Cognitive and Motor Dual Task on Multi-area Brain Activation and Gait Performance in Individuals with Parkinson’s Disease

Yan-Ci Liu
National Taiwan University

Yea-Ru Yang
National Yang-Ming University

Nai-Chen Yeh
National Yang-Ming University

Pei-Hsin Ku
National Yang-Ming University

Chia-Feng Lu
National Yang-Ming University

Ray-Yau Wang (✉ rywang@ym.edu.tw)
National Yang-Ming University

Research

Keywords: Brain activities, cognitive dual task, gait performance, motor dual task, Parkinson’s disease

Posted Date: March 3rd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-258545/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

Background

In people with Parkinson’s disease (PD), gait performance deteriorating during dual task walking compared to single-task walking has been noted in previous studies. However, the effects of different types of dual task on gait performance and brain activation were still unknown.

Methods

This study investigated the walking performance changes and multi-area brain activities during cognitive and motor dual task walking in people with PD. Twenty-eight participants with PD were recruited and performed single walking (SW), walking while performing a cognitive task (WCT), and walking while performing a motor task (WMT) at their self-selected speed. Gait performance including walking speed, cadence, stride length, stride time, swing cycle, temporal and spatial variability and dual task cost (DTC) were recorded. Brain activation of the prefrontal cortex (PFC), premotor cortex (PMC), and supplementary motor areas (SMA) were measured by functional near-infrared spectroscopy during walking.

Results

Results showed the walking performance deteriorated upon performing a secondary task, especially the cognitive task. Also, a higher and sustained activation in PMC and SMA during WCT as compared with WMT and SW in the late phase of walking was found. Moreover, gait performance was negatively correlated with PMC and SMA activity during different walking tasks.

Conclusions

Individuals with PD demonstrated gait deterioration during dual task walking, especially WCT. The SMA and PMC were further activated in people with PD when performing cognitive dual task walking.

Trial registration

TCTR20190118010. Registered 18 January 2019, retrospectively registered.

Introduction

Performing a secondary task during walking, defined as dual task walking, is necessary in daily living(1). According to the types of secondary task, dual task walking can be classified as motor or cognitive. Motor dual task walking refers to conducting motor tasks such as carrying or manipulating objects during walking, while cognitive dual task walking implies conducting attentional tasks, including mental tracking, verbal fluency, conversational tasks, or memory tasks during walking(2).

Parkinson’s disease (PD) is a neurological degenerative disease which leads to motor impairments such as difficulty in task switching, functional walking, and postural control. In addition, cognitive impairment
in people with PD has also been observed, including impairments in executive function, attention, and memory(3–5). The impairments of cognitive and sensorimotor processing due to PD may therefore lead to difficulties in complex activities, such as dual task walking(1, 6–8). Previous studies have found a decrement in gait speed and stride length and an increase in stride-to-stride variability during cognitive and motor dual task walking in PD patients(1, 9–12).

Although the prefrontal cortex (PFC) has been considered to play a crucial role in locomotion(13) and dual tasks(14–16), the mechanisms underlying dual task walking are still unclear. Results from functional magnetic resonance imaging (fMRI) studies have suggested the PFC is an important mediator of cognitive dual tasks(14–17). Several studies using functional near-infrared spectroscopy (fNIRS) showed the PFC was activated significantly during dual task walking in healthy adults(18–20) and elderly(20–23). Although the activity of the PFC was documented by fNIRS, the activity in other brain areas involved in adapting walking speed and posture, such as the premotor cortex (PMC) and supplementary motor areas (SMA)(24, 25), were less studied under dual task walking condition. Our previous fNIRS study showed that in addition to PFC, higher brain activation was observed in PMC and SMA during cognitive and motor dual task walking in young adults as compared with single walking(26). Similarly, we also found the SMA and PMC were crucial during cognitive and motor dual task walking in patients with stroke(27).

Regarding brain activations during dual task walking in people with PD, Nieuwhof et al. reported the HbO2 concentration in PFC significantly increased during walking combined with the serial subtraction task or the digit span task than during quiet standing(28). Maidan et al. found that the PFC did not activate significantly during walking combined with the serial subtraction task as compared with single walking31. These results may indicate the inability of PFC to further recruit for more difficult tasks such as dual task walking, due to already highly activated during single walking task. However, the activities in PMC and SMA to adapt to the challenges of dual task walking are not immediately known. Therefore, the aim of this study was to investigate the cognitive and motor dual task walking performance and multi-area brain activities in people with PD.

**Methods**

**Participants**

Individuals with PD were enrolled between March 2017 and November 2019. The inclusion criteria included (1) aged between 20 and 90 and (2) diagnosed with idiopathic PD, with the diagnostic criteria for PD defined as the presence of at least two of four features (resting tremor, bradykinesia, rigidity, and asymmetric onset), and one of which had to be resting tremor or bradykinesia(29), (3) stage 1 to 3 on the Hoehn and Yahr scale, (4) ability to walk 10 meters independently without an assistive device, (5) ability to use upper extremity to hold a tray for motor dual task assessment, (6) stable medical condition, and (7) mini-mental state examination (MMSE) scores ≥ 24. The exclusion criteria were (1) history of malignant tumors, (2) any neurological or orthopedic disease that might affect the experiment, (3) history
of mental illness within 5 years, (4) alcohol addiction within the last 12 months, (5) history of using central nervous system drugs, e.g. anti-epileptic or anti-depressant drugs, in the recent month.

All participants were informed about the research procedures and signed the written consent form. The study protocol was approved by the Institutional Review Board of National Yang-Ming University registered at http://www.clinicaltrials.in.th/ (TCTR20190118010).

**Study design**

This was a cross-sectional study. The characteristic data including age, gender, MMSE scores, Hoehn and Yahr stage, and the time since diagnosis of PD were obtained before the study measurements. Participants were asked to walk on a walkway back and forth for 60 seconds under the 3 walking conditions as described below. Gait performance and brain activity were recorded simultaneously during each walking trial.

1. **Single-walking (SW):** Participants were asked to walk at their comfortable speed.

2. **Walking while performing a cognitive task (WCT):** Participants were asked to keep walking while serially subtracting 3 from a three-digit number.

3. **Walking while performing a motor task (WMT):** Participants were asked to keep walking while carrying a tray with a cup of water on it with both hands.

Each walking condition was repeated 2 times (a total of 6 walking trials) in random order. There was a 60-second resting period between each walking trial.

Before each walking trial started, participants were asked to stand quietly in a comfortable position for at least 15 seconds to stabilize their hemodynamics. Verbal instruction was provided by the assessor to inform participants of the coming next walking condition to be performed.

**Gait performance**

Gait performance was recorded and analyzed by the GAITRite walkway system (CIR System, Inc., Havertown, PA, USA) which has a sensor pad connected to a laptop. This walkway is 4.75 m long and 0.89 m wide, with a 4.30-m long and 0.61-m wide pressure-sensitive area. When the participant walked along the walkway, the temporal and spatial gait parameters were recorded and analyzed.

The participants were asked to walk from one end to the other back and forth, and to turn outside the area of the electronic walkway. The average values from the 2 trials of each walking condition were calculated for data analysis. The gait parameters of interest included speed (cm/s), cadence (steps/min), stride length (cm), stride time (s), swing cycle (% of the gait cycle), and temporal and spatial variability. Temporal variability was calculated as the coefficient of variation (standard deviation / mean × 100%) of the stride time. Spatial variability
was calculated as the coefficient of variation (standard deviation / mean × 100%) of the stride length. Dual task cost (DTC) was calculated using the following formula: (dual task walking speed-single walking speed) / single walking speed × 100%. The DTC was used to quantify the interference of dual tasking on walking.\(^{(30)}\)

**Brain activation**

A multichannel wearable fNIRS imaging system (NIRSport, NIRx Medical Technologies LLC, Glen Head, NY, USA) was used to detect the hemodynamics of the bilateral PFC, PMC, SMA, as previously reported\(^{(26, 27)}\). The instrument exports and receives the dual-wavelength (760 and 850 nm) near infrared signals by 8 LED light sources and 8 detectors attached on the head cap which is compatible with the international 10–5 system. The standard surface positions for a human head was set approximately 3.0 cm between any 2 adjacent positions\(^{(31)}\). There were 14 source-detector channels to detect changes in local blood hemodynamics with a sample rate of 7.81 Hz. The locations of the fNIRS channels have been validated by structural T1-weighted MRI in our previous study\(^{(26)}\).

Participants were asked to wear a backpack which contained the fNIRS control box and a connected laptop for data acquisition. The whole data acquisition set weighed less than 1 kg, which exerted minimal influence on gait performance.

The procedure of signal processing in this study was the same as that of our previous study. To reduce physical artifacts, data was rejected based on coefficient of variation which set at CV\(_{\text{chan}}\)>15 \(\%\) and CV\(_{\text{trail}}\)>10 \(\%\)\(^{(26)}\). The remaining fNIRS signals were bandpass-filtered (low-cut frequency of 0.005 Hz and high-cut frequency of 0.03 Hz) to eliminate the effects of heartbeat, respiration, and low-frequency signal drifts for each wavelength\(^{(32)}\). Wavelet filtering was used to remove the motion artifacts from fNIRS signals\(^{(33)}\). The preprocessed signals were converted to concentration changes in oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR) using the modified Beer-Lambert law for each channel\(^{(34–36)}\). The 5-second baseline collected before each walking block was the relative changes in HbO and HbR concentrations. The HbO and HbR changes were averaged over 2 repetitions for each walking condition to improve signal-to-noise ratio\(^{(32, 36)}\). The HOMER2 fNIRS processing package was used to preprocess the signals, including filtering, artifact removal and conversion for further analysis\(^{(37)}\).

Neuronal activation typically coupled with a rapid increase in HbO and a relatively lower-amplitude reduction in HbR based on neurovascular coupling. Therefore, the index of hemoglobin differential (Hbdiff = HbO − HbR) was used to evaluate the brain activation changes in this study\(^{(24, 26, 38, 39)}\). The 60-second walking trial was divided into two phases: early and late phase of the walking task. The period between 5 and 20 seconds after task onset was defined as the early phase to reflect the immediate hemodynamic response to the walking condition. The period between 20 and 40 seconds after task onset was defined as the late phase to assess sustained activation in specific brain areas\(^{33}\).
Statistical analysis

A repeated one-way ANOVA was used to analyze the differences in the gait performance under the 3 different walking conditions. Post hoc test with Bonferroni correction was used to determine the significant differences in pairwise comparisons (SW and WCT, SW and WMT, WCT and WMT). One-sided \( t \) test with false discovery rate correction (FDR) of multiple comparisons for 14 channels was used to determine the significant increase in brain activation under each walking condition and phase. A one-way ANOVA with repeated measure was used to compare the brain activation between the 3 walking conditions. Paired \( t \) test with the FDR correction of multiple comparisons for 3 walking conditions was then used as post hoc test. The Pearson correlation coefficient was used to examine the correlation between brain activation (early and late stage respectively) in each channel and the gait parameters of gait performance. Gait performance and correlation coefficient were analyzed by SPSS 24.0 software (SPSS Inc., USA), and the changes in brain activation were analyzed by customized script developed on MATLAB. The significance level was set at \( p < 0.05 \).

Results

A total of twenty-eight individuals (17 men, 11 women) with PD participated in this study. The mean age was 66.1 years old (ranging from 47 to 83 years old), and the mean PD duration was 74.6 months (ranging from 6 to 240 months). The average of Hoehn and Yahr stage was 1.6 (ranging from stage 1 to 3). The characteristic data of all participants are shown in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>66.1 ± 8.0</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>17/11</td>
</tr>
<tr>
<td>MMSE</td>
<td>28.0 ± 1.8</td>
</tr>
<tr>
<td>Onset duration (months)</td>
<td>74.6 ± 57.7</td>
</tr>
<tr>
<td>Hoehn and Yahr stage</td>
<td>1.6 ± 0.7</td>
</tr>
</tbody>
</table>

Values are mean ± SD or frequency

Abbreviations: MMSE, Mini-mental state examination

Gait performance

Gait performances under the 3 different walking conditions are shown in Table 2. Participants with PD walked more slowly, with shorter stride length, shorter swing cycle, and longer stride time during both the cognitive and motor dual task walking comparing to during single-walking (\( p < 0.05 \)). In addition,
decreased cadence and increased temporal variability were only seen during WCT. Comparison of the different types of the dual tasks showed that participants with PD walked with lower cadence and longer stride time during WCT than during WMT (p < 0.05). The dual task cost was also greater during WCT than during WMT (p < 0.05).

Table 2
Gait performance under three different walking conditions (n = 28)

<table>
<thead>
<tr>
<th></th>
<th>SW</th>
<th>WCT</th>
<th>WMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speed (cm/s)</td>
<td>94.1 ± 19.6</td>
<td>77.0 ± 23.3*</td>
<td>81.7 ± 19.8*</td>
</tr>
<tr>
<td>Cadence</td>
<td>108.5 ± 8.5</td>
<td>98.9 ± 12.3†</td>
<td>105.8 ± 10.5</td>
</tr>
<tr>
<td>Stride length (cm)</td>
<td>104.3 ± 17.9</td>
<td>92.7 ± 21.4*</td>
<td>92.3 ± 17.5*</td>
</tr>
<tr>
<td>Stride time (s)</td>
<td>1.11 ± 0.08</td>
<td>1.23 ± 0.16*</td>
<td>1.14 ± 0.11*</td>
</tr>
<tr>
<td>Swing cycle (%)</td>
<td>33.9 ± 2.4</td>
<td>32.3 ± 3.2*</td>
<td>32.5 ± 2.3*</td>
</tr>
<tr>
<td>Temporal variability</td>
<td>6.45 ± 9.37</td>
<td>9.29 ± 9.52†</td>
<td>5.76 ± 5.27</td>
</tr>
<tr>
<td>Spatial variability</td>
<td>6.79 ± 5.27</td>
<td>9.41 ± 6.13</td>
<td>8.18 ± 6.36</td>
</tr>
<tr>
<td>Speed DTC</td>
<td>0.20 ± 0.13†</td>
<td>0.14 ± 0.10</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± SD.

Abbreviations: SW, single walking; WCT, walking while performing cognitive task; WMT, walking while performing motor task

*, p < 0.05 as compared with SW, †, p < 0.05 as compared with WMT

Brain activation

Participants with PD showed increased brain activation in most of the channels except for the right PFC (Ch.2) in the early phase during SW. However, there was no sustained activation observed in any channel in the late phase. During both types of dual task walking, the cortical Hbdiff were significantly increased in all 14 channels in the early phase. Similar to SW, there was no sustained activation during WMT and WCT in any channel in the late phase (Fig. 1).

The pairwise comparisons of hemodynamic responses during different walking conditions in the early and late phases are shown in Fig. 2. The early activation did not differ between SW and WCT, but there was a higher level of Hbdiff sustained in the bilateral PMC (Ch.7 and 8 in left PMC, Ch.5, 6, 9 and 10 in right PMC) and SMA (Ch.11 and 12) in the late phase of WCT (Fig. 2a). As for the comparison between WMT and SW, there was no significant difference in any of channels in either the early or the late phases (Fig. 2b). When comparing different dual task walking conditions, higher cortical Hbdiff was demonstrated during WCT in the late phase in all the channels except for the right PFC (Ch.2) than during WMT (Fig. 2c).
The relations of brain activation and gait performance

The relations of brain activity (in early and late phase) and gait performance during single walking and dual task walking are shown in Tables 3 and 4. During SW, the early phase of brain activity in the right PFC (Ch. 2) and left PMC (Ch. 7) correlated with speed, cadence, and stride time. In the late phase, bilateral PFC, PMC, and SMA (all the channels except Ch. 5, 6, 10, 14) significantly correlated with gait parameters including speed, stride time, stride length, and cadence. During WCT, brain activity in the right PFC (Ch. 2) negatively correlated with cadence, and the right PMC (Ch. 6) positively correlated with spatial variability in the early phase. In the late phase, results showed that the activity in the bilateral PFC correlated with speed, cadence, stride time, and stride length. Also, there was a significant correlation between activities in the right PFC (Ch. 2), left PMC (Ch. 3, 7, 8) and SMA (Ch. 11) and swing cycle. During WMT, the speed, cadence, stride time, swing cycle, and stride length correlated with the early phase activation in the bilateral PFC, PMC, and left SMA. In the late phase, activation in the bilateral PFC, PMC, and SMA (all the channels except Ch. 7, 9, 10) correlated significantly with all of the gait parameters.
Table 3
The correlations between brain activity in different brain areas and gait parameters in early phase (from 5 to 20s after the task onset)

<table>
<thead>
<tr>
<th>Walking condition</th>
<th>Brain area</th>
<th>Gait parameters</th>
<th>Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>SW</td>
<td>R’t PFC (Ch.2)</td>
<td>Cadence</td>
<td>-0.559**</td>
</tr>
<tr>
<td></td>
<td>R’t PFC (Ch.2)</td>
<td>Stride time</td>
<td>0.595**</td>
</tr>
<tr>
<td></td>
<td>L’t PMC (Ch.7)</td>
<td>Speed</td>
<td>-0.406*</td>
</tr>
<tr>
<td></td>
<td>L’t PMC (Ch.7)</td>
<td>Stride time</td>
<td>-0.423*</td>
</tr>
<tr>
<td>WCT</td>
<td>R’t PFC (Ch.2)</td>
<td>Cadence</td>
<td>-0.418*</td>
</tr>
<tr>
<td></td>
<td>R’t PMC (Ch.6)</td>
<td>Spatial variability</td>
<td>0.432*</td>
</tr>
<tr>
<td>WMT</td>
<td>L’t PFC (Ch.1)</td>
<td>Swing cycle</td>
<td>-0.514*</td>
</tr>
<tr>
<td></td>
<td>R’t PFC (Ch.2)</td>
<td>Swing cycle</td>
<td>-0.443*</td>
</tr>
<tr>
<td></td>
<td>L’t PMC (Ch.4)</td>
<td>Speed</td>
<td>-0.402*</td>
</tr>
<tr>
<td></td>
<td>R’t PMC (Ch.5)</td>
<td>Swing cycle</td>
<td>-0.405*</td>
</tr>
<tr>
<td></td>
<td>L’t SMA (Ch.11)</td>
<td>Speed</td>
<td>-0.407*</td>
</tr>
<tr>
<td></td>
<td>L’t SMA (Ch.11)</td>
<td>Stride time</td>
<td>0.410*</td>
</tr>
<tr>
<td></td>
<td>L’t SMA (Ch.13)</td>
<td>Speed</td>
<td>-0.507*</td>
</tr>
<tr>
<td></td>
<td>L’t SMA (Ch.13)</td>
<td>Cadence</td>
<td>-0.414*</td>
</tr>
<tr>
<td></td>
<td>L’t SMA (Ch.13)</td>
<td>Stride length</td>
<td>-0.431*</td>
</tr>
<tr>
<td></td>
<td>L’t SMA (Ch.13)</td>
<td>Stride time</td>
<td>0.497*</td>
</tr>
</tbody>
</table>

This table only shows the correlations with statistical significance.

Abbreviations: SW, single walking; WCT, walking while performing cognitive task; WMT, walking while performing motor task; L’t, left side of; R’t, right side of; PFC, prefrontal cortex, PMC, premotor cortex; SMA, Supplementary area
Table 4
The correlations between brain activity in different brain areas and gait parameters in late phase (from 20 to 40s after the task onset)

<table>
<thead>
<tr>
<th>Walking condition</th>
<th>Brain area</th>
<th>Gait parameters</th>
<th>Correlation coefficient</th>
<th>Brain area</th>
<th>Gait parameters</th>
<th>Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>SW</td>
<td>L't PFC (Ch.1)</td>
<td>Stride time</td>
<td>0.440*</td>
<td>L't PMC (Ch.7)</td>
<td>Stride length</td>
<td>-0.505**</td>
</tr>
<tr>
<td></td>
<td>L't PFC (Ch.1)</td>
<td>Swing cycle</td>
<td>-0.416*</td>
<td>L't PMC (Ch.8)</td>
<td>Speed</td>
<td>-0.437*</td>
</tr>
<tr>
<td></td>
<td>R't PFC (Ch.2)</td>
<td>Speed</td>
<td>-0.493*</td>
<td>L't PMC (Ch.8)</td>
<td>Stride length</td>
<td>-0.420*</td>
</tr>
<tr>
<td></td>
<td>R't PFC (Ch.2)</td>
<td>Cadence</td>
<td>-0.464*</td>
<td>R't PMC (Ch.9)</td>
<td>Speed</td>
<td>-0.434*</td>
</tr>
<tr>
<td></td>
<td>R't PFC (Ch.2)</td>
<td>Stride length</td>
<td>-0.412*</td>
<td>R't PMC (Ch.9)</td>
<td>Stride length</td>
<td>-0.406*</td>
</tr>
<tr>
<td></td>
<td>R't PFC (Ch.2)</td>
<td>Stride time</td>
<td>0.497*</td>
<td>L't SMA (Ch.11)</td>
<td>Speed</td>
<td>-0.474*</td>
</tr>
<tr>
<td></td>
<td>L't PMC (Ch.3)</td>
<td>Speed</td>
<td>-0.441*</td>
<td>L't SMA (Ch.11)</td>
<td>Stride length</td>
<td>-0.428*</td>
</tr>
<tr>
<td></td>
<td>L't PMC (Ch.3)</td>
<td>Stride length</td>
<td>-0.397*</td>
<td>R't SMA (Ch.12)</td>
<td>Speed</td>
<td>-0.414*</td>
</tr>
<tr>
<td></td>
<td>L't PMC (Ch.4)</td>
<td>Speed</td>
<td>-0.449*</td>
<td>R't SMA (Ch.12)</td>
<td>Stride length</td>
<td>-0.433*</td>
</tr>
<tr>
<td></td>
<td>L't PMC (Ch.4)</td>
<td>Stride length</td>
<td>-0.403*</td>
<td>L't SMA (Ch.13)</td>
<td>Speed</td>
<td>-0.441*</td>
</tr>
<tr>
<td></td>
<td>L't PMC (Ch.7)</td>
<td>Speed</td>
<td>-0.437*</td>
<td>L't SMA (Ch.13)</td>
<td>Stride time</td>
<td>0.408*</td>
</tr>
<tr>
<td>WCT</td>
<td>L't PFC (Ch.1)</td>
<td>Speed</td>
<td>-0.438*</td>
<td>R't PFC (Ch.2)</td>
<td>Stride time</td>
<td>0.474*</td>
</tr>
<tr>
<td></td>
<td>L't PFC (Ch.1)</td>
<td>Cadence</td>
<td>-0.425*</td>
<td>R't PFC (Ch.2)</td>
<td>Swing cycle</td>
<td>-0.505*</td>
</tr>
<tr>
<td></td>
<td>L't PFC (Ch.1)</td>
<td>Stride time</td>
<td>0.413*</td>
<td>L't PMC (Ch.3)</td>
<td>Swing cycle</td>
<td>-0.462*</td>
</tr>
<tr>
<td></td>
<td>R't PFC (Ch.2)</td>
<td>Speed</td>
<td>-0.510*</td>
<td>L't PMC (Ch.7)</td>
<td>Swing cycle</td>
<td>-0.470*</td>
</tr>
</tbody>
</table>

This table only shows the correlations with statistical significance.

Abbreviations: SW, single walking; WCT, walking while performing cognitive task; WMT, walking while performing motor task; L’t, left side of; R’t, right side of; PFC, prefrontal cortex; PMC, premotor cortex; SMA, Supplementary area; DTC, dual task cost
<table>
<thead>
<tr>
<th>Walking condition</th>
<th>Brain area</th>
<th>Gait parameters</th>
<th>Correlation coefficient</th>
<th>Brain area</th>
<th>Gait parameters</th>
<th>Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>R't PFC (Ch.2)</td>
<td>Cadence</td>
<td>-0.473*</td>
<td>L't PMC (Ch.8)</td>
<td>Swing cycle</td>
<td>-0.453*</td>
<td></td>
</tr>
<tr>
<td>R't PFC (Ch.2)</td>
<td>Stride length</td>
<td>-0.459*</td>
<td>L't SMA (Ch.11)</td>
<td>Swing cycle</td>
<td>-0.485*</td>
<td></td>
</tr>
<tr>
<td>WMT</td>
<td>L't PFC (Ch.1)</td>
<td>Cadence</td>
<td>-0.409*</td>
<td>L't PMC (Ch.8)</td>
<td>Stride length</td>
<td>-0.474*</td>
</tr>
<tr>
<td></td>
<td>Stride time</td>
<td>0.496*</td>
<td>L't PMC (Ch.8)</td>
<td>DTC</td>
<td>0.433*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Swing cycle</td>
<td>-0.439*</td>
<td>L't SMA (Ch.11)</td>
<td>Speed</td>
<td>-0.513**</td>
<td></td>
</tr>
<tr>
<td>R't PFC (Ch.2)</td>
<td>Speed</td>
<td>-0.490*</td>
<td>L't SMA (Ch.11)</td>
<td>Stride length</td>
<td>-0.461*</td>
<td></td>
</tr>
<tr>
<td>R't PFC (Ch.2)</td>
<td>Stride length</td>
<td>-0.438*</td>
<td>L't SMA (Ch.11)</td>
<td>Stride time</td>
<td>0.478*</td>
<td></td>
</tr>
<tr>
<td>R't PFC (Ch.2)</td>
<td>Stride time</td>
<td>0.495*</td>
<td>L't SMA (Ch.11)</td>
<td>Spatial variability</td>
<td>0.449*</td>
<td></td>
</tr>
<tr>
<td>R't PFC (Ch.2)</td>
<td>Swing cycle</td>
<td>-0.478*</td>
<td>R't SMA (Ch.12)</td>
<td>Speed</td>
<td>-0.406*</td>
<td></td>
</tr>
<tr>
<td>L't PMC (Ch.3)</td>
<td>Speed</td>
<td>-0.429*</td>
<td>R't SMA (Ch.12)</td>
<td>Stride time</td>
<td>0.396*</td>
<td></td>
</tr>
<tr>
<td>L't PMC (Ch.3)</td>
<td>Stride time</td>
<td>0.440*</td>
<td>R't SMA (Ch.12)</td>
<td>Spatial variability</td>
<td>0.411*</td>
<td></td>
</tr>
<tr>
<td>L't PMC (Ch.3)</td>
<td>DTC</td>
<td>0.402*</td>
<td>R't SMA (Ch.12)</td>
<td>DTC</td>
<td>0.430*</td>
<td></td>
</tr>
<tr>
<td>L't PMC (Ch.4)</td>
<td>Speed</td>
<td>-0.472*</td>
<td>L't SMA (Ch.13)</td>
<td>Speed</td>
<td>-0.530**</td>
<td></td>
</tr>
<tr>
<td>L't PMC (Ch.4)</td>
<td>Cadence</td>
<td>-0.393*</td>
<td>L't SMA (Ch.13)</td>
<td>Stride length</td>
<td>-0.478*</td>
<td></td>
</tr>
<tr>
<td>L't PMC (Ch.4)</td>
<td>Stride time</td>
<td>0.493*</td>
<td>L't SMA (Ch.13)</td>
<td>Stride time</td>
<td>0.493*</td>
<td></td>
</tr>
<tr>
<td>L't PMC (Ch.4)</td>
<td>DTC</td>
<td>0.474*</td>
<td>L't SMA (Ch.13)</td>
<td>Spatial variability</td>
<td>0.428*</td>
<td></td>
</tr>
</tbody>
</table>

This table only shows the correlations with statistical significance.

Abbreviations: SW, single walking; WCT, walking while performing cognitive task; WMT, walking while performing motor task; L't, left side of; R't, right side of; PFC, prefrontal cortex, PMC, premotor cortex; SMA, Supplementary area; DTC, dual task cost
<table>
<thead>
<tr>
<th>Walking condition</th>
<th>Brain area</th>
<th>Gait parameters</th>
<th>Correlation coefficient</th>
<th>Brain area</th>
<th>Gait parameters</th>
<th>Correlation coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R’t PMC (Ch.5)</td>
<td>DTC</td>
<td>0.498**</td>
<td>L’t SMA (Ch.13)</td>
<td>DTC</td>
<td>0.426*</td>
</tr>
<tr>
<td></td>
<td>R’t PMC (Ch.6)</td>
<td>Stride time</td>
<td>0.442*</td>
<td>R’t SMA (Ch.14)</td>
<td>Stride time</td>
<td>0.426*</td>
</tr>
<tr>
<td></td>
<td>R’t PMC (Ch.6)</td>
<td>DTC</td>
<td>0.565**</td>
<td>R’t SMA (Ch.14)</td>
<td>Spatial variability</td>
<td>0.439*</td>
</tr>
<tr>
<td></td>
<td>L’t PMC (Ch.8)</td>
<td>Speed</td>
<td>-0.522**</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This table only shows the correlations with statistical significance.

Abbreviations: SW, single walking; WCT, walking while performing cognitive task; WMT, walking while performing motor task; L’t, left side of; R’t, right side of; PFC, prefrontal cortex, PMC, premotor cortex; SMA, Supplementary area; DTC, dual task cost

**Discussion**

To our knowledge, this is the first study to report multi-area brain activation and walking performance during different types (cognitive and motor) of dual task walking in individuals with PD. Both types of dual tasks exerted negative impact on gait performance including speed, stride length, and swing and stride time. The interference of the cognitive task was greater than the motor task on gait performance, with higher and sustained activation in the PMC and SMA during late phase of cognitive dual task walking than motor dual task walking in participants with PD.

The negative effects of motor and cognitive dual tasks on walking noted in this study were in line with previous results in people with PD (1, 2, 12). In addition, the cognitive dual task exerted more negative effects on cadence and temporal variability than the motor dual task. Galletly and Brauer found the gait speed and stride length was significantly decreased more during walking with the serial subtraction task than walking with the button press task (40). Rochester and colleagues also found that the cognitive dual task had a greater effect on gait performance in PD subjects than motor dual task (41). Taking this together, the dual task walking was a challenge to people with PD and cognitive dual task walking was even more challenging, as also indicated by the higher dual task cost noted in present study.

Previously, we found that the secondary tasks, both the cognitive and the motor, exerted a negative influence on walking performance in healthy adults (33), healthy elderly (42), and people with stroke (34). However, the cognitive task did not seem to exert greater impact than the motor task on walking, as indicated by gait variability and dual task cost in healthy adults, elderly, and in people with stroke (33, 34, 42). It has been suggested that performing dual tasks requires specific cognitive functions, such as set shifting, divided or alternating attention, and response inhibition (43). The global cognitive function of the participants in above mentioned studies (33, 34, 42) was similar to that of the participants in present study.
The particularly negative impact of the cognitive dual task on gait performance may thus be specific to people with PD, which may be associated with impairments in executive function(41, 44, 45). Executive function, one of the cognitive domains, is needed for planning, monitoring, and executing a sequence of motor acts(23). Impairments in executive function have been reported in people with PD(23) and such deficits may limit those with PD to compensate their walking abilities through cognitive strategies, especially during cognitive dual task walking(2). In addition to dual task cost, the particular challenge of the cognitive dual task on walking was also demonstrated by increasing the gait variability. It is noted that the higher gait variability indicates less stability during gait and greater fall risks(46). This important message is suggested to advise people with PD, since cognitive dual task walking is frequently performed during daily activities.

The PFC has been recognized as the key area for executive function(26, 47, 48). Executive function is involved in many daily activities, especially walking. Another task in addition to walking increases attentional demand, prefrontal load, and interferes with gait performance(26, 28). However, brain activity may react differently in neurologically involved people, such as in people with PD. It is interesting to note that the bilateral PFC did not activate more during dual task walking than during SW in the present study. However, our previous study and other studies showed that the PFC was activated significantly during dual task walking in healthy adults and elderly(20-22, 26). In line with present study, Maidan et al., reported no activation difference in the PFC while executing cognitive dual task walking as compared with SW in people with PD(23). In addition, they also found hyperactivity in the PFC during SW in PD population as compared with healthy age-matched adults(23). It is possible that the PFC is highly activated in people with PD to compensate for the deficit in automaticity, even in relatively simple tasks(49, 50). Wu et al., found that PD patients had greater activity in the prefrontal cortex, cerebellum, premotor cortex, parietal cortex, and precuneus while performing automatic movement when compared with healthy controls, as demonstrated by fMRI(51). This compensatory phenomenon of higher activation during a single task may reflect the lower efficiency of the neural network(50). Therefore, people with PD may recruit other brain areas for complex activities. As shown in the present study, recruiting more PMC and SMA activity may be the strategy used to cope with the challenging cognitive dual task walking. We further noted that almost all the brain areas measured in this study were activated more while performing WCT than when performing WMT. Taking together, even by activating more brain areas during WCT, the interference or the negative impact of the cognitive task on walking was still more significant than WMT in people with PD.

The PMC is known to involve motor planning and selection and locomotion(24). The SMA is responsible for posture control and for coordinating movements(25). The PMC and SMA were significantly activated during both cognitive and motor dual task walking according to our previous study in healthy adults(26). Therefore, additional neural processing occurred at least in the PMC and SMA for dual task walking. However, in people with PD, the activations of PMC and SMA during motor dual task walking were not significantly higher than during SW, but were significantly higher during cognitive dual task walking. The activity in different brain areas during dual task walking are less studied and need further elucidation in
people with PD. However, according to our results on brain activation and walking performance, it is reasonable to suggest that the cognitive dual task gait training may be a potential intervention to promote plasticity of the motor cortex and dual task walking ability in individuals with PD.

We also examined the relationships between brain activation and walking performance in this study, and found a negative correlation between brain activation and gait performance in general. That is, the higher the brain activation during single and dual task walking, the worse the gait demonstrated. These relationships were also noted in patients with stroke\textsuperscript{34}. Therefore, we speculate that in people with impaired neuromotor control, the increased brain activation in the motor- and cognitive-related areas may not be able to sufficiently fulfill the walking demands, even during single walking.

The present study looked into the different dual task gait performance and multi-area brain activities in people with PD, which has not yet been reported by previous studies. However, there are several limitations that should be noted. First, the sample size of the present study was relatively small, and a study with a larger sample size is needed to validate our findings. Despite the small sample size in our present study, the statistical power was greater than 0.99, indicating that the possibility of a Type 2 error was very low. Second, the clinical disability of most included patients was mild (Hoehn and Yahr stage I-II), therefore, the generalizations of our findings need to consider the severity of the disease. Third, all the participants were tested during the “on-medication” status, thus, it is unclear whether the results could be applied to the off-medication status.

**Conclusion**

In people with PD, both motor and cognitive dual tasks exerted negative impact on walking performance. The impact of the cognitive task on walking was still more significant than motor task even by further activating the PMC and SMA in individuals with PD.

**Abbreviations**

PD: Parkinson’s disease; SW: single walking; WCT: walking while performing a cognitive task; WMT: walking while performing a motor task; DTC: dual task cost; PFC: prefrontal cortex; PMC: premotor cortex; SMA: supplementary motor areas; fNIRS: functional near-infrared spectroscopy; MRI: magnetic resonance imaging; MMSE: Mini-mental state examination;

**Declarations**

**Acknowledgements**

The authors would like to thank the study participants.

**Funding**
Support for this study was provided by the Ministry of Science and Technology of the Republic of China (Grant No. MOST-106-2314-B-010-040-MY3). The funding body had no role in the study design, data collection, analysis, and interpretation, or preparation of the manuscript.

**Availability of data and materials**

The datasets used and/or analyzed for this study are available from the corresponding author on reasonable request.

**Authors’ contributions**

YCL and RYW designed the study and drafted the manuscript. YRY assisted with the study design. YCL, NCY and PHK conducted the experiments. YRY and CFL assisted with data analysis. RYW finalized the manuscript. All authors read and approved the final manuscript.

**Ethics approval and consent to participate**

The study protocol was approved by the institutional review board of Institutional Review Board of National Yang-Ming University. Participants consented to participate following an explanation of the procedure and review of the informed consent.

**Consent for publication**

Not applicable

**Competing interests**

The authors declare that they have no competing interests

**References**


**Figures**

(a)

(b)

(c)

**Figure 1**
Illustrations of brain activation level. (a) during SW, (b) during WCT, and (c) during WMT. The t values of significant activation with FDR correction for the multiple comparison in early or late phase are color-coded under the axis for each channel. The horizontal solid lines depict the concentration level of zero, and the vertical solid lines label the time of zero for the task onset.

(a)

(b)

(c)

Figure 2
Illustrations of brain activation level between different walking conditions. (a) during WCT and during SW, (b) during WMT and during SW, and (c) during WCT and WMT. The t values of significant activations with FDR correction for the multiple comparison in early or late phase are color-coded under the axis for each channel. The horizontal solid lines depict the concentration level of zero, and the vertical solid lines label the time of zero for the task onset.