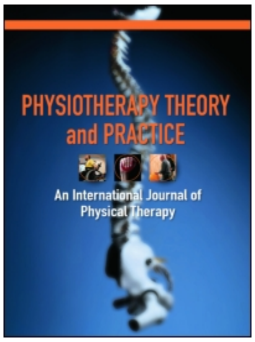

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Increased prefrontal cortical activation during challenging walking conditions in persons with lower limb amputation – an fNIRS observational study

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ABSTRACT

Background: Lower limb amputation (LLA) alters the sensorimotor control systems. Despite the self-reports of increased attention during mobility, the interaction between mobility and cognitive control mechanisms is not fully understood.

Objective: Concurrently evaluate walking performance and prefrontal cortical (PFC) activity in persons with and without LLA during different walking conditions.

Methods: Thirty-nine persons with LLA and thirty-three able-bodied controls participated. Walking performance was evaluated using the Figure-of 8-walk-test during three conditions: 1) UW (Usual walking with self-selected walking speed); 2) WCT (walking and carrying a tray with two cups filled with water); and 3) WUT (walking on uneven terrain). PFC activity was assessed using functional near-infrared spectroscopy (fNIRS). Linear mixed models were used to detect changes between groups and between walking conditions within each group.

Results: Between-group comparisons showed increased PFC activity in persons with LLA during UW and WUT, and a significant decrease in walking performance during WCT and WUT compared to controls. Within-group comparisons showed increased PFC activity during WUT compared with UW and WCT and an overall difference in walking performance between the conditions (WU > WUT > WCT) in both groups. However, the effect of walking condition on PFC activity and walking performance was not modified by group ($P > .1$).

Conclusion: The results suggest that persons with LLA have increased attentional demands during walking but choose the same cognitive-mobility strategy during challenging walking conditions as able-bodied persons. However, the attentional demands seem to depend on the complexity of the task.

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Cognitive load; attention; artificial limb; gait; neuroimaging

Introduction

Persons with a lower limb amputation (LLA) have altered sensorimotor inputs and outputs from and to the prosthetic limb (Knaepen et al., 2015). This may challenge prosthetic mobility and have an impact on gait quality and attentional demands, particularly in challenging walking environments (Hafner, Morgan, Abrahamson, and Amtmann, 2016b). Many people with LLA have reported increased attention and concentration needs when walking, which might reflect an increased use of cognitive resources during ambulation (Miller, Speechley, and Deathe, 2001; Morgan, Hafner, Kartin, and Kelly, 2018).

Prior research on LLA recognizes the impact cognitive function has on walking performance (Coffey et al., 2012; Frengopoulos et al., 2017; Morgan, Hafner, Kartin, and Kelly, 2018) and the interaction between cognition and mobility has commonly been assessed using dual-task methods which challenge the attentional capacities (Morgan, Hafner, Kartin, and Kelly, 2018; Yogev-Seligmann, Hausdorff, and Giladi, 2008). To our knowledge, only a limited number of dual-task studies in persons with LLA exists (Frengopoulos et al., 2018a; Hunter et al., 2018; Lamoth, Ainsworth, Polomski, and Houdijk, 2010; Morgan, Hafner, and Kelly, 2016, 2017; Pruziner et al., 2019) and cognitive tasks like serial subtractions or the Stroop test have been used together with walking tasks. The results indicate that both walking and cognitive performance decreases when adding a concurrent cognitive task in combination with walking (Hunter et al., 2018; Morgan, Hafner, and Kelly, 2017; Pruziner et al., 2019), and a decrease in performance is observed regardless of time since amputation and etiology (Frengopoulos et al., 2018a).

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Studies have also indicated that adding a concurrent cognitive task does not affect walking performance in a different way in persons with lower limb amputation compared with able-bodied controls (Lamoth, Ainsworth, Polomski, and Houdijk, 2010; Morgan, Hafner, and Kelly, 2016; Pruziner et al., 2019). However, a previous study has reported that the gait quality (i.e. increased asymmetry) while dual-task walking on an unstable surface was different between persons with and without transfemoral amputation (Morgan, Hafner, and Kelly, 2017). This might indicate that the use of cognitive resources depends on the environmental conditions.

Except for a recent study (Pruziner et al., 2019), dual-task studies in persons with LLA have mainly looked at cognitive and mobility performance and not on the underlying cortical activation during the performance. Pruziner et al. (2019) evaluated both gait mechanics (i.e. dual-task walking with a visual task) and cortical activity by electroencephalography (EEG) in a population with and without transtibial amputation and both groups showed overall similar cortical dynamics. Cortical structures play an important role in the control of mobility during daily activities (Hamacher et al., 2015). Neuroimaging studies have revealed that several different cortical and subcortical regions are involved during walking (Hamacher et al., 2015) and the literature describes two pathways (Bayot et al., 2018; Herold et al., 2017): 1) a direct locomotor pathway (primary motor cortex, cerebellum and spinal cord); and 2) indirect locomotor pathway (prefrontal cortex (PFC), premotor areas, and basal ganglia). During attentional demanding and challenging walking conditions, the activation of the indirect locomotor pathway increases and the PFC, in particular, plays a key role (Clark, 2015; Hamacher et al., 2015; Yogev-Seligmann, Hausdorff, and Giladi, 2008). According to the capacity sharing theory (Kahneman, 1973), the attentional capacity is limited; hence, there might be a risk of attentional overload during challenging mobility conditions.

Several studies have examined PFC activation during dual-task walking using functional near-infrared spectroscopy (fNIRS) (Herold et al., 2017; Vitorio et al., 2017) and mixed findings have been reported. Several studies report increased PFC activity during dual-task walking when using cognitive tasks (Fraser et al., 2016; Holtzer et al., 2011; Mirelman et al., 2017) or motor tasks (Clark, Rose, Ring, and Porges, 2014; Osofundiya, Benden, Dowdy, and Mehta, 2016). However, a decreased PFC activation has been observed in dual-task walking with a visual task in older persons (Beurskens, Helmich, Rein, and Bock, 2014) and during different complex walking paths in younger persons (Lin and Lin, 2016). When comparing different challenging dual tasks, the magnitude of the PFC activation seems to depend on: type of task and its complexity (Clark, Rose, Ring, and Porges, 2014); age (Holtzer et al., 2011; Lin and Lin, 2016; Mirelman et al., 2017); and presence of pathology (Maidan et al., 2016; Mori, Takeuchi, and Izumi, 2018). One recent study on persons with transfemoral amputation during straight-path walking showed increased brain activity in the prefrontal and motor cortex compared to healthy controls (Möller, Rusaw, Hagberg, and Ramstrand, 2019). However, knowledge of neuronal processes required during challenging mobility conditions in home and community is still incomplete (Hamacher et al., 2015; Pruziner et al., 2019). New knowledge about PFC activation during mobility for persons with LLA can help us to gain a better understanding of cognitive and cortical control mechanisms during mobility and may contribute to better planning of rehabilitation strategies. The present study aimed to evaluate PFC activity by fNIRS and walking performance in persons with and without LLA during different challenging walking conditions. Our main hypothesis was that there would be increased PFC activation and reduced walking performance in persons with LLA compared with able-bodied controls during all walking conditions. Secondly, we also hypothesized that the walking conditions would differentially affect PFC activation and/or walking performance in people with LLA compared with able-bodied controls.

Method

The current observational study is part of a larger project examining mobility in persons with LLA. The Regional Committee for Medical and Health Research Ethics in Norway (2015/1245) approved the study which was performed according to the principles of the Declaration of Helsinki. All participants signed an informed consent prior to participation.

The main hypothesis was to investigate between-group comparisons. To identify the minimum sample size, an a priori power analysis was conducted based on walking speed (Wezenberg et al., 2013). Power was set to 90%, alpha to .05 and power analysis (by Stata/SE 14.2 for Windows, College Station, TX, USA) estimated to a total sample size of 20. To increase the robustness of the analyses, a sample size of more than 30 persons in each group was considered appropriate.

Participants

Inclusion criteria: 1) 18 years or older; 2) ability to walk without an assistive device for at least 500 m; 3) no psychiatric or neurologic comorbidities; 4) no diagnosis of dementia; and 5) no comorbidities impacting the ability to complete the protocol. For persons with LLA, additional criteria were: 1) unilateral transtibial or transfemoral/knee-disarticulation; 2) non-vascular or non-diabetic etiology of amputation; and 3) walking with a prosthesis for at least 1 year. Participants were recruited from: 1) local prosthetic workshops and rehabilitation centers through flyers; 2) Facebook groups for the two prosthetic user organizations in Norway; and 3) friends, family and peers of the participants.

Baseline cognitive and physical function

Baseline cognitive function was measured by the Montreal Cognitive Assessment (MoCA), which is a tool for screening global cognition (Frengopoulos et al., 2017; Frengopoulos, Payne, Viana, and Hunter, 2018b; Nasreddine et al., 2005) and the Trail Making Test (TMT-A and TMT-B) which is a tool for measuring cognitive flexibility and executive functions (Tombaugh, 2004). Persons with LLA also performed the Amputee Mobility Predictor (AMP) (Gailey et al., 2002), a performance-based measure of mobility and the Prosthetic Limb Users Survey of Mobility (PLUS-M) (Amtmann et al., 2014), a self-report measure of mobility for persons with LLA.

Walking performance

The Figure-of-eight Walk test (F8W) (time and number of steps) was used, which is a valid measure of walking skill and involves straight and curved-path walking and is designed to stimulate more of the complexity of walking in daily life than straight-path walking (Hess, Brach, Piva, and VanSwearingen, 2010; Schack, Mirtaheri, Steen, and Gjøvaag, 2019). Three different walking conditions were used: 1) UW = Usual walking with self-selected walking speed; 2) WCT = walking and carrying a tray with two cups filled with water; and 3) WUT = walking on uneven terrain. WCT and WUT are known to be challenging mobility conditions for persons with LLA (Hafner, Morgan, Abrahamson, and Amtmann, 2016b). The uneven terrain consisted of six foam mats (185 cm long, 60 cm wide and 1.5 cm thick, Airex® Coronella, Airex AG, Switzerland). An additional foam mat of the same material as the six foam mats was cut into slices and these slices were placed underneath the larger mats with eight slices around each of the cones in the F8W (Schack, Mirtaheri, Steen, and Gjøvaag, 2019). Before applying the fNIRS equipment, the walking conditions were explained and demonstrated to the participants and they could practice the F8W (one to two laps) in each condition before data collection.

PFC activity

A portable continuous-wave NIRSport system (NIRStar, NIRX Medical Technologies LLC, Glen Head, NY, USA) with two wavelengths (760 nm, 850 nm) was used during the experiments. The system had 16 active optodes; 8 sources and 8 detectors, resulting in 20 channels in total with a sampling frequency of 7.81 Hz. The optodes were placed in a cap (EasyCap, GmbH, Germany) based on the 10–20 international standardized EEG system (Herold, Wiegel, Scholkmann, and Müller, 2018) (Figure 1). The source and detector separation was approximately 3 cm. To ensure the correct position of the measuring cap, the Cz position was used as a reference point and the cap was centered between the nasion and the inion as well as between the left and right preauricular points. The optodes mainly covered the left and right prefrontal cortex representing Broadmann areas (BA) 8, 9 10, 11, 45 and 46 (Morais, Balardin, and Sato, 2018; Rorden and Brett, 2000) (Figure 1). A block design with a random order of the three walking conditions was used. Each condition was repeated 5 times and began with a rest period of 60 seconds. The duration of each walking trial was 20 seconds, considering the temporal delay of 2 to 5 seconds in the hemodynamic response (Herold et al., 2017). The participants walked in the figure-of-eight-pattern during the trials and the total time duration was used in the subsequent analysis of the signals. The participants returned to the starting position in the figure-of-eight after each trial and rested for 40 seconds. The stimulus presentation software NIRSStim (NIRX Medical Technologies LLC, Glen Head, NY, USA) triggered the onset of each walking trial. Heart rate (HR) was measured simultaneously during the walking trials using SOMNOtouch NIBP (SOMNOmedics, Randersacker, Germany). HR was used as a regressor for filtering the fNIRS signal (Herold, Wiegel, Scholkmann, and Müller, 2018; Tachtsidis and Scholkmann, 2016).

fNIRS data analysis

The nirsLAB v201706 software (https://www.nitrc.org/projects/fnirs_downstate/) was used to analyze the signals. The relative coefficient of variation (CV) was initially calculated for the raw signals for both wavelengths in order to estimate the signal-to-noise quality for each channel (Lu et al., 2015). The default CV (7.5%) was used as signal quality control since high standard deviation from unfiltered data might indicate the presence of motion artifact (Morais et al., 2017). The differential pathlength factor was calculated according to the participants' age for both wavelengths (Herold et al., 2017). The last 20 seconds of the rest

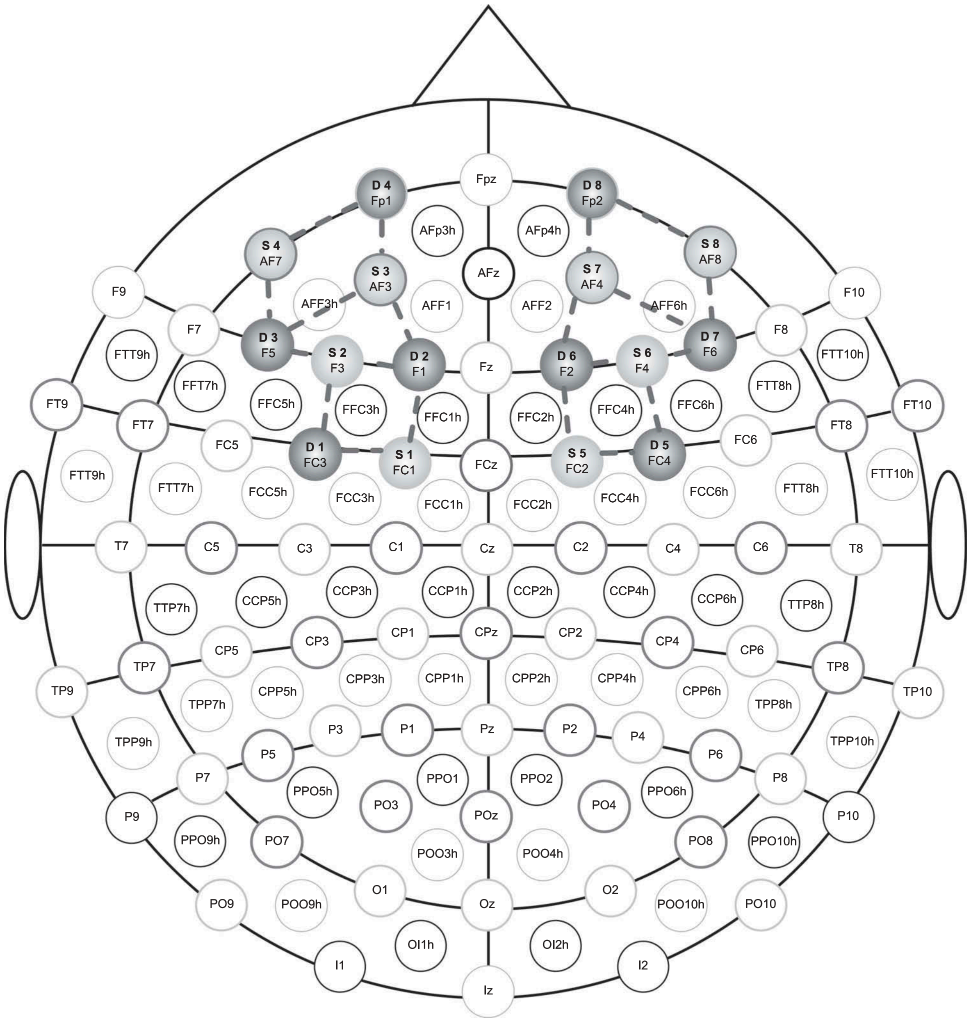

Figure 1. Illustrates the location of the optode sources and detectors on the scalp. The labels starting with S (S1, S2 … S8)(light gray color) represent the sources. The labels starting with D (D1, D2, …, D8)(dark gray color) represent the detectors. The 20 source-detector pairs called channels are illustrated with bars.

period preceding UW were used as baseline (Herold, Wiegel, Scholkmann, and Müller, 2018). The relative changes of oxygenated hemoglobin (OxyHb) and deoxygenated hemoglobin (deoxyHb) were then calculated using the modified Beer–Lambert's law. In previous studies, it has been reported that OxyHb appears to be a more sensitive and reliable parameter for measuring mobility-dependent changes in cerebral blood flow (Harada, Miyai, Suzuki, and Kubota, 2009; Holtzer et al., 2011; Miyai et al., 2001). Accordingly, we used the changes in OxyHb as a primary outcome for PFC activation.

The general linear model (GLM) as incorporated in nirsLAB was used to analyze the hemodynamic signals. HR measurements were synchronized with the NIRS data and loaded as a user-defined regressor. In addition, the effect of motion artifacts and serial temporal correlation (Tachtsidis and Scholkmann, 2016) were reduced via an autoregressive model with the prewhitening iterative reweighted least square algorithms inside the GLM engine (Barker, Rosso, Sparto, and Huppert, 2016). The canonical hemodynamic response function (HRF) was used as a base function for the GLM. The GLM model-fitting coefficients for each channel were exported to SPSS for further statistical analysis.

Statistical analyses

Score distributions were evaluated for normality using histograms and Q-Q plots and found normally distributed for all variables. Descriptive statistics with means and standard deviations (SD) were calculated for participants' demographic and health characteristics. Continuous data were compared using the Student's t-test and categorical data were compared using the chi-square test. Linear mixed effects models using a random intercept for subject, with group (persons with LLA and able-bodied controls) as between-subject factor, walking conditions (UW, WCT, and WUT) as repeated within-subject factor and interaction terms between group and walking condition were estimated for each of the 20 channels (PFC activation), F8 W time and steps as the dependent variables. We calculated the effect sizes (Cohen's *d*) and used the following definition: 0.01 = very small 0.2 = small; 0.5 = medium; 0.8 = large; 1.2 = very large and 2.0 = huge (Sawilowsky, 2009). We performed pairwise posthoc tests for all combinations of walking conditions and groups, and Bonferroni adjusted for three multiple tests. Significant group-by-condition interactions would indicate that the walking condition differentially affected PFC activation or walking performance in people with LLA compared with able-bodied controls. To help the interpretation of the data, Pearson's correlation analysis was conducted to investigate potential relationships between "time since amputation" and age to PFC activation and walking performance. Furthermore, we conducted Pearson's correlation analysis between PFC activation and mobility scores (PLUS-M and AMP) for persons with LLA.

Results

Participants

Seventy-four persons volunteered to participate in this study. Two persons with LLA were excluded because of technical problems. Thirty-nine persons with LLA and thirty-three able-bodied persons completed the study and their personal characteristics are summarized in Table 1. There were no significant differences between the groups in relation to age, sex, height, weight, MoCa score or TMT. The level of amputation was: transtibial (n = 20), transfemoral (n = 11) and knee-disarticulation (n = 8). All persons with LLA wore energy-storing prosthetic feet. Six of the persons with transfemoral amputation/knee-disarticulation used different types of mechanical knees, while the others (13) used micro-processor-controlled prosthetic knees. PLUS-M T-scores for persons with LLA indicate that average mobility for participants with LLA was higher than approximately 80% of people with lower-limb loss.

Table 1. Participant demographics and characteristics.

	Able-bodied controls (N = 33)	Persons with LLA (N = 39)	*p*-value
Sex (female/male), n	14/19	17/22	0.92
Age, years	53.6 (12.4)	51.7 (12.3)	0.51
Weight, kg	82.9 (15.7)	84.2 (19.7)	0.76
Height, m	1.76 (0.1)	1.76 (0.1)	0.89
MoCA	27.5 (1.7)	27.1 (1.9)	0.60
TMT-A, s	29.9 (7.8)	34.0 (12.0)	0.09
TMT-B, s	70.9 (24.8)	81.0 (31.4)	0.13
Time since amputation, years	N/A	22 (18)	
Amputation etiology			
Cancer, n	N/A	6	
Trauma, n	N/A	24	
Infection (non-diabetic), n	N/A	1	
Congenital, n	N/A	6	
Other (non-diabetic), n	N/A	2	
PLUS-M	N/A	58.4 (7.6)	
AMP	N/A	42.9 (2.2)	

Values are means (SD) except for sex and amputation etiology which is the number of observations (n). MoCA = The Montreal Cognitive Assessment (Scale range 0–30; higher scores indicate greater cognitive function). TMT-A = Trail Making Test A. TMT-B = Trail Making Test B. PLUS-M = Prosthetic Limb Users Survey of Mobility (T-score ranging between 21.8 and 71.4, higher score indicates greater mobility). AMP = Amputee Mobility Predictor (Scale 0–47, higher scores indicate better mobility). N/A = not applicable. Clinical data were compared using Student's t-test. Sex was compared using the chi-square test.

Changes in PFC activation

Between-group comparisons for each condition (UW, WCT, WUT) are shown separately in Figure 2 a, b, c, respectively. A large variability in PFC activation was found across all channels in both groups. The observed results revealed a significant increase in PFC activation during UW (channel 5, $p = .039$, Cohen's $d = 0.62$; channel 18, p = .036, Cohen's $d = 0.58$) and WUT (channel 2, p = .042, Cohen's $d = 0.51$; channel 4, p = .051, Cohen's $d = 0.51$; channel 5, $p = .039$, Cohen's $d = 0.55$; channel 14, $p = .009$, Cohen's $d = 0.63$) in persons with LLA compared with able-bodied controls. No significant differences were observed between groups during WCT ($p > .1$).

In persons with LLA, within-group comparisons showed a significantly higher PFC activation in WUT compared to UW (channel 4, $p = .039$, Cohen's $d = 0.44$) and WCT (channel 4, $p = .003$, Cohen's $d = 0.50$; channel 5, $p = .033$, Cohen's $d = 0.45$; channel 14, $p = .018$, Cohen's $d = 0.37$), respectively. In the able-bodied controls, the results were similar showing a significant increase in PFC activation during WUT compared to UW (channel 3, $p = .039$, Cohen's $d = 0.54$; channel 6, $p = .045$, Cohen's $d = 0.43$; channel 7, $p = .039$, Cohen's $d = 0.49$) and WCT (channel 4, $p = .039$, Cohen's $d = 0.74$), respectively. Both groups were not significantly different when comparing UW and WCT in all channels. The effect of walking condition on PFC activity was not modified by group, the interaction term group x condition was non-significant in all the statistical models.

Changes in walking performance

Table 2 shows the results from the F8W performance in each group. Between-group comparisons of the F8W parameters revealed significant differences in both time and number of steps during WCT and WUT, but not in UW. Within-group comparisons revealed significant differences in F8W time ($p < .01$) and the number of steps ($p < 0\ .001$) in both groups between the three walking conditions, except for F8W steps between UW and WUT for able-bodied controls ($p = .105$). However, the interaction term group x condition was non-significant (F8W time, $p = .108$; F8 W steps, $p = .073$).

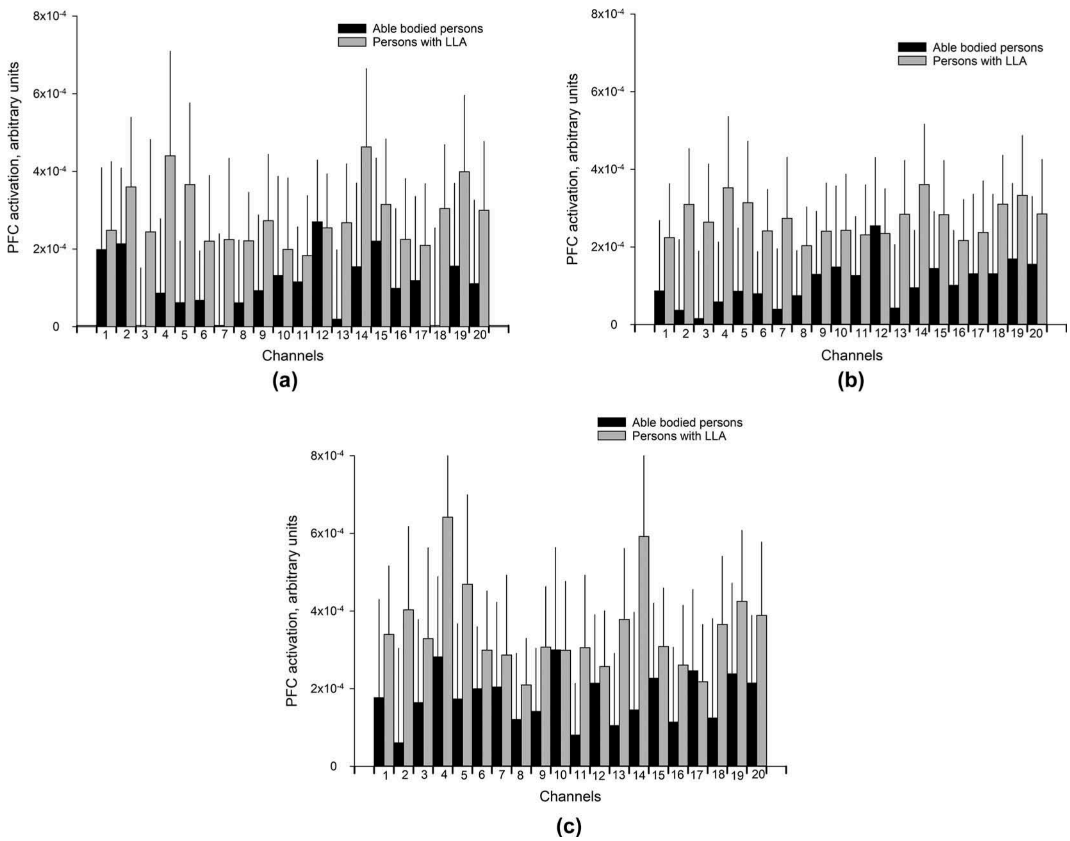

Figure 2. a, b, c. Bar charts of the mean PFC activation (Arbitrary Unit) with 95% confidence intervals (shown as light gray lines) for each of the 20 channels in condition.

UW (Usual walking with self-selected walking speed), WCT (walking and carrying a tray with two cups filled with water) and WUT (walking on uneven terrain), respectively, for both groups.

Table 2. Figure-of-eight Walk test (F8W) parameters for the participants.

Walking condition	Variable	Persons with LLA (N = 39)	Able-bodied controls (N = 33)	Mean difference	95% CI of the difference	Between-groups *p*-values (Bonferroni adjusted)	Effect size Cohen's *d*
UW	Time, s.	9.0 (2.0)	8.0 (1.9)	.9	−.03–1.86	0.177	0.51
	Steps, n.	13.8 (2.5)	12.6 (2.0)	1.2	.12–2.36	0.090	0.68
WCT	Time, s.	10.6 (2.2)	9.4 (2.0)	1.2	.28–2.17	**0.033**	0.77
	Steps, n.	15.8 (2.9)	14.3 (1.9)	1.5	.41–2.66	**0.021**	0.61
WUT	Time, s.	10.1 (2.4)	8.6 (1.9)	1.4	.50–2.39	**0.009**	0.69
	Steps, n.	15.0 (3.0)	13.1 (1.9)	1.9	.81–3.05	**0.003**	0.76

Values are means (SD). s. = seconds. n. = number. UW = Usual walking with self-selected walking speed. WCT = Walking and carrying a tray with two cups filled with water. WUT = Walking on uneven terrain. Figure-of-eight Walk test (F8 W) parameters were compared and mean difference estimated using linear mixed effects models. Bold numbers are significant values after Bonferroni adjustment for multiple tests. CI = confidence interval.

Correlation analysis

Age was not significantly correlated with PFC activity in any channels of all three walking conditions in both groups, while age was correlated with F8W time and steps in all conditions in persons with LLA (F8W time (r = 0.48 – 0.57 and p = <0.001 – 0.002); F8W steps (r = 0.41 – 0.53 and p = .001 0.01)) and able-bodied controls (F8 W time (r = 0.47 – 0.54 and p = .001 – 0.006); F8W steps (r = 0.42 – 0.51 and p = .002 – 0.02)), respectively. "Time since amputation" was not significantly correlated with PFC activity or walking performance in any of the walking conditions. For persons with LLA, we found a significant negative correlation between PFC activity during WUT and PLUS-M (ch 10: r = −0.473; $p < .011$) and AMP (ch 18: r = −0.508, $p < .003$; ch 20: r = −0.457, $p < .011$)

Discussion

The aim of the current study was to evaluate the cortical activity and walking performance during different challenging walking conditions in persons with and without LLA. The results partially confirmed our hypothesis. The results from the between-group comparison showed an increased PFC activation with a medium effect size ($0.58 < d < 0.62$) in persons with LLA compared with able-bodied controls during UW, which was accompanied by a non-significant difference in walking performance. In the context of neural compensation, this suggests that increased levels of brain activity might be necessary to maintain walking performance and support mobility for persons with LLA (Debaere et al., 2004; Holtzer et al., 2015; Stern, 2009). The results suggest that persons with LLA might have less capacity for processing other concurrent cognitive tasks like talking in a mobile phone, due to the assumption that the brain capacity for information processing is limited (Kahneman, 1973; Woollacott and Shumway-Cook, 2002). This limitation might increase the risk of attentional overload during community mobility and consequently increase the risk of falling (Bayot et al., 2018) and reduce participation in social activities (Gallagher, O'Donovan, Doyle, and Desmond, 2011; Miller, Deathe, Speechley, and Koval, 2001).

It is interesting that the largest increase in PFC activity for persons with LLA, in contrast to able-bodied controls, was observed in channels 4 and 14 (Figure 2a–c) during all three walking conditions. These channels roughly represent the dorsolateral prefrontal area (dlPFC) (BA 9) in the left and right hemispheres, respectively. Although the function of the dlPFC is not fully understood, it appears to be involved in the processing of sensory information and may play a significant role during attention-demanding tasks (Debaere et al., 2004; MacDonald, Cohen, Stenger, and Carter, 2000). A possible explanation might be that increased levels of sensory information processing in dlPFC might be necessary to support mobility due to the lack of sensorimotor inputs and outputs from and to the prosthetic limb in persons with LLA (Knaepen et al., 2015)

The within-group results showed an increased PFC activity during WUT, in comparison with UW, which was accompanied by a significant decrease in walking performance (F8W time) in both groups. Increased activation of the PFC accompanied by a decrease in walking performance might indicate neural inefficiency rather than neural compensation (Stern, 2009). The results suggest that the PFC networks assessed in this study, might not be able to adequately support WUT and consequently a reduction in performance occurs. The results indicate that uneven terrain, which is an environmental condition often faced during community mobility, is a demanding activity for both able-bodied persons and persons with LLA (Gallagher, O'Donovan, Doyle, and Desmond, 2011; Morgan, Hafner, and Kelly, 2017).

The results showed in addition that the difference in PFC activation and walking performance between the groups was not differentially affected by walking conditions (i.e. the interaction term group x condition was non-significant). Several studies have reported similar findings that the addition of a secondary task during walking did not affect persons with LLA in a different way compared with able-bodied controls. (Lamoth, Ainsworth, Polomski, and Houdijk, 2010; Morgan, Hafner, and Kelly, 2016; Pruziner et al., 2019). Although individual differences and large variability in PFC activity are presented in both groups related to how walking conditions are handled, the results in the current study might suggest that persons with LLA in comparison with able-bodied controls use the same cognitive-mobility strategy in order to cope with challenging walking conditions (Pruziner et al., 2019; Stern, 2009).

Contrary to our hypothesis, between-group comparison of WCT and within-group comparison of UW and WCT showed a non-significant difference in PFC activation. A possible explanation for the results may be due to the "carrying a load" task. This task might be characterized as a complex vision-motor task (Bond and Morris, 2000) including both a motor task ("carrying the tray") and visual tasks ("looking at the cups to avoid spilling any water" with deprivation of visual feedback by "not being able to look at the ground") (Woollacott and Shumway-Cook, 2002). It has been reported that dual-task walking with a visual task might not induce increased activation of PFC in comparison with single-task walking (Beurskens, Helmich, Rein, and Bock, 2014). This might explain the non-significant difference in PFC activation between UW and WCT in both groups in the present study. WCT might induce activation in other deeper regions of the brain (Hamacher et al., 2015; Yogev-Seligmann, Hausdorff, and Giladi, 2008), which is not possible to examine with fNIRS due to the limited penetration depth of the fNIRS signals (Herold et al., 2017). The results, therefore, agree with the literature (Clark, Rose, Ring, and Porges, 2014; Lin and Lin, 2016; Mirelman et al., 2014), that the type and complexity of the secondary task influence PFC activation. Within-group analysis revealed that both groups reduced the walking speed and increased the number of steps during WCT compared with UW and WUT. Reducing the gait speed as a compensatory strategy when simultaneously performing a cognitive task has been reported in the literature in both healthy older adults (Yogev-Seligmann, Hausdorff, and Giladi, 2008) and persons with LLA (Hunter et al., 2018). Since the instruction to focus on "not spilling any water" was given, the participants might not have prioritized the walking performance (Yogev-Seligmann, Hausdorff, and Giladi, 2012). In the current study, walking performance involved curved-path walking (F8W) and increasing the time and number of steps while turning has been reported to increase the risk of falling in persons with LLA (Dite, Connor, and Curtis, 2007).

Only a limited number of channels showed significant differences between the groups, although almost all channels during all the walking conditions showed an increase in PFC activation for persons with LLA in comparison with able-bodied controls. The non-significant results could be due to the advanced level of experience of prosthetic users in the current study (Pruziner et al., 2019), as the mobility measures (AMP and PLUS-M) showed that persons with LLA had a high mobility level (Gailey et al., 2002; Hafner et al., 2016a). Prosthetic experience and good mobility might possibly result in lower attentional demands due to motor learning and sensorimotor adjustments that occur during rehabilitation (Geurts et al., 1991; Pruziner et al., 2019; Yogev-Seligmann, Hausdorff, and Giladi, 2012). The results from the correlation analysis between PFC activity during WUT and the mobility scores (PLUS-M and AMP) showed that high levels of mobility are associated with lower attentional demands during walking. However, the results did not show any significant correlations between "time since amputation" and PFC activity in any of the walking conditions. The explanation might be due to the long experience of most of the participants, as 88% had more than 5 years of experience as prosthetic walkers. An association between PFC activity and "time since amputation" might be observed in prosthetic users with less experience and lower mobility level compared to the participants in the present study.

In addition, power analysis based on PFC activation between groups may have revealed the need of a higher sample size to gain adequate statistical power. The large variability in PFC activation, which is also reported in previous fNIRS studies (de Lima-pardini et al., 2017; Perrey, 2014; Quaresima et al., 2009), might support this notion. Although we did increase the robustness of the analysis by increasing the power to 90% and the sample size to above 30, the study may have had insufficient statistical power to detect differences with respect to the results of PFC activation.

Limitations

The present study consisted of relatively active persons with LLA of non-diabetic or non-vascular etiology. They all walked without an assistive device, which might limit the generalizability of the results. The sample might not be representative of all prosthetic users, especially those with amputation due to vascular causes or persons with a lower mobility level (e.g. due to older age or comorbidities). In addition, there was a large age range of participants in both groups, but there was no significant difference between the groups related to age. Baseline cognitive function was only assessed using MoCA and TMT (A and B) which are screening tools to assess cognition and therefore might provide limited information about cognition. Spatio-temporal parameters of gait were not measured and might have provided additional information about walking performance and the quality of gait (Holtzer et al., 2015; Morgan, Hafner, and Kelly, 2017). During the preprocessing of fNIRS signals, we controlled for heart rate, but not for other systemic changes like blood pressure or respiratory rate, which might have changed during the walking conditions. Thus, we cannot exclude the influence of these confounding factors (Tachtsidis and Scholkmann, 2016). Furthermore, we used a laboratory setting for the examination, which does not replicate ecologic environmental dimensions and might have influenced the cognitive processes.

Clinical implications

The results of the present study indicate the importance of addressing walking limitations in the context of environmental challenges that persons with LLA face in their daily lives. Developing rehabilitation interventions for persons with LLA with a focus on dual-task abilities in complex environments might reduce the attentional demands over time and improve safety, increase community participation and increase quality of life.

Conclusion

Persons with LLA showed an increased PFC activation compared with able-bodied persons during UW and WUT. The activation of PFC seems to depend on the nature and complexity of the task and was not significantly different between groups in WCT. Persons with LLA had reduced walking performance during WCT and WUT compared to able-bodied controls. However, the challenging walking conditions did not affect PFC activation and walking performance in a different way in persons with LLA compared with able-bodied controls. This suggests that persons with LLA have increased attentional demands during complex walking but use the same cognitive-mobility strategy during challenging walking conditions as able-bodied persons.

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Disclosure Statement

The authors declare no conflicts of interest.

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