variability is associated with hemodynamic activity in sensorimotor cortical areas.

Acknowledgements

This work was supported by the Center for Research in Human Movement Variability of the University of Nebraska Omaha and the National Institutes of Health (P20GM109090 and R15HD08682).

References

- [1]. Stergiou N, Harbourne RT, Cavanaugh JT, Optimal movement variability: A new theoretical perspective for neurologic physical therapy, *J. Neurol. Phys. Ther.* 30 (2006) 120–129. doi: 10.1097/01.NPT.0000281949.48193.d9. [PubMed: 17029655]
- [2]. Hausdorff JM, Gait dynamic, fractals and falls: Finding meaning in the stride-to-stride fluctuations of human walking, *Hum. Mov. Sci.* 26 (2007) 555–589. [PubMed: 17618701]
- [3]. Hausdorff JM, Gait dynamics in Parkinson's disease: Common and distinct behavior among stride length, gait variability, and fractal-like scaling, *Chaos.* 19 (2009) 1–14. doi: 10.1063/1.3147408.
- [4]. Brach JS, Berlin JE, VanSwearingen JM, Newman AB, Studenski SA, Gait variability : methods, modeling and meaning Example of Increased Stride Time Variability in Elderly Fallers Quantification of Stride-to-Stride Fluctuations, *J. Neuroeng. Rehabil.* 2 (2005) 1–10. doi: 10.1186/1743-0003-2-21. [PubMed: 15730560]
- [5]. Buzzi UH, Stergiou N, Kurz MJ, Hageman PA, Heide J, Nonlinear dynamics indicates aging affects variability during gait, *Clin. Biomech.* 18 (2003) 435–443. doi: 10.1016/S0268-0033(03)00029-9.
- [6]. Frenkel-Toledo S, Giladi C, Peretz N, Herman T, Gruendlinger L, Hausdorff JM, Example of Increased Stride Time Variability in Elderly Fallers Quantification of Stride-to-Stride Fluctuations, *J. Neuroeng. Rehabil.* 2 (2005) 1–10. doi:10.1186/1743-0003-2-23. [PubMed: 15730560]
- [7]. Goldberger AL, Amaral LAN, Hausdorff JM, Ivanov PC, Peng C-K, Stanley HE, Fractal dynamics in physiology: Alterations with disease and aging, *Proc. Natl. Acad. Sci.* 99 (2002) 2466–2472. doi:10.1073/pnas.012579499. [PubMed: 11875196]
- [8]. Hausdorff JM, Edelberg HK, Mitchell SL, Goldberger AL, Wei JY, Increased gait unsteadiness in community-dwelling elderly failers, *Arch. Phys. Med. Rehabil.* 78 (1997) 278–283. [PubMed: 9084350]
- [9]. Hausdorff JM, Cudkowicz ME, Firtion R, Wei JY, Goldberger AL, Gait variability and basal ganglia disorders: Stride-to-stride variations of gait cycle timing in Parkinson's disease and Huntington's disease, *Mov. Disord.* 13 (1998) 428–437. [PubMed: 9613733]
- [10]. Hausdorff JM, Rios DA, Edelberg HK, Gait variability and fall risk in community-living older adults: A 1-year prospective study, *Arch. Phys. Med. Rehabil.* 82 (2001) 1050–1056. doi: 10.1053/apmr.2001.24893. [PubMed: 11494184]
- [11]. Hausdorff JM, Lowenthal J, Herman T, Gruendlinger L, Peretz C, Giladi N, Rhythmic auditory stimulation modulates gait variability in Parkinson's disease, *Eur. J. Neurosci.* 26 (2007) 2369–2375. doi:10.1111/j.1460-9568.2007.05810.x. [PubMed: 17953624]
- [12]. Herman T, Giladi N, Gurevich T, Hausdorff JM, Gait instability and fractal dynamics of older adults with a "cautious" gait: Why do certain older adults walk fearfully?, *Gait Posture.* 21 (2005) 178–185. doi:10.1016/j.gaitpost.2004.01.014. [PubMed: 15639397]
- [13]. Kurz MJ, Stergiou N, The aging humans neuromuscular system expresses less certainty for selecting joint kinematics during gait, *Neurosci. Lett.* 348 (2003) 155–158. doi: 10.1016/S0304-3940(03)00736-5. [PubMed: 12932817]
- [14]. Goldberger AL, Rigney DR, West BJ, Chaos and fractals in human physiology, *Sci. Am.* 262 (1990) 42–49.
- [15]. Goldberger AL, Peng CK, Lipsitz LA, What is physiologic complexity and how does it change with aging and disease?, *Neurobiol. Aging.* 23 (2002) 23–26. doi: 10.1016/S0197-4580(01)00266-4. [PubMed: 11755014]
- [16]. Bürki CN, Bridenbaugh SA, Reinhardt J, Stippich C, Kressig RW, Blatow M, Imaging gait analysis: An fMRI dual task study, *Brain Behav.* 7 (2017) 1–13. doi: 10.1002/brb3.724.
- [17]. Dobkin BH, Firestine A, West M, Saremi K, Woods R, Ankle dorsiflexion as an fMRI paradigm to assay motor control for walking during rehabilitation, *Neuroimage.* 23 (2004) 370–381. doi: 10.1016/j.neuroimage.2004.06.008. [PubMed: 15325385]
- [18]. Labriffe M, Annweiler C, Amirova LE, Gauquelin-Koch G, Ter Minassian A, Leiber L-M, Beauchet O, Custaud M-A, Dinomais M, Brain Activity during Mental Imagery of Gait Versus Gait-Like Plantar Stimulation: A Novel Combined Functional MRI Paradigm to Better

- Understand Cerebral Gait Control, *Front. Hum. Neurosci.* 11 (2017) 1–15. doi: 10.3389/fnhum.2017.00106. [PubMed: 28149275]
- [19]. la Fougère C, Zwergal A, Rominger A, Förster S, Fesl G, Dieterich M, Brandt T, Strupp M, Bartenstein P, Jahn K, Real versus imagined locomotion: A [18F]-FDG PET-fMRI comparison, *Neuroimage*. 50 (2010) 1589–1598. doi: 10.1016/j.neuroimage.2009.12.060. [PubMed: 20034578]
- [20]. Luft AR, Macko RF, Forrester LW, Villagra F, Ivey F, Sorkin JD, Whitall J, McCombe-Waller S, Katzel L, Goldberg AP., D.F. Hanley, Treadmill exercise activates subcortical neural networks and improves walking after stroke: A randomized controlled trial, *Stroke*. 39 (2008) 3341–3350. [PubMed: 18757284]
- [21]. Phillips JP, Sullivan KJ, Butner PA, Caprihan A, Provost B, Bernitsky-Beddingfield A, Ankle dorsiflexion fMRI in children with cerebral palsy undergoing intensive treadmill training : a pilot study, *Dev. Med. Child Neurol.* 49 (2007) 39–44. [PubMed: 17209975]
- [22]. Gwin JT, Gramann K, Makeig S, Ferris DP, Electrocortical activity is coupled to gait cycle phase during treadmill walking, *Neuroimage*. 54 (2011) 1289–1296. doi: 10.1016/j.neuroimage.2010.08.066. [PubMed: 20832484]
- [23]. Kurz MJ, Wilson TW, Arpin DJ, Stride-time variability and sensorimotor cortical activation during walking, *Neuroimage*. 59 (2012) 1602–1607. doi: 10.1016/j.neuroimage.2011.08.084. [PubMed: 21920441]
- [24]. Miyai I, Tanabe HC, Sase I, Eda H, Oda I, Konishi I, Tsunazawa Y, Suzuki T, Yanagida T, Kubota K, Cortical mapping of gait in humans: A near-infrared spectroscopic topography study, *Neuroimage*. 14 (2001) 1186–1192. doi: 10.1006/nimg.2001.0905. [PubMed: 11697950]
- [25]. Miyai I, Yagura H, Hatakenaka M, Oda I, Konishi I, Kubota K, Longitudinal Optical Imaging Study for Locomotor Recovery after Stroke, *Stroke*. 34 (2003) 2866–2870. [PubMed: 14615624]
- [26]. Miyai I, Suzuki M, Hatakenaka M, Kubota K, Effect of body weight support on cortical activation during gait in patients with stroke, *Exp. Brain Res.* 169 (2006) 85–91. doi: 10.1007/s00221-005-0123-x. [PubMed: 16237521]
- [27]. Harada T, Miyai I, Suzuki M, Kubota K, Gait capacity affects cortical activation patterns related to speed control in the elderly, *Exp. Brain Res.* 193 (2009) 445–454. doi: 10.1007/s00221-008-1643-y. [PubMed: 19030850]
- [28]. Koenraadt KLM, Roelofsen EGJ, Duysens J, Keijsers NLW, Cortical control of normal gait and precision stepping: An fNIRS study, *Neuroimage*. 85 (2014) 415–422. doi: 10.1016/j.neuroimage.2013.04.070. [PubMed: 23631980]
- [29]. Kurz MJ, Wilson TW, Arpin DJ, An fNIRS exploratory investigation of the cortical activity during gait in children with spastic diplegic cerebral palsy., *Brain Dev.* 36 (2014) 870–7. doi: 10.1016/j.braindev.2014.01.003. [PubMed: 24508407]
- [30]. Cui X, Baker JM, Liu N, Reiss AL, Sensitivity of fNIRS measurement to head motion: An applied use of smartphones in the lab., *J. Neurosci. Methods*. 245 (2015) 37–43. doi: 10.1016/j.jneumeth.2015.02.006. [PubMed: 25687634]
- [31]. Piper SK, Krueger A, Koch SP, Mehnert J, Habermehl C, Steinbrink J, Obrig H, Schmitz CH, A wearable multi-channel fNIRS system for brain imaging in freely moving subjects, *Neuroimage*. 85 (2014) 1–20. doi:10.1016/j.neuroimage.2013.06.062.A. [PubMed: 24321364]
- [32]. Cope M, Delpy DT, System for long-term measurement of cerebral blood and tissue oxygenation on newborn infants by near infra-red transillumination, *Med. Biol. Eng. Comput.* 26 (1988) 289–294. doi:10.1007/BF02447083. [PubMed: 2855531]
- [33]. Obrig H, Villringer A, Beyond the visible - Imaging the human brain with light, *J. Cereb. Blood Flow Metab.* 23 (2003) 1–18. doi: 10.1097/01.WCB.0000043472.45775.29.
- [34]. Klem G, Luders H, Jasper H, Elger C, The ten-twenty electrode system of the International Federation, *Electroencephalogr. Clin. Neurophysiol.* 10 (1958) 371–375. doi: 10.1016/0013-4694(58)90053-1.
- [35]. Okamoto M, Dan H, Sakamoto K, Takeo K, Shimizu K, Kohno S, Oda I, Isobe S, Suzuki T, Kohyama K, Dan I, Three-dimensional probabilistic anatomical cranio-cerebral correlation via the international 10–20 system oriented for transcranial functional brain mapping, *Neuroimage*. 21 (2004) 99–111. doi:10.1016/j.neuroimage.2003.08.026. [PubMed: 14741647]

- [36]. Okamoto M, Dan I, Automated cortical projection of head-surface locations for transcranial functional brain mapping, *Neuroimage*. 26 (2005) 18–28. doi: 10.1016/j.neuroimage.2005.01.018. [PubMed: 15862201]
- [37]. Boas DA, Dale AM, Franceschini MA, Diffuse optical imaging of brain activation: Approaches to optimizing image sensitivity, resolution, and accuracy, *Neuroimage*. 23 (2004). doi: 10.1016/j.neuroimage.2004.07.011.
- [38]. Zhang Y, Brooks DH, Franceschini MA, Boas DA, Eigenvector-based spatial filtering for reduction of physiological interference in diffuse optical imaging, *J. Biomed. Opt.* 10 (2005) 11014. doi: 10.1117/1.1852552. [PubMed: 15847580]
- [39]. Choi JT, Bastian AJ, Adaptation reveals independent control networks for human walking, *Nat. Neurosci.* 10 (2007) 1055–1062. doi:10.1038/nn1930. [PubMed: 17603479]
- [40]. Hackney ME, Earhart GM, Backward walking in Parkinson's disease, *Mov. Disord.* 24 (2009) 218–223. doi:10.1002/mds.22330. [PubMed: 18951535]
- [41]. Winter DA, Pluck N, Yang JF, Backward walking: A simple reversal of forward walking?, *J. Mot. Behav.* 21 (1989) 291–305. doi: 10.1080/00222895.1989.10735483. [PubMed: 15136266]
- [42]. Diamond SG, Perdue KL, Boas DA, A cerebrovascular response model for functional neuroimaging including dynamic cerebral autoregulation, *Math. Biosci.* 220 (2009) 102–117. doi: 10.1016/j.mbs.2009.05.002. [PubMed: 19442671]
- [43]. Obrig H, Neufang M, Wenzel R, Kohl M, Steinbrink J, Einhupl K, Villringer A, Spontaneous low frequency oscillations of cerebral hemodynamics and metabolism in human adults, *Neuroimage*. 12 (2000) 623–639. doi: 10.1006/nimg.2000.0657. [PubMed: 11112395]
- [44]. Saager RB, Telleri NL, Berger AJ, Two-detector Corrected Near Infrared Spectroscopy (C-NIRS) detects hemodynamic activation responses more robustly than single-detector NIRS, *Neuroimage*. 55 (2011) 1679–1685. doi: 10.1016/j.neuroimage.2011.01.043. [PubMed: 21256223]
- [45]. Toronov V, Franceschini MA, Filiaci M, Fantini S, Wolf M, Michalos A, Gratton E, Near-infrared study of fluctuations in cerebral hemodynamics during rest and motor stimulation: Temporal analysis and spatial mapping, *Med. Phys.* 27 (2000) 801–815. doi: 10.1118/1.598943. [PubMed: 10798703]
- [46]. Gagnon L, Cooper RJ, Yucel MA, Perdue KL, Greve DN, Boas DA, Short separation channel location impacts the performance of short channel regression in NIRS, *Neuroimage*. 59 (2012) 2518–2528. doi: 10.1016/j.neuroimage.2011.08.095. [PubMed: 21945793]
- [47]. Hoshi Y, Kobayashi N, Tamura M, Interpretation of near-infrared spectroscopy signals: a study with a newly developed perfused rat brain model, *J. Appl. Physiol.* 90 (2001) 1657–1662. <http://jap.physiology.org/content/90/5/1657%5Cnhttp://jap.physiology.org/content/jap/90/5/1657.full.pdf%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/11299252>. [PubMed: 11299252]
- [48]. Suzuki M, Miyai I, Ono T, Kubota K, Activities in the frontal cortex and gait performance are modulated by preparation. An fNIRS study, *Neuroimage*. 39 (2008) 600–607. doi: 10.1016/j.neuroimage.2007.08.044. [PubMed: 17950626]
- [49]. Hanakawa T, Fukuyama H, Katsumi Y, Honda M, Shibasaki H, Enhanced lateral premotor activity during paradoxical gait in parkinson's disease, *Ann. Neurol.* 45 (1999) 329–336. [PubMed: 10072047]

Highlights

- Changes in stride-time variability corresponded with changes in hemodynamic activity in the motor cortex during walking.
- Hemodynamic response and stride-time variability did not differ between forward and backward treadmill walking conditions.
- Measures of body movement and relative head movement during forward and backward walking did not suggest that motion contamination from head movement was confounding fNIRS results.

Figure 1.

The 24 fNIRS channels were grouped into regions of interest located above the supplementary motor area (SMA) in pink, pre-central gyrus (PreCG) in blue, post-central gyrus (PostCG) in yellow, and superior parietal lobule (SPL) in green. Cz was located between channels 19 and 20 based on the International 10/20 System [34].

Figure 2.
Experimental setup.

Figure 3.

Range of movement for the sternum marker in the medial-lateral, anterior-posterior, and vertical directions. Body movement range in the anterior-posterior direction was 48.68% greater during the backward walking condition relative to the forward walking condition, but this difference was not significant (Backward: 83.754, 64.938 to 99.900 mm; Forward: 56.331, 51.882 to 70.186 mm; $P = 0.050$). Range of body movement did not differ significantly between conditions for the medial-lateral (Backward: 40.052, 29.514 to 52.918 mm; Forward: 29.996, 25.433 to 43.340 mm; $P = 0.489$) or vertical (Backward: 20.758, 17.826 to 26.218 mm; Forward: 17.516, 17.169 to 18.782 mm; $P = 0.770$) directions. Differences with a $P > 0.100$ are indicated by †.

Figure 4.

Range of movement for the left temple marker, relative to the sternum marker, in the medial-lateral, anterior-posterior, and vertical directions. Relative head movement range was not significantly different between conditions for medial-lateral (Backward: 21.835, 19.613 to 24.034 mm; Forward: 20.527, 17.403 to 25.060 mm; $P = 1.000$), anterior-posterior (Backward: 28.443, 27.297 to 31.802 mm; Forward: 27.522, 24.210 to 29.520 mm; $P = 0.340$), and vertical (Backward: 12.385, 10.440 to 17.156 mm; Forward: 12.991, 10.653 to 17.285 mm; $P = 0.931$) directions.

Figure 5.

Maximum oxyHb concentration in regions of interest for forward and backward walking. OxyHb concentration in the SMA (Backward: 0.050, 0.030 to 0.094 mMol $\times$ mm; Forward: 0.032, 0.022 to 0.085 mMol $\times$ mm; $P = 0.695$), PreCG (Backward: 0.036, 0.020 to 0.083 mMol $\times$ mm; Forward: 0.036, 0.025 to 0.060 mMol $\times$ mm; $P = 0.922$), PostCG (Backward: 0.027, 0.015 to 0.082 mMol $\times$ mm; Forward: 0.048, 0.028 to 0.061 mMol $\times$ mm; $P = 0.695$), and SPL (Backward: 0.041, 0.010 to 0.083 mMol $\times$ mm; Forward: 0.057, 0.035 to 0.071 mMol $\times$ mm; $P = 0.625$) was not significantly different between conditions.

Figure 6.

Minimum deoxyHb concentrations in regions of interest during forward and backward walking conditions. DeoxyHb was significantly lower in the SMA during backward walking compared to forward walking (Backward: -0.010 , -0.016 to -0.005 mMol $\times$ mm; Forward: -0.003 , -0.008 to -0.0003 mMol $\times$ mm; $P = 0.020$). There were no conditional differences in deoxyHb concentration for the PreCG (Backward: -0.003 , -0.005 to -0.001 ; Forward: -0.004 , -0.012 to -0.001 ; $P = 0.375$), PostCG (Backward: -0.002 , -0.004 to -0.001 mMol $\times$ mm; Forward: -0.002 , -0.004 to -0.0002 mMol $\times$ mm; $P = 0.846$), or SPL (Backward: -0.004 , -0.012 to 0.0004 mMol $\times$ mm; Forward: -0.002 , -0.003 to -0.0004 mMol $\times$ mm; $P = 0.375$).

Figure 7. Inter-stride interval (ISI) coefficient of variation (CoV) for forward and backward walking conditions. CoV was significantly greater during backward walking (Backward: 4.662, 4.306 to 4.903%; Forward: 3.366, 2.928 to 4.037%; $P = 0.004$).

Figure 8. Correlation between PreCG oxyHb concentration and ISI standard deviation during forward walking ($R = 0.66$, $P = 0.044$).

Table 1.

Root mean square for relative head movement (left temple marker - sternum marker) and body movement (sternum marker). There were no significant differences in root mean square body movement or relative head movement. The root mean square of anterior-posterior body movement as 15.87% greater during forward walking compared to backward walking, but this difference did not reach significance. Values are reported as: median (interquartile range). Differences with a $P \leq 0.100$ are indicated by †.

Root Mean Square of Head and Body Movement			
Movement Direction	Backward Walking	Forward Walking	Significance
Body Movement			
Anterior-Posterior	586.909 (528.072 - 618.015) mm	680.023 (617.479 - 738.023) mm	$P = 0.063^\dagger$
Medial-Lateral	2649.584 (2647.144 - 2655.643) mm	2657.229 (2645.505 - 2657.962) mm	$P = 0.730$
Vertical	1427.835 (1411.046 - 1468.054) mm	1427.005 (1407.106 - 1473.442) mm	$P = 0.931$
Head Movement			
Anterior-Posterior	57.785 (43.858 - 71.334) mm	58.981 (47.995 - 69.698) mm	$P = 0.605$
Medial-Lateral	57.706 (54.143 - 64.106) mm	56.791 (53.001 - 61.832) mm	$P = 0.865$
Vertical	243.933 (242.887 - 249.836) mm	245.349 (243.230 - 249.544) mm	$P = 0.865$

Table 2.

Total path length for relative head movement (left temple marker - sternum marker) and body movement (sternum marker). There were no significant differences in total path length for body movement or relative head movement.

Movement Direction	Total Line Path of Head and Body Movement		Significance
	Backward Walking	Forward Walking	
Body Movement			
Anterior-Posterior	624.650 (576.776 - 677.459) mm	682.091 (660.764 - 804.468) mm	P = 0.136
Medial-Lateral	664.269 (473.655 - 716.637) mm	517.545 (387.080 - 625.563) mm	P = 0.436
Vertical	498.867 (439.837 - 526.192) mm	482.329 (367.161 - 516.470) mm	P = 0.605
Composite	1155.430 (1026.836 - 1249.969) mm	1100.157 (1000.124 - 1347.253) mm	P = 0.796
Head Movement			
Anterior-Posterior	591.797 (523.011 - 654.506) mm	510.472 (474.312 - 571.486) mm	P = 0.190
Medial-Lateral	509.946 (473.250 - 565.731) mm	469.977 (440.562 - 581.675) mm	P = 0.730
Vertical	343.536 (307.771 - 354.676) mm	327.021 (275.545 - 328.934) mm	P = 0.340
Composite	963.461 (947.557 - 1048.949) mm	877.193 (834.155 - 1064.411) mm	P = 0.605